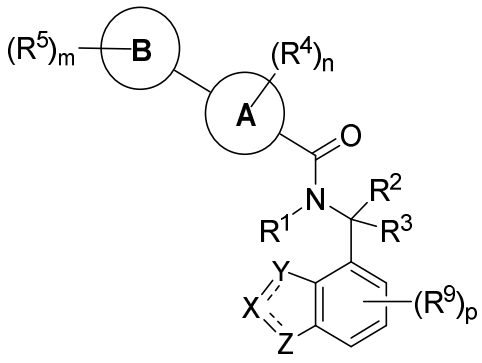
CLAIMS

1. A compound of Formula I:



(**I**)

or a pharmaceutically acceptable salt thereof;

wherein

⋯ is an optional double bond;

X is CH or N;

Y and Z are each independently selected from the group consisting of NH, NR^9, O, S, N, CH, and CR^9;

Ring A is selected from the group consisting of C_{6-10} aryl, 5-6 membered heteroaryl, C_{4-10} cycloalkyl, and 4-10 membered heterocycloalkyl;

Ring B is selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, Ring B is absent and m is 0;

R^1 is selected from the group consisting of H, C_{1-6} alkyl, and C_{3-6} cycloalkyl, wherein alkyl and cycloalkyl are each optionally substituted with R^6;

R^2 and R^3 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, R^2 and R^3, together with the atom to which they are attached, form a ring selected from the group consisting of C_{3-7} cycloalkyl and 3-7 membered heterocycloalkyl;

each R^4 is independently selected from the group consisting of C_{1-6} alkyl, halo, OH, OR^6, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl$)_2$, $NHCOR^6$, CN, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, and COR^6;

alternatively, two R^4, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and

4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^5 is independently selected from the group consisting of H, C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OR^6, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, $NHCOR^6$, CN, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, COR^6, and SO_2R^6;

alternatively, two R^5, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and 4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^6 is independently selected from the group consisting of C_{1-6} alkyl, C_{0-6} alkyl-C_{6-10} aryl, C_{0-6} alkyl-5-10 membered heteroaryl, OC_{1-6} alkyl, C_{3-6} cycloalkyl, halo, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

each R^7 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OC_{1-6} alkyl, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, CN, COR^8, and SO_2R^8;

each R^8 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

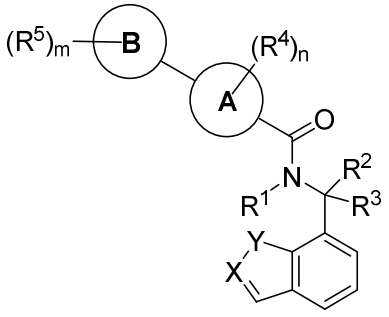
each R^9 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, CN, OH, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

m is 0, 1, 2, or 3;

n is 1, 2, or 3; and

p is 0, 1, 2, or 3.

2. The compound of claim 1, wherein the compound of Formula I is a compound of Formula Ia:



(**Ia**)

or a pharmaceutically acceptable salt thereof;

wherein

X is CH or N;

Y is NH, O, or S;

Ring A is phenyl or 5-6 membered heteroaryl;

Ring B is selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

R^1 is H or C_{1-6} alkyl;

R^2 and R^3 are each independently H or C_{1-6} alkyl;

each R^4 is independently selected from the group consisting of C_{1-6} alkyl, halo, OH, OC_{1-6} alkyl, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, C_{1-6} haloalkyl, and COR^6;

each R^5 is independently selected from the group consisting of H, C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, CN, COR^6, and SO_2R^6;

each R^6 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

m is 1, 2, or 3; and

n is 0, 1, 2, or 3.

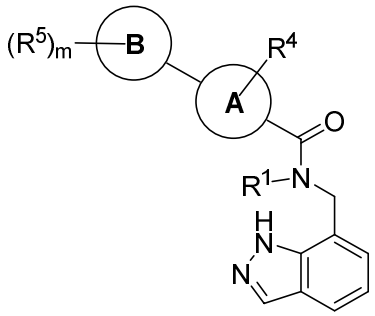
3. The compound of claim 1 or 2, wherein Ring A is selected from the group consisting of phenyl, pyridine, pyrimidine, and pyrazine.

4. The compound of any one of claims 1-3, wherein Ring A is selected from the group consisting of phenyl, pyridine, pyridazine, pyrimidine, imidazole, pyrazole, and C_{3-6} cycloalkyl.

5. The compound of any one of claims 1-4, wherein R^1 is C_{1-6} alkyl or C_{3-6} cycloalkyl, optionally substituted with C_{1-6} alkyl.

6. The compound of any one of claims 1-5, wherein Y is NH, X is N, and Z is CH.

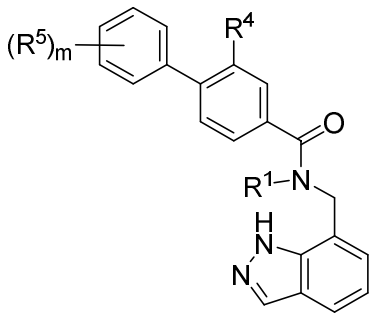
7. The compound of any one of claims 1-6, wherein the compound of Formula I is a compound of Formula Ib:



(**Ib**)

or a pharmaceutically acceptable salt thereof.

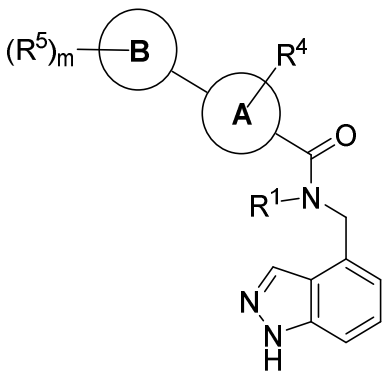
8. The compound of any one of claims 1-7, wherein the compound of Formula I is a compound of Formula Ic:



(**Ic**)

or a pharmaceutically acceptable salt thereof.

9. The compound of claim 1, wherein the compound of Formula I is a compound of Formula Id:



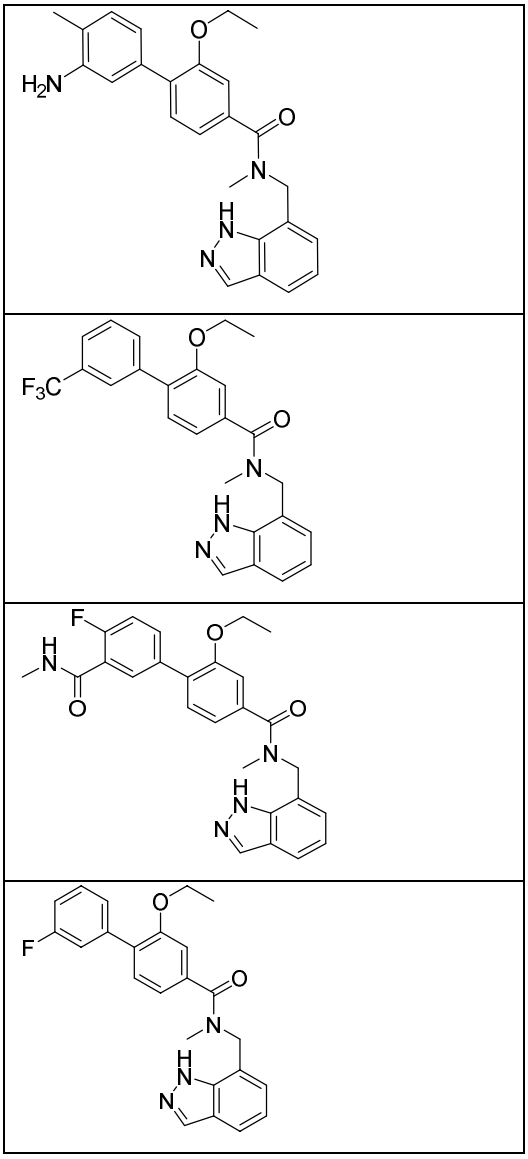
(**Id**)

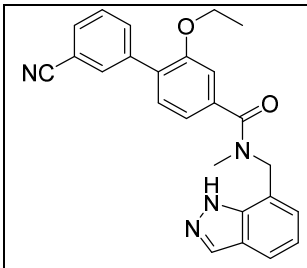
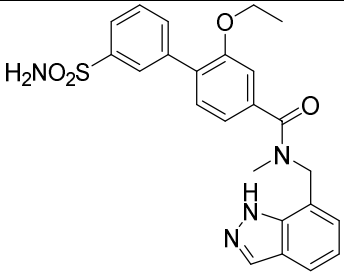
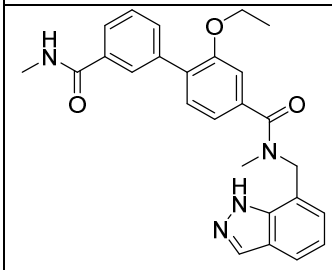
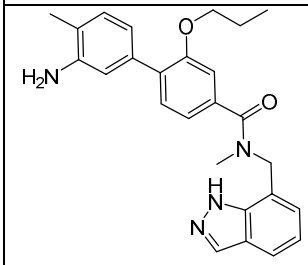
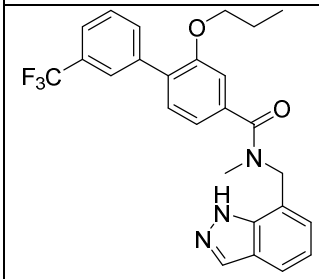
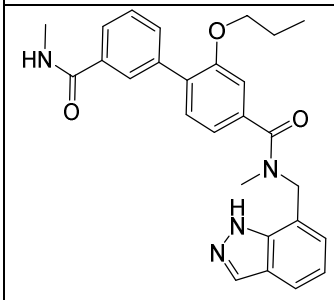
or a pharmaceutically acceptable salt thereof.

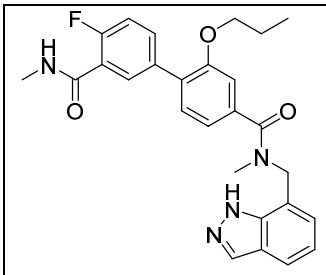
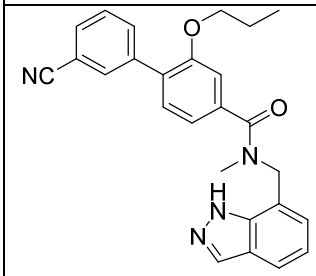
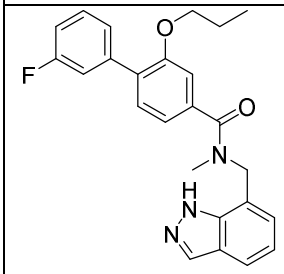
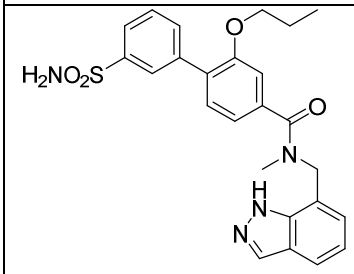
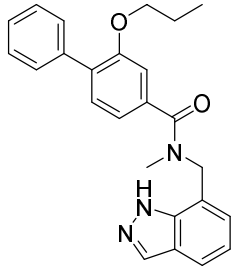
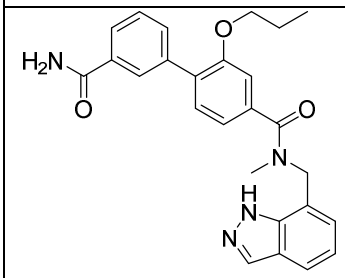
10. The compound of any one of claims 1-9, wherein R^4 is OC_{1-6} alkyl.

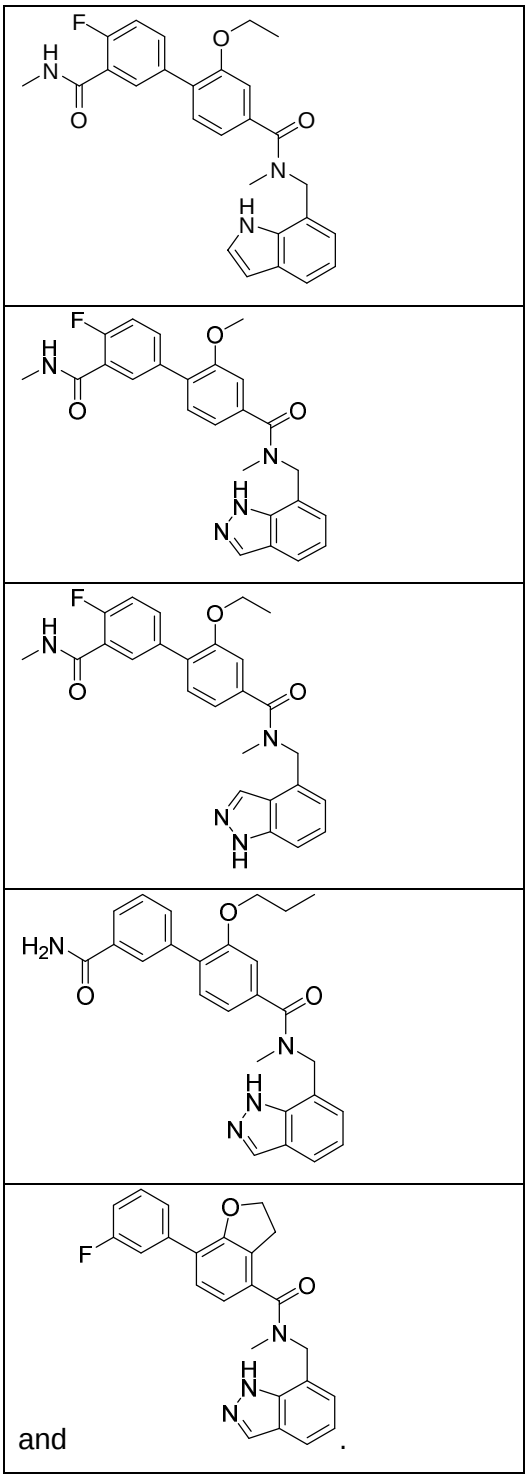
11. The compound of any one of claims 1-10, wherein R^5 is selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, NH_2, CN, $CONH_2$, $CONH(C_{1-6}$ alkyl), and SO_2NH_2.

12. The compound of any one of claims 1-11, wherein the compound of Formula I, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of:

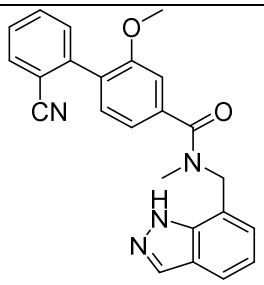
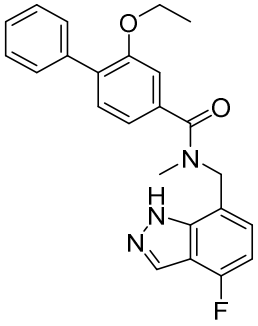
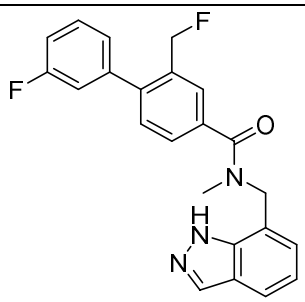
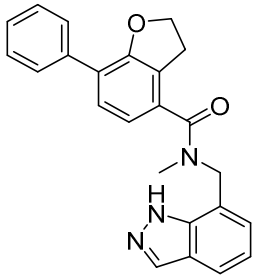
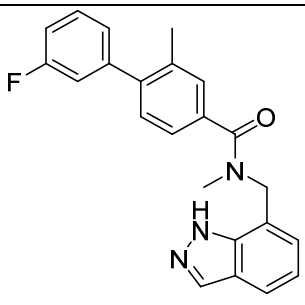


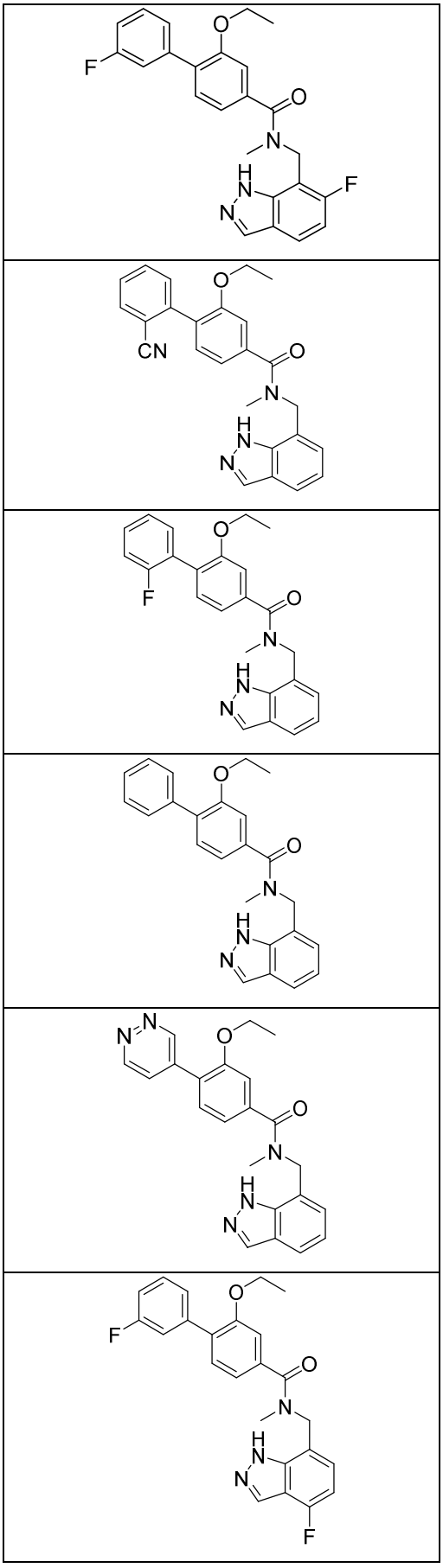







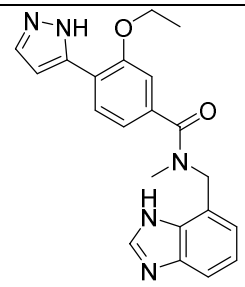
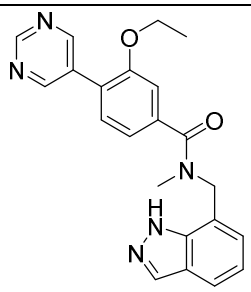
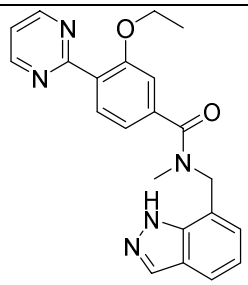
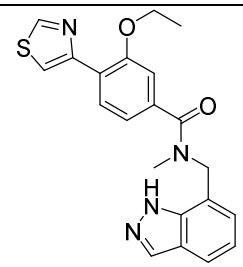
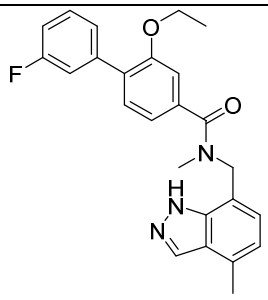
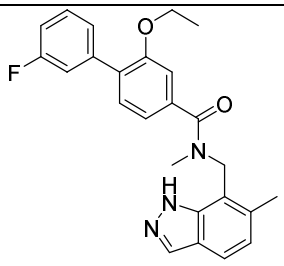







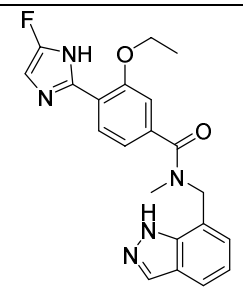
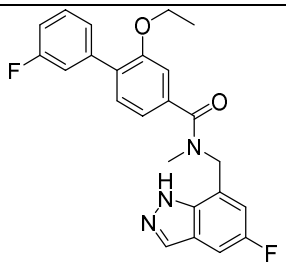
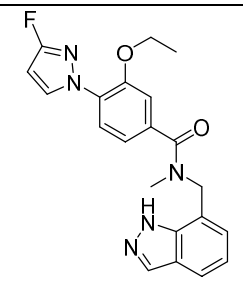
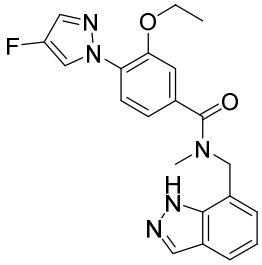
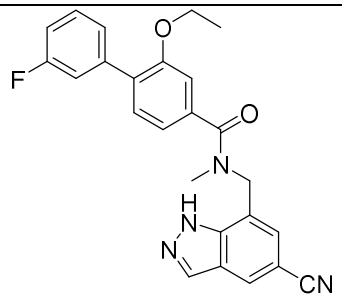
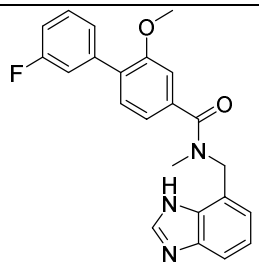


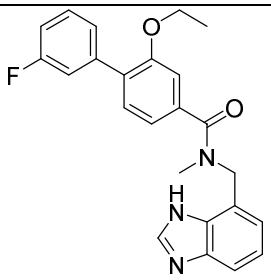
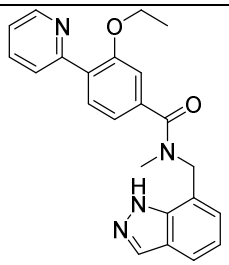
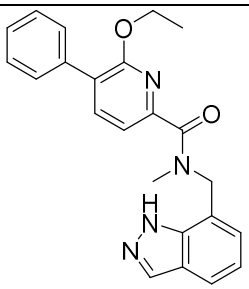
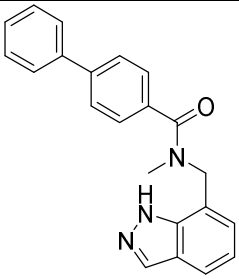
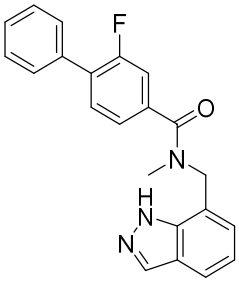
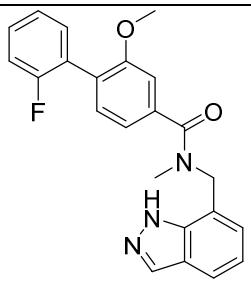
13. The compound of any one of claims 1-11, wherein the compound of Formula I, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of:

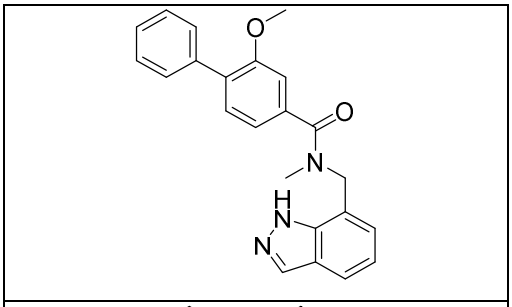
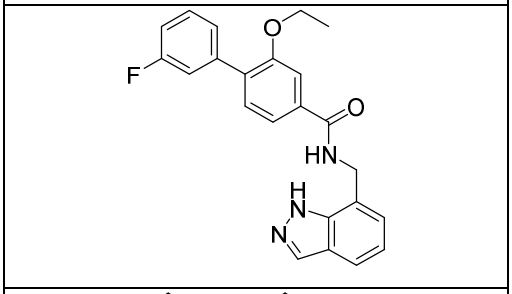
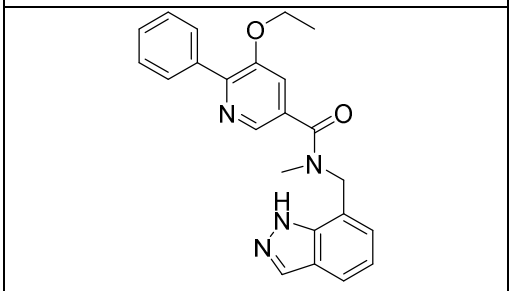
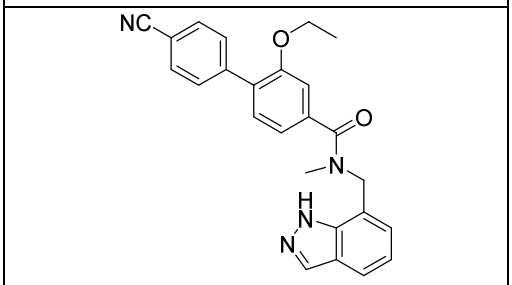
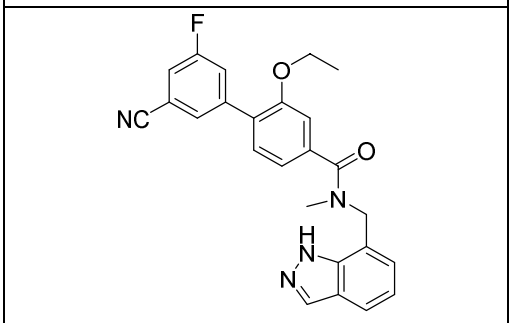
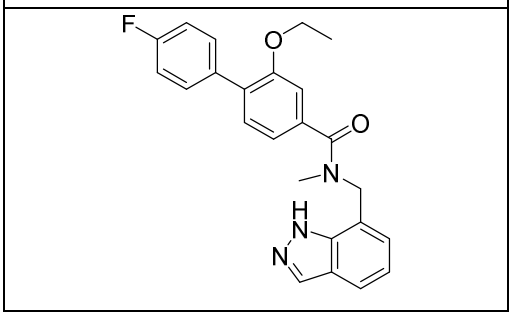






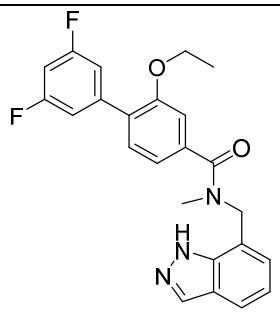
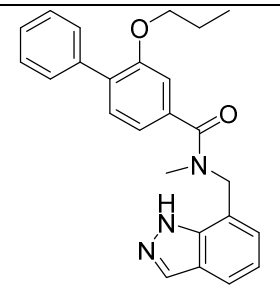
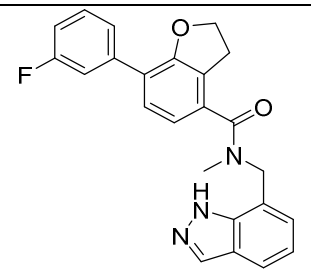
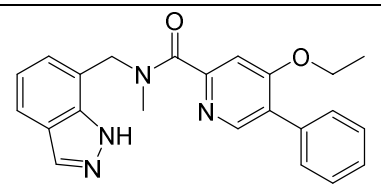
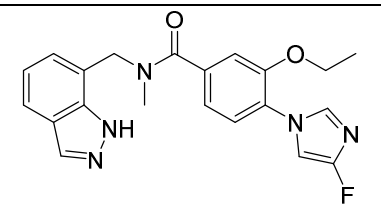
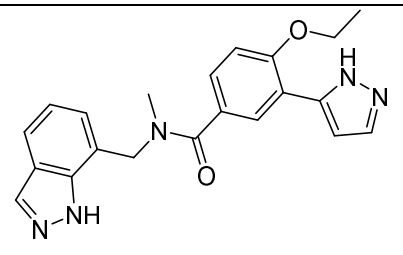


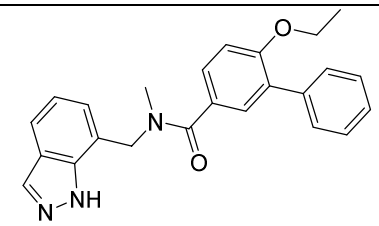
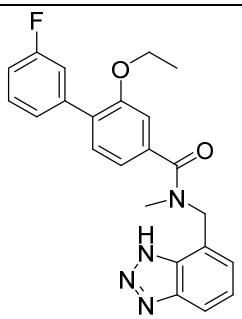
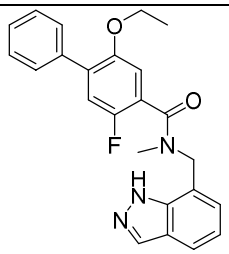
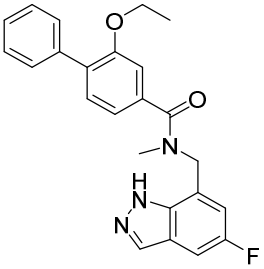
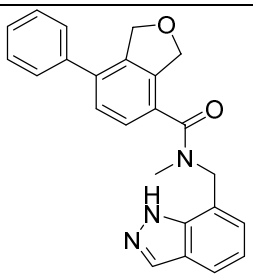
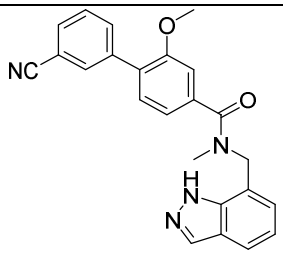







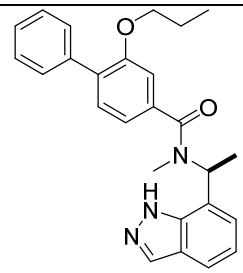
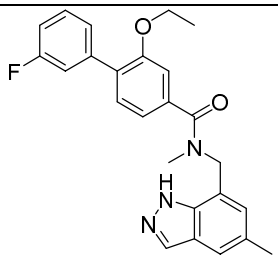
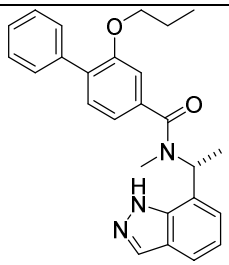
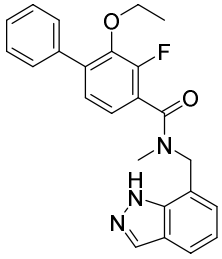
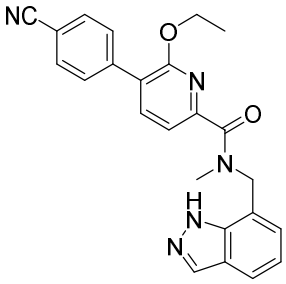
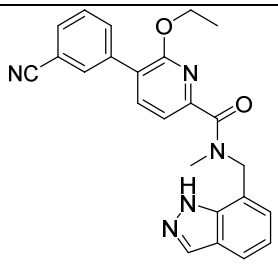







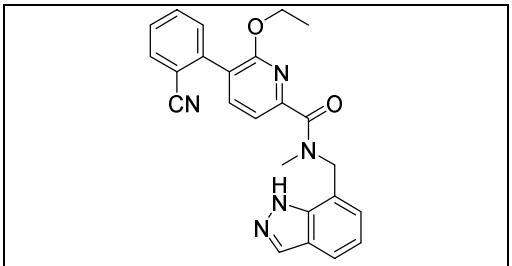







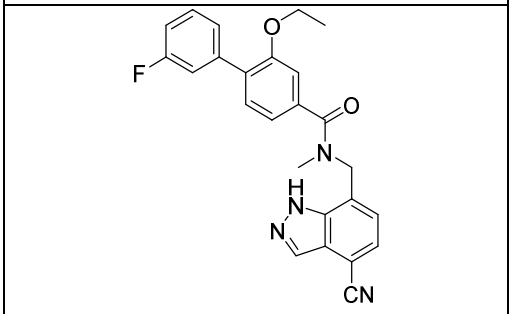







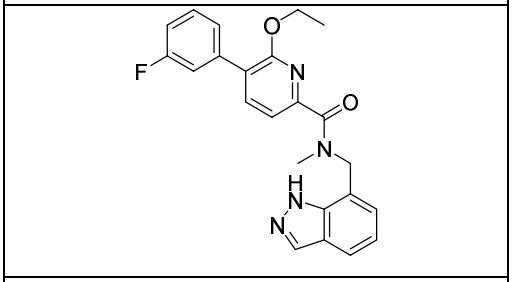







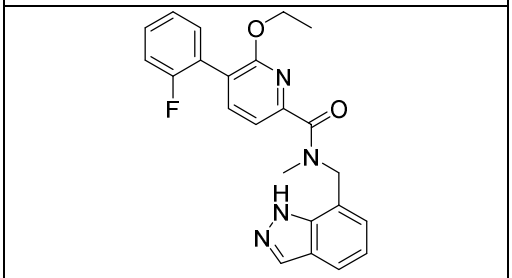







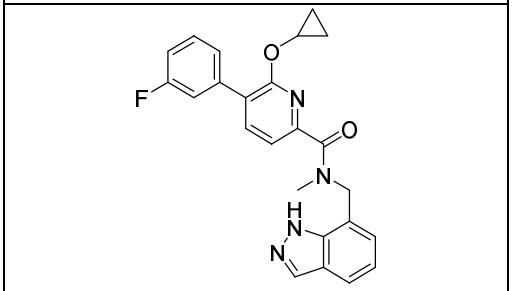







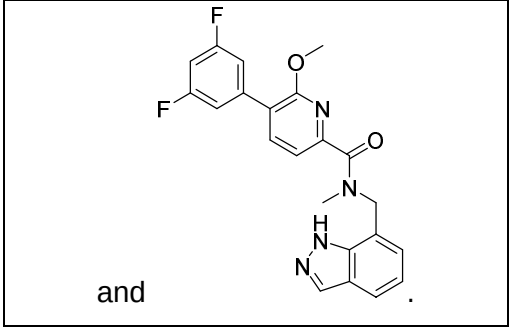






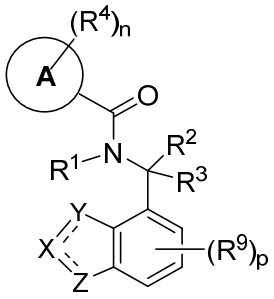






and .

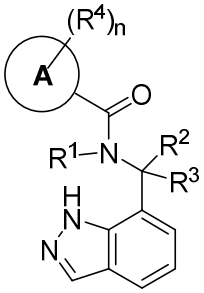
14. The compound of claim 1, wherein the compound of Formula I is a compound of Formula II:



(**II**)

or a pharmaceutically acceptable salt thereof.

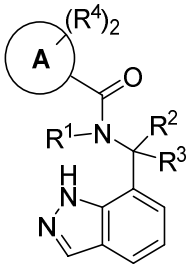
15. The compound of claim 14, wherein the compound of Formula II is a compound of Formula IIa:



(**IIa**)

or a pharmaceutically acceptable salt thereof.

16. The compound of claim 14, wherein the compound of Formula II is a compound of Formula IIb:

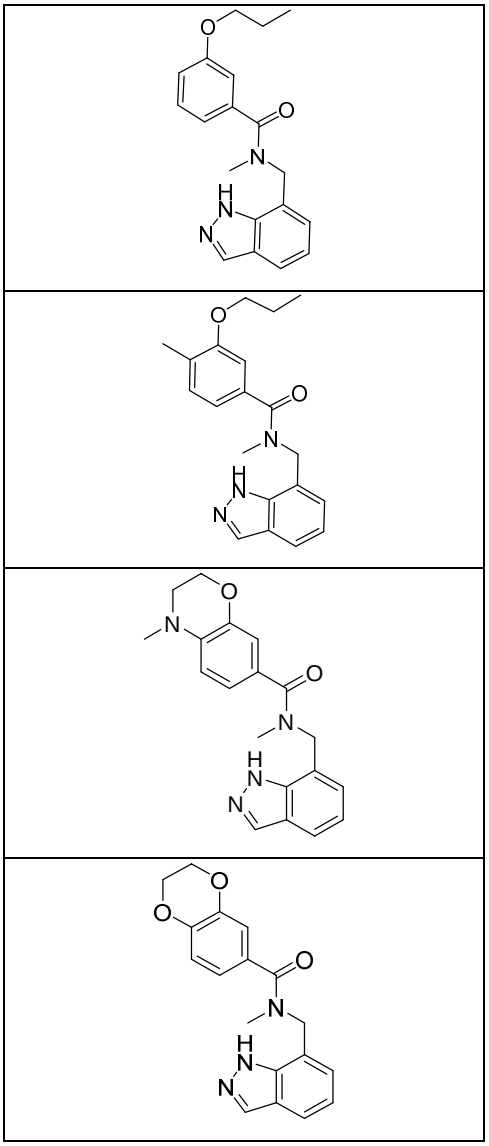


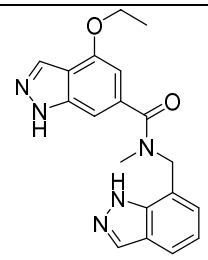
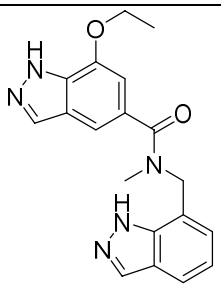
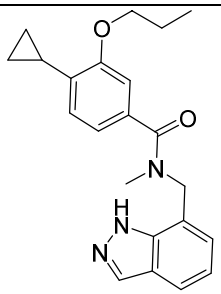
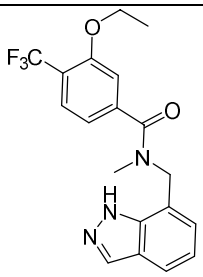
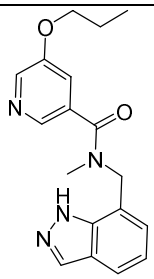
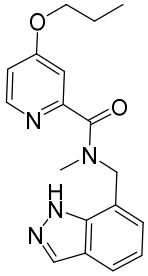
(**IIb**)

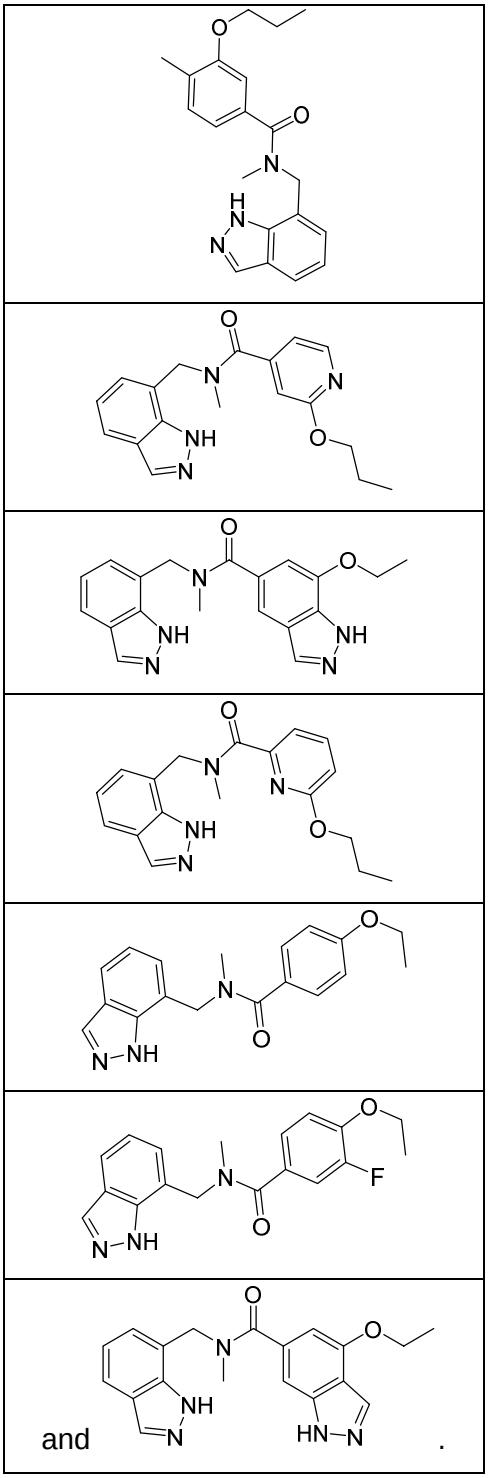
or a pharmaceutically acceptable salt thereof;

wherein two R^4, together with Ring A, form a ring selected from the group consisting of dihydrobenzooxazine, dihydrobenzodioxine, indazole, and indole, all of which are optionally substituted with one, two, or three R^7.

17. The compound of any one of claims 14-16, wherein the compound of Formula II, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of:

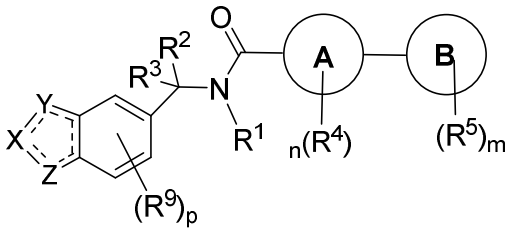




and .

18. A compound of Formula III:



(**III**)

or a pharmaceutically acceptable salt thereof;

wherein

--- is an optional double bond;

X is CH, N, NH, or N(C_{1-6} alkyl);

Y and Z are each independently selected from the group consisting of NH, NR^9, O, S, N, CH, and CR^9;

Ring A is selected from the group consisting of C_{6-10} aryl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl, and 4-10 membered heterocycloalkyl;

Ring B is selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, Ring B is absent and m is 0;

R^1 is selected from the group consisting of H, C_{1-6} alkyl, and C_{3-6} cycloalkyl, wherein alkyl and cycloalkyl are each optionally substituted with R^6;

R^2 and R^3 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, R^2 and R^3, together with the atom to which they are attached, form a ring selected from the group consisting of C_{3-7} cycloalkyl and 3-7 membered heterocycloalkyl;

each R^4 is independently selected from the group consisting of C_{1-6} alkyl, halo, OH, OR^6, NH_2, NH(C_{1-6} alkyl), N(C_{1-6} alkyl)$_2$, $NHCOR^6$, CN, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, and COR^6;

alternatively, two R^4, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and 4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^5 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OR^6, NH_2, NH(C_{1-6} alkyl), N(C_{1-6} alkyl)$_2$, $NHCOR^6$, CN, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, COR^6, and SO_2R^6;

alternatively, two R^5, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and

4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^6 is independently selected from the group consisting of C_{1-6} alkyl, C_{0-6} alkyl-C_{6-10} aryl, C_{0-6} alkyl-5-10 membered heteroaryl, OC_{1-6} alkyl, C_{3-6} cycloalkyl, halo, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl$)_2$;

each R^7 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OC_{1-6} alkyl, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl$)_2$, CN, COR^8, and SO_2R^8;

each R^8 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl$)_2$;

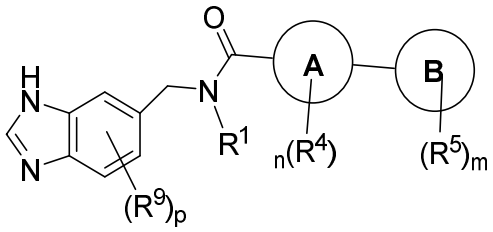
each R^9 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, CN, OH, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl$)_2$;

m is 0, 1, 2, or 3;

n is 1, 2, or 3; and

p is 0, 1, 2, or 3.

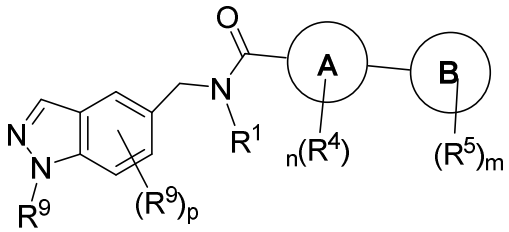
19. The compound of claim 18, wherein the compound of Formula III is a compound of Formula IIIa:



(**IIIa**)

or a pharmaceutically acceptable salt thereof.

20. The compound of claim 18, wherein the compound of Formula III is a compound of Formula IIIb:

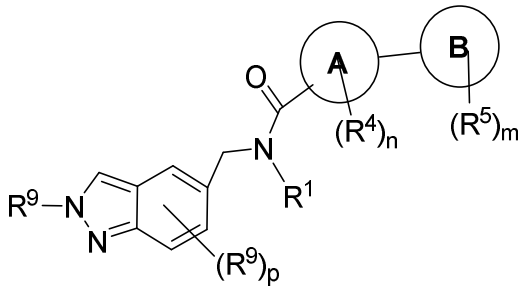


(**IIIb**)

wherein p is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof.

21. The compound of claim 18, wherein the compound of Formula III is a compound of Formula IIIc:

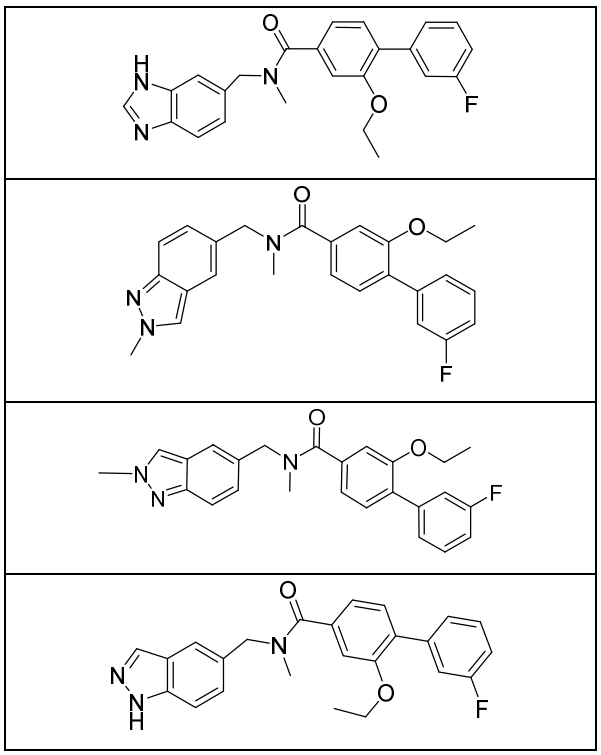


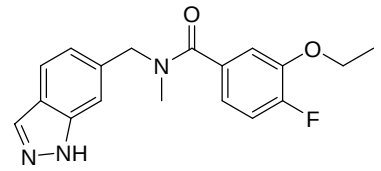
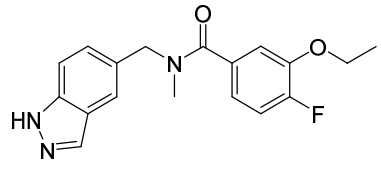
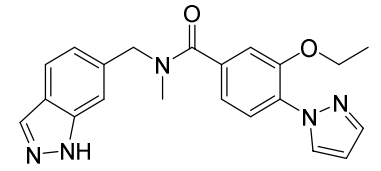
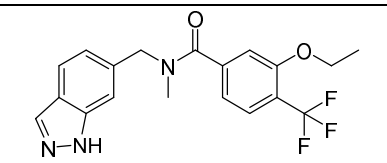
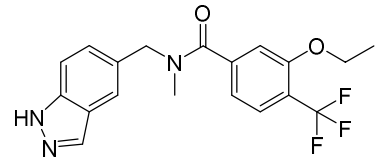
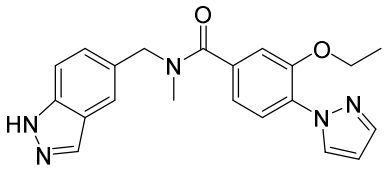
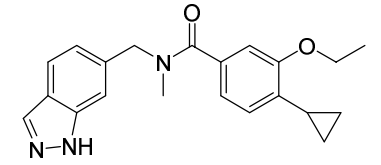
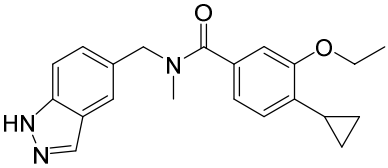
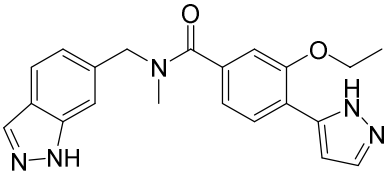
(**IIIc**)

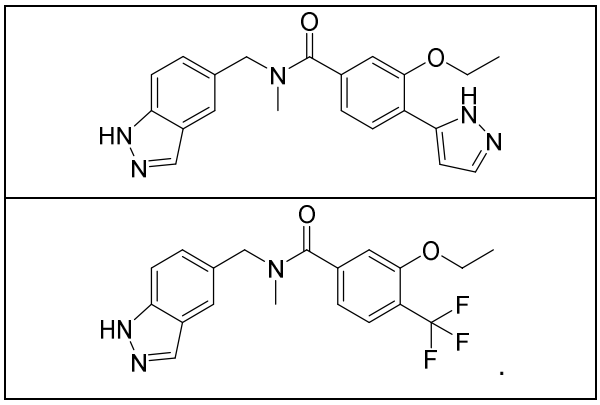
wherein p is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof.

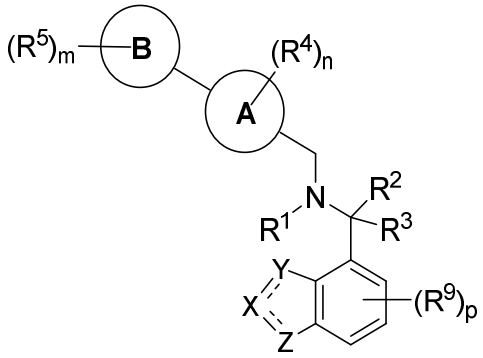
22. The compound of any one of claims 18-21, wherein the compound of Formula III, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of:





23. A compound of Formula IV:



(**IV**)

or a pharmaceutically acceptable salt thereof;

wherein

--- is an optional double bond;

X is CH, N, NH, or N(C_{1-6} alkyl);

Y and Z are each independently selected from the group consisting of NH, NR^9, O, S, N, CH, and CR^9;

Ring A is selected from the group consisting of C_{6-10} aryl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl, and 4-10 membered heterocycloalkyl;

Ring B is selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, Ring B is absent and m is 0;

R^1 is selected from the group consisting of H, C_{1-6} alkyl, and C_{3-6} cycloalkyl, wherein alkyl and cycloalkyl are each optionally substituted with R^6;

R^2 and R^3 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, R^2 and R^3, together with the atom to which they are attached, form a ring selected from the group consisting of C_{3-7} cycloalkyl and 3-7 membered heterocycloalkyl;

each R^4 is independently selected from the group consisting of C_{1-6} alkyl, halo, OH, OR^6, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, $NHCOR^6$, CN, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, and COR^6;

alternatively, two R^4, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and 4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^5 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OR^6, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, $NHCOR^6$, CN, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, COR^6, and SO_2R^6;

alternatively, two R^5, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and 4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^6 is independently selected from the group consisting of C_{1-6} alkyl, C_{0-6} alkyl-C_{6-10} aryl, C_{0-6} alkyl-5-10 membered heteroaryl, OC_{1-6} alkyl, C_{3-6} cycloalkyl, halo, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

each R^7 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OC_{1-6} alkyl, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, CN, COR^8, and SO_2R^8;

each R^8 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

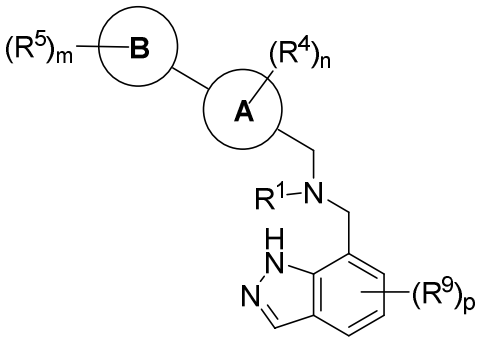
each R^9 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, CN, OH, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

m is 0, 1, 2, or 3;

n is 1, 2, or 3; and

p is 0, 1, 2, or 3.

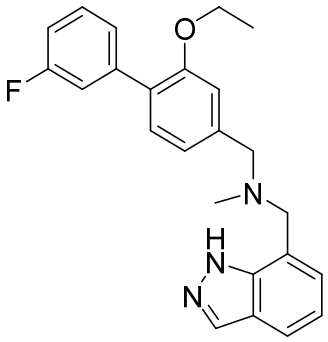
24. The compound of claim 23, wherein the compound of Formula IV is a compound of Formula IVa:



(**IVa**)

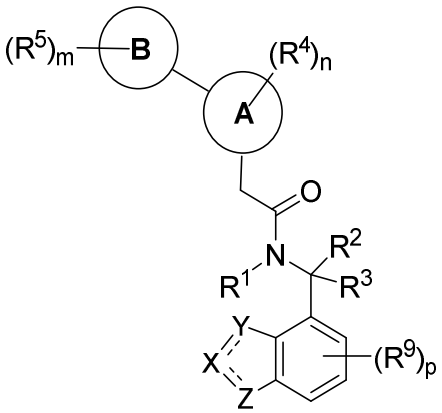
or a pharmaceutically acceptable salt thereof.

25. The compound of claim 23 or 24, wherein the compound of Formula IV is



or a pharmaceutically acceptable salt thereof.

26. A compound of Formula V:



(**V**)

or a pharmaceutically acceptable salt thereof;

wherein

$\cdots$ is an optional double bond;

X is CH, N, NH, or N(C_{1-6} alkyl);

Y and Z are each independently selected from the group consisting of NH, NR^9, O, S, N, CH, and CR^9;

Ring A is selected from the group consisting of C_{6-10} aryl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl, and 4-10 membered heterocycloalkyl;

Ring B is selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, Ring B is absent and m is 0;

R^1 is selected from the group consisting of H, C_{1-6} alkyl, and C_{3-6} cycloalkyl, wherein alkyl and cycloalkyl are each optionally substituted with R^6;

R^2 and R^3 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, R^2 and R^3, together with the atom to which they are attached, form a ring selected from the group consisting of C_{3-7} cycloalkyl and 3-7 membered heterocycloalkyl;

each R^4 is independently selected from the group consisting of C_{1-6} alkyl, halo, OH, OR^6, NH_2, NH(C_{1-6} alkyl), N(C_{1-6} alkyl)$_2$, $NHCOR^6$, CN, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, and COR^6;

alternatively, two R^4, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and 4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^5 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OR^6, NH_2, NH(C_{1-6} alkyl), N(C_{1-6} alkyl)$_2$, $NHCOR^6$, CN, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, COR^6, and SO_2R^6;

alternatively, two R^5, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and 4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^6 is independently selected from the group consisting of C_{1-6} alkyl, C_{0-6} alkyl-C_{6-10} aryl, C_{0-6} alkyl-5-10 membered heteroaryl, OC_{1-6} alkyl, C_{3-6} cycloalkyl, halo, NH_2, NH(C_{1-6} alkyl), and N(C_{1-6} alkyl)$_2$;

each R^7 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OC_{1-6} alkyl, NH_2, NH(C_{1-6} alkyl), N(C_{1-6} alkyl)$_2$, CN, COR^8, and SO_2R^8;

each R^8 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl$)_2$;

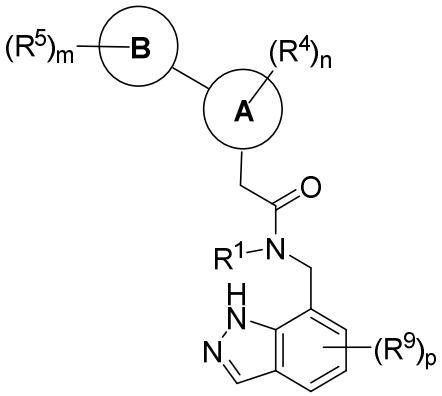
each R^9 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, CN, OH, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl$)_2$;

m is 0, 1, 2, or 3;

n is 1, 2, or 3; and

p is 0, 1, 2, or 3.

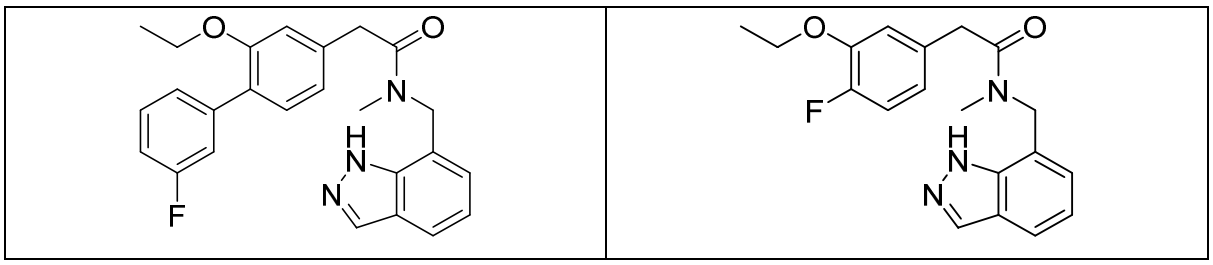
27. The compound of claim 26, wherein the compound of Formula V is a compound of Formula Va:



(**Va**)

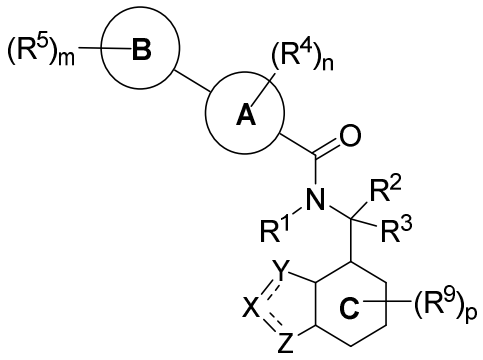
or a pharmaceutically acceptable salt thereof.

28. The compound of claim 26 or 27, wherein the compound of Formula V is selected from the group consisting of



or a pharmaceutically acceptable salt thereof.

29. A compound of Formula VI:



(**VI**)

or a pharmaceutically acceptable salt thereof;

wherein

--- is an optional double bond;

X is CH, N, NH, or N(C_{1-6} alkyl);

Y and Z are each independently selected from the group consisting of NH, NR^9, O, S, N, CH, and CR^9;

Ring A is selected from the group consisting of C_{6-10} aryl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl, and 4-10 membered heterocycloalkyl;

Ring B is selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, Ring B is absent and m is 0;

Ring C is pyridine;

R^1 is selected from the group consisting of H, C_{1-6} alkyl, and C_{3-6} cycloalkyl, wherein alkyl and cycloalkyl are each optionally substituted with R^6;

R^2 and R^3 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, R^2 and R^3, together with the atom to which they are attached, form a ring selected from the group consisting of C_{3-7} cycloalkyl and 3-7 membered heterocycloalkyl;

each R^4 is independently selected from the group consisting of C_{1-6} alkyl, halo, OH, OR^6, NH_2, NH(C_{1-6} alkyl), N(C_{1-6} alkyl)$_2$, $NHCOR^6$, CN, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, and COR^6;

alternatively, two R^4, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and 4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^5 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OR^6, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, $NHCOR^6$, CN, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, COR^6, and SO_2R^6;

alternatively, two R^5, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and 4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^6 is independently selected from the group consisting of C_{1-6} alkyl, C_{0-6} alkyl-C_{6-10} aryl, C_{0-6} alkyl-5-10 membered heteroaryl, OC_{1-6} alkyl, C_{3-6} cycloalkyl, halo, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

each R^7 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OC_{1-6} alkyl, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, CN, COR^8, and SO_2R^8;

each R^8 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

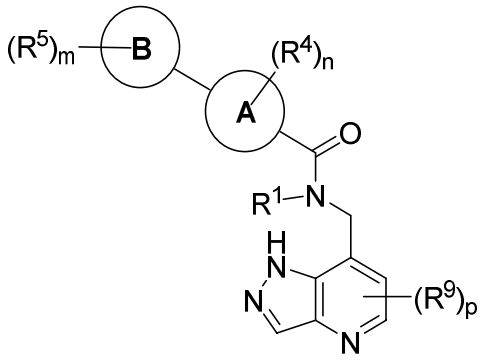
each R^9 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, CN, OH, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

m is 0, 1, 2, or 3;

n is 1, 2, or 3; and

p is 0, 1, 2, or 3.

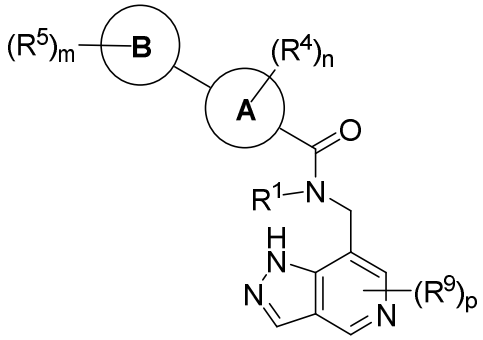
30. The compound of claim 29, wherein the compound of Formula VI is a compound of Formula VIa:



(**VIa**)

or a pharmaceutically acceptable salt thereof.

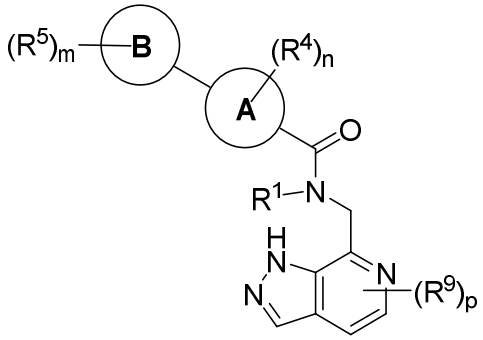
31. The compound of claim 29, wherein the compound of Formula VI is a compound of Formula VIb:



(**VIb**)

or a pharmaceutically acceptable salt thereof.

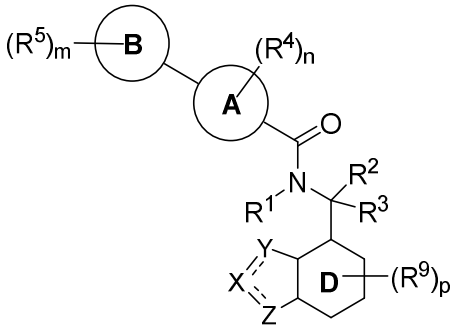
32. The compound of claim 29, wherein the compound of Formula VI is a compound of Formula VIc:



(**VIc**)

or a pharmaceutically acceptable salt thereof.

33. A compound of Formula VII:



(**VII**)

or a pharmaceutically acceptable salt thereof, wherein

--- is an optional double bond;

X is CH, N, NH, or N(C_{1-6} alkyl);

Y and Z are each independently selected from the group consisting of NH, NR^9, O, S, N, CH, and CR^9;

Ring A is selected from the group consisting of C_{6-10} aryl, 5-10 membered heteroaryl, C_{3-10} cycloalkyl, and 4-10 membered heterocycloalkyl;

Ring B is selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, Ring B is absent and m is 0;

Ring D is phenyl or pyridine;

R^1 is selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, OC_{1-6} alkyl, OC_{3-6} cycloalkyl, O(C_{0-6} alkyl-C_{6-10} aryl), C_{0-6} alkyl-C_{6-10} aryl, and OH, wherein alkyl, aryl, and cycloalkyl are each optionally substituted with R^6;

R^2 and R^3 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, R^2 and R^3, together with the atom to which they are attached, form a ring selected from the group consisting of C_{3-7} cycloalkyl and 3-7 membered heterocycloalkyl;

each R^4 is independently selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halo, OH, OR^6, NH_2, NH(C_{1-6} alkyl), N(C_{1-6} alkyl)$_2$, C_{1-6} alkyl-$NHCOR^6$, $NHCOR^6$, CN, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, and COR^6;

alternatively, two R^4, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and 4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^5 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OR^6, NH_2, NH(C_{1-6} alkyl), N(C_{1-6} alkyl)$_2$, $NHCOR^6$, CN, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, COR^6, and SO_2R^6;

alternatively, two R^5, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and 4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^6 is independently selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl, C_{0-6} alkyl-C_{6-10} aryl, C_{0-6} alkyl-5-10 membered heteroaryl, OC_{1-6} alkyl, C_{3-6} cycloalkyl, 3-6 membered heterocycloalkyl, halo, NH_2, NH(C_{1-6} alkyl), and N(C_{1-6} alkyl)$_2$;

each R^7 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OC_{1-6} alkyl, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, CN, COR^8, and SO_2R^8;

each R^8 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

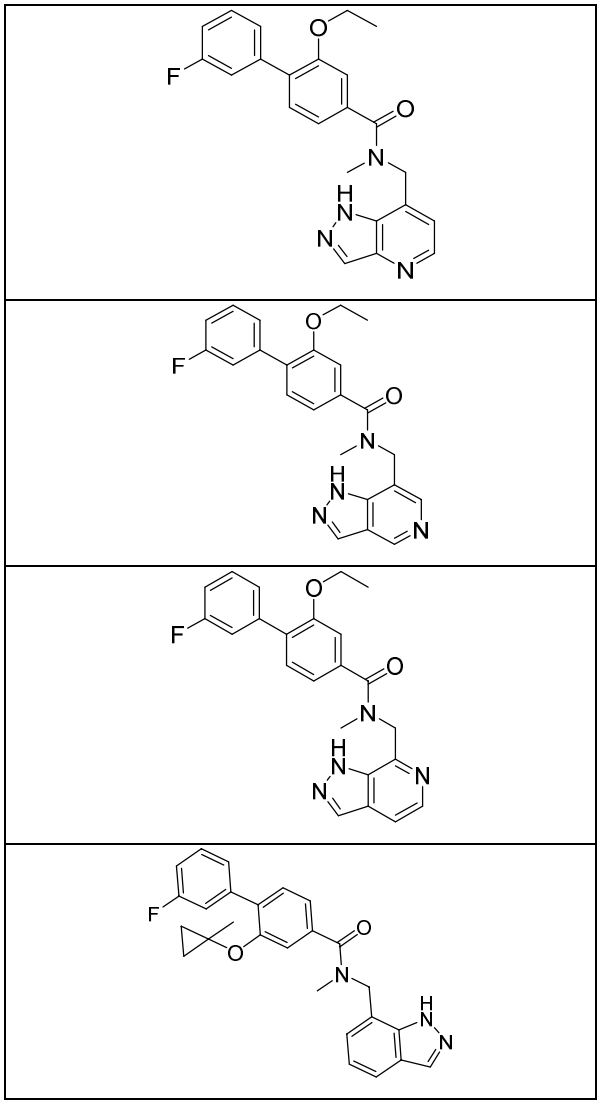
each R^9 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkyl-OH, OC_{1-6} alkyl, C_{1-6} alkyl-O-C_{1-6} alkyl, $O(C_{3-6}$ cycloalkyl), halo, CN, OH, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

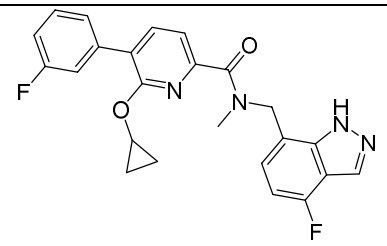
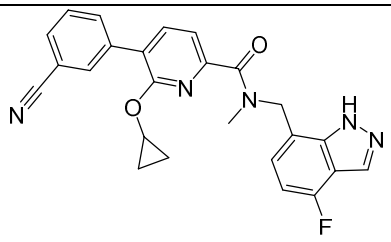
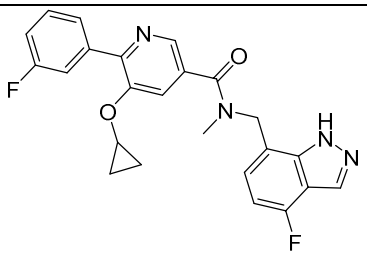
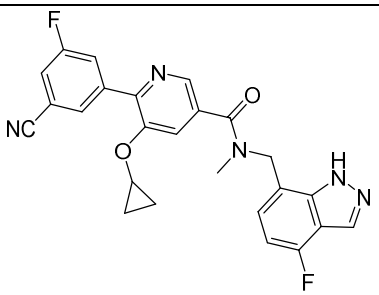
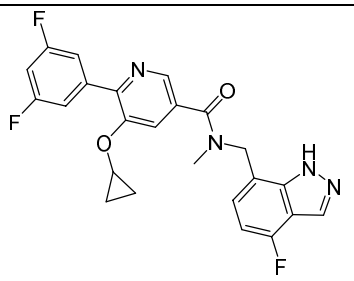
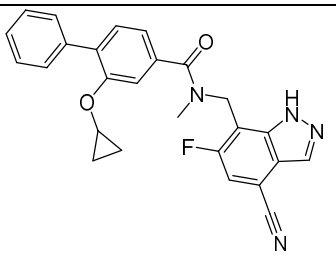
m is 0, 1, 2, or 3;

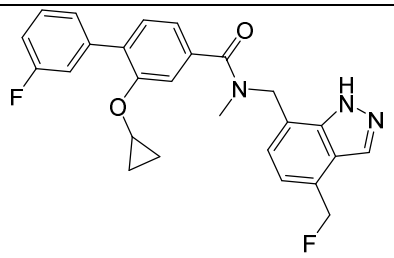
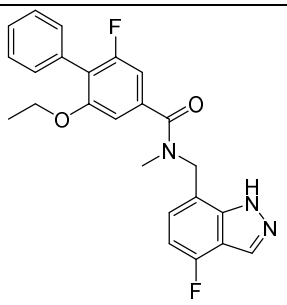
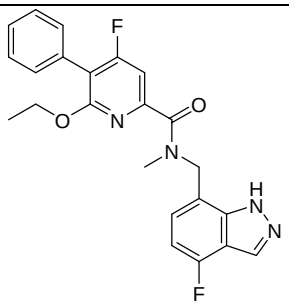
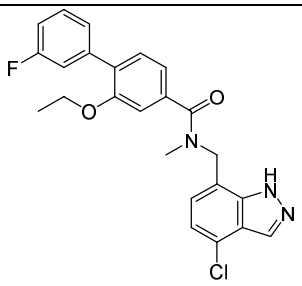
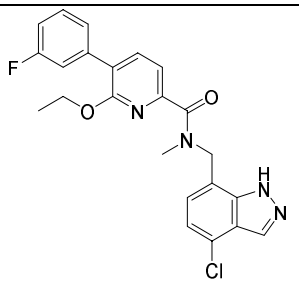
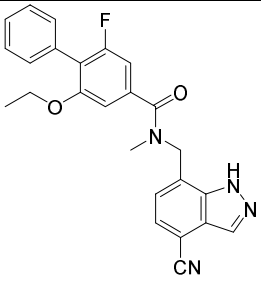
n is 0, 1, 2, or 3; and

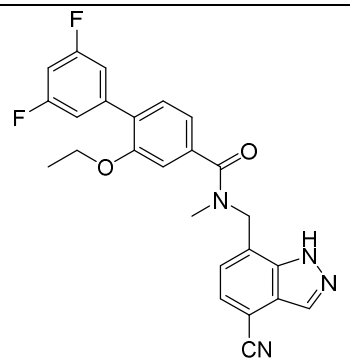
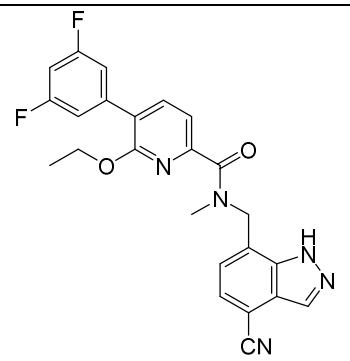
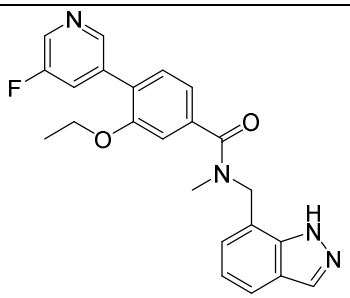
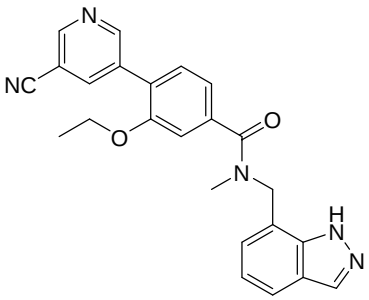
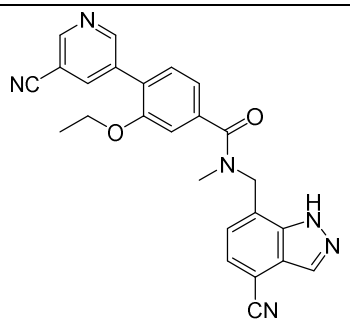
p is 0, 1, 2, or 3.

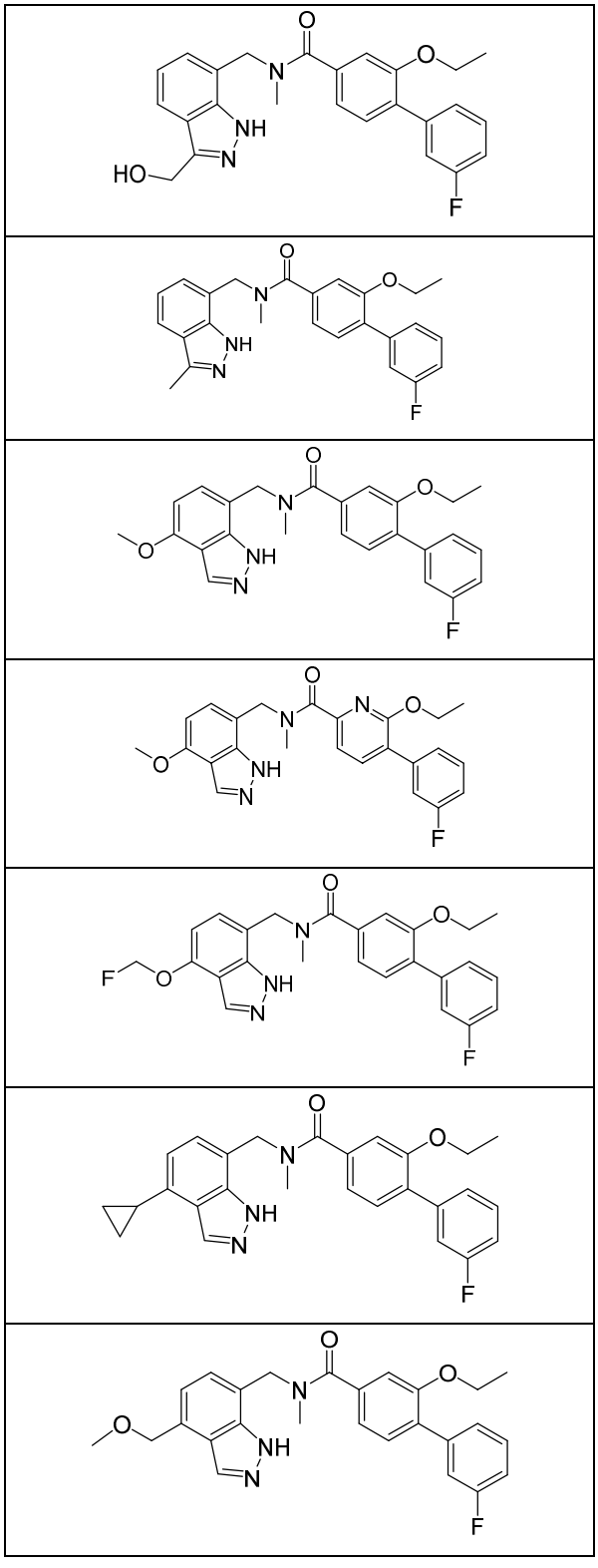
34. The compound of any one of claims 39-33, wherein the compound of Formula VI, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of:

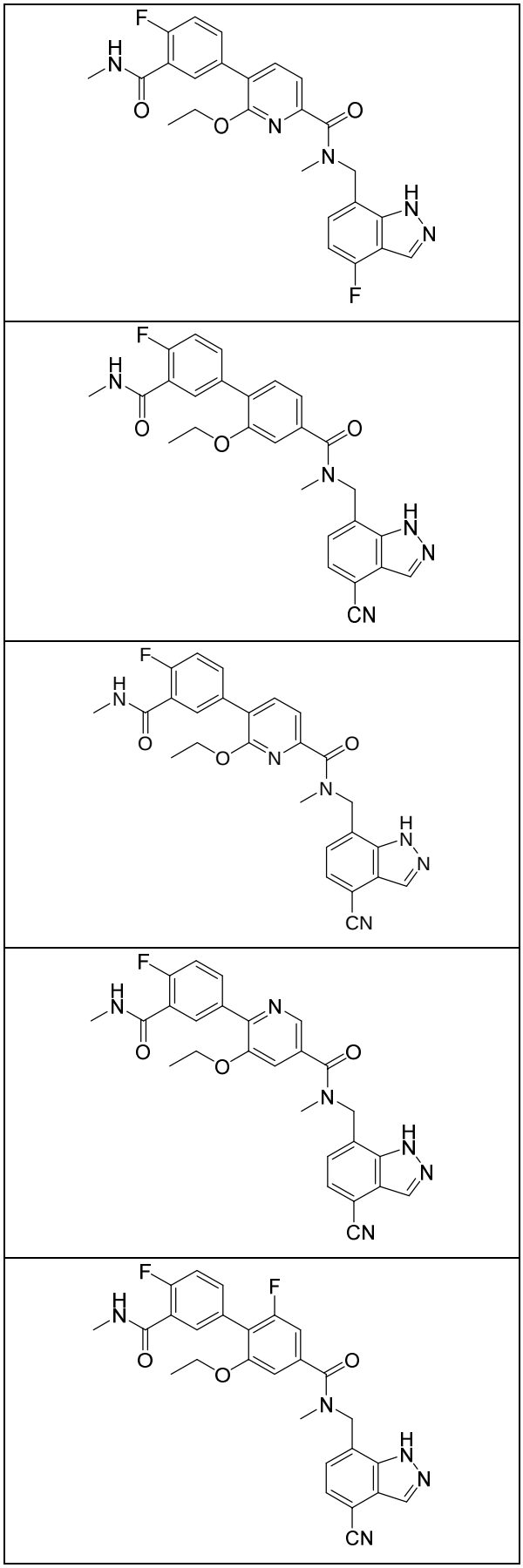


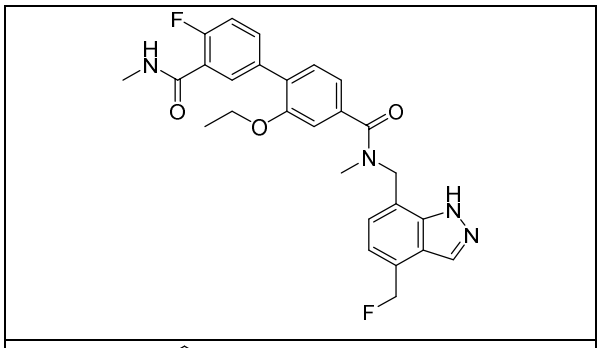







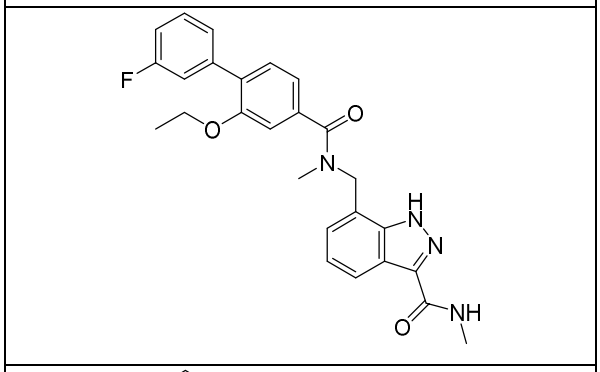







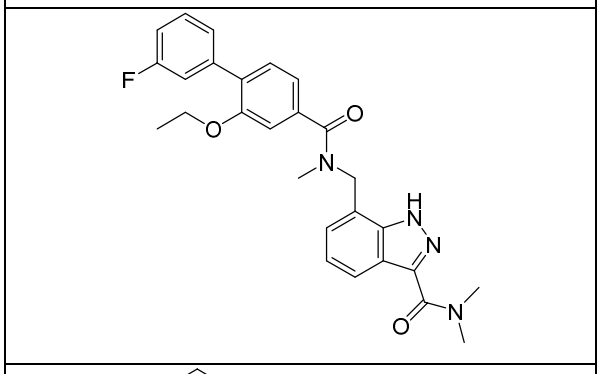






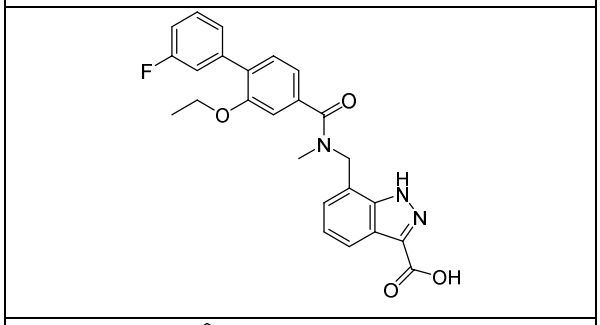


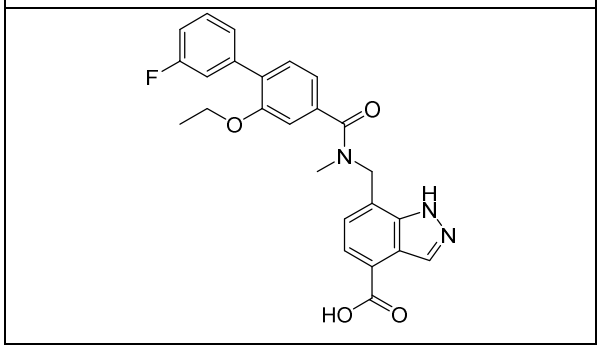


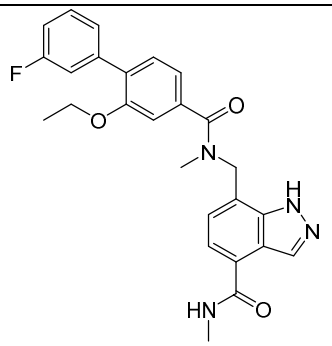
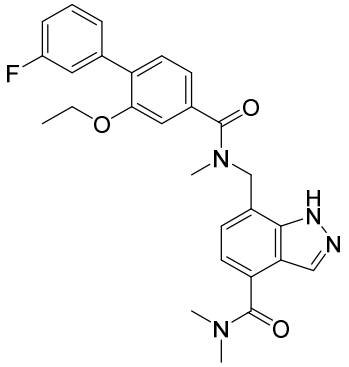
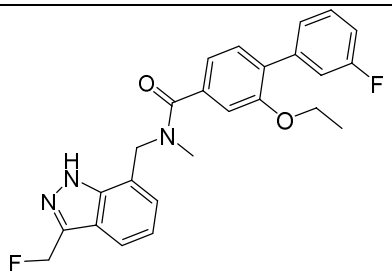
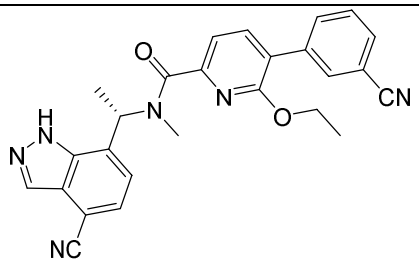
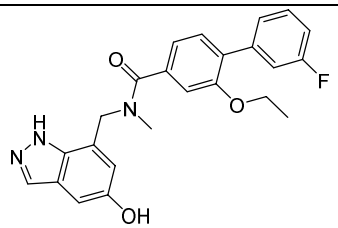


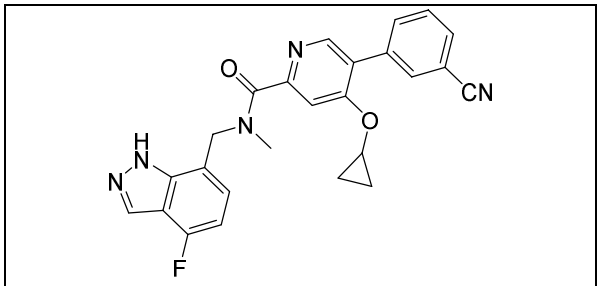
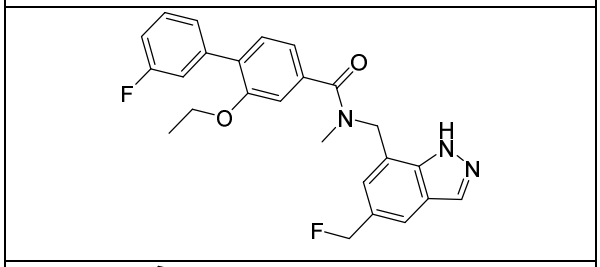
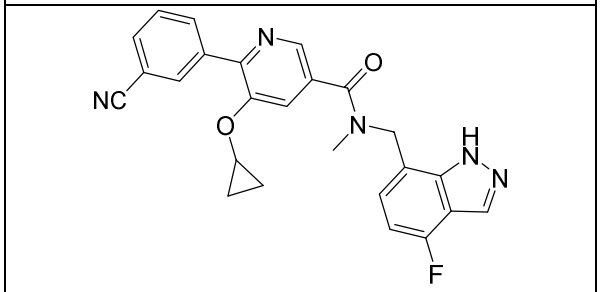
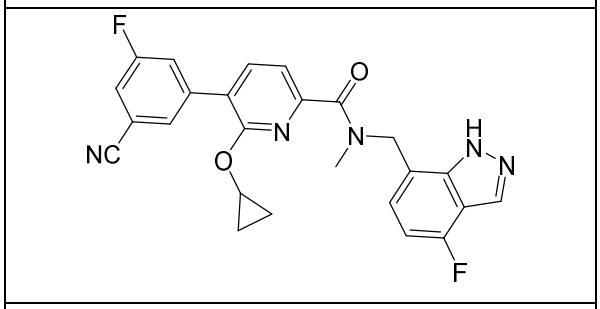
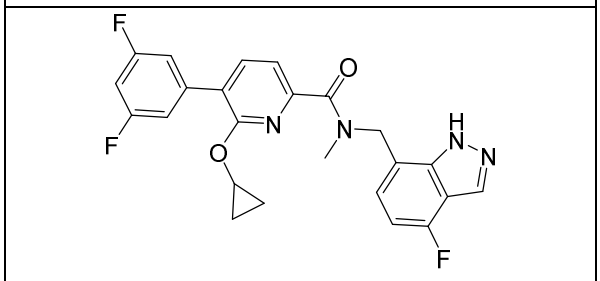
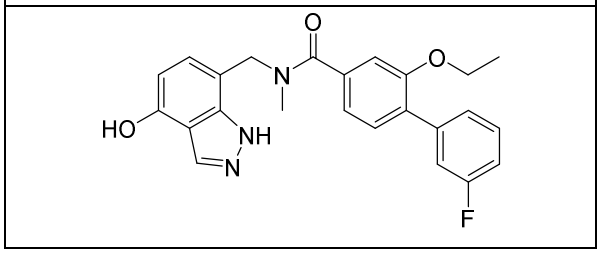


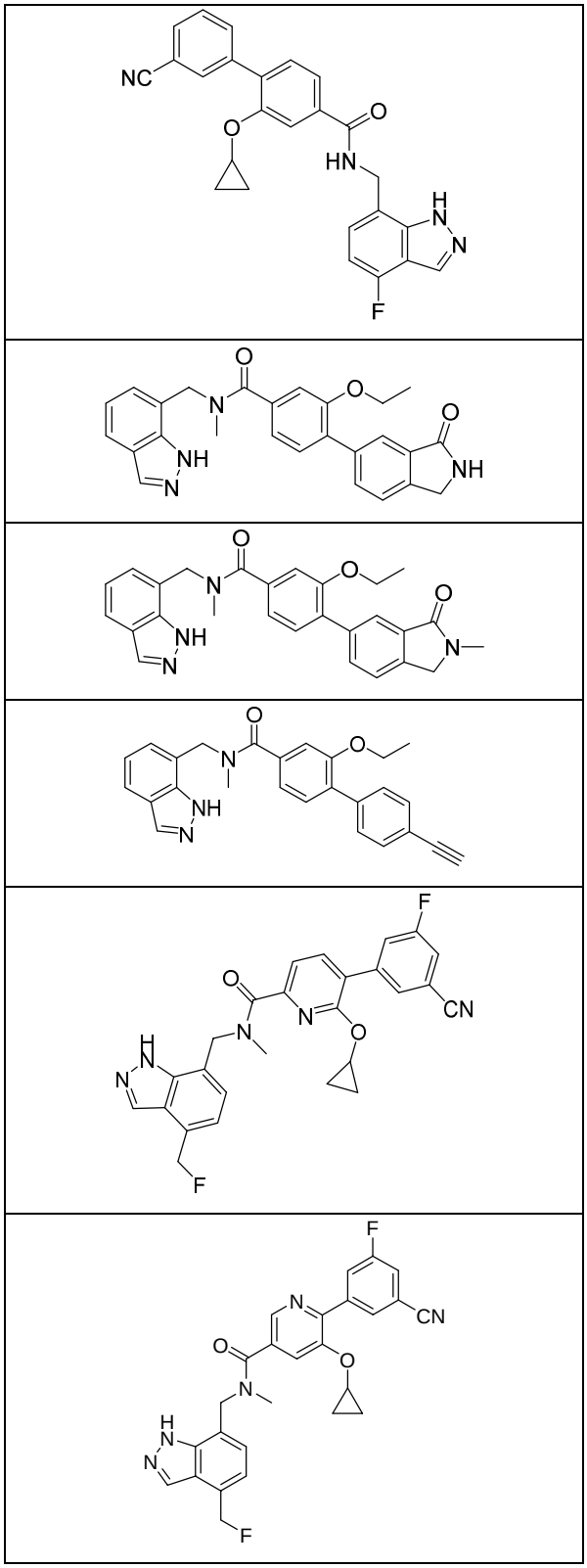


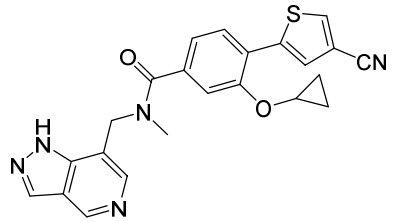
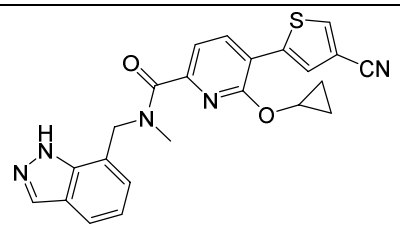
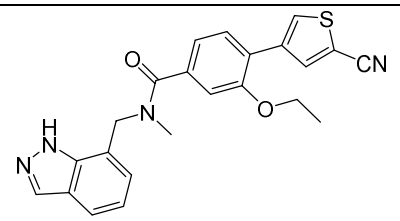
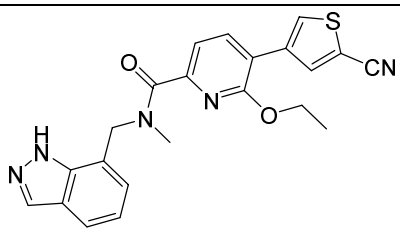
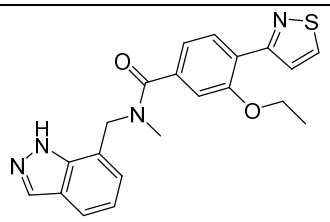
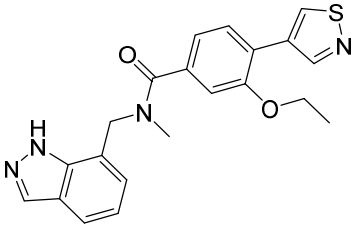
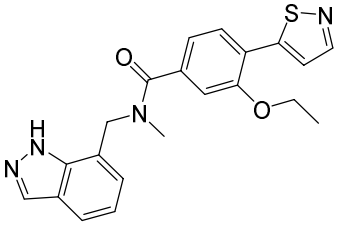


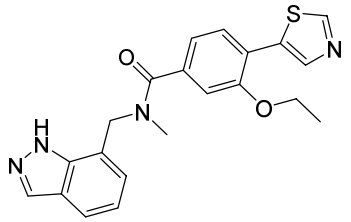
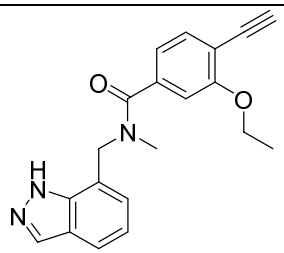
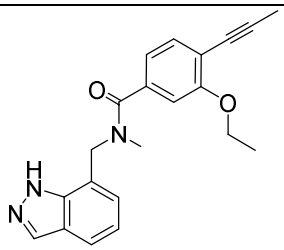
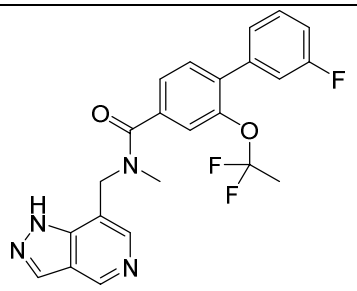
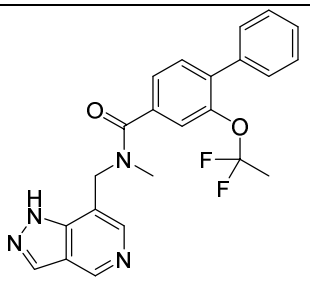
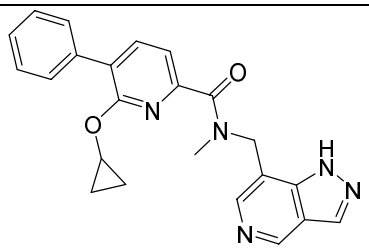


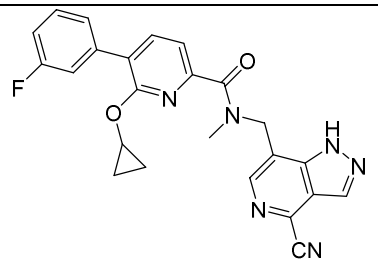
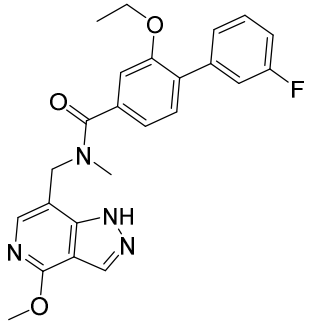
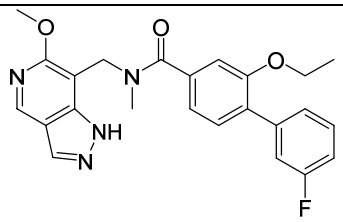
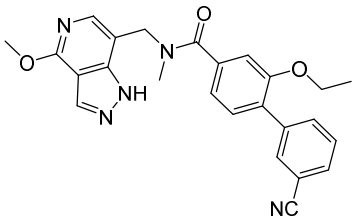
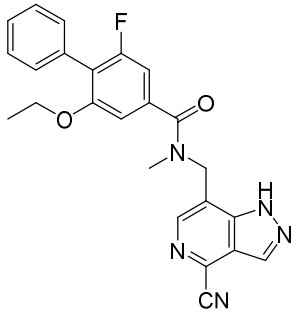
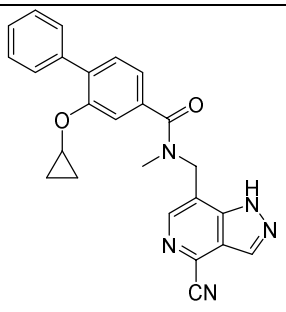






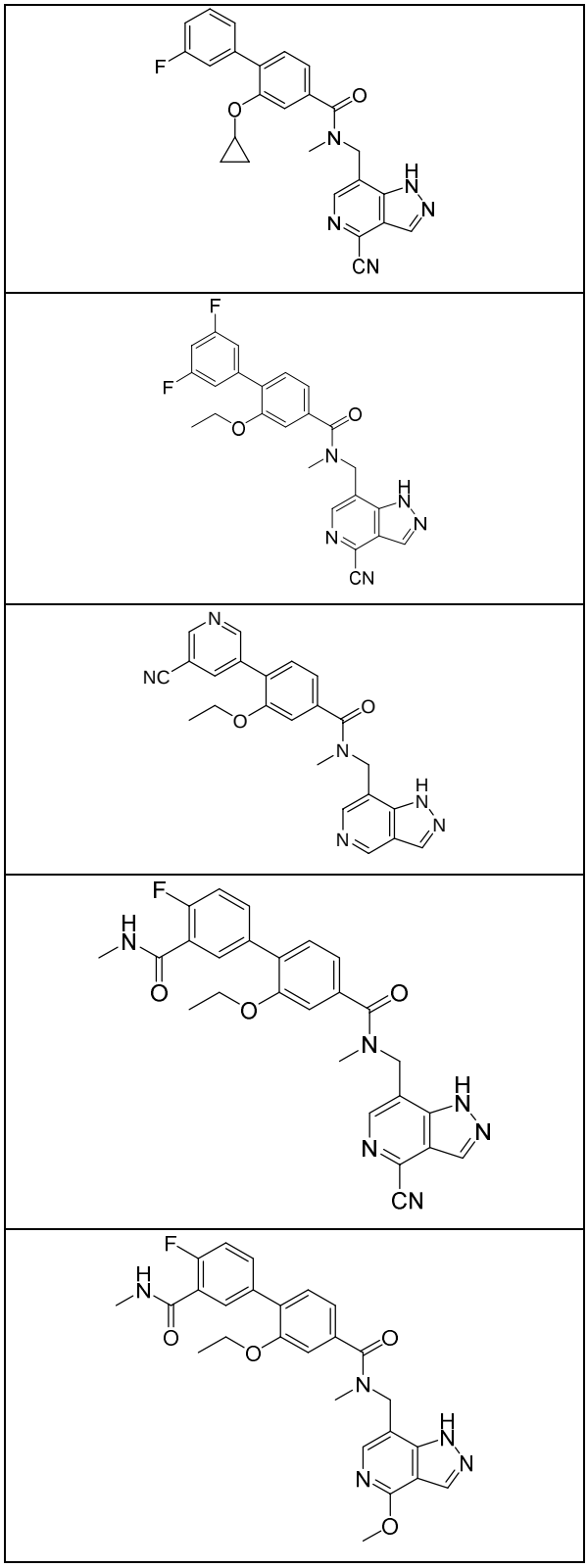







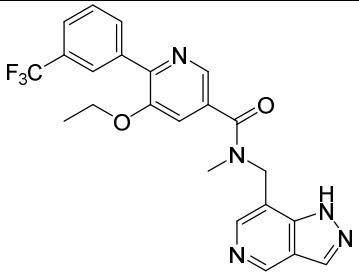
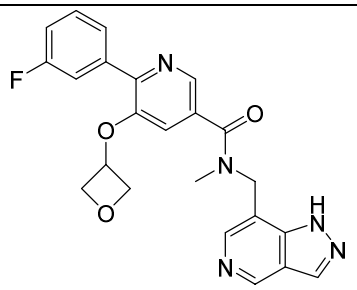
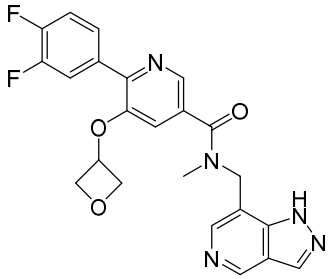
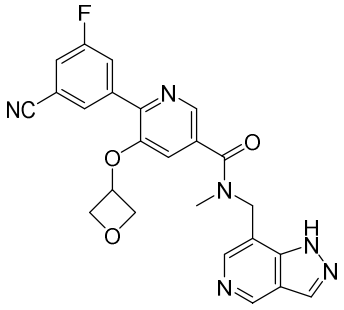
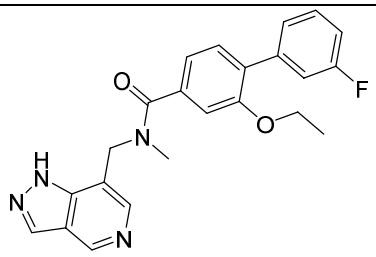
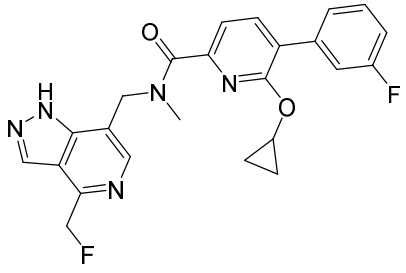


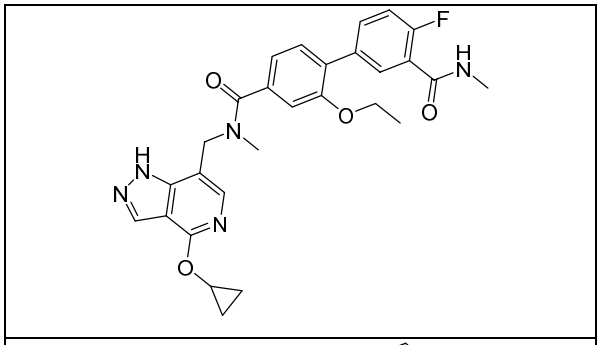








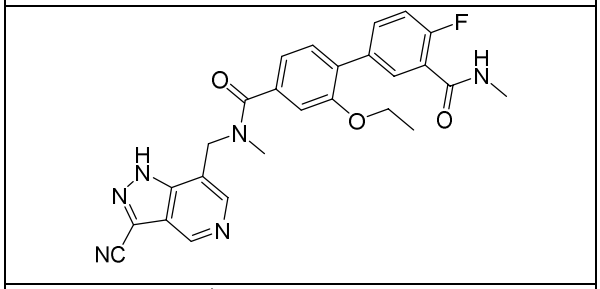







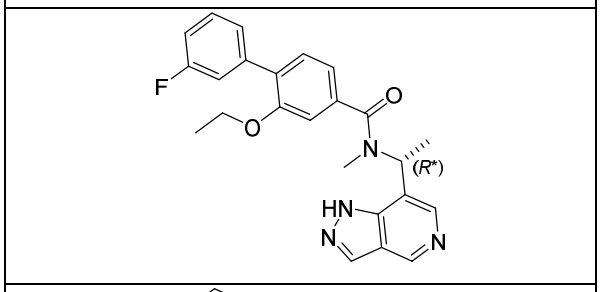







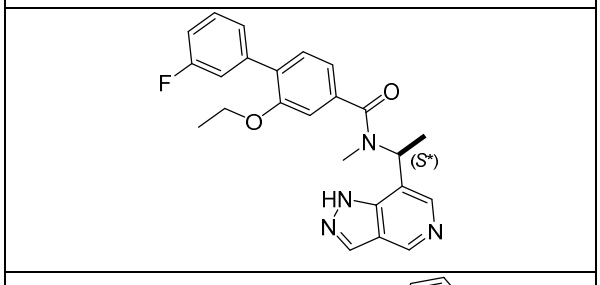


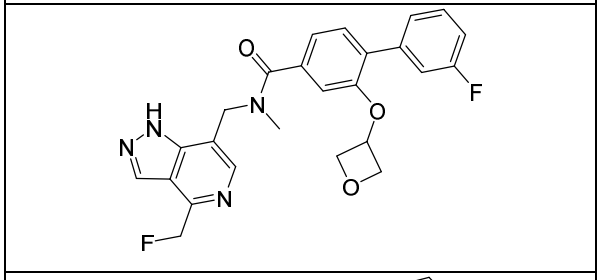







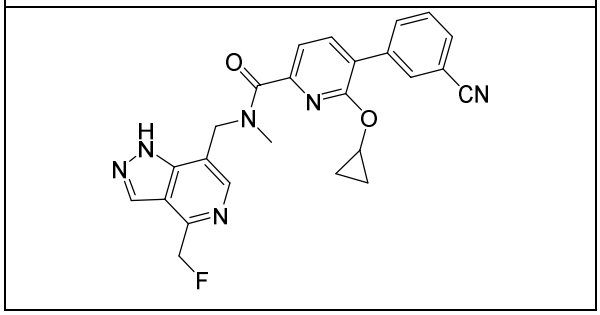


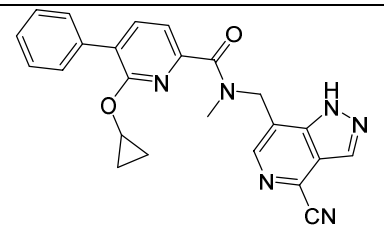
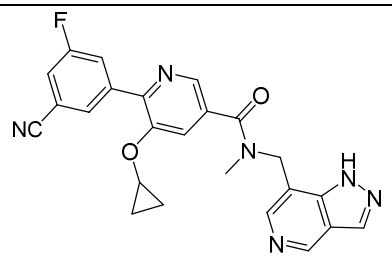
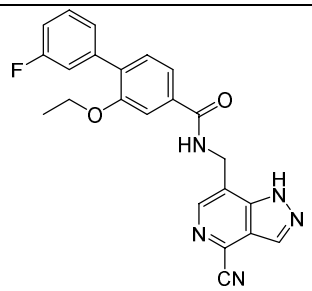
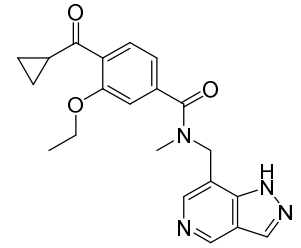
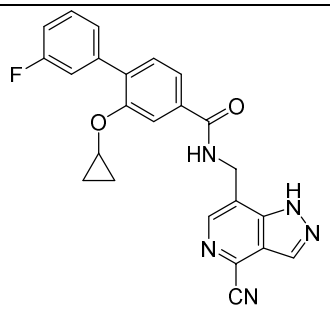
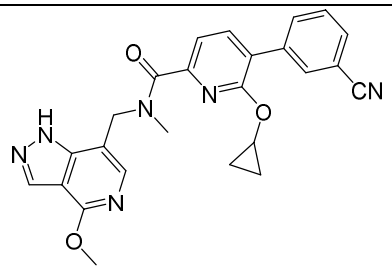


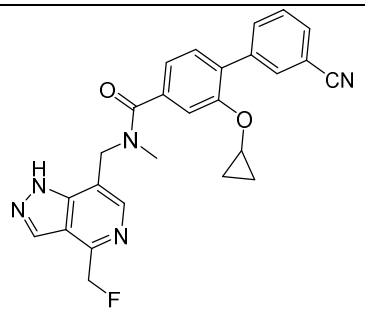
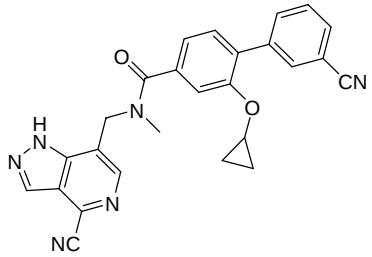
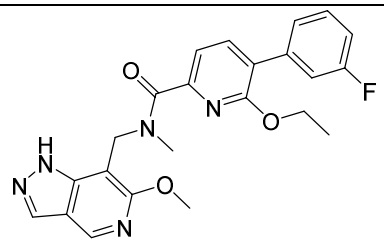
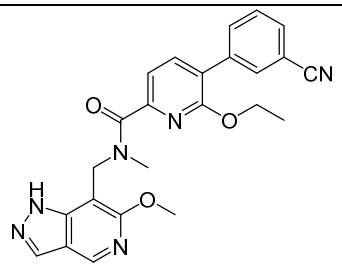
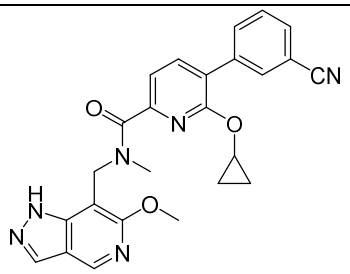
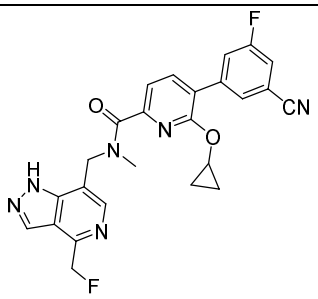


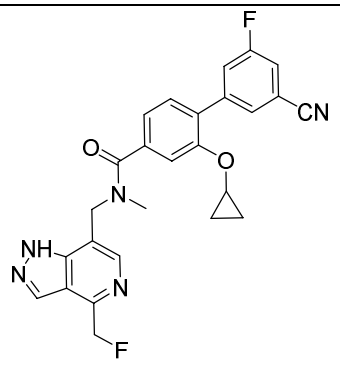
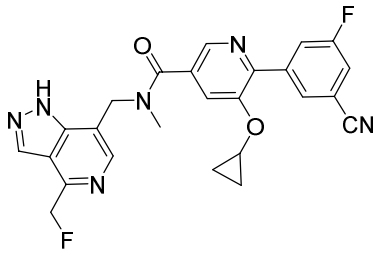
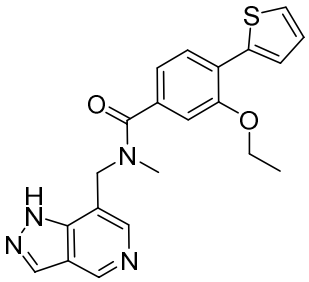
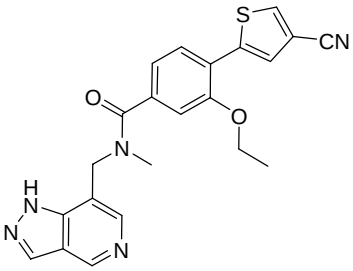
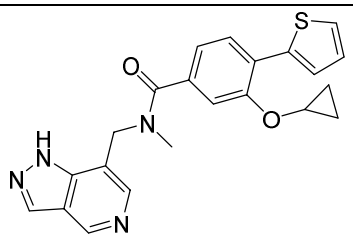
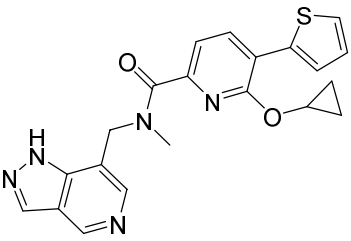


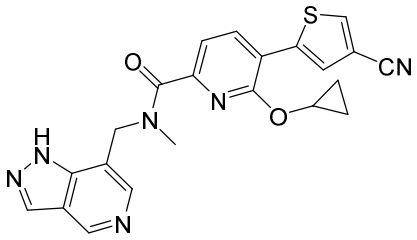
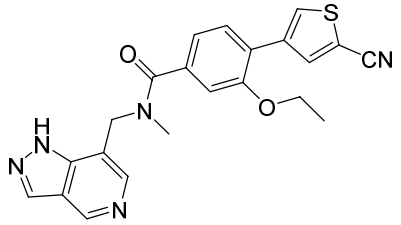
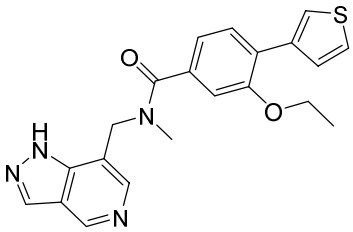
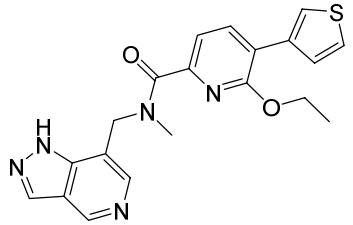
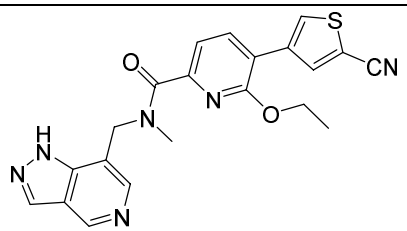
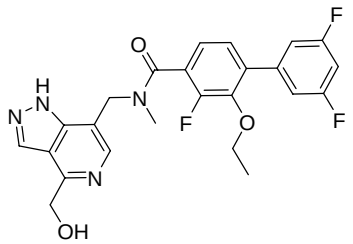
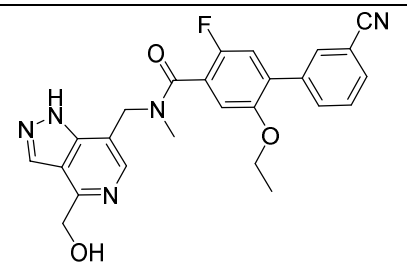


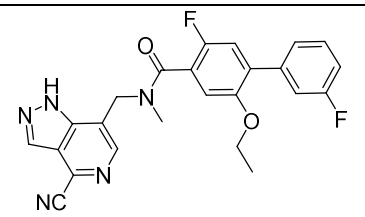
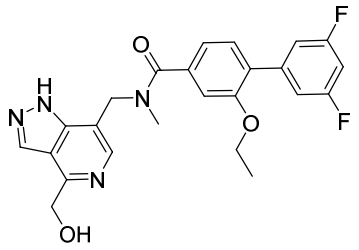
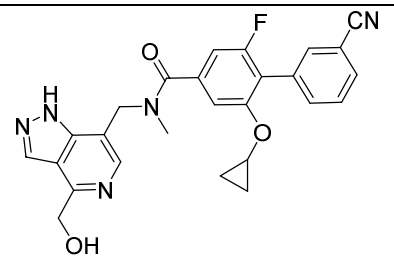
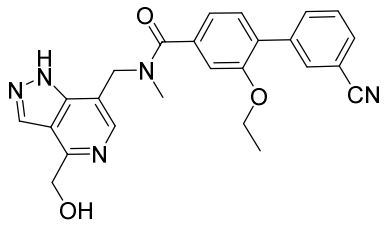
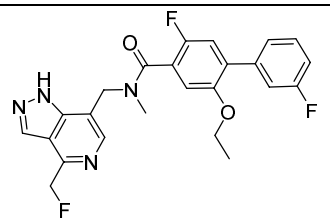
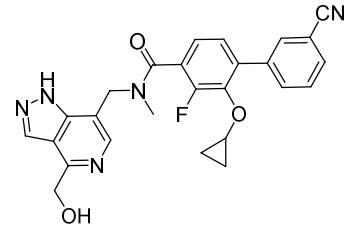
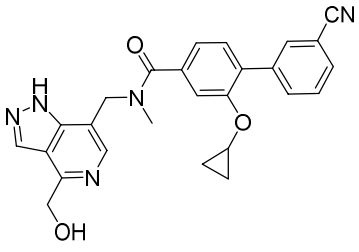


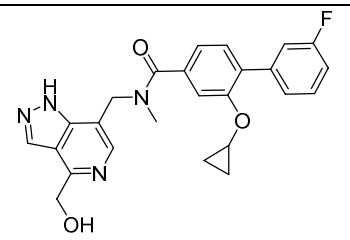
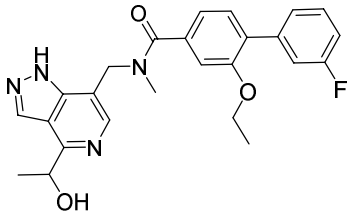
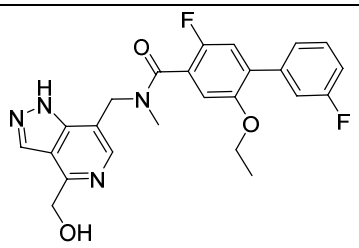
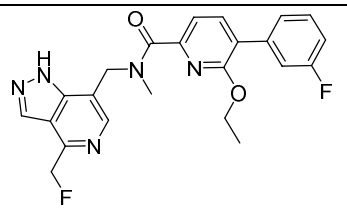
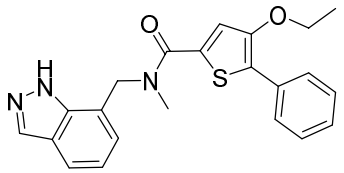
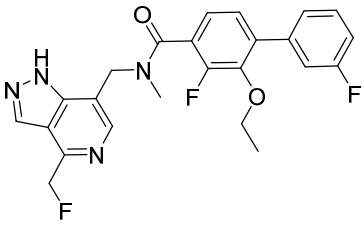
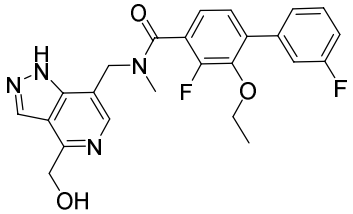







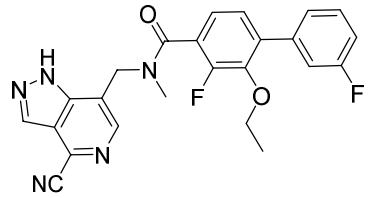
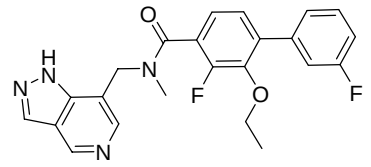
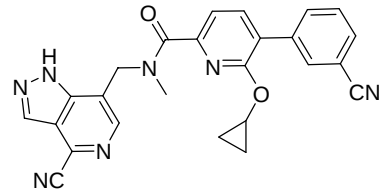
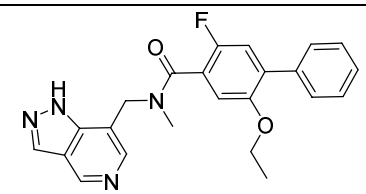
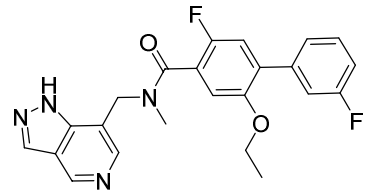
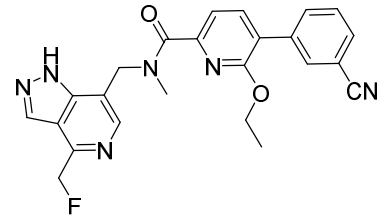
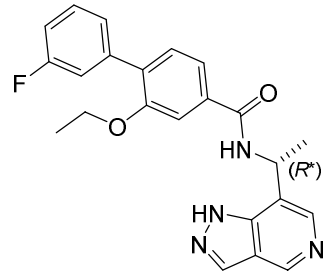







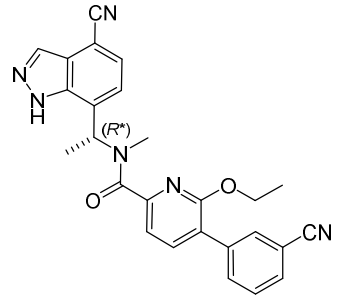
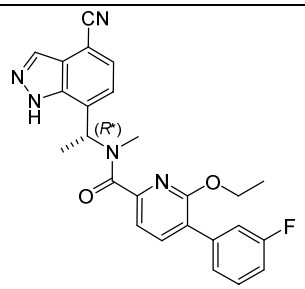
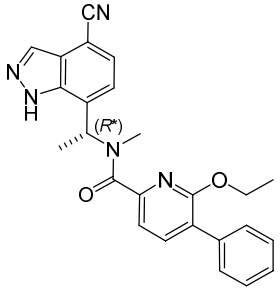
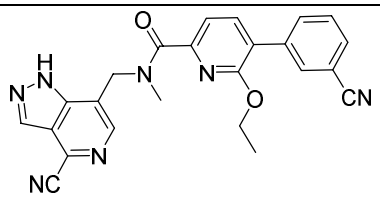
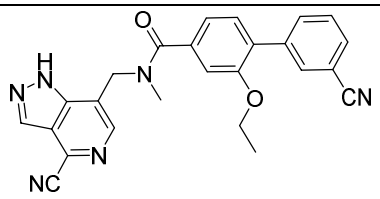
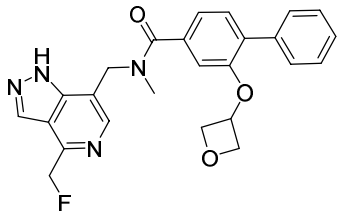







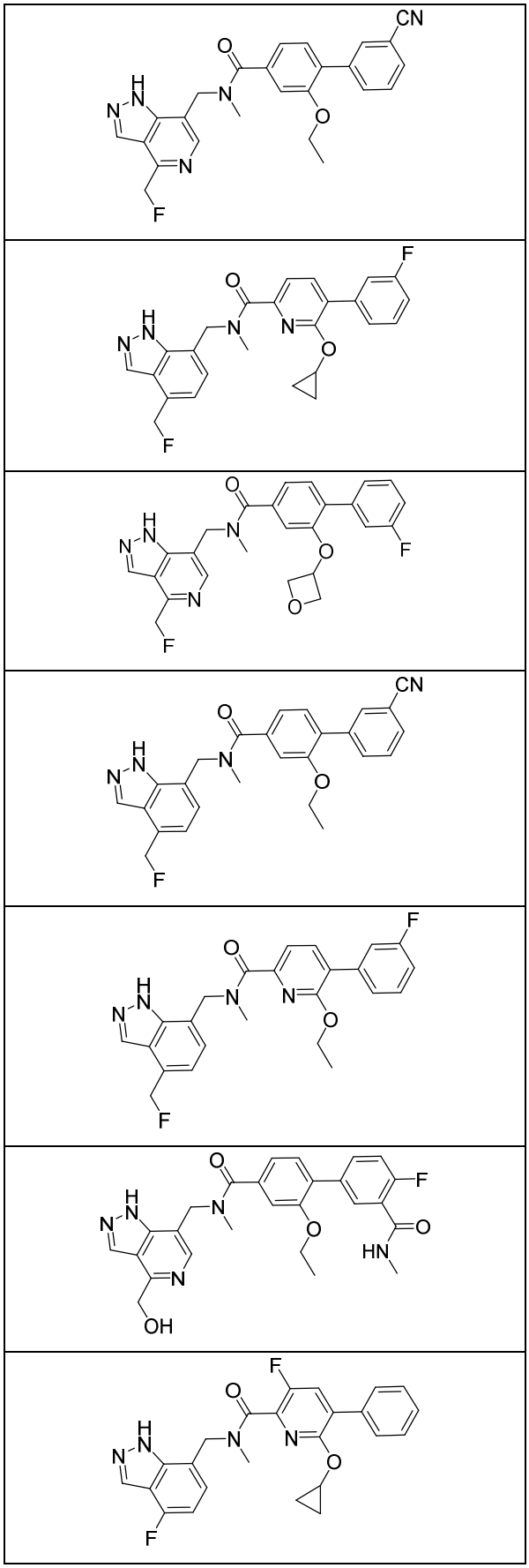








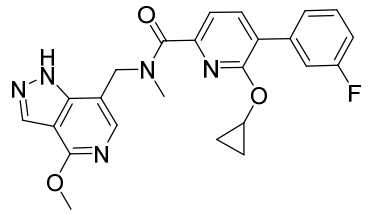
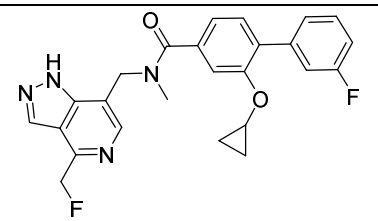
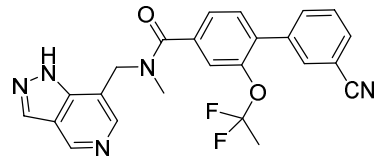
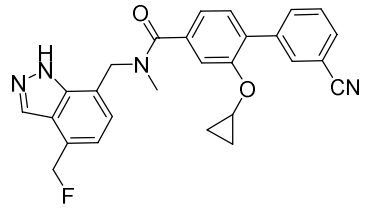
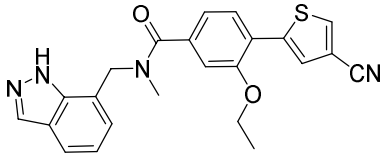
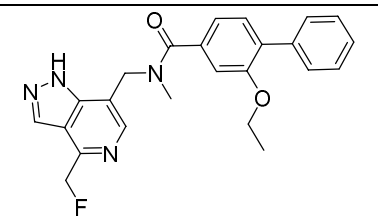
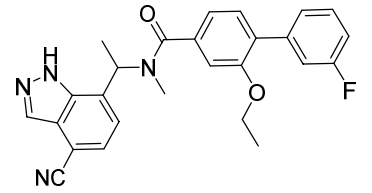
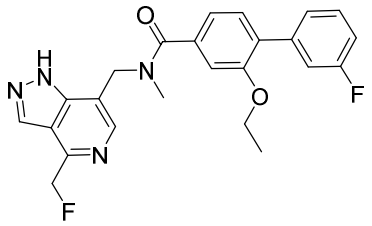








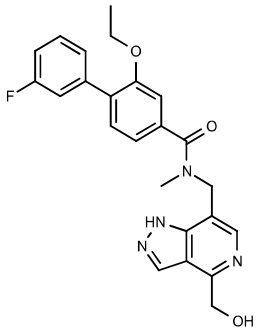
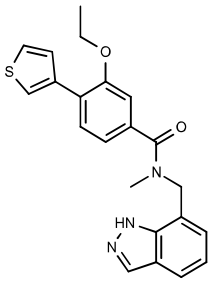
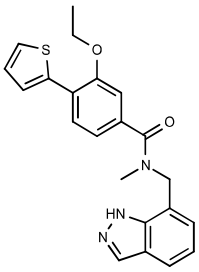
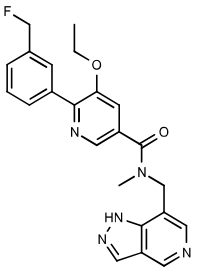
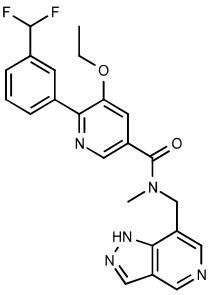








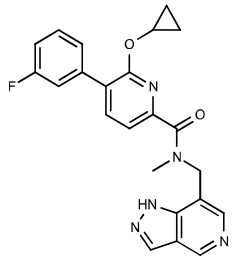
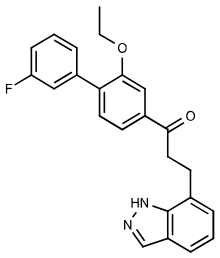
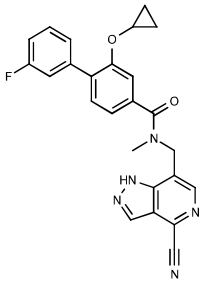
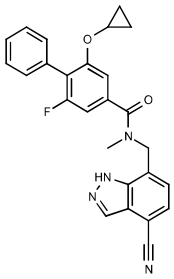
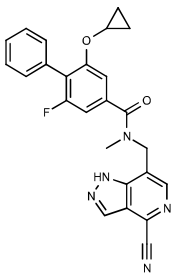
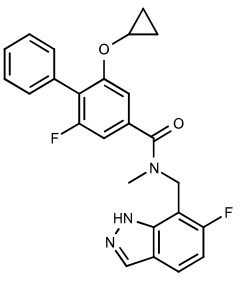








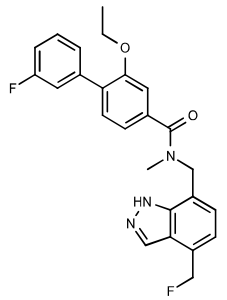
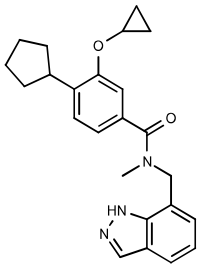
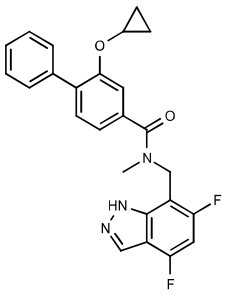
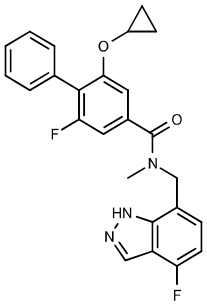
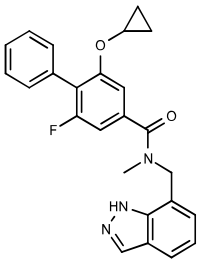







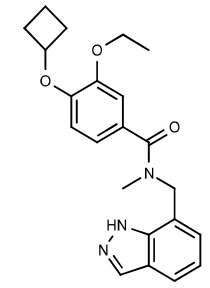
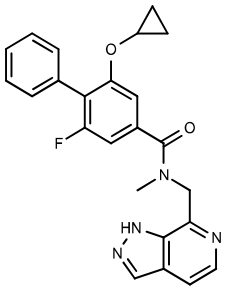
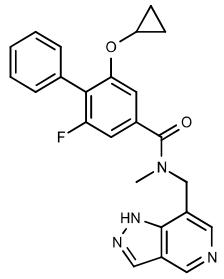
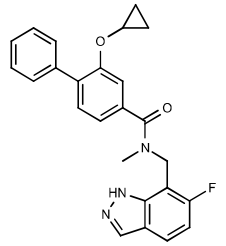
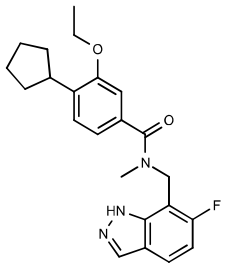
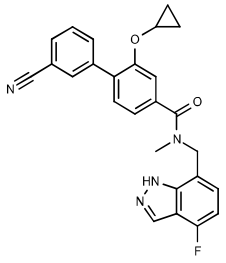


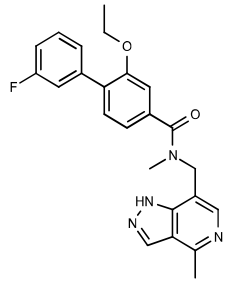
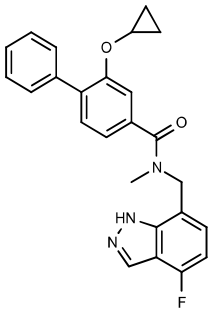
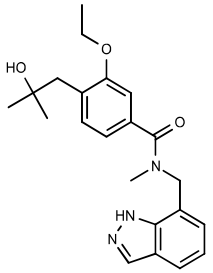
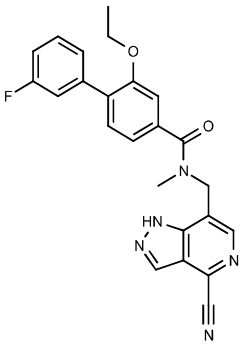
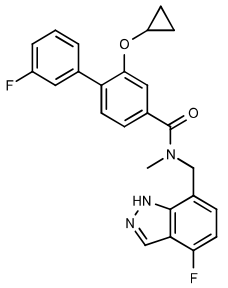









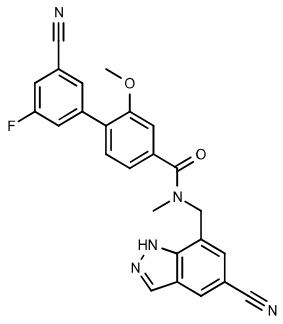
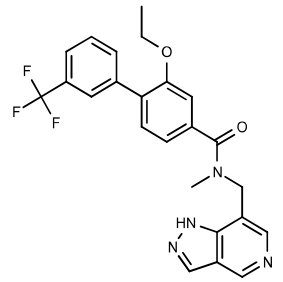
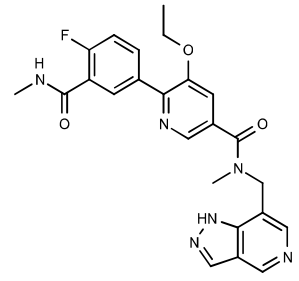
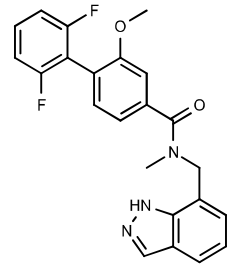
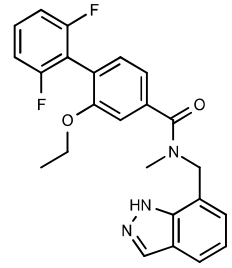






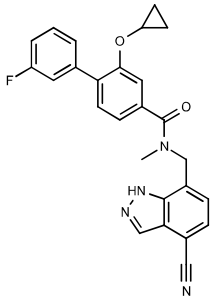
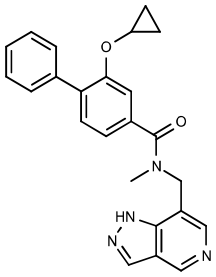
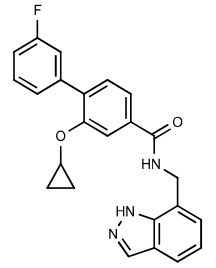
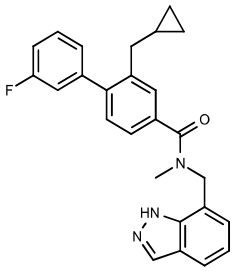
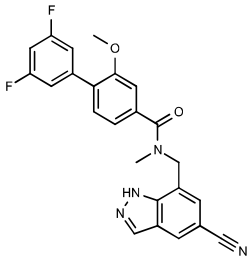
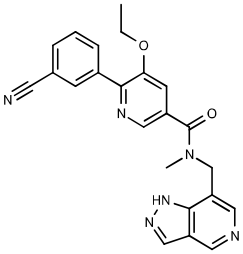







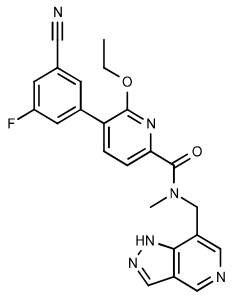
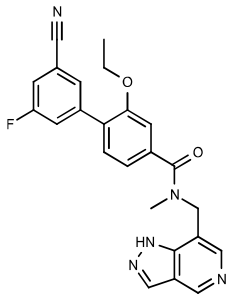
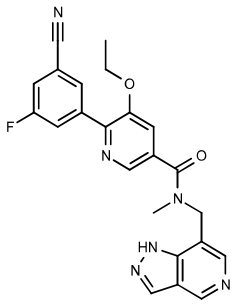
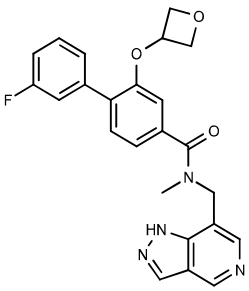
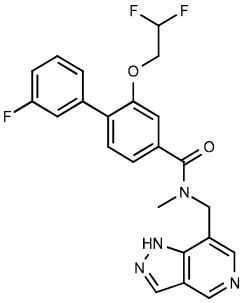






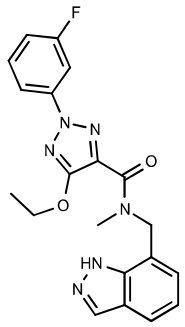
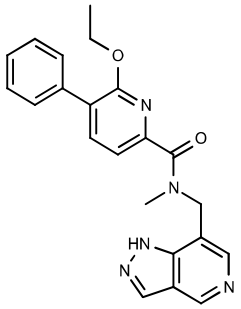
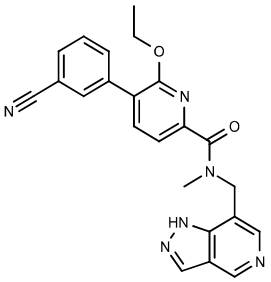
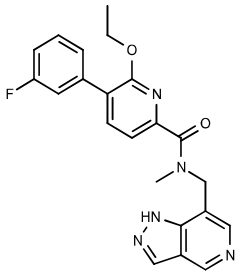
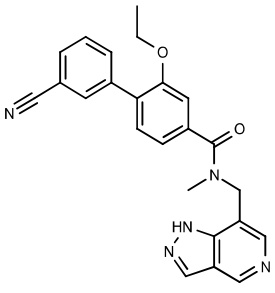







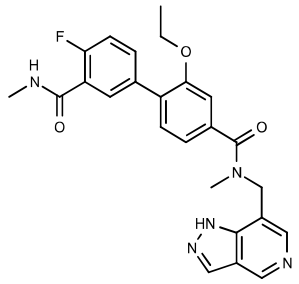
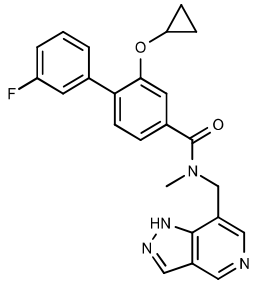
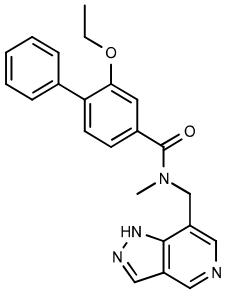
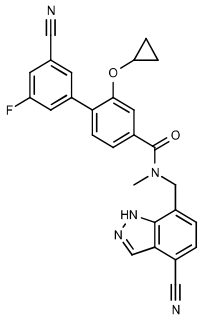
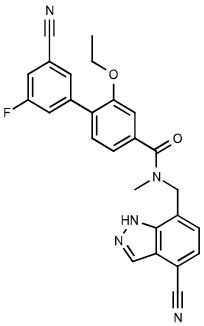






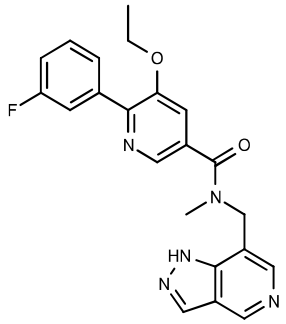
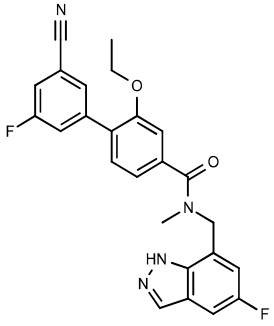
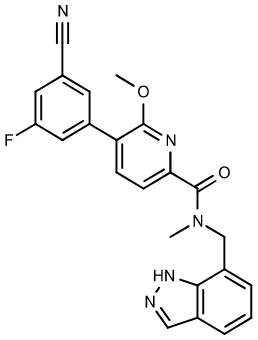
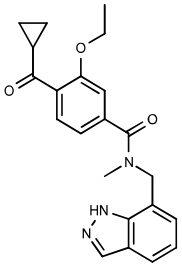
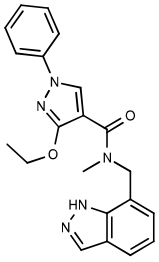






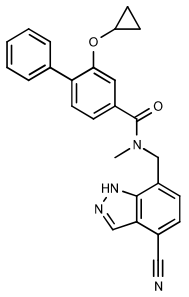
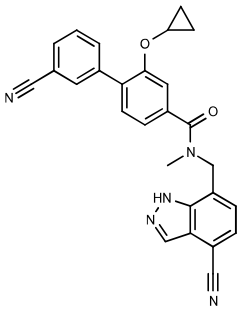
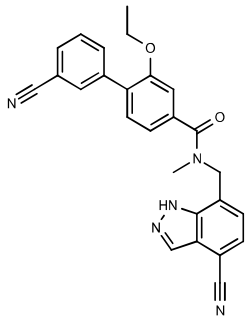
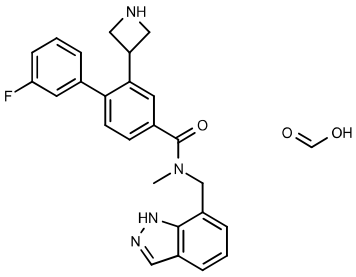
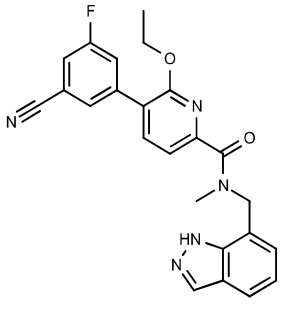







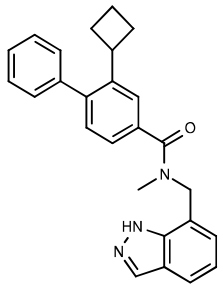
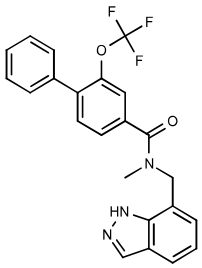
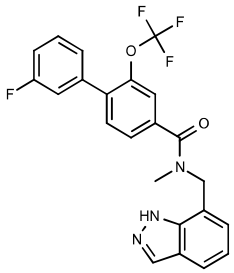
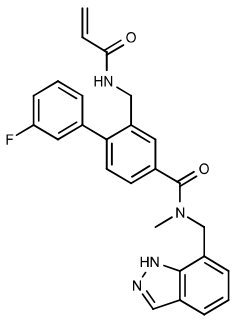
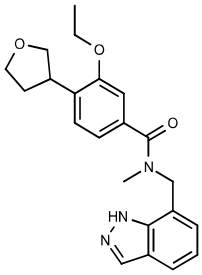






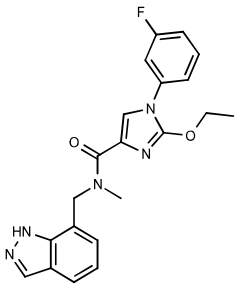
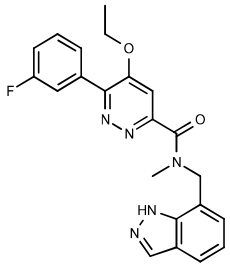
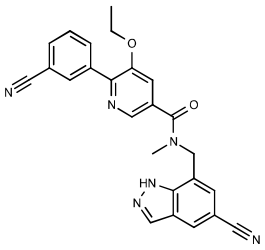
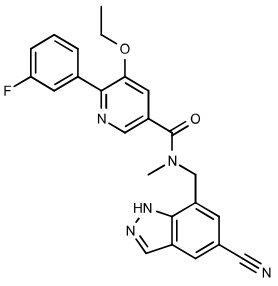
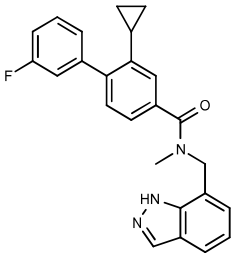






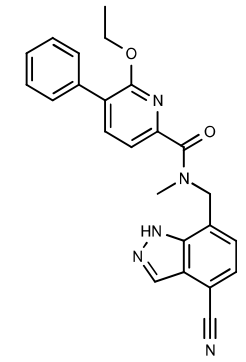
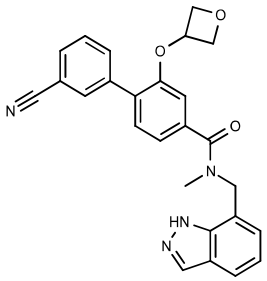
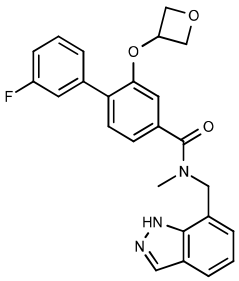
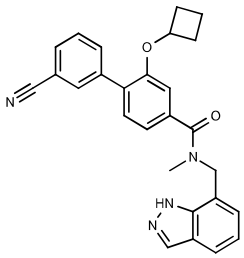
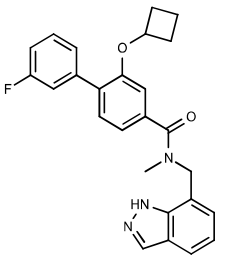






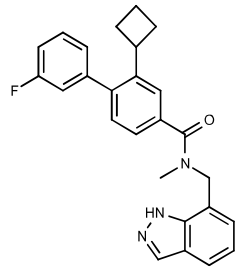
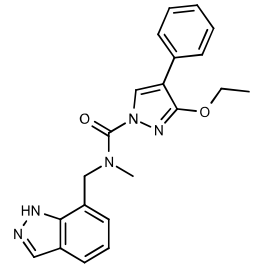
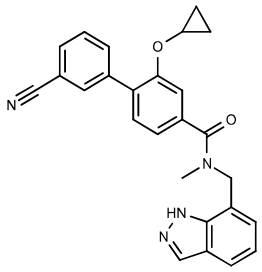
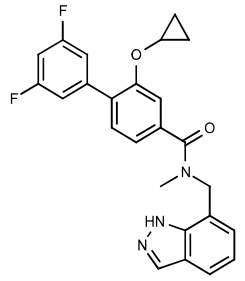
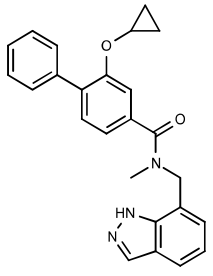






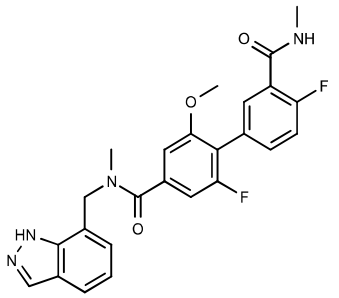
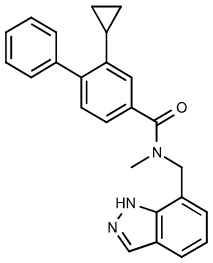
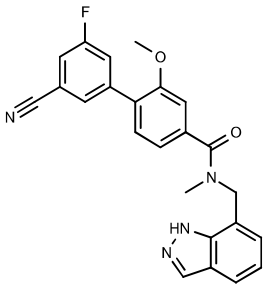
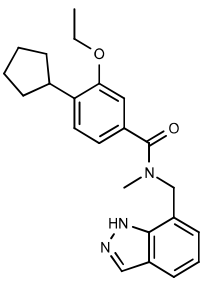
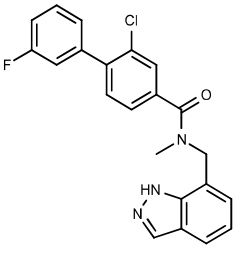






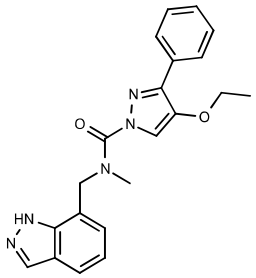
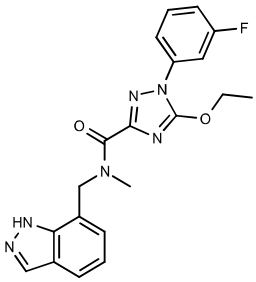
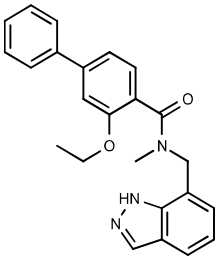
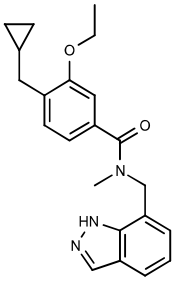
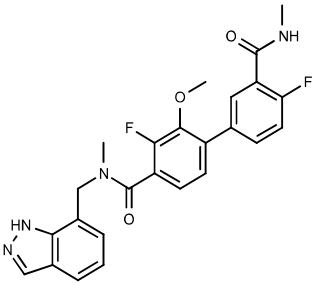






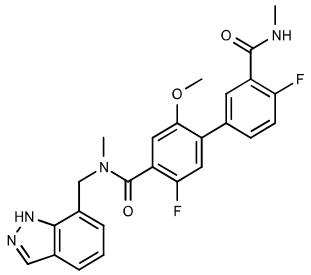
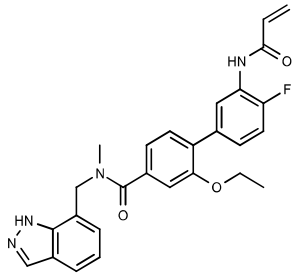
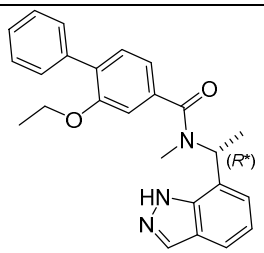
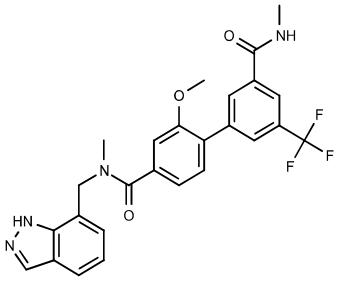
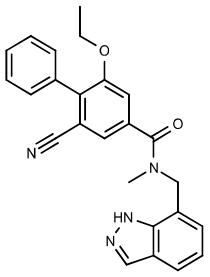
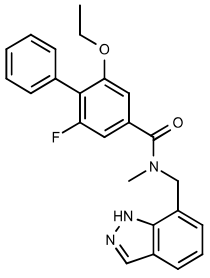






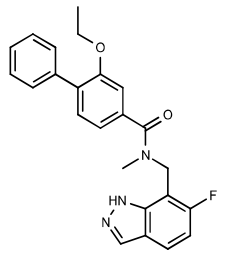
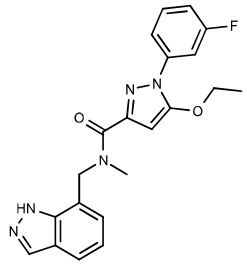
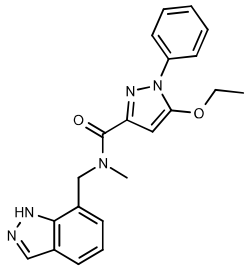
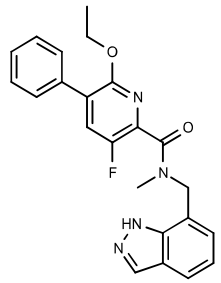
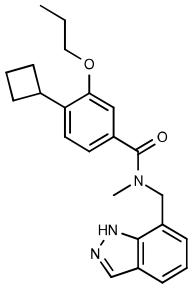
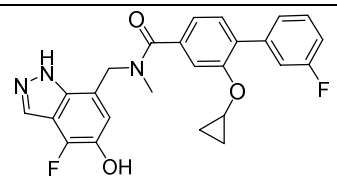






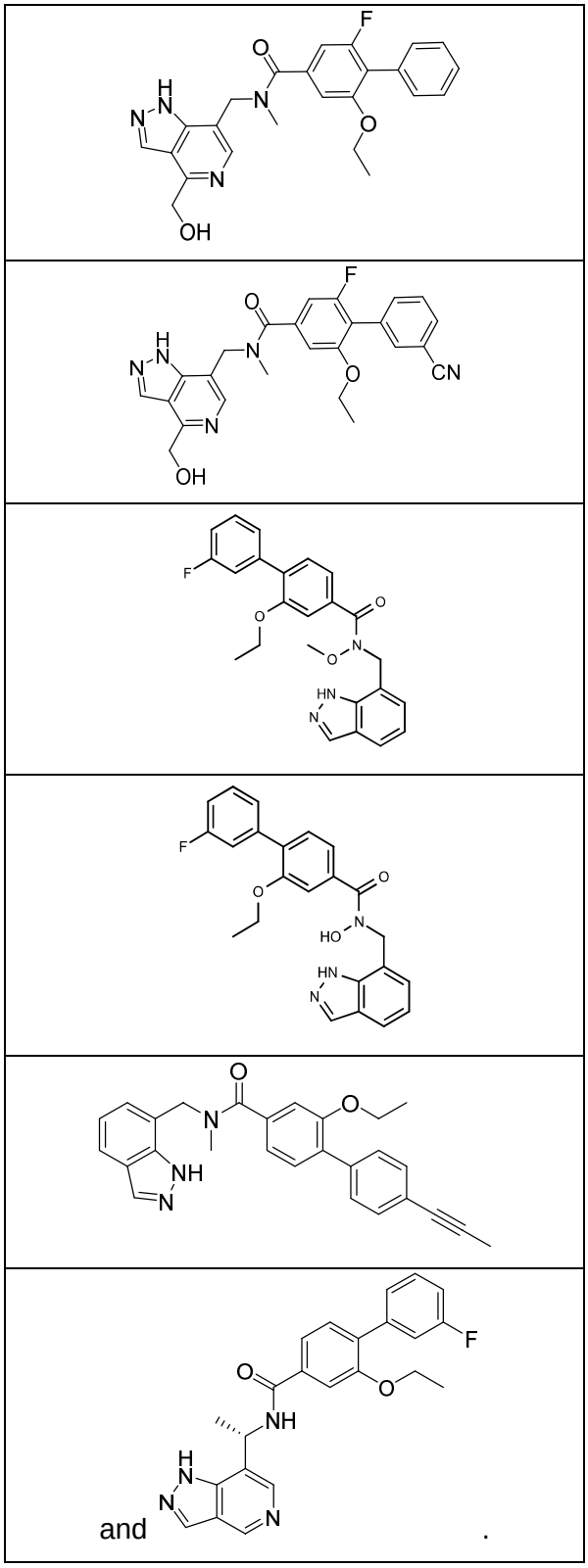






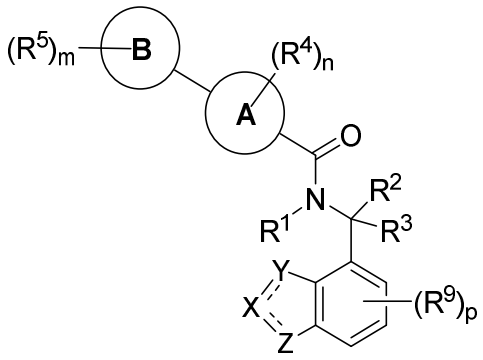









and .

35. A compound of Formula X:



(**X**)

or a pharmaceutically acceptable salt thereof;

wherein

⎓ is an optional double bond;

X is CH, N, NH, or N(C_{1-6} alkyl);

Y and Z are each independently selected from the group consisting of NH, NR^9, O, S, N, CH, and CR^9;

Ring A is selected from the group consisting of C_{6-10} aryl, 5-6 membered heteroaryl, C_{3-10} cycloalkyl, and 4-10 membered heterocycloalkyl;

Ring B is selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl, and 3-6 membered heterocycloalkyl;

alternatively, Ring B is absent and m is 0;

R^1 is selected from the group consisting of H, C_{1-6} alkyl, and C_{3-6} cycloalkyl, wherein alkyl and cycloalkyl are each optionally substituted with R^6;

R^2 and R^3 are each independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and 4-10 membered heterocycloalkyl, wherein alkyl, cycloalkyl, and heterocycloalkyl are each optionally substituted with R^6;

alternatively, R^2 and R^3, together with the atom to which they are attached, form a ring selected from the group consisting of C_{3-7} cycloalkyl and 3-7 membered heterocycloalkyl;

each R^4 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} alkyl-O-C_{1-6} alkyl, halo, OH, OR^6, NH_2, NH(C_{1-6} alkyl), N(C_{1-6} alkyl)$_2$, $NHCOR^6$, CN, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, and COR^6 wherein alkyl, cycloalkyl, and heterocycloalkyl are each optionally substituted with R^6;

alternatively, two R^4, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and 4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^5 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OR^6, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, $NHCOR^6$, CN, C_{3-7} cycloalkyl, 3-7 membered heterocycloalkyl, COR^6, and SO_2R^6;

alternatively, two R^5, together with the atoms to which they are attached, form a ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{4-6} cycloalkyl, and 4-6 membered heterocycloalkyl all of which are optionally substituted with one, two, or three R^7;

each R^6 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, C_{0-6} alkyl-C_{6-10} aryl, C_{0-6} alkyl-5-10 membered heteroaryl, OC_{1-6} alkyl, C_{3-6} cycloalkyl, halo, OH, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

each R^7 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} haloalkyl, halo, OH, OC_{1-6} alkyl, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, CN, COR^8, and SO_2R^8;

each R^8 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, NH_2, $NH(C_{1-6}$ alkyl), and $N(C_{1-6}$ alkyl)$_2$;

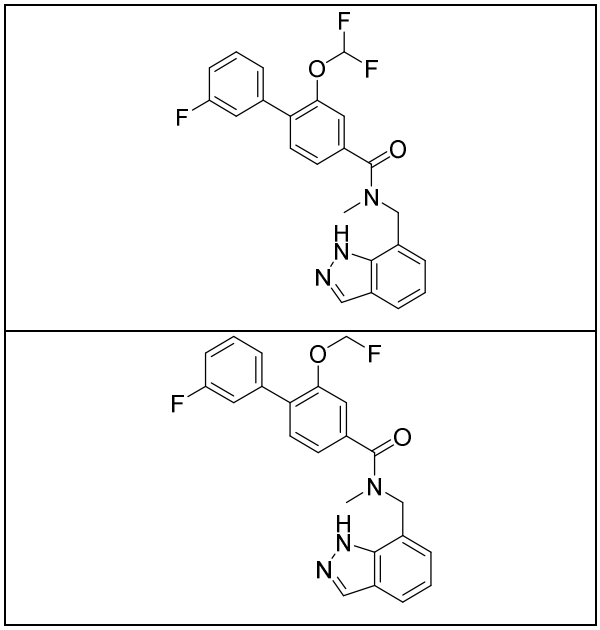
each R^9 is independently selected from the group consisting of C_{1-6} alkyl, OC_{1-6} alkyl, halo, CN, OH, NH_2, $NH(C_{1-6}$ alkyl), $N(C_{1-6}$ alkyl)$_2$, $C(O)NHR^8$, $C(O)N(R^8)_2$, and $NHC(O)R^8$;

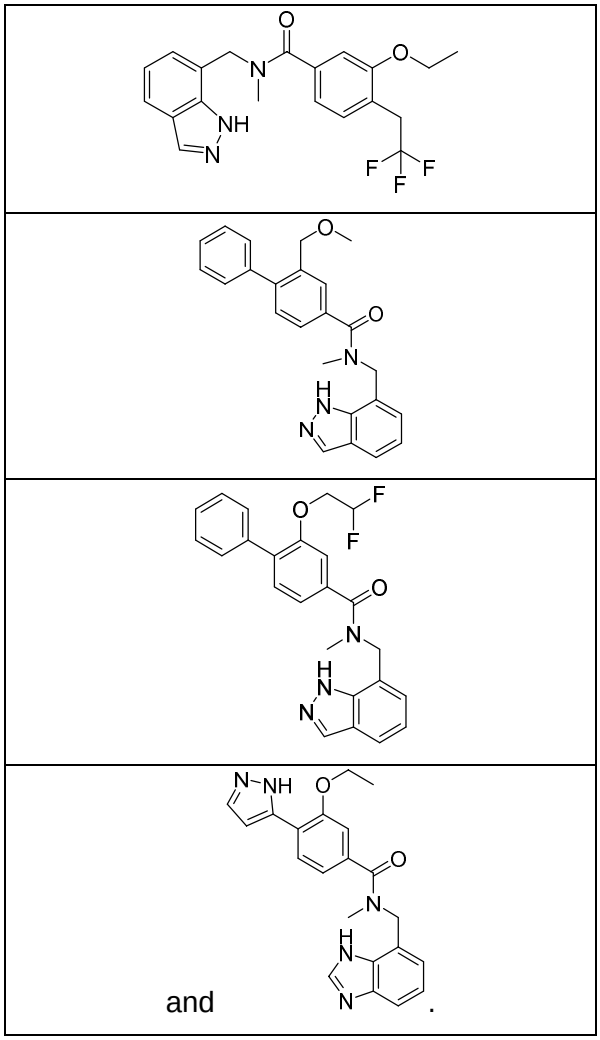
m is 0, 1, 2, or 3;

n is 1, 2, or 3; and

p is 0, 1, 2, or 3.

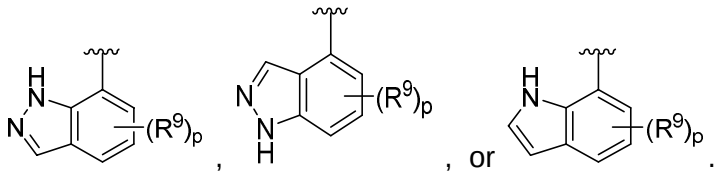
36. The compound of claim 35, wherein the compound of Formula X, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of:





and .

37. The compound of any one of claims 1, 14, 23, 26, 33, and 35 wherein the compound of Formulae I, II, IV, VII, and X has one of the following core structures:



, , or .

38. A pharmaceutical composition comprising a compound of any one of claims 1-37, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

39. A compound according to any one of claims 1-37, or the pharmaceutical composition of claim 38, for use in inhibiting NLRP3 inflammasome in a subject in need thereof.

40. A compound according to any one of claims 1-37, or the pharmaceutical composition of claim 38, for use in treating inflammation in a subject in need thereof.

41. A compound according to any one of claims 1-37, or the pharmaceutical composition of claim 38, for use in treating inflammaging in a subject in need thereof.

42. A compound according to any one of claims 1-37, or the pharmaceutical composition of claim 38, for use in treating cryopyrin-associated periodic syndrome (CAPS) in a subject in need thereof.

43. A compound according to any one of claims 1-37, or the pharmaceutical composition of claim 38, for use in treating a disease or disorder of the inner ear in a subject in need thereof.

44. The compound for use according to claim 43, wherein the disease or disorder of the inner ear is selected from the group consisting of hearing loss, hearing impairment, vertigo, Meniere's disease, and tinnitus.

45. Use of a compound according to any one of claims 1-37, or the pharmaceutical composition of claim 38, in the manufacture of a medicament for inhibiting NLRP3 inflammasome in a subject in need thereof.

46. Use of a compound according to any one of claims 1-37, or the pharmaceutical composition of claim 38, in the manufacture of a medicament for treating inflammation in a subject in need thereof.

47. Use of a compound according to any one of claims 1-37, or the pharmaceutical composition of claim 38, in the manufacture of a medicament for treating inflammaging in a subject in need thereof.

48. Use of a compound according to any one of claims 1-37, or the pharmaceutical composition of claim 38, in the manufacture of a medicament for treating cryopyrin-associated periodic syndrome (CAPS) in a subject in need thereof.

49. Use of a compound according to any one of claims 1-37, or the pharmaceutical composition of claim 38, in the manufacture of a medicament for treating a disease or disorder of the inner ear in a subject in need thereof.

50. The use according to claim 49, wherein the disease or disorder of the inner ear is selected from the group consisting of hearing loss, hearing impairment, vertigo, Meniere's disease, and tinnitus.