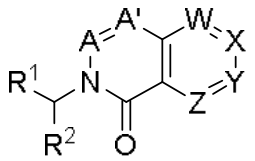
CLAIMS

1. A compound of Formula I:



(**I**)

or a pharmaceutically acceptable salt thereof;

wherein:

A and A' are each, independently, CH, CR^8, or N;

W and Z are each, independently, N, CH, C-halo, C-(C_1-C_3 alkyl), or C-(C_1-C_3 alkoxy);

X and Y are each, independently, N, CH, or CR^3;

provided that at least one of W, X, Y, or Z is CH;

R^1 is selected from the group consisting of 6-10 membered aryl, 5-10 membered heteroaryl, 3-10 membered heterocycloalkyl, and 3-10 membered cycloalkyl, all of which are optionally substituted with one, two, or three R^8;

R^2 is selected from the group consisting of 6-10 membered aryl, 5-10 membered heteroaryl, 3-10 membered heterocycloalkyl, and 3-10 membered cycloalkyl, all of which are optionally substituted with one, two, or three R^6;

R^3 is independently, at each occurrence, selected from the group consisting of halogen, OR^4, NR^4R^4, SO_2R^4, SO_2NHR^4, $NHSO_2R^4$, $C(O)OR^4$, $C(O)NHR^4$, $C(O)R^4$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, 3-7 membered cycloalkyl, C_4-C_7 cycloalkenyl, C_6-C_{10} aryl, 5-6 membered heteroaryl, and 5-7 membered heterocyclyl, wherein alkyl, alkenyl, or alkynyl are each optionally substituted one, two, or three times with R^4, and wherein aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^5;

R^4 is independently, at each occurrence, selected from the group consisting of H, $(CH_2)_{0-3}$-(C_3-C_7 cycloalkyl), $(CH_2)_{0-3}$-(C_4-C_7 cycloalkenyl), $(CH_2)_{0-3}$-(C_6-C_{10} aryl), $(CH_2)_{0-3}$-(5-6 membered heteroaryl), and $(CH_2)_{0-3}$-(5-7 membered heterocyclyl), wherein the aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^5;

R^5 is independently, at each occurrence, selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_1-C_3 alkylamine, 3-10 membered cycloalkyl, halogen, COOH, C(O)O(C_1-C_6 alkyl), O$(CH_2)_{1-3}$-OH, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)$_2$, OH, CN, $(CH_2)_{0-3}$-(C_6-C_{10} aryl), $(CH_2)_{0-3}$-(5-6 membered heteroaryl), and $(CH_2)_{0-3}$-(5-7 membered heterocyclyl), wherein the aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^7;

R^6 is independently, at each occurrence, selected from the group consisting of C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_1-C_3 alkylamine, halogen, OH, NO_2, NH_2, $NH(C_1$-C_6 alkyl), $N(C_1$-C_6 alkyl)$_2$, $(CH_2)_{1-4}OH$, $S(O)_{0-2}H$, $S(O)_{0-2}NH_2$, or CN;

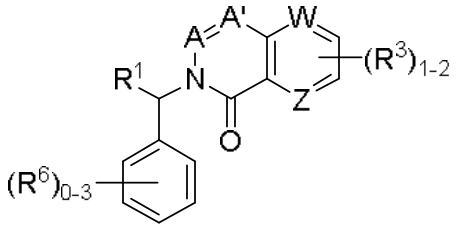
alternatively, two R^6, together with the atoms to which they are attached, can form 5-10 membered heteroaryl, 6-10 membered aryl, 3-10 membered heterocycloalkyl, or 3-10 membered cycloalkyl;

R^7 is independently, at each occurrence, selected from the group consisting of substituents independently selected from C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, halogen, NH_2, $NH(C_1$-C_6 alkyl), $N(C_1$-C_6 alkyl)$_2$, SO_2NH_2, $SO_2NH(C_1$-C_6 alkyl), $SO_2N(C_1$-C_6 alkyl)$_2$, $(CH_2)_{1-2}$-OH, $C(O)(CH_2)_{1-2}$-OH, $C(O)(C_1$-C_6 alkyl), and $C(O)O(C_1$-C_6 alkyl);

alternatively, two R^7, together with the atoms to which they are attached, can form 5-10 membered heteroaryl, 6-10 membered aryl, 3-10 membered heterocycloalkyl, or 3-10 membered cycloalkyl; and

R^8 is independently, at each occurrence, selected from the group consisting of C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_1-C_3 alkylamine, 3-6 membered cycloalkyl, halogen, OH, NO_2, NH_2, $NH(C_1$-C_6 alkyl), $N(C_1$-C_6 alkyl)$_2$, $(CH_2)_{1-4}OH$, $S(O)_{0-2}H$, $S(O)_{0-2}NH_2$, or CN.

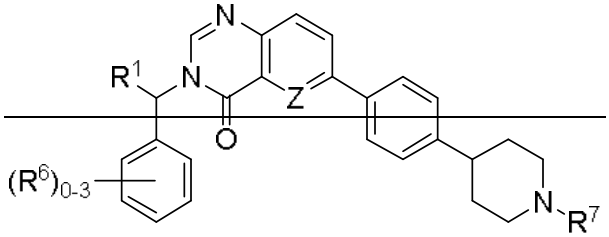
2. The compound of claim 1, wherein the compound of Formula I is a compound of Formula Ia:



(**Ia**)

or a pharmaceutically acceptable salt thereof.

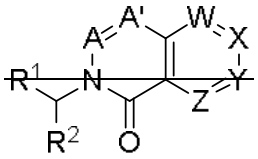
~~3. The compound according to claim 1 or 2, wherein the compound of Formula I is a compound of Formula Ib:~~



(Ib)

or a pharmaceutically acceptable salt thereof.

4. A compound of Formula I:



(I)

or a pharmaceutically acceptable salt thereof;

wherein:

A and A' are each, independently, CH, CR^8, or N;

W and Z are each, independently, N, CH, C-halo, C-(C_1-C_3 haloalkyl), C-(C_1-C_3 alkyl), or C-(C_1-C_3 alkoxy);

X and Y are each, independently, N, CH, or CR^3;

provided that at least one of W, X, Y, or Z is CH;

R^1 is selected from the group consisting of 6-10 membered aryl, 5-10 membered heteroaryl, 3-10 membered heterocycloalkyl, and 3-10 membered cycloalkyl, all of which are optionally substituted with one, two, or three R^8;

R^2 is selected from the group consisting of 6-10 membered aryl, 5-10 membered heteroaryl, 3-10 membered heterocycloalkyl, and 3-10 membered cycloalkyl, all of which are optionally substituted with one, two, or three R^6;

R^3 is independently, at each occurrence, selected from the group consisting of halogen, OR^4, NR^4R^4, SO_2R^4, SO_2NHR^4, $NHSO_2R^4$, $C(O)OR^4$, $C(O)NHR^4$, $C(O)R^4$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, 3-7 membered cycloalkyl, C_4-C_7 cycloalkenyl, C_6-C_{10} aryl, 5-6 membered heteroaryl, and 5-7 membered heterocyclyl, wherein alkyl, alkenyl, or alkynyl are each optionally substituted one, two, or three times with R^4, and wherein aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^5;

R^4 is independently, at each occurrence, selected from the group consisting of H, $(CH_2)_{0-3}$-(C_3-C_7 cycloalkyl), $(CH_2)_{0-3}$-(C_4-C_7 cycloalkenyl), $(CH_2)_{0-3}$-(C_6-C_{10} aryl), $(CH_2)_{0-3}$-(5-6 membered heteroaryl), and $(CH_2)_{0-3}$-(5-7 membered heterocyclyl), wherein the aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^5;

R^5 is independently, at each occurrence, selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_1-C_3 alkylamine, 3-10 membered cycloalkyl, halogen, COOH, C(O)O(C_1-C_6 alkyl), O(CH_2)$_{1-3}$-OH, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)$_2$, OH, CN, $(CH_2)_{0-3}$-(C_6-C_{10} aryl), $(CH_2)_{0-3}$-(5-6 membered heteroaryl), and $(CH_2)_{0-3}$-

~~(5-7 membered heterocyclyl), wherein the aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^7;~~

~~R^6 is independently, at each occurrence, selected from the group consisting of C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_1-C_3 alkylamine, halogen, OH, NO_2, NH_2, $NH(C_1$-C_6 alkyl), $N(C_1$-C_6 alkyl)$_2$, $(CH_2)_{1-4}OH$, $S(O)_{0-2}H$, $S(O)_{0-2}NH_2$, or CN;~~

~~alternatively, two R^6, together with the atoms to which they are attached, can form 5-10 membered heteroaryl, 6-10 membered aryl, 3-10 membered heterocycloalkyl, or 3-10 membered cycloalkyl;~~

~~R^7 is independently, at each occurrence, selected from the group consisting of substituents independently selected from C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6~~ haloalkoxy, halogen, NH_2, $NH(C_1$-C_6 alkyl), $N(C_1$-C_6 alkyl)$_2$, SO_2NH_2, $SO_2NH(C_1$-C_6 alkyl), ~~$SO_2N(C_1$-C_6 alkyl)$_2$, $(CH_2)_{1-2}$-OH, C(O)$(CH_2)_{1-2}$-OH, C(O)$(C_1$-C_6 alkyl), and C(O)O$(C_1$-C_6 alkyl);~~

~~alternatively, two R^7, together with the atoms to which they are attached, can form 5-10 membered heteroaryl, 6-10 membered aryl, 3-10 membered heterocycloalkyl, or 3-10 membered cycloalkyl; and~~

~~R^8 is independently, at each occurrence, selected from the group consisting of C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_1-C_3 alkylamine, 3-6 membered~~ cycloalkyl, halogen, OH, NO_2, NH_2, $NH(C_1$-C_6 alkyl), $N(C_1$-C_6 alkyl)$_2$, $(CH_2)_{1-4}OH$, $S(O)_{0-2}H$, ~~$S(O)_{0-2}NH_2$, or CN.~~

~~5. The compound of any one of claims 1-4, wherein Z is CH.~~

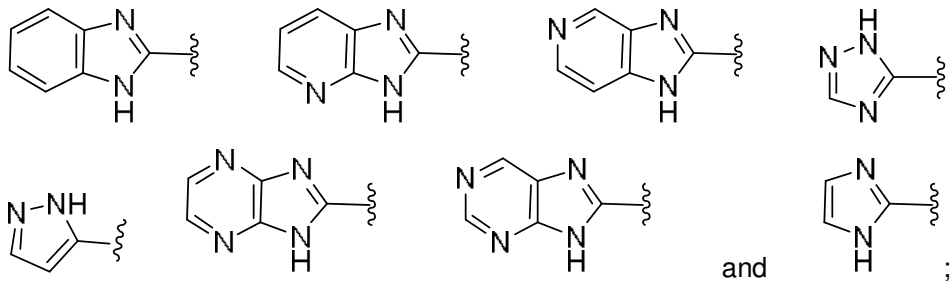
~~6. The compound of any one of claims 1-4, wherein Z is N.~~

~~7~~3. The compound of ~~any one of~~ claim~~s~~ 1-~~4~~ or 2, wherein Z is CF.

~~8~~4. The compound of any one of claims 1-~~7~~3, wherein R^6 is independently, at each occurrence, hydroxy or halo.

~~9~~5. The compound of any one of claims 1-~~8~~4, wherein R^1 is selected from the group consisting of benzimidazole, imidazopyrazine, purine, imidazole, pyrazole, triazole, and imidazopyridine.

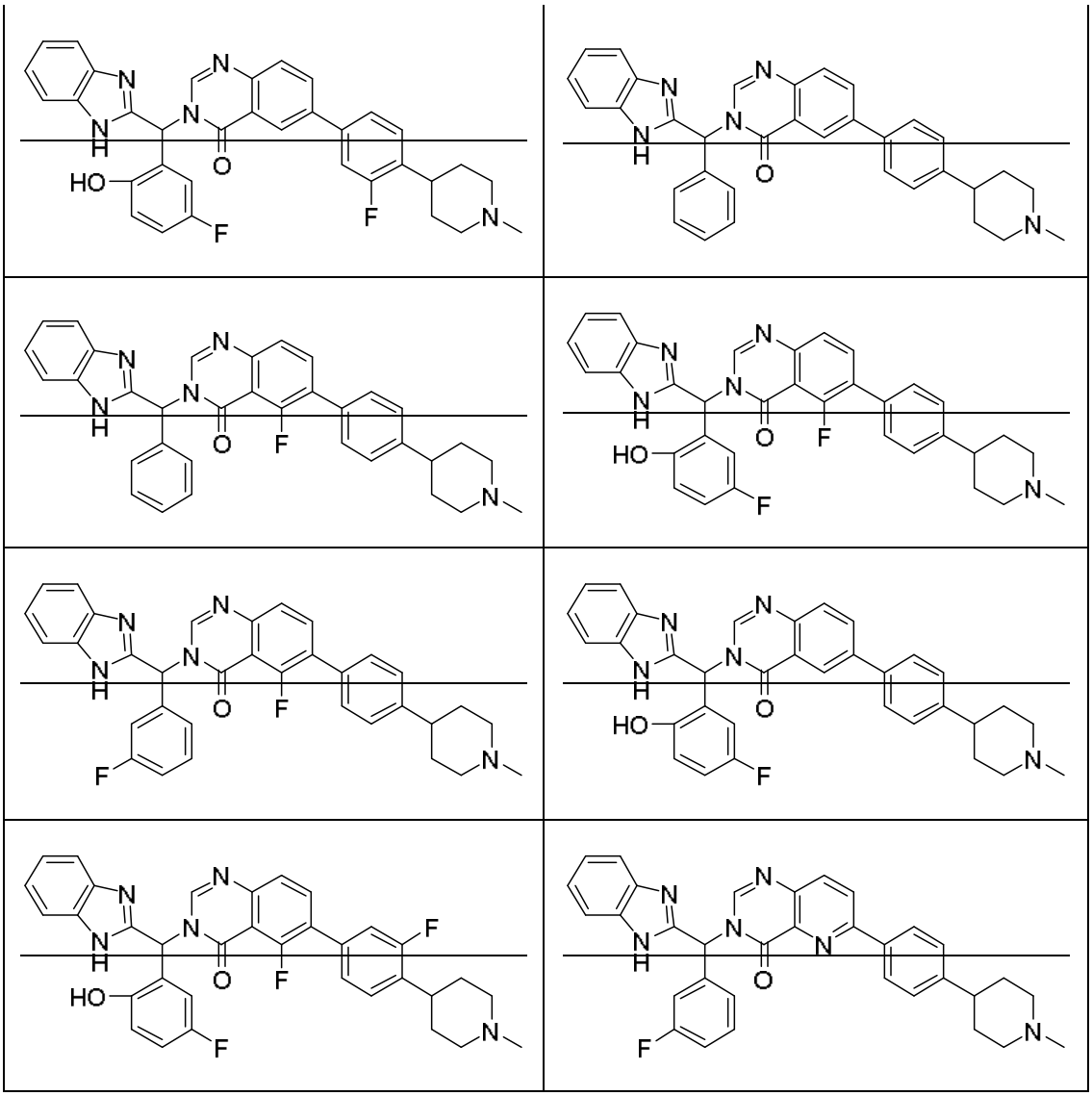
~~10~~6. The compound of any one of claims 1-~~8~~4, wherein R^1 is selected from the group consisting of:

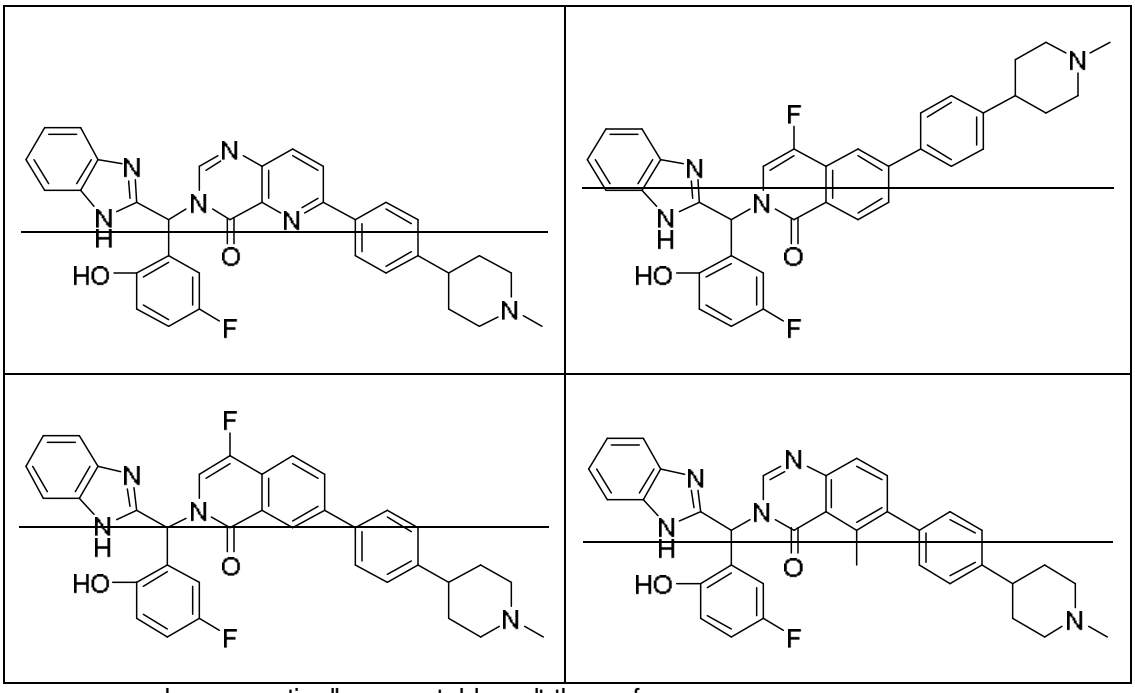


and ;

all of which are optionally substituted with one, two, or three R^8.

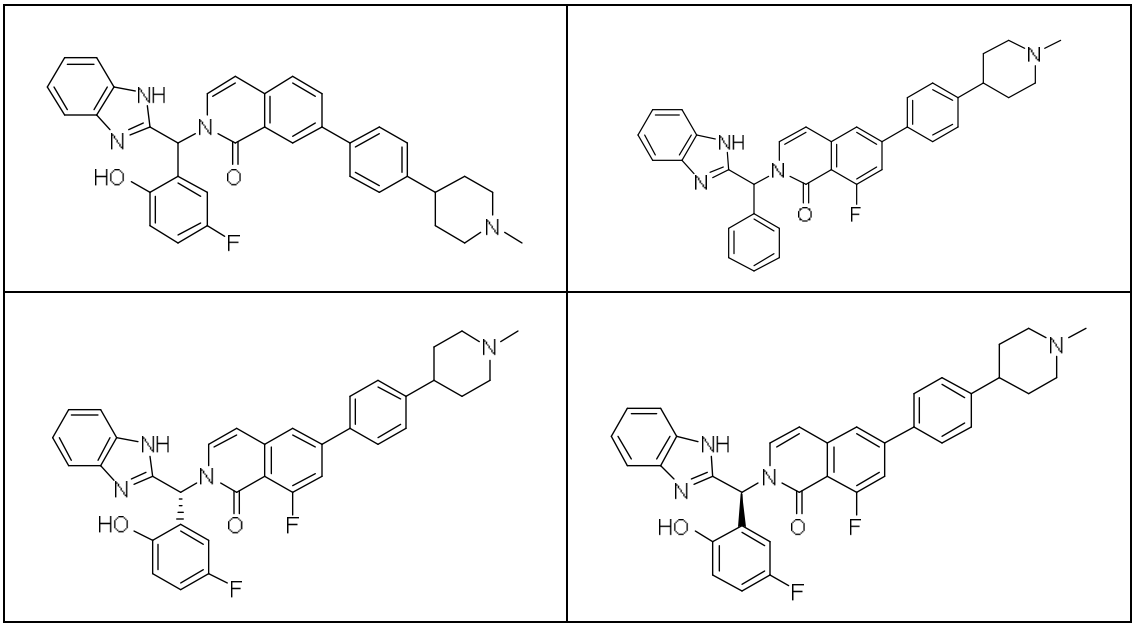
~~11. The compound of claim 1, wherein the compound of Formula I is selected from the group consisting of:~~

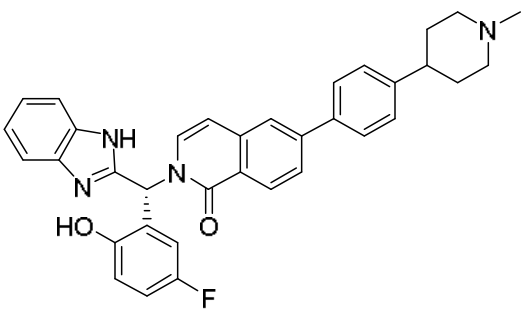
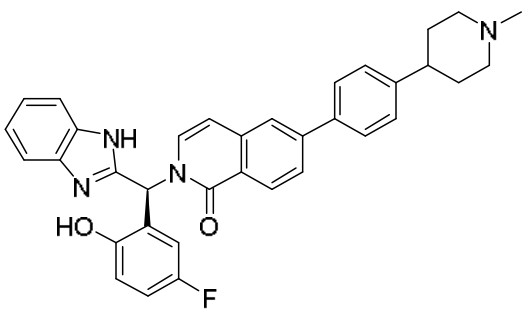
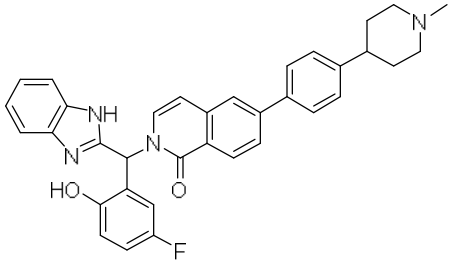
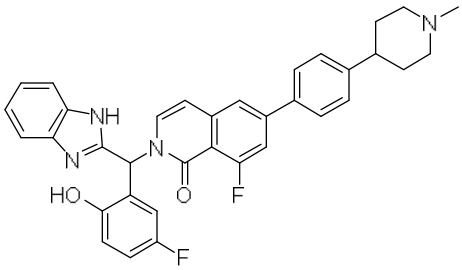
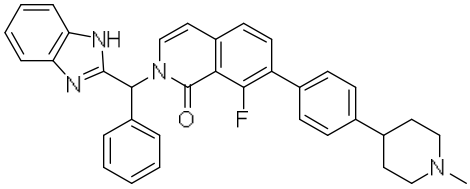
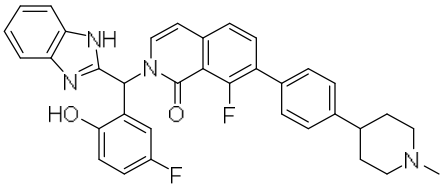
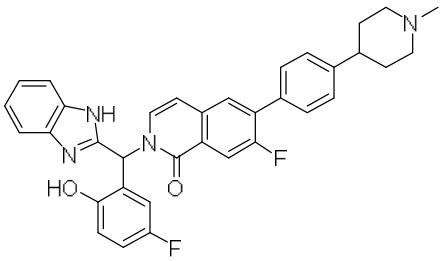
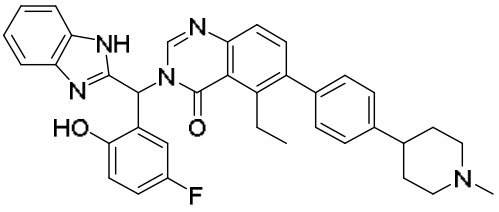
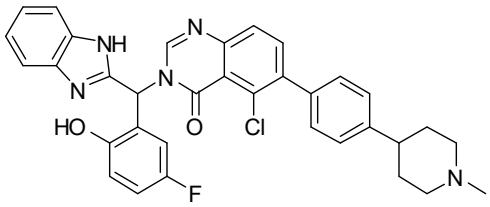
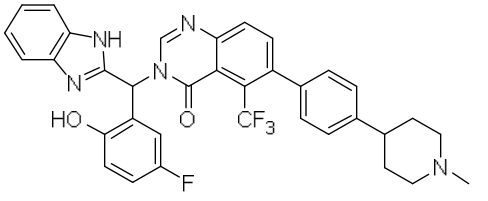


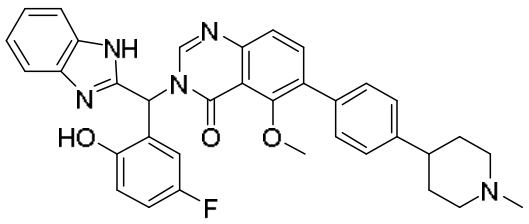
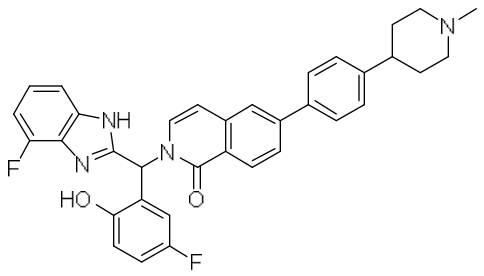
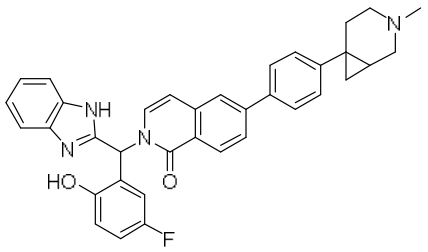
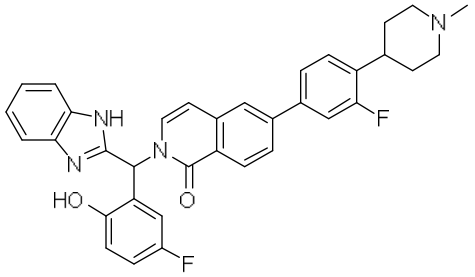
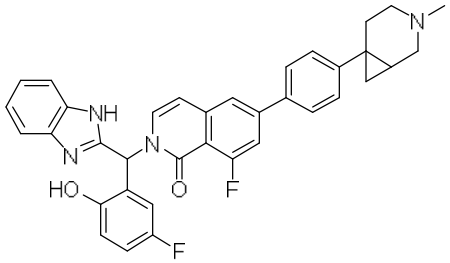
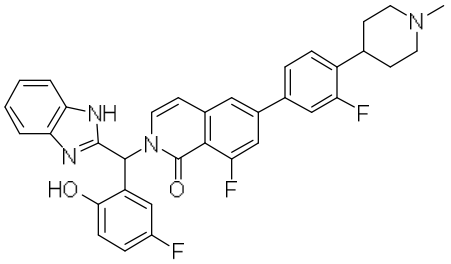
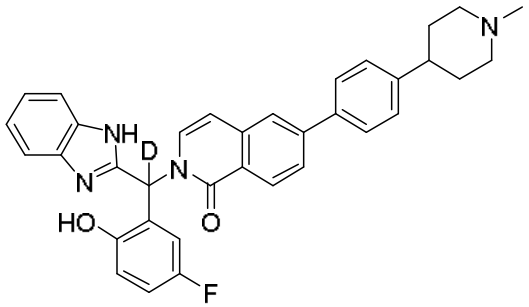
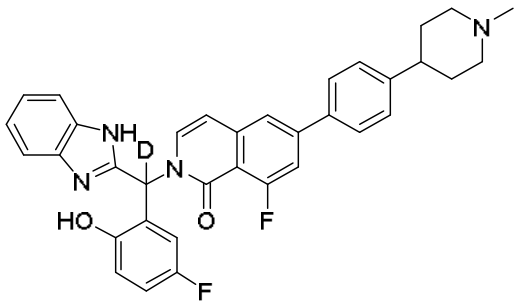
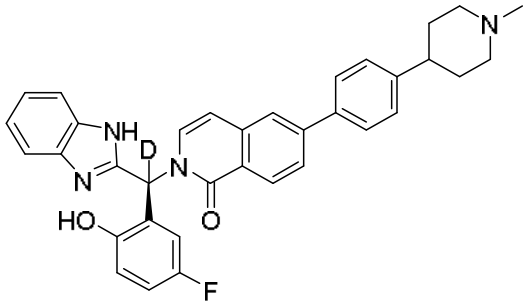
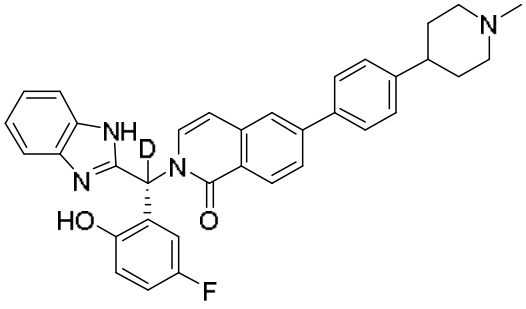


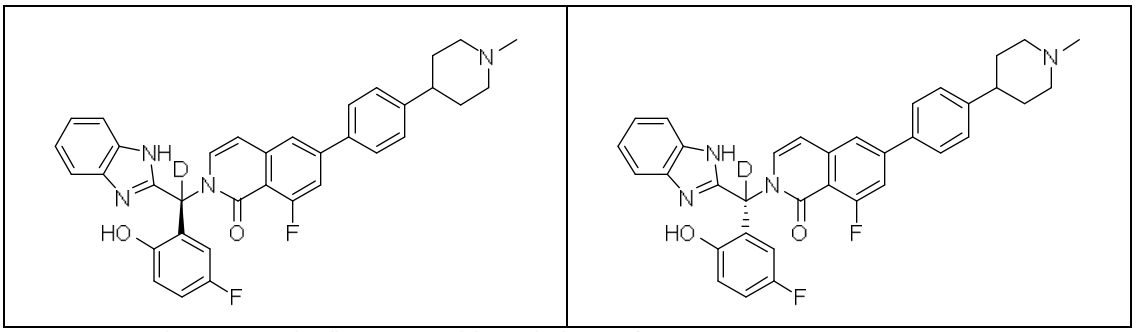
~~or a pharmaceutically acceptable salt thereof.~~

127. The compound of claim 1, wherein the compound of Formula I is selected from the group consisting of



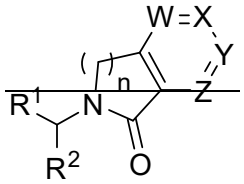
	
	
	
	
	



or a pharmaceutically acceptable salt thereof.

~~13. A compound of Formula II:~~



~~(II)~~

or a pharmaceutically acceptable salt thereof;

~~wherein~~

~~W and Z are each, independently, N, CH, C-halo, C-(C_1-C_3 alkyl), or C-(C_1-C_3 alkoxy);~~

~~X and Y are each, independently, N, CH, or CR^3;~~

~~provided that at least one of W, X, Y, or Z is CH;~~

~~R^1 is selected from the group consisting of 6-10 membered aryl, 5-10 membered heteroaryl, 3-10 membered heterocycloalkyl, and 3-10 membered cycloalkyl, all of which are~~ optionally substituted with one, two, or three R^8;

~~R^2 is selected from the group consisting of 6-10 membered aryl, 5-10 membered heteroaryl, 3-10 membered heterocycloalkyl, and 3-10 membered cycloalkyl, all of which are optionally substituted with one, two, or three R^6;~~

~~R^3 is independently, at each occurrence, selected from the group consisting of halogen, OR^4, NR^4R^4, SO_2R^4, SO_2NHR^4, $NHSO_2R^4$, $C(O)OR^4$, $C(O)NHR^4$, $C(O)R^4$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, 3-7 membered cycloalkyl, C_4-C_7 cycloalkenyl, C_6-C_{10} aryl, 5-6 membered heteroaryl, and 5-7 membered heterocyclyl, wherein alkyl, alkenyl, or alkynyl~~ are each optionally substituted one, two, or three times with R^4, and wherein aryl, heteroaryl, ~~or heterocyclyl are each optionally substituted one, two, or three times with R^5;~~

~~R^4 is independently, at each occurrence, selected from the group consisting of H, $(CH_2)_{0-3}$-(C_3-C_7 cycloalkyl), $(CH_2)_{0-3}$-(C_4-C_7 cycloalkenyl), $(CH_2)_{0-3}$-(C_6-C_{10} aryl), $(CH_2)_{0-3}$-(5-6 membered heteroaryl), and $(CH_2)_{0-3}$-(5-7 membered heterocyclyl), wherein the aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^5;~~

~~R^5 is independently, at each occurrence, selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_1-C_3 alkylamine, 3-10 membered cycloalkyl, halogen, COOH, C(O)O(C_1-C_6 alkyl), O$(CH_2)_{1-3}$-OH, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)$_2$, OH, CN, $(CH_2)_{0-3}$-(C_6-C_{10} aryl), $(CH_2)_{0-3}$-(5-6 membered heteroaryl), O$(CH_2)_{0-3}$-(4-7 membered heterocyclyl), and $(CH_2)_{0-3}$-(4-7 membered heterocyclyl), wherein the alkyl, alkoxy, aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^7;~~

~~R^6 is independently, at each occurrence, selected from the group consisting of C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_1-C_3 alkylamine, halogen, OH, NO_2, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)$_2$, $(CH_2)_{1-4}$OH, $S(O)_{0-2}$H, $S(O)_{0-2}NH_2$, or CN;~~

alternatively, two R^6, together with the atoms to which they are attached, can form 5-~~10 membered heteroaryl, 6-10 membered aryl, 3-10 membered heterocycloalkyl, or 3-10 membered cycloalkyl;~~

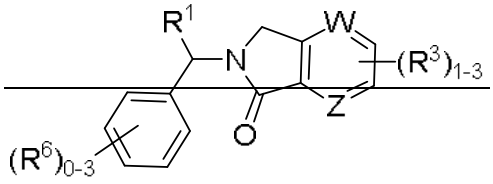
~~R^7 is independently, at each occurrence, selected from the group consisting of substituents independently selected from C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, halogen, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)$_2$, SO_2NH_2, SO_2NH(C_1-C_6 alkyl), SO_2N(C_1-C_6 alkyl)$_2$, $(CH_2)_{1-2}$-OH, C(O)$(CH_2)_{1-2}$-OH, C(O)(C_1-C_6 alkyl), and C(O)O(C_1-C_6 alkyl);~~

alternatively, two R^7, together with the atoms to which they are attached, can form 5-~~10 membered heteroaryl, 6-10 membered aryl, 3-10 membered heterocycloalkyl, or 3-10 membered cycloalkyl;~~

~~R^8 is independently, at each occurrence, selected from the group consisting of C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_1-C_3 alkylamine, 3-6 membered cycloalkyl, halogen, OH, NO_2, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)$_2$, $(CH_2)_{1-4}$OH, $S(O)_{0-2}$H, $S(O)_{0-2}NH_2$, or CN; and~~

~~n is 1 or 2.~~

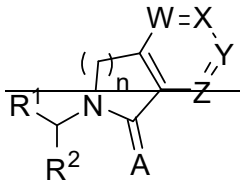
~~14. The compound of claim 13, wherein the compound of Formula II is a compound of Formula IIa:~~



~~(**IIa**)~~

~~or a pharmaceutically acceptable salt thereof.~~

15. A compound of Formula X:



(X)

or a pharmaceutically acceptable salt thereof;

wherein

A is O or S;

W and Z are each, independently, N, CH, C-halo, C-(C_1-C_3-alkyl), or C-(C_1-C_3 alkoxy);

X and Y are each, independently, N, CH, or CR^3;

provided that at least one of W, X, Y, or Z is CH;

R^1 is selected from the group consisting of 6-10 membered aryl, 5-10 membered heteroaryl, 3-10 membered heterocycloalkyl, and 3-10 membered cycloalkyl, all of which are optionally substituted with one, two, or three R^8;

R^2 is selected from the group consisting of 6-10 membered aryl, 5-10 membered heteroaryl, 3-10 membered heterocycloalkyl, and 3-10 membered cycloalkyl, all of which are optionally substituted with one, two, or three R^6;

R^3 is independently, at each occurrence, selected from the group consisting of halogen, OR^4, NR^4R^4, SO_2R^4, SO_2NHR^4, $NHSO_2R^4$, $C(O)OR^4$, $C(O)NHR^4$, $C(O)R^4$, C_1-C_6 alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, 3-7 membered cycloalkyl, C_4-C_7-cycloalkenyl, C_6-C_{10}-aryl, 5-6 membered heteroaryl, and 5-7 membered heterocyclyl, wherein alkyl, alkenyl, or alkynyl are each optionally substituted one, two, or three times with R^4, and wherein aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^5;

R^4 is independently, at each occurrence, selected from the group consisting of H, $(CH_2)_{0-3}$-(C_3-C_7-cycloalkyl), $(CH_2)_{0-3}$-(C_4-C_7-cycloalkenyl), $(CH_2)_{0-3}$-(C_6-C_{10}-aryl), $(CH_2)_{0-3}$-(5-6 membered heteroaryl), and $(CH_2)_{0-3}$-(5-7 membered heterocyclyl), wherein the aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^5;

R^5 is independently, at each occurrence, selected from the group consisting of C_1-C_6 alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_1-C_3-alkylamine, 3-10 membered cycloalkyl, halogen, COOH, C(O)O(C_1-C_6-alkyl), $O(CH_2)_{1-3}$-OH, NH_2, NH(C_1-C_6-alkyl), N(C_1-C_6-alkyl)$_2$, OH, CN, $(CH_2)_{0-3}$-(C_6-C_{10}-aryl), $(CH_2)_{0-3}$-(5-6 membered heteroaryl), $O(CH_2)_{0-3}$-(4-7 membered heterocyclyl), and $(CH_2)_{0-3}$-(4-7 membered heterocyclyl), wherein the alkyl, alkoxy, aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^7;

R^6 is independently, at each occurrence, selected from the group consisting of C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_1-C_3 alkylamine, halogen, OH, NO_2, NH_2, $NH(C_1$-C_6 alkyl), $N(C_1$-C_6 alkyl)$_2$, $(CH_2)_{1-4}OH$, $S(O)_{0-2}H$, $S(O)_{0-2}NH_2$, or CN;

alternatively, two R^6, together with the atoms to which they are attached, can form 5-10 membered heteroaryl, 6-10 membered aryl, 3-10 membered heterocycloalkyl, or 3-10 membered cycloalkyl;

R^7 is independently, at each occurrence, selected from the group consisting of substituents independently selected from C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, halogen, NH_2, $NH(C_1$-C_6 alkyl), $N(C_1$-C_6 alkyl)$_2$, SO_2NH_2, $SO_2NH(C_1$-C_6 alkyl), $SO_2N(C_1$-C_6 alkyl)$_2$, $(CH_2)_{1-2}$-OH, $C(O)(CH_2)_{1-2}$-OH, $C(O)(C_1$-C_6 alkyl), and $C(O)O(C_1$-C_6 alkyl);

alternatively, two R^7, together with the atoms to which they are attached, can form 5-10 membered heteroaryl, 6-10 membered aryl, 3-10 membered heterocycloalkyl, or 3-10 membered cycloalkyl;

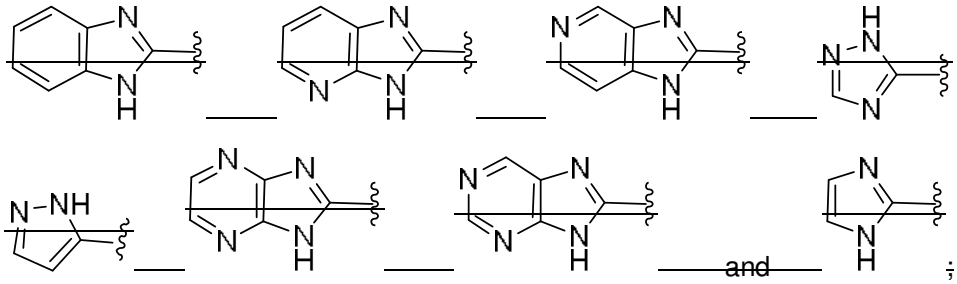
R^8 is independently, at each occurrence, selected from the group consisting of C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_1-C_3 alkylamine, 3-6 membered cycloalkyl, halogen, OH, NO_2, NH_2, $NH(C_1$-C_6 alkyl), $N(C_1$-C_6 alkyl)$_2$, $(CH_2)_{1-4}OH$, $S(O)_{0-2}H$, $S(O)_{0-2}NH_2$, or CN; and

n is 1 or 2.

16. The compound of any one of claims 13-15, wherein R^6 is independently, at each occurrence, hydroxy or halo.

17. The compound of any one of claims 13-16, wherein R^1 is selected from the group consisting of benzimidazole, imidazopyrazine, purine, imidazole, pyrazole, triazole, and imidazopyridine.

18. The compound of any one of claims 13-16, wherein R^1 is selected from the group consisting of:



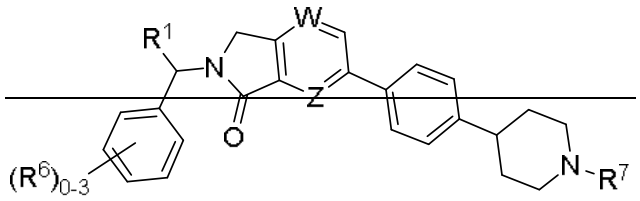
and ;

all of which are optionally substituted with one, two, or three R^8.

~~19. The compound of any one of claims 13-18, wherein R^3 is phenyl or C_2-C_3 alkynyl, wherein phenyl is optionally substituted one or two times with R^5, and alkynyl is optionally substituted one or two times with R^4.~~

~~20. The compound of any of claims 13-19, wherein R^3 is phenyl substituted with one or two R^5, and R^5 is selected from the group consisting of piperidine, pyridine, and thiomorpholine dioxide, all of which are optionally substituted with one or two R^7.~~

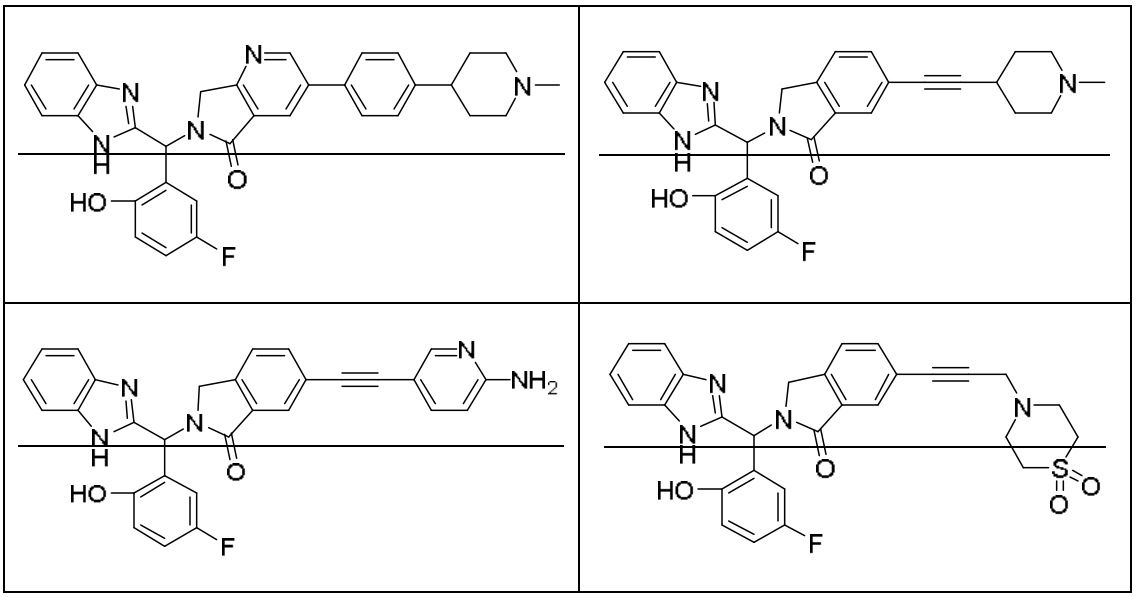
~~21. The compound of any one of claims 13-18, wherein the compound of Formula II is a~~ compound of Formula IIb:

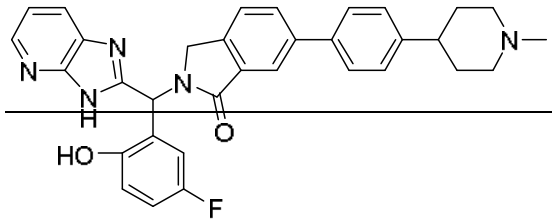
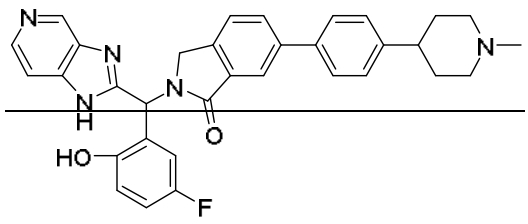
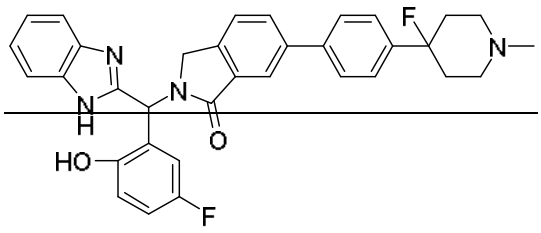
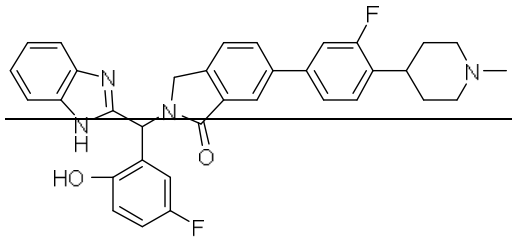
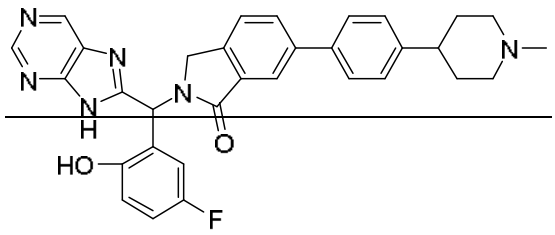
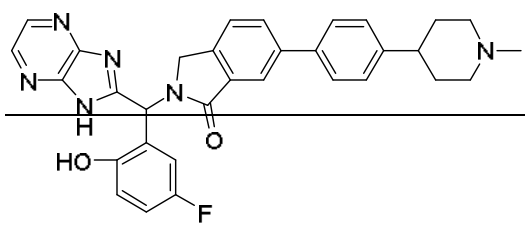
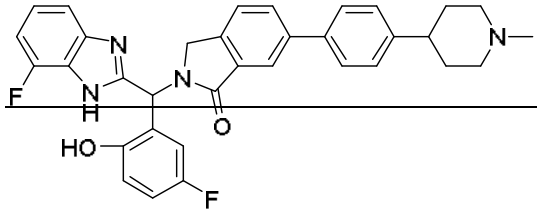
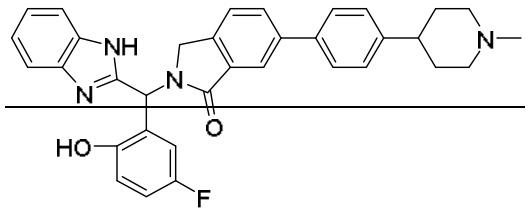
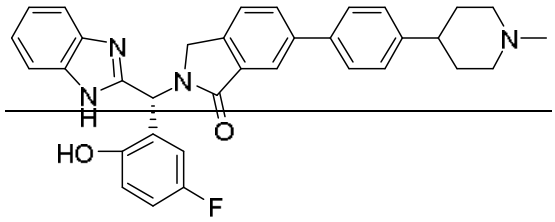
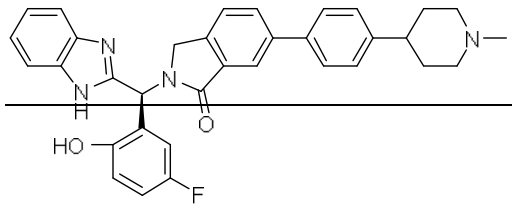
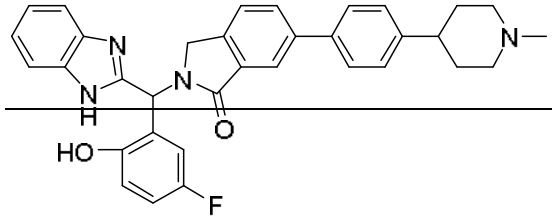
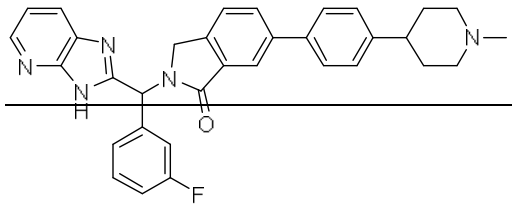


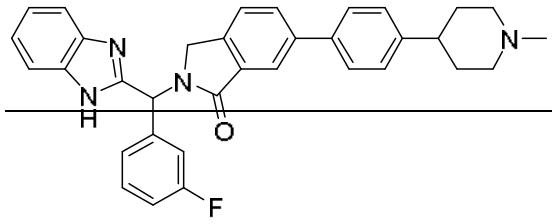
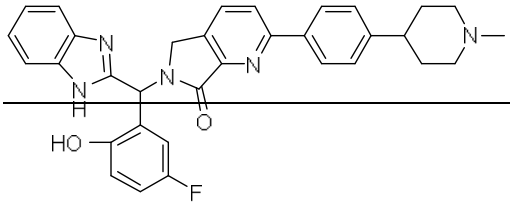
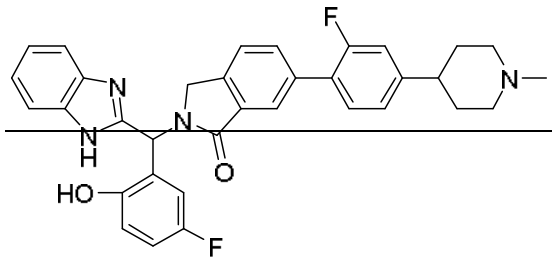
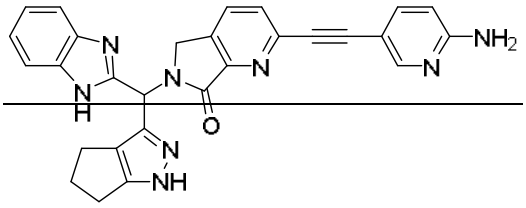
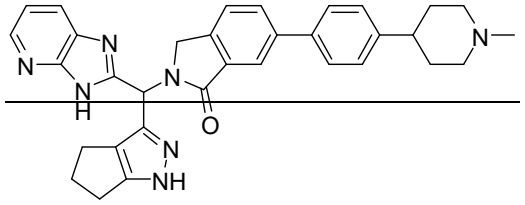
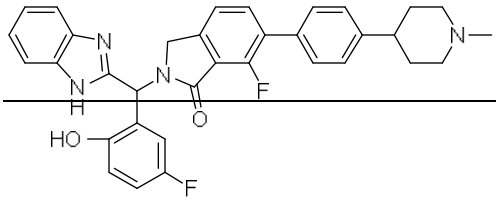
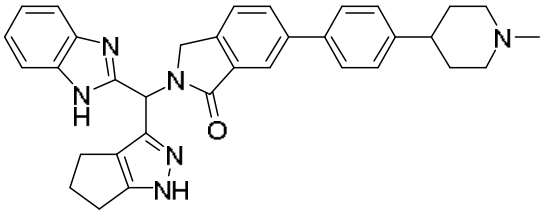
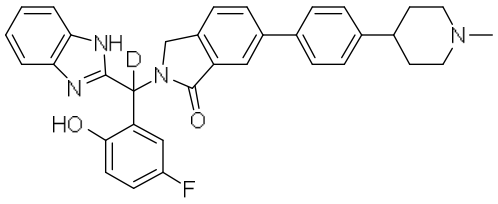
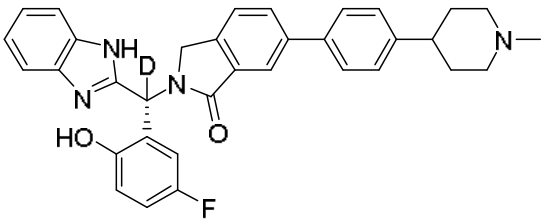
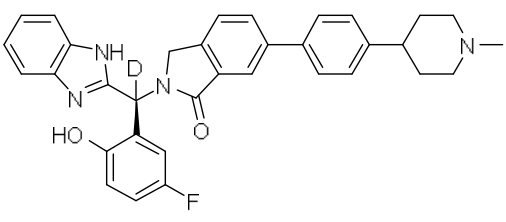
~~(IIb)~~

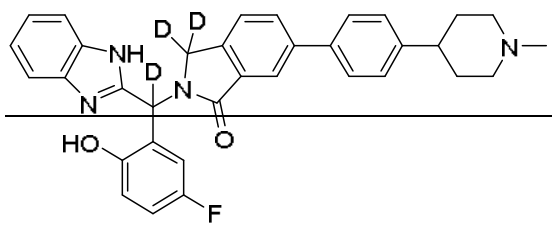
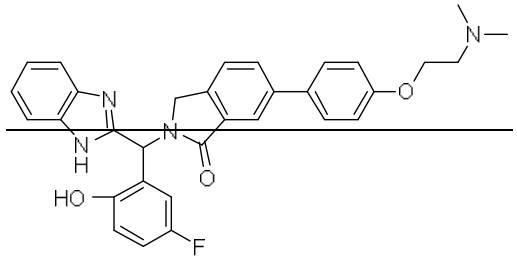
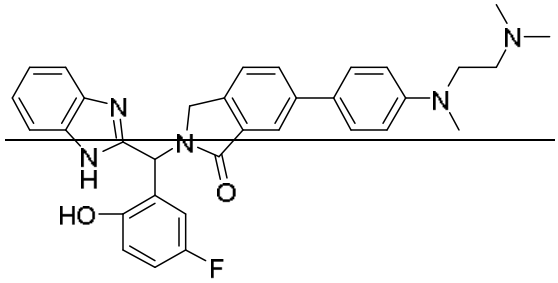
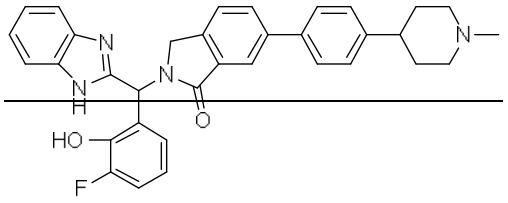
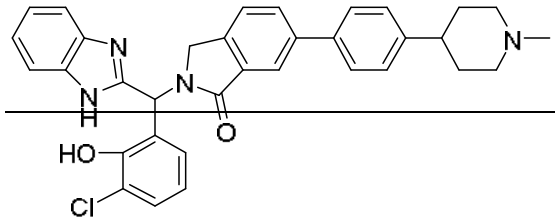
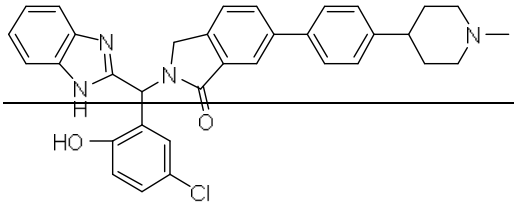
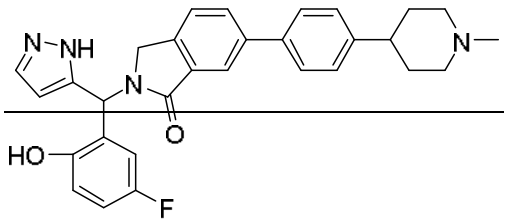
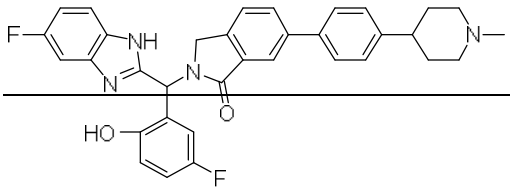
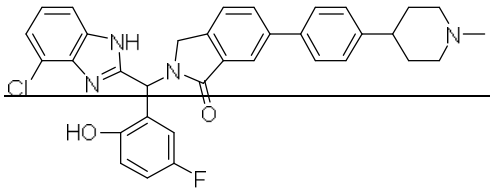
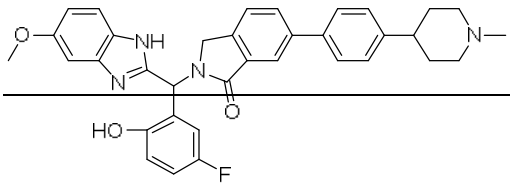
~~or a pharmaceutically acceptable salt thereof.~~

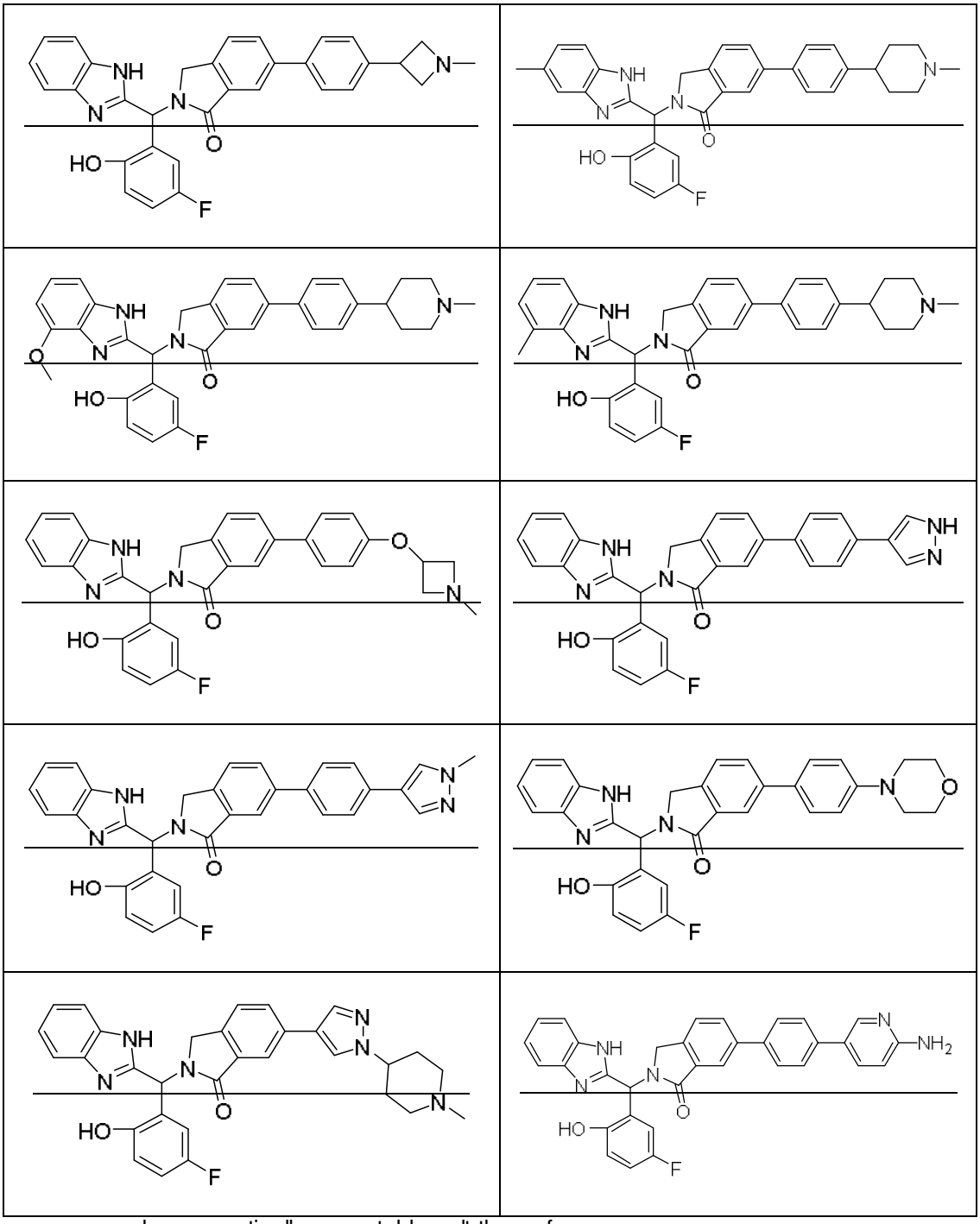
~~22. The compound of claim 13, wherein the compound of Formula II is selected from the group consisting of:~~



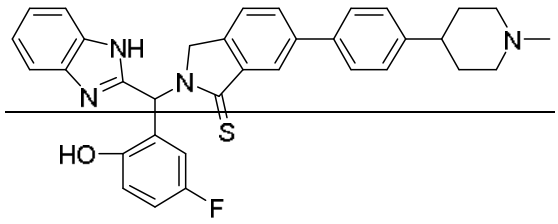
	
	
	
	
	

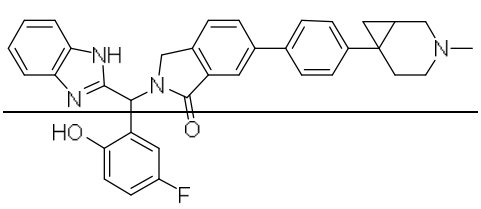
	
	
	
	
	

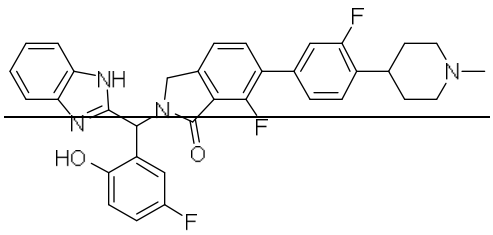


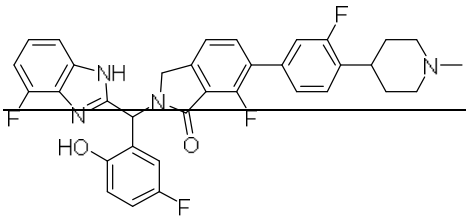
~~or a pharmaceutically acceptable salt thereof.~~

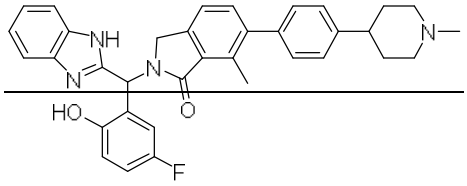
~~23. The compound of claim 15, wherein the compound of Formula X is selected from the group consisting of~~

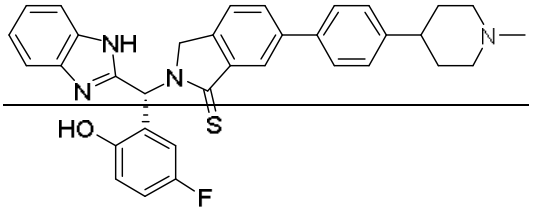


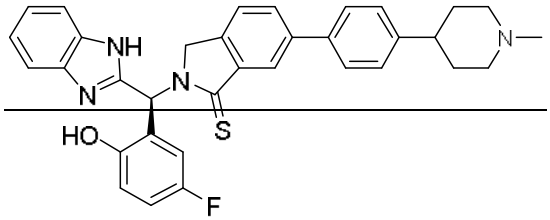


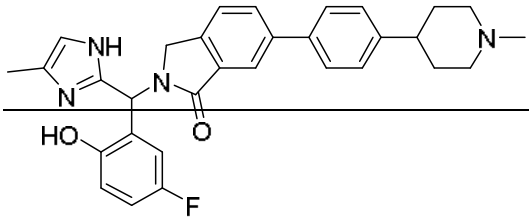


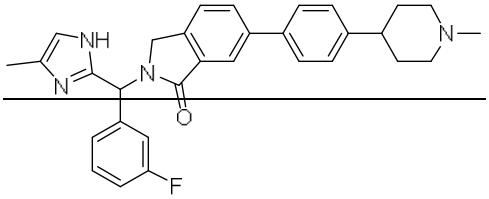


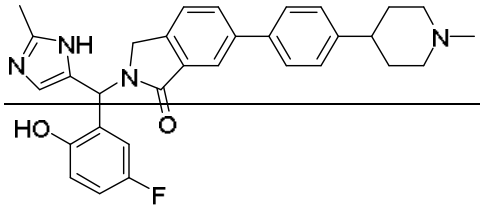
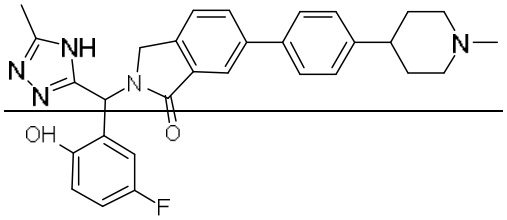
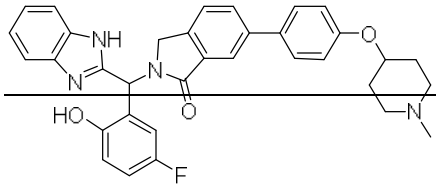
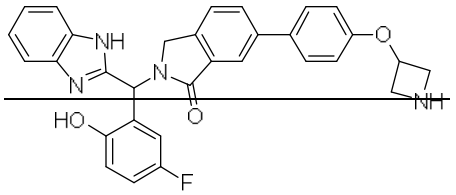
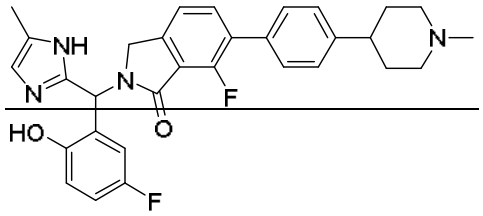
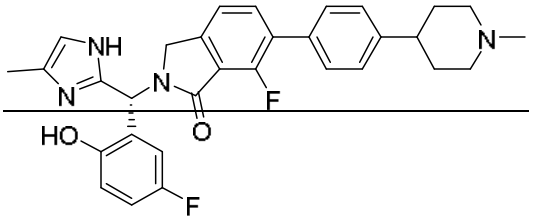
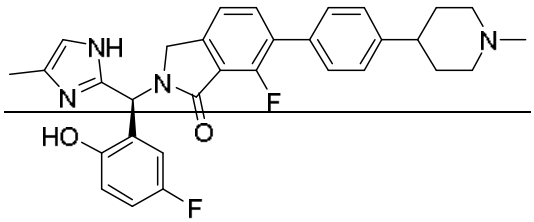
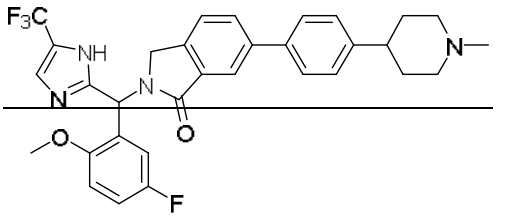
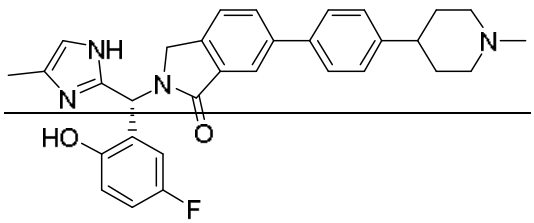
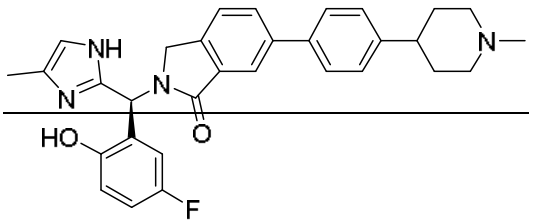


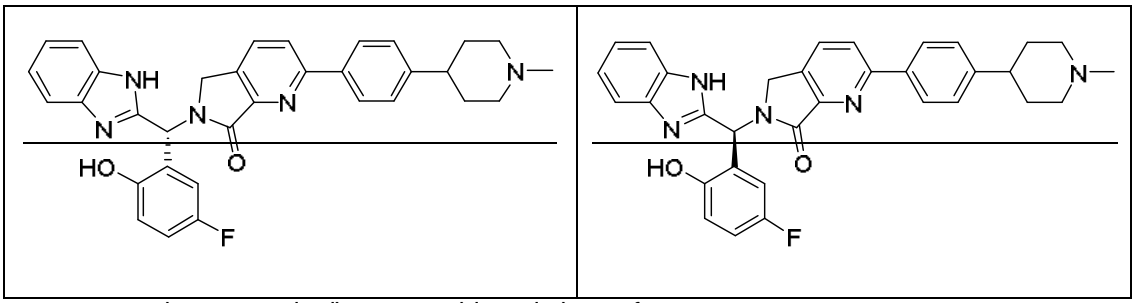






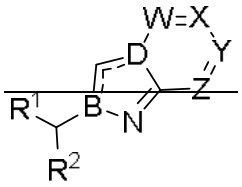




or a pharmaceutically acceptable salt thereof.

~~24. A compound of Formula III:~~



~~(III)~~

~~or a pharmaceutically acceptable salt thereof;~~

~~wherein~~

~~==== is a single or double bond;~~

~~B and D are each, independently, C or N;~~

~~W and Z are each, independently, N, CH, C-halo, C-(C_1-C_3 alkyl), or C-(C_1-C_3 alkoxy);~~

~~X and Y are each, independently, N, CH, or CR^3;~~

~~provided that at least one of W, X, Y, or Z is CH;~~

~~R^1 is selected from the group consisting of 6-10 membered aryl, 5-10 membered heteroaryl, 3-10 membered heterocycloalkyl, and 3-10 membered cycloalkyl, all of which are optionally substituted with one, two, or three R^8;~~

~~R^2 is selected from the group consisting of 6-10 membered aryl, 5-10 membered heteroaryl, 3-10 membered heterocycloalkyl, and 3-10 membered cycloalkyl, all of which are optionally substituted with one, two, or three R^6;~~

~~R^3 is independently, at each occurrence, selected from the group consisting of halogen, OR^4, NR^4R^4, SO_2R^4, SO_2NHR^4, $NHSO_2R^4$, $C(O)OR^4$, $C(O)NHR^4$, $C(O)R^4$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, 3-7 membered cycloalkyl, C_4-C_7 cycloalkenyl, C_6-C_{10} aryl,~~ 5-6 membered heteroaryl, and 5-7 membered heterocyclyl, wherein alkyl, alkenyl, or alkynyl ~~are each optionally substituted one, two, or three times with R^4, and wherein aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^5;~~

~~R^4 is independently, at each occurrence, selected from the group consisting of H,~~

~~$(CH_2)_{0-3}$-(C_3-C_7 cycloalkyl), $(CH_2)_{0-3}$-(C_4-C_7 cycloalkenyl), $(CH_2)_{0-3}$-(C_6-C_{10} aryl), $(CH_2)_{0-3}$-(5-6 membered heteroaryl), and $(CH_2)_{0-3}$-(5-7 membered heterocyclyl), wherein the aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^5;~~

~~R^5 is independently, at each occurrence, selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6-alkoxy, C_1-C_6 haloalkoxy, C_1-C_3 alkylamine, 3-10 membered cycloalkyl, halogen, COOH, C(O)O(C_1-C_6 alkyl), O$(CH_2)_{1-3}$-OH, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)$_2$, OH, CN, $(CH_2)_{0-3}$-(C_6-C_{10} aryl), $(CH_2)_{0-3}$-(5-6 membered heteroaryl), and $(CH_2)_{0-3}$-(5-7 membered heterocyclyl), wherein the aryl, heteroaryl, or heterocyclyl are each optionally substituted one, two, or three times with R^7;~~

~~R^6 is independently, at each occurrence, selected from the group consisting of C_1-C_3~~ alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_1-C_3 alkylamine, halogen, OH, NO_2, ~~NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)$_2$, $(CH_2)_{1-4}$OH, S$(O)_{0-2}$H, S$(O)_{0-2}NH_2$, or CN;~~

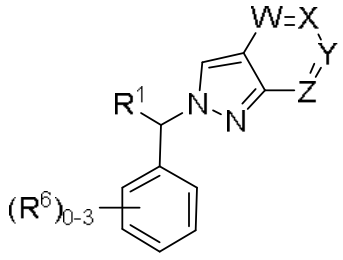
~~alternatively, two R^6, together with the atoms to which they are attached, can form 5-10 membered heteroaryl, 6-10 membered aryl, 3-10 membered heterocycloalkyl, or 3-10 membered cycloalkyl;~~

~~R^7 is independently, at each occurrence, selected from the group consisting of substituents independently selected from C_1-C_6 alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6 haloalkoxy, halogen, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)$_2$, SO_2NH_2, SO_2NH(C_1-C_6 alkyl),~~ SO_2N(C_1-C_6 alkyl)$_2$, $(CH_2)_{1-2}$-OH, C(O)$(CH_2)_{1-2}$-OH, C(O)(C_1-C_6 alkyl), and C(O)O(C_1-C_6 ~~alkyl);~~

~~alternatively, two R^7, together with the atoms to which they are attached, can form 5-10 membered heteroaryl, 6-10 membered aryl, 3-10 membered heterocycloalkyl, or 3-10 membered cycloalkyl; and~~

~~R^8 is independently, at each occurrence, selected from the group consisting of C_1-C_3 alkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_1-C_3 alkylamine, 3-6 membered cycloalkyl, halogen, OH, NO_2, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)$_2$, $(CH_2)_{1-4}$OH, S$(O)_{0-2}$H,~~ S$(O)_{0-2}NH_2$, or CN.

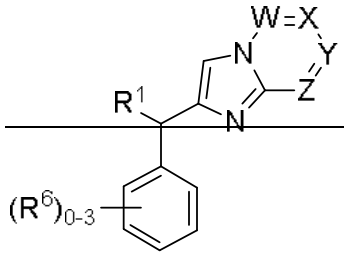
~~25. The compound of claim 24, wherein the compound of Formula III is a compound of Formula IIIa:~~



(~~**IIIa**~~)

~~or a pharmaceutically acceptable salt thereof.~~

~~26. The compound of claim 24, wherein the compound of Formula III is a compound of Formula IIIb:~~

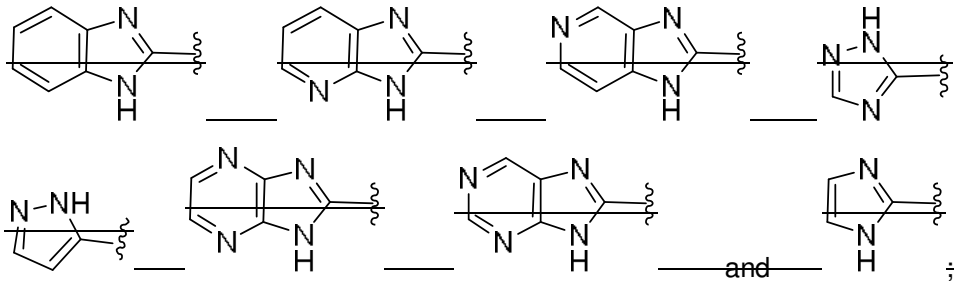


(**IIIb**)

~~or a pharmaceutically acceptable salt thereof.~~

~~27. The compound of any one of claims 24-26, wherein R^1 is selected from the group consisting of benzimidazole, imidazopyrazine, purine, imidazole, pyrazole, triazole, and imidazopyridine.~~

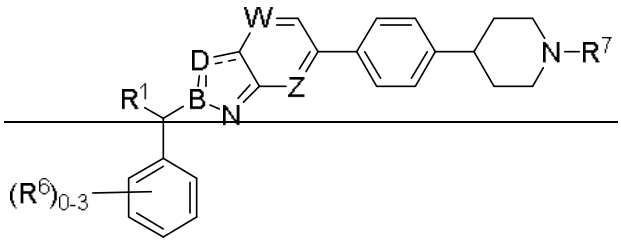
~~28. The compound of any one of claims 24-26, wherein R^1 is selected from the group consisting of:~~



~~all of which are optionally substituted with one, two, or three R^8.~~

~~29. The compound of any of claims 24-28, wherein Y is CR^3, and R^3 is 6-10 membered aryl substituted with one or two R^5.~~

~~30. The compound of claim 24, wherein the compound of Formula III is a compound of Formula IIIc:~~



~~(IIIc)~~

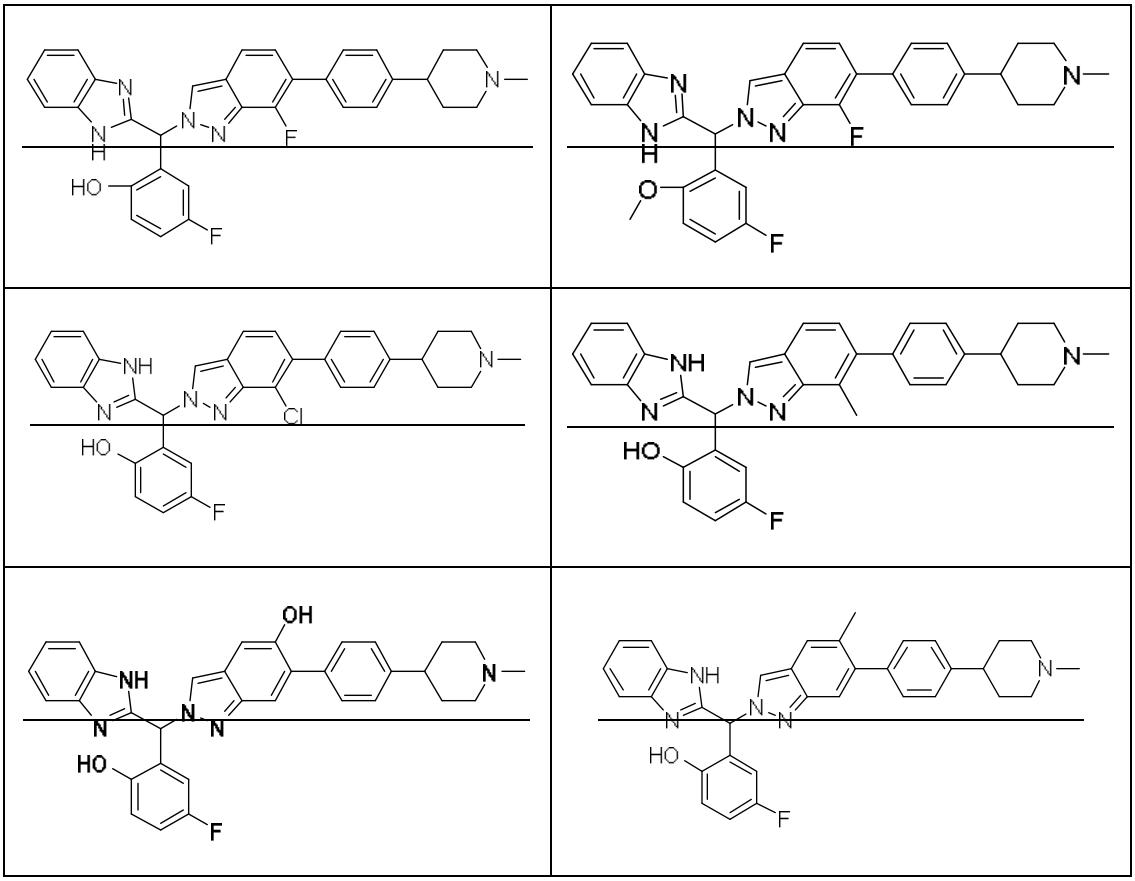
~~or a pharmaceutically acceptable salt thereof.~~

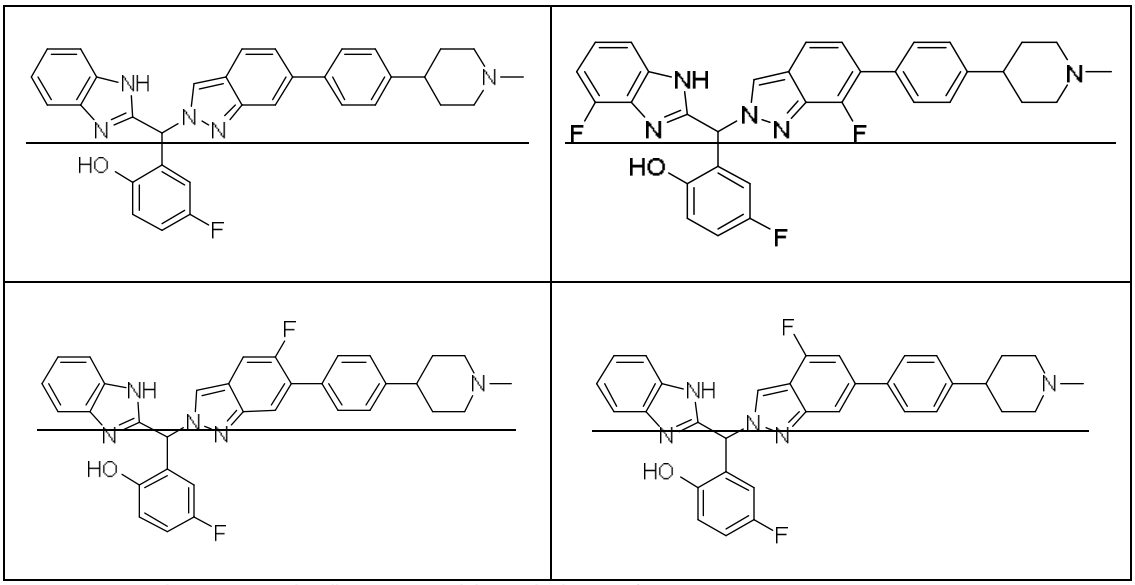
~~31. The compound of any of claims 24-30, wherein Z is CF.~~

32. The compound of any of claims 24-30, wherein Z is CH.

~~33. The compound of any of claims 24-30, wherein Z is N.~~

~~34. The compound of claim 24, wherein the compound of Formula III is selected from the group consisting of:~~





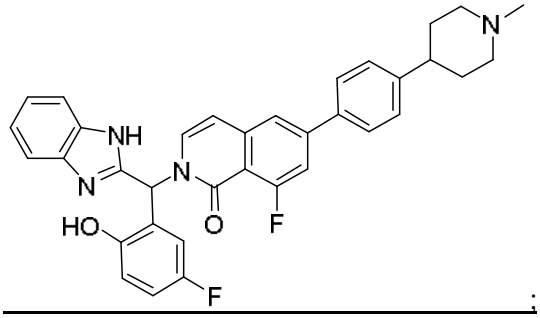
~~or a pharmaceutically acceptable salt thereof.~~

~~358~~. The compound of any one of claims 1-~~106~~, ~~13-21, and 24-33,~~ wherein R^7 is C_1-C_3 alkyl.

9. The compound of any one of claims 1-6, and 8, wherein W is CH.

10. The compound of any one of claims 1-6, 8, and 9, wherein R^3 is phenyl substituted one time with piperidine, wherein piperidine is substituted one time with R^7.

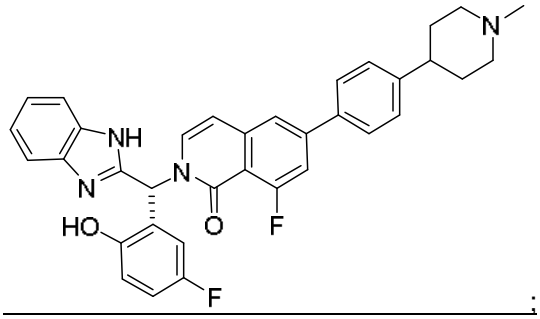
11. The compound of any one of claims 1-6, and 8-10, wherein the compound of Formula I is



;

or a pharmaceutically acceptable salt thereof.

12. The compound of claim 11, wherein the compound of Formula I is



;

or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition comprising a compound of any one the preceding claims, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

14. Use of a compound or pharmaceutical composition of any one of the preceding claims in the manufacture of a medicament for the treatment of cancer.

15. The use according to claim 14, wherein the cancer is selected from the group consisting of lung cancer, colon cancer, breast cancer, endometrial cancer, thyroid cancer, glioma, squamous cell carcinoma, and prostate cancer.

16. The use according to claim 14, wherein the cancer is non-small cell lung cancer (NSCLC).

17. The use according to any one of claims 14-16, wherein the medicament further comprises osimertinib.

18. The use according to any one of claims 14-16, wherein the medicament is for co-administration with a therapeutically effective amount of osimertinib.