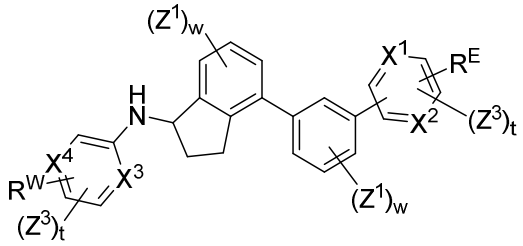
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A compound of formula (I):



(I)

or a pharmaceutically acceptable salt, stereoisomer, mixture of stereoisomers, solvate, or tautomer thereof, wherein:

each of X^1, X^2, X^3 and X^4 are independently N, CH or CZ^3;

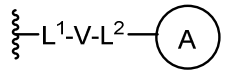
each Z^1 is independently is halo, $-OR^a$, $-NO_2$, cyano, $-NR^aR^b$, $-N_3$, $-S(O)_2R^a$, $-C_{1-6}$ alkyl, $-C_{1-6}$ haloalkyl, $-C_{2-6}$alkenyl, $-C_{2-6}$ alkynyl, $-O-C_{1-6}$ alkyl, $-O-C_{1-6}$ haloalkyl, $-C_{3-8}$ cycloalkyl, or $-C_{1-6}$ alkylC_{3-8} cycloalkyl; and

wherein each alkyl, alkenyl, alkynyl, and cycloalkyl is optionally substituted with 1 to 4 groups independently selected from oxo, $-NO_2$, $-N_3$, $-OR^a$, halo, and cyano;

each w is independently 0, 1 or 2;

each Z^3 is independently halo, $-OR^a$, $-N_3$, $-NO_2$, cyano, $-NR^1R^2$, $-S(O)_2R^a$, $-S(O)_2NR^aR^b$, $-NR^aS(O)_2R^a$, $-NR^aC(O)R^a$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-NR^aC(O)OR^a$, $-NR^aC(O)NR^1R^2$, $-OC(O)NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2NR^aR^b$, $-C_{1-6}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{2-6}$ alkynyl, $-O-C_{1-6}$ alkyl, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ haloalkyl, $-O-C_{1-6}$ cyanoalkyl, $-O-C_{1-6}$ haloalkyl, $-C_{3-8}$ cycloalkyl, $-C_{1-6}$ alkylC_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, and R^N; and

wherein the alkyl, alkenyl, alkynyl, C_{3-8} cycloalkyl, aryl, heteroaryl, or heterocyclyl group is optionally substituted with 1 to 4 groups independently selected from oxo, $-NO_2$, $-N_3$, $-OR^a$, halo, cyano, $-NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-O-C_{1-6}$cyanoalkyl, $-C(O)NR^aR^b$, $-NR^aC(O)R^a$, $-NR^aC(O)OR^a$, $-S(O)_2R^a$, $-NR^aS(O)_2R^b$, $-SO_2NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2NR^aR^b$ and $-C_{3-8}$ cycloalkyl;

R^N is independently $-C_{1-6}$ alkylNR^1R^2, $-OC_{1-6}$ alkylNR^1R^2, $-C_{1-6}$ alkyl-$O-C_{1-6}$ alkylNR^1R^2, $-NR^aC_{1-6}$ alkylNR^1R^2, $-C_{1-6}$ alkyl$C(O)NR^1R^2$, $-O-C_{1-6}$ alkyl$C(O)NR^1R^2$, $-O-C_{1-6}$ alkyl$C(O)OR^1$, $-SC_{1-6}$ alkylNR^1R^2, $-C_{1-6}$ alkylOR^a, or ;

wherein:

L^1 is independently a bond, -O-, $-NR^a$-, -S-, -S(O)-, or $-S(O)_2$-;

V is independently selected from a bond, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

wherein each alkyl, alkenyl, or alkynyl is optionally independently substituted with $-OR^a$, halo, cyano, $-NR^aR^b$ or $-C_{3-8}$ cycloalkyl;

L^2 is independently a bond, -O-, $-NR^a-$, -S-, -S(O)-, or $-S(O)_2-$;

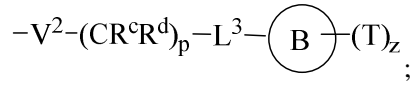
ring A is independently cycloalkyl, aryl, heteroaryl, or heterocyclyl;

wherein each cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from oxo, $-NO_2$, $-N_3$, $-OR^a$, halo, cyano, $-C_{1-6}$ alkyl, $-C_{1-6}$ haloalkyl, $-C_{2-6}$ alkenyl, $-C_{2-6}$ alkynyl, $-O-C_{1-6}$ haloalkyl, $-NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-O-C_{1-6}$ cyanoalkyl, $-C(O)NR^aR^b$, $-NR^aC(O)R^a$, $-NR^aC(O)OR^a$, $-NR^aC(O)OR^a$, $-C(O)N(R^a)OR^b$, $-S(O)_2R^a$, $-S(O)_2NR^aR^b$, $-NR^aS(O)_2R^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2NR^aR^b$, C_{3-8} cycloalkyl, and $-C_{1-6}$ alkylC_{3-8} cycloalkyl; and

wherein the alkyl, alkenyl, or alkynyl group is optionally independently substituted with $-OR^a$, halo, cyano, $-NR^aR^b$ or $-C_{3-8}$ cycloalkyl;

each t is independently 0, 1 or 2;

R^E and R^W are each independently $-NR^1R^2$, $-C_{1-6}$ alkylNR^1R^2, $-O-C_{1-6}$ alkylNR^1R^2, $-C_{1-6}$ alkyl-O-C_{1-6}alkylNR^1R^2, $-NR^a-C_{1-6}$ alkylNR^1R^2, $-C_{1-6}$ alkyl$N^+R^1R^2R^3$, -S-C_{1-6} alkylNR^1R^2, $-C(O)NR^1R^2$, $-S(O)_2R^a$, $-(CH_2)_uS(O)_2NR^1R^2$, $-(CH_2)_uNR^aS(O)_2NR^aR^b$, $-S(O)_2NR^aC_{1-6}$ alkylNR^1R^2, $-NR^aS(O)_2C_{1-6}$ alkylNR^1R^2, $-(CH_2)_uC(O)NR^aS(O)_2NR^aR^b$, $-(CH_2)_uN^+R^1R^2O^-$, $-(CH_2)_uP^+R^bR^cR^d$, $-(CH_2)_uP^+R^cR^dO^-$, $-(CH_2)_uP^+O[NR^aR^b][NR^cR^d]$, $-(CH_2)_uNR^cP(O)(OR^c)_2$, $-(CH_2)_uCH_2OP(O)(OR^c)(OR^d)$, $-(CH_2)_uOP(O)(OR^c)(OR^d)$, $-(CH_2)_uOP(O)NR^aR^b)(OR^a)$, or



;

wherein:

V^2 is independently a bond, -O-, $-NR^a-$, -S-, -SO-, $-SO_2-$, $-C(O)NR^a-$, $-NR^aC(O)-$, $-S(O)_2NR^1-$, or $-NR^aS(O)_2-$;

L^3 is independently a bond, -O-, $-NR^a-$, -S-, -SO-, $-SO_2-$, $-C(O)NR^a-$, $-NR^aC(O)-$, $-S(O)_2NR^1-$, or $-NR^aS(O)_2-$;

ring B is independently cycloalkyl, aryl, heteroaryl, or heterocyclyl;

T is independently hydrogen, $-OR^a$, $-(CH_2)_qNR^1R^2$, $-(CH_2)_qNR^aC(O)R^e$, or $-(CH_2)_qC(O)R^e$;

p is independently 0, 1, 2, 3, 4, or 5;

q is independently 0, 1, 2, 3, 4, or 5;

u is 0, 1, 2, 3, or 4;

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

wherein the alkyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl of R^E or R^W is optionally substituted with 1 to 3 substituents independently selected from the group consisting of $-NR^aR^b$, halo, cyano, oxo, $-OR^a$, $-C_{1-6}$ alkyl, $-C_{1-6}$ haloalkyl, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ alkylNR^aR^b, $-C_{1-6}$ hydroxyalkyl, $-C_{3-8}$ cycloalkyl, and $-C_{1-3}$ alkylC_{3-8}cycloalkyl;

provided that at least one of V^2, L^3, ring B and T contains a nitrogen atom;

each R^1 is independently selected from hydrogen, $-C_{1-8}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{2-6}$ alkynyl, $-C_{3-6}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, $-C_{1-6}$ alkylheterocyclyl, $-C_{1-6}$ alkyl$C(O)OR^a$, $-C_{2-6}$ alkenyl$C(O)OR^a$, $-S(O)_2R^a$, $-S(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2R^a$, and $-C_{1-6}$ alkylC_{3-8}cycloalkyl;

wherein each alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from $-OR^a$, cyano, halo, C_{1-6} alkyl, $-C_{1-6}$ alkylOR^a, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ haloalkyl, C_{3-8} cycloalkyl, $-C_{1-3}$ alkylC_{3-8}cycloalkyl, $-C(O)R^a$, $-C_{1-6}$ alkyl$C(O)R^a$, $-C(O)OR^a$, $-C_{1-6}$ alkyl$C(O)OR^a$, $-NR^aR^b$, $-OC(O)NR^aR^b$, $NR^aC(O)OR^b$, $-C_{1-6}$ alkylNR^aR^b, $-C(O)NR^aR^b$, $-C_{1-6}$ alkyl$C(O)NR^aR^b$, $-S(O)_2R^a$, $-C_{1-6}$ alkyl$S(O)_2R^a$, $-S(O)_2NR^aR^b$, $-C_{1-6}$ alkyl$S(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2R^b$, $-C_{1-6}$ alkyl$C(O)NR^aS(O)_2R^b$, $-NR^aC(O)R^b$, and $-C_{1-6}$alkyl$NR^aC(O)R^b$;

each R^2 is independently selected from hydrogen, $-C_{1-6}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{2-6}$ alkynyl, $-C_{3-6}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, $-C_{1-6}$ alkylheterocyclyl, $-C_{2-6}$ alkyl-OR^a, $-C_{1-6}$ alkyl$C(O)OR^a$, and $-C_{2-6}$ alkenyl$C(O)OR^a$;

wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from $-OR^a$, cyano, halo, C_{1-6}alkyl, $-C_{1-6}$ alkylOR^a, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ haloalkyl, $-C_{3-8}$ cycloalkyl, $-C_{1-3}$ alkylC_{3-8}cycloalkyl, $-C(O)R^a$, $-C_{1-6}$ alkyl$C(O)R^a$, $-C(O)OR^a$, $-C_{1-6}$ alkyl$C(O)OR^a$, $-NR^aR^b$, $-C_{1-6}$ alkylNR^aR^b, $-C(O)NR^aR^b$, C_{1-6} alkyl$C(O)NR^aR^b$, $-S(O)_2R^a$, $-C_{1-6}$ alkyl$S(O)_2R^a$, $-S(O)_2NR^aR^b$, $-C_{1-6}$ alkyl$S(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2R^{\mathbf{b}}$ and $-NR^aC(O)R^b$;

or R^1 and R^2 combine to form a heterocyclyl optionally substituted with 1 to 3 groups independently selected from oxo, $-C_{1-6}$ alkyl, $-C_{3-8}$ cycloalkyl, $-C_{2-6}$ alkenyl, $-C_{2-6}$ alkynyl, $-OR^a$, $-C(O)OR^a$, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ alkylOR^a, $-C_{1-6}$ haloalkyl, $-C_{1-3}$ alkylC_{3-8}cycloalkyl, $-C(O)R^a$, C_{1-6} alkyl$C(O)R^a$, $-C_{1-6}$ alkyl$C(O)OR^a$, $-NR^aR^b$, $-C_{1-6}$alkylNR^aR^b, $-C(O)NR^aR^b$, $-C_{1-6}$ alkyl$C(O)NR^aR^b$, $-S(O)_2R^a$, $-C_{1-6}$ alkyl$S(O)_2R^a$, $-S(O)_2NR^aR^b$, $-C(O)N{=}S(O)R^aNR^aR^b$, $-C(O)N{=}S(O)R^aNR^aC(O)R^b$, and $-C_{1-6}$ alkyl$S(O)_2NR^aR^b$;

each R^3 is independently hydrogen, $-C_{1-6}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{3-6}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, $-C_{1-6}$ alkylheterocyclyl, $-C_{2-6}$ alkyl-OR^a, $-C_{1-6}$ alkyl$C(O)OR^a$, or $-C_{2-6}$ alkenyl$C(O)OR^a$;

each R^a is independently selected from hydrogen, -C_{1-6} alkyl, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6}alkylheterocyclyl;

each R^b is independently selected from hydrogen, -C_{1-6} alkyl, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6} alkylheterocyclyl;

or R^a and R^b may combine together to form a heterocyclyl optionally substituted with 1 to 4 groups independently selected from -OR^f, cyano, halo, -C_{1-6} alkylOR^f, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, -C_{3-8} cycloalkyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -$C(O)R^f$, -C_{1-6} alkyl$C(O)R^f$, -$C(O)OR^f$, -C_{1-6} alkyl$C(O)OR^f$, -NR^fR^g, -C_{1-6} alkylNR^fR^g, -$C(O)NR^fR^g$, -C_{1-6} alkyl$C(O)NR^fR^g$, -$S(O)_2R^f$, -C_{1-6} alkyl$S(O)_2R^f$, -$S(O)_2NR^fR^g$, -C_{1-6} alkyl$S(O)_2NR^fR^g$, -$C(O)NR^fS(O)_2R^g$ and –$NR^fC(O)R^g$;

each R^c is independently selected from hydrogen, -OH, -C_{1-6} alkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8} cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6} alkylheterocyclyl;

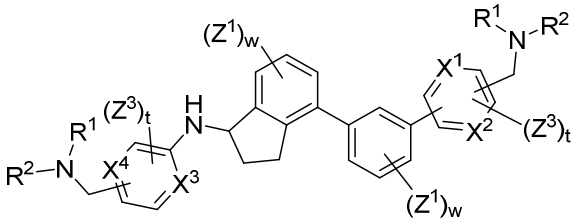
each R^d is independently selected from hydrogen, -C_{1-6} alkyl, -C_3-C_8cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6} alkylheterocyclyl;

each R^e is independently selected from hydrogen, -C_{1-6} alkyl, -O-C_{1-6}alkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -O-C_{3-8} cycloalkyl, -O-aryl, -O-heteroaryl, -O-heterocyclyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6}alkylheteroaryl, -NR^fR^g, -C_{1-6} alkylNR^fR^g, -$C(O)NR^fR^g$, -C_{1-6} alkyl$C(O)NR^fR^g$, -$NHS(O)_2R^f$, -C_{1-6} alkyl$S(O)_2R^f$, and -C_{1-6} alkyl$S(O)_2NR^fR^g$;

each R^f is independently selected from hydrogen, -C_{1-6} alkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8} cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6} alkylheterocyclyl; and

each R^g is independently selected from hydrogen, -C_{1-6} alkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8} cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6} alkylheterocyclyl.

2. A compound of formula (II):



(II)

or a pharmaceutically acceptable salt, stereoisomer, mixture of stereoisomers, solvate, or tautomer thereof, wherein:

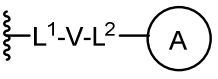
each of X^1, X^2, X^3 and X^4 are independently N, CH or CZ^3;

each Z^1 is independently halo, -OR^a, cyano, or -C_{1-6} alkyl;

each w is independently 0, 1 or 2;

each Z^3 is independently halo, $-OR^a$, $-N_3$, $-NO_2$, cyano, $-NR^1R^2$, $-SO_2R^a$, $-SO_2NR^aR^b$, $-NR^aSO_2R^a$, $-NR^aC(O)R^a$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-NR^aC(O)OR^a$, $-NR^aC(O)NR^1R^2$, $-OC(O)NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2NR^aR^b$, $-C_{1-6}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{2-6}$ alkynyl, $-O-C_{1-6}$ alkyl, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ haloalkyl, $-O-C_{1-6}$ cyanoalkyl, $-O-C_{1-6}$ haloalkyl, $-C_{3-8}$ cycloalkyl, $-C_{1-6}$ alkylC_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, and R^N; and

wherein the alkyl, alkenyl, alkynyl, C_{3-8} cycloalkyl, aryl, heteroaryl, or heterocyclyl group is optionally substituted with 1 to 4 groups independently selected from oxo, $-NO_2$, $-N_3$, $-OR^a$, halo, cyano, $-NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-O-C_{1-6}$cyanoalkyl, $-C(O)NR^aR^b$, $NR^aC(O)R^a$, $-NR^aC(O)OR^a$, $-S(O)_2R^a$, $-NR^aS(O)_2R^b$, $-S(O)_2NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2NR^aR^b$ and $-C_{3-8}$ cycloalkyl;

R^N is independently $-C_{1-6}$ alkylNR^1R^2, $-OC_{1-6}$ alkylNR^1R^2, $-C_{1-6}$ alkylOC_{1-6} alkylNR^1R^2, $-NR^a-C_{1-6}$ alkylNR^1R^2, $-C_{1-6}$ alkyl$C(O)NR^1R^2$, $-O-C_{1-6}$ alkyl$C(O)NR^1R^2$, $-O-C_{1-6}$ alkyl$C(O)OR^1$, $-S-C_{1-6}$ alkylNR^1R^2, $-C_{1-6}$ alkylOR^a, or 

;

wherein: L^1 is independently a bond, -O-, $-NR^a$-, -S-, -S(O)-, or $-S(O)_2$-;

V is independently selected from a bond, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

wherein each alkyl, alkenyl, or alkynyl is optionally independently substituted with $-OR^a$, halo, cyano, $-NR^aR^b$ or $-C_{3-8}$ cycloalkyl;

L^2 is independently a bond, -O-, $-NR^a$-, -S-, -S(O)-, or $-S(O)_2$-;

ring A is independently cycloalkyl, aryl, heteroaryl, or heterocyclyl;

wherein each cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from oxo, $-NO_2$, $-N_3$, $-OR^a$, halo, cyano, $-C_{1-6}$ alkyl, $-C_{1-6}$ haloalkyl, $-C_{2-6}$alkenyl, $-C_{2-6}$ alkynyl, $-O-C_{1-6}$ haloalkyl, NR^aR^b, $-C(O)R^a$, $-C(O)OR^a$, $-OC_{1-6}$ alkylCN, $-C(O)NR^aR^b$, $-NR^aC(O)R^a$, $-NR^aC(O)OR^a$, $-NR^aC(O)OR^a$, $-C(O)N(R^a)OR^b$, $-S(O)_2R^a$, $-S(O)_2NR^aR^b$, $-NR^aS(O)_2R^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2NR^aR^b$, $-C_{3-8}$cycloalkyl, heteroaryl, and $-C_{1-6}$alkylC_{3-8} cycloalkyl; and

wherein the alkyl, alkenyl, or alkynyl group is optionally independently substituted with $-OR^a$, halo, cyano, $-NR^aR^b$ or $-C_{3-8}$ cycloalkyl;

each t is independently 0, 1 or 2;

each R^1 is independently selected from hydrogen, $-C_{1-8}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{2-6}$ alkynyl, $-C_{3-6}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl,

-C_{1-6} alkylheterocyclyl, -C_{1-6} alkylC(O)OR^a, -C_{2-6} alkenylC(O)OR^a, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)NR^aS(O)_2R^a$, and -C_{1-6} alkylC_{3-8}cycloalkyl;

wherein each alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from -OR^a, cyano, halo, C_{1-6}alkyl, -C_{1-6} alkylOR^a, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, C_{3-8} cycloalkyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -$C(O)R^a$, -C_{1-6} alkylC(O)R^a, -C(O)OR^a, -C_{1-6} alkylC(O)OR^a, -NR^aR^b, -$OC(O)NR^aR^b$, -$NR^aC(O)OR^b$, -C_{1-6} alkylNR^aR^b, -$C(O)NR^aR^b$, -C_{1-6} alkylC(O)NR^aR^b, -SO_2R^a, -C_{1-6} alkylSO_2R^a, -$SO_2NR^aR^b$, -C_{1-6} alkyl$SO_2NR^aR^b$, -$C(O)NR^aSO_2R^b$, -C_{1-6} alkylC(O)$NR^aSO_2R^b$, -$NR^aC(O)R^b$, and -C_{1-6}alkyl$NR^aC(O)R^b$;

each R^2 is independently selected from hydrogen, -C_{1-6} alkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, -C_{3-6} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, -C_{1-6} alkylheterocyclyl, -C_{2-6} alkyl-OR^a, -C_{1-6} alkylC(O)OR^a, and -C_{2-6} alkenylC(O)OR^a;

wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from -OR^a, cyano, halo, C_{1-6} alkyl, -C_{1-6} alkylOR^a, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, -C_{3-8} cycloalkyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -$C(O)R^a$, -C_{1-6} alkylC(O)R^a, -C(O)OR^a, -C_{1-6} alkylC(O)OR^a, -NR^aR^b, -C_{1-6} alkylNR^aR^b, -$C(O)NR^aR^b$, C_{1-6} alkylC(O)NR^aR^b, -$S(O)_2R^a$, -C_{1-6} alkyl$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -C_{1-6} alkyl$S(O)_2NR^aR^b$, -$C(O)NR^aS(O)_2R^b$ and -$NR^aC(O)R^b$;

or R^1 and R^2 combine to form a heterocyclyl optionally substituted with 1 to 3 groups independently selected from oxo, -C_{1-6} alkyl, -C_{3-8} cycloalkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, -OR^a, -C(O)OR^a, -C_{1-6} cyanoalkyl, -C_{1-6} alkylOR^a, -C_{1-6} haloalkyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -$C(O)R^a$, -C_{1-6} alkylC(O)R^a, -C_{1-6} alkylC(O)OR^a, -NR^aR^b, -C_{1-6}alkylNR^aR^b, -$C(O)NR^aR^b$, -C_{1-6} alkylC(O)NR^aR^b, -$S(O)_2R^a$, -C_{1-6} alkyl$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -C(O)N=S(O)$R^aNR^aR^b$, -C(O)N=S(O)$R^aNR^aC(O)R^b$, and -C_{1-6} alkyl$S(O)_2NR^aR^b$;

each R^3 is independently hydrogen, -C_{1-6} alkyl, -C_{2-6} alkenyl, -C_{3-6} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, -C_{1-6} alkylheterocyclyl, -C_{2-6} alkyl-OR^a, -C_{1-6} alkylC(O)OR^a, or -C_{2-6} alkenylC(O)OR^a;

each R^a is independently selected from hydrogen, -C_{1-6} alkyl, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6}alkylheterocyclyl;

each R^b is independently selected from hydrogen, -C_{1-6} alkyl, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6} alkylheterocyclyl;

or R^a and R^b may combine together to form a heterocyclyl optionally substituted with 1 to 4 groups independently selected from -OR^f, cyano, halo, -C_{1-6} alkylOR^f, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, -C_{3-8} cycloalkyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -$C(O)R^f$, -C_{1-6} alkylC(O)R^f, -C(O)OR^f, -C_{1-6} alkylC(O)OR^f,

$-NR^fR^g$, $-C_{1-6}$ alkylNR^fR^g, $-C(O)NR^fR^g$, $-C_{1-6}$ alkyl$C(O)NR^fR^g$, $-S(O)_2R^f$, $-C_{1-6}$ alkyl$S(O)_2R^f$, $-S(O)_2NR^fR^g$, $-C_{1-6}$ alkyl$S(O)_2NR^fR^g$, $-C(O)NR^fS(O)_2R^g$ and $-NR^fC(O)R^g$;

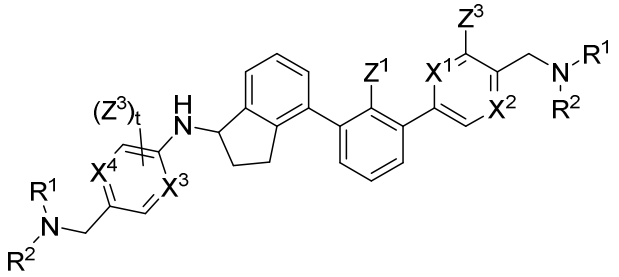
each R^c is independently selected from hydrogen, -OH, $-C_{1-6}$ alkyl, $-C_{3-8}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-3}$ alkylC_{3-8} cycloalkyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, and $-C_{1-6}$ alkylheterocyclyl;

R^d is independently selected from hydrogen, $-C_{1-6}$ alkyl, $-C_3-C_8$cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-3}$ alkylC_{3-8}cycloalkyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, and $-C_{1-6}$ alkylheterocyclyl;

each R^f is independently selected from hydrogen, $-C_{1-6}$ alkyl, $-C_{3-8}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-3}$ alkylC_{3-8} cycloalkyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, and $-C_{1-6}$ alkylheterocyclyl; and

each R^g is independently selected from hydrogen, $-C_{1-6}$ alkyl, $-C_{3-8}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-3}$ alkylC_{3-8} cycloalkyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, and $-C_{1-6}$ alkylheterocyclyl.

3. A compound of formula (IIA):



(IIA)

or a pharmaceutically acceptable salt thereof, wherein:

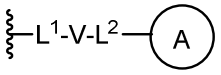
each of X^1, X^2, X^3 and X^4 are independently N, CH or CZ^3;

each Z^1 is independently halo, $-OR^a$, cyano, or $-C_{1-6}$ alkyl;

each w is independently 0, 1 or 2;

each Z^3 is independently halo, $-OR^a$, $-N_3$, $-NO_2$, cyano, $-NR^1R^2$, $-SO_2R^a$, $-SO_2NR^aR^b$, $-NR^aSO_2R^a$, $-NR^aC(O)R^a$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-NR^aC(O)OR^a$, $-NR^aC(O)NR^1R^2$, $-OC(O)NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2NR^aR^b$, $-C_{1-6}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{2-6}$ alkynyl, $-O-C_{1-6}$ alkyl, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ haloalkyl, $-O-C_{1-6}$ cyanoalkyl, $-O-C_{1-6}$ haloalkyl, $-C_{3-8}$ cycloalkyl, $-C_{1-6}$ alkylC_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, and R^N; and

wherein the alkyl, alkenyl, alkynyl, C_{3-8} cycloalkyl, aryl, heteroaryl, or heterocyclyl group is optionally substituted with 1 to 4 groups independently selected from oxo, $-NO_2$, $-N_3$, $-OR^a$, halo, cyano, $-NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-O-C_{1-6}$cyanoalkyl, $-C(O)NR^aR^b$, $NR^aC(O)R^a$, $-NR^aC(O)OR^a$, $-S(O)_2R^a$, $-NR^aS(O)_2R^b$, $-S(O)_2NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2NR^aR^b$ and $-C_{3-8}$ cycloalkyl;

R^N is independently -C_{1-6} alkylNR^1R^2, -OC_{1-6} alkylNR^1R^2, -C_{1-6} alkylOC_{1-6} alkylNR^1R^2, -NR^a-C_{1-6} alkylNR^1R^2, -C_{1-6} alkylC(O)NR^1R^2, -O-C_{1-6} alkylC(O)NR^1R^2, -O-C_{1-6} alkylC(O)OR^1, -S-C_{1-6} alkylNR^1R^2, -C_{1-6} alkylOR^a, or 

;

wherein: L^1 is independently a bond, -O-, -NR^a-, -S-, -S(O)-, or -$S(O)_2$-;

V is independently selected from a bond, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

wherein each alkyl, alkenyl, or alkynyl is optionally independently substituted with -OR^a, halo, cyano, -NR^aR^b or -C_{3-8} cycloalkyl;

L^2 is independently a bond, -O-, -NR^a-, -S-, -S(O)-, or -$S(O)_2$-;

ring A is independently cycloalkyl, aryl, heteroaryl, or heterocyclyl;

wherein each cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from oxo, -NO_2, -N_3, -OR^a, halo, cyano, -C_{1-6} alkyl, -C_{1-6} haloalkyl, -C_{2-6}alkenyl, -C_{2-6} alkynyl, -O-C_{1-6} haloalkyl, NR^aR^b, -C(O)R^a, -C(O)OR^a, -OC_{1-6} alkylCN, -C(O)NR^aR^b, -NR^aC(O)R^a, -NR^aC(O)OR^a, -NR^aC(O)OR^a, -C(O)N(R^a)OR^b, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$NR^aS(O)_2R^b$, -$NR^aS(O)_2NR^aR^b$, -C(O)$NR^aS(O)_2NR^aR^b$, -C_{3-8}cycloalkyl, heteroaryl, and -C_{1-6}alkylC_{3-8} cycloalkyl; and

wherein the alkyl, alkenyl, or alkynyl group is optionally independently substituted with -OR^a, halo, cyano, -NR^aR^b or -C_{3-8} cycloalkyl;

each t is independently 0, 1 or 2;

each R^1 is independently selected from hydrogen, -C_{1-8} alkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, -C_{3-6} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, -C_{1-6} alkylheterocyclyl, -C_{1-6} alkylC(O)OR^a, -C_{2-6} alkenylC(O)OR^a, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -C(O)$NR^aS(O)_2R^a$, and -C_{1-6} alkylC_{3-8}cycloalkyl;

wherein each alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from -OR^a, cyano, halo, C_{1-6}alkyl, -C_{1-6} alkylOR^a, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, C_{3-8} cycloalkyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -C(O)R^a, -C_{1-6} alkylC(O)R^a, -C(O)OR^a, -C_{1-6} alkylC(O)OR^a, -NR^aR^b, -OC(O)NR^aR^b, -NR^aC(O)OR^b, -C_{1-6} alkylNR^aR^b, -C(O)NR^aR^b, -C_{1-6} alkylC(O)NR^aR^b, -SO_2R^a, -C_{1-6} alkylSO_2R^a, -$SO_2NR^aR^b$, -C_{1-6} alkyl$SO_2NR^aR^b$, -C(O)$NR^aSO_2R^b$, -C_{1-6} alkylC(O)$NR^aSO_2R^b$, -NR^aC(O)R^b, and -C_{1-6}alkylNR^aC(O)R^b;

each R^2 is independently selected from hydrogen, -C_{1-6} alkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, -C_{3-6} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, -C_{1-6} alkylheterocyclyl, -C_{2-6} alkyl-OR^a, -C_{1-6} alkylC(O)OR^a, and -C_{2-6} alkenylC(O)OR^a;

wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from $-OR^a$, cyano, halo, C_{1-6} alkyl, $-C_{1-6}$ alkylOR^a, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ haloalkyl, $-C_{3-8}$ cycloalkyl, $-C_{1-3}$ alkylC_{3-8}cycloalkyl, $-C(O)R^a$, $-C_{1-6}$ alkyl$C(O)R^a$, $-C(O)OR^a$, $-C_{1-6}$ alkyl$C(O)OR^a$, $-NR^aR^b$, $-C_{1-6}$ alkylNR^aR^b, $-C(O)NR^aR^b$, C_{1-6} alkyl$C(O)NR^aR^b$, $-S(O)_2R^a$, $-C_{1-6}$ alkyl$S(O)_2R^a$, $-S(O)_2NR^aR^b$, $-C_{1-6}$ alkyl$S(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2R^b$ and $-NR^aC(O)R^b$;

or R^1 and R^2 combine to form a heterocyclyl optionally substituted with 1 to 3 groups independently selected from oxo, $-C_{1-6}$ alkyl, $-C_{3-8}$ cycloalkyl, $-C_{2-6}$ alkenyl, $-C_{2-6}$ alkynyl, $-OR^a$, $-C(O)OR^a$, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ alkylOR^a, $-C_{1-6}$ haloalkyl, $-C_{1-3}$ alkylC_{3-8}cycloalkyl, $-C(O)R^a$, $-C_{1-6}$ alkyl$C(O)R^a$, $-C_{1-6}$ alkyl$C(O)OR^a$, $-NR^aR^b$, $-C_{1-6}$alkylNR^aR^b, $-C(O)NR^aR^b$, $-C_{1-6}$ alkyl$C(O)NR^aR^b$, $-S(O)_2R^a$, $-C_{1-6}$ alkyl$S(O)_2R^a$, $-S(O)_2NR^aR^b$, $-C(O)N=S(O)R^aNR^aR^b$, $-C(O)N=S(O)R^aNR^aC(O)R^b$, and $-C_{1-6}$ alkyl$S(O)_2NR^aR^b$;

each R^3 is independently hydrogen, $-C_{1-6}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{3-6}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, $-C_{1-6}$ alkylheterocyclyl, $-C_{2-6}$ alkyl-OR^a, $-C_{1-6}$ alkyl$C(O)OR^a$, or $-C_{2-6}$ alkenyl$C(O)OR^a$;

each R^a is independently selected from hydrogen, $-C_{1-6}$ alkyl, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ haloalkyl, $-C_{3-8}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-3}$ alkylC_{3-8}cycloalkyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, and $-C_{1-6}$alkylheterocyclyl;

each R^b is independently selected from hydrogen, $-C_{1-6}$ alkyl, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ haloalkyl, $-C_{3-8}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-3}$ alkylC_{3-8}cycloalkyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, and $-C_{1-6}$ alkylheterocyclyl;

or R^a and R^b may combine together to form a heterocyclyl optionally substituted with 1 to 4 groups independently selected from $-OR^f$, cyano, halo, $-C_{1-6}$ alkylOR^f, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ haloalkyl, $-C_{3-8}$ cycloalkyl, $-C_{1-3}$ alkylC_{3-8}cycloalkyl, $-C(O)R^f$, $-C_{1-6}$ alkyl$C(O)R^f$, $-C(O)OR^f$, $-C_{1-6}$ alkyl$C(O)OR^f$, $-NR^fR^g$, $-C_{1-6}$ alkylNR^fR^g, $-C(O)NR^fR^g$, $-C_{1-6}$ alkyl$C(O)NR^fR^g$, $-S(O)_2R^f$, $-C_{1-6}$ alkyl$S(O)_2R^f$, $-S(O)_2NR^fR^g$, $-C_{1-6}$ alkyl$S(O)_2NR^fR^g$, $-C(O)NR^fS(O)_2R^g$ and $-NR^fC(O)R^g$;

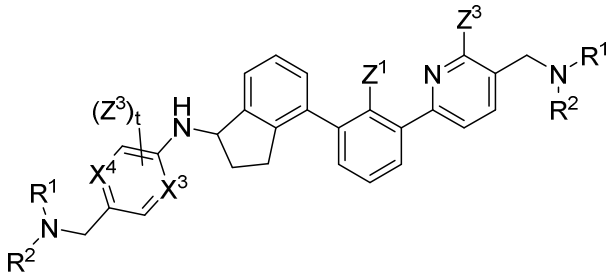
each R^c is independently selected from hydrogen, -OH, $-C_{1-6}$ alkyl, $-C_{3-8}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-3}$ alkylC_{3-8} cycloalkyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, and $-C_{1-6}$ alkylheterocyclyl;

R^d is independently selected from hydrogen, $-C_{1-6}$ alkyl, $-C_3$-C_8cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-3}$ alkylC_{3-8}cycloalkyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, and $-C_{1-6}$ alkylheterocyclyl;

each R^f is independently selected from hydrogen, $-C_{1-6}$ alkyl, $-C_{3-8}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-3}$ alkylC_{3-8} cycloalkyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, and $-C_{1-6}$ alkylheterocyclyl; and

each R^g is independently selected from hydrogen, $-C_{1-6}$ alkyl, $-C_{3-8}$ cycloalkyl, aryl, heteroaryl, heterocyclyl, $-C_{1-3}$ alkylC_{3-8} cycloalkyl, $-C_{1-6}$ alkylaryl, $-C_{1-6}$ alkylheteroaryl, and $-C_{1-6}$ alkylheterocyclyl.

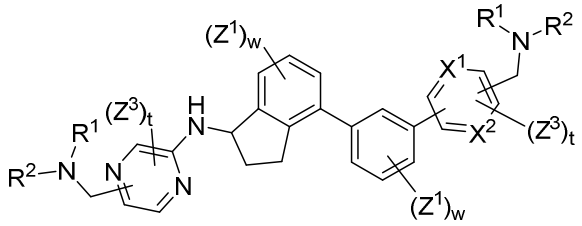
4. The compound of claim 1, wherein the compound is of formula (IIC):



(IIC)

or a pharmaceutically acceptable salt thereof.

5. A compound of formula (VI):



(VI)

or a pharmaceutically acceptable salt thereof, wherein:

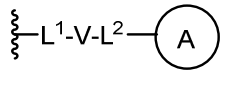
each of X^1 and X^2 are independently N, CH or CZ^3;

each Z^1 is independently halo, $-OR^a$, cyano, or $-C_{1-6}$ alkyl;

each w is independently 0, 1 or 2;

each Z^3 is independently halo, $-OR^a$, $-N_3$, $-NO_2$, cyano, $-NR^1R^2$, $-SO_2R^a$, $-SO_2NR^aR^b$, $-NR^aSO_2R^a$, $-NR^aC(O)R^a$, $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^aR^b$, $-NR^aC(O)OR^a$, $-NR^aC(O)NR^1R^2$, $-OC(O)NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2NR^aR^b$, $-C_{1-6}$ alkyl, $-C_{2-6}$ alkenyl, $-C_{2-6}$ alkynyl, $-O-C_{1-6}$ alkyl, $-C_{1-6}$ cyanoalkyl, $-C_{1-6}$ haloalkyl, $-O-C_{1-6}$ cyanoalkyl, $-O-C_{1-6}$ haloalkyl, $-C_{3-8}$ cycloalkyl, $-C_{1-6}$ alkylC_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, and R^N; and

wherein the alkyl, alkenyl, alkynyl, C_{3-8} cycloalkyl, aryl, heteroaryl, or heterocyclyl group is optionally substituted with 1 to 4 groups independently selected from oxo, $-NO_2$, $-N_3$, $-OR^a$, halo, cyano, $-NR^aR^b$, $-C(O)R^a$, $-C(O)OR^a$, $-O-C_{1-6}$cyanoalkyl, $-C(O)NR^aR^b$, $NR^aC(O)R^a$, $-NR^aC(O)OR^a$, $-S(O)_2R^a$, $-NR^aS(O)_2R^b$, $-S(O)_2NR^aR^b$, $-NR^aS(O)_2NR^aR^b$, $-C(O)NR^aS(O)_2NR^aR^b$ and $-C_{3-8}$ cycloalkyl;

R^N is independently $-C_{1-6}$ alkylNR^1R^2, $-OC_{1-6}$ alkylNR^1R^2, $-C_{1-6}$ alkylOC_{1-6} alkylNR^1R^2, $-NR^a-C_{1-6}$ alkylNR^1R^2, $-C_{1-6}$ alkyl$C(O)NR^1R^2$, $-O-C_{1-6}$ alkyl$C(O)NR^1R^2$, $-O-C_{1-6}$ alkyl$C(O)OR^1$, $-S-C_{1-6}$ alkylNR^1R^2, $-C_{1-6}$ alkylOR^a, or ;

wherein: L^1 is independently a bond, -O-, $-NR^a$-, -S-, -S(O)-, or $-S(O)_2$-;

V is independently selected from a bond, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

wherein each alkyl, alkenyl, or alkynyl is optionally independently substituted with -OR^a, halo, cyano, -NR^aR^b or -C_{3-8} cycloalkyl;

L^2 is independently a bond, -O-, -NR^a-, -S-, -S(O)-, or -$S(O)_2$-;

ring A is independently cycloalkyl, aryl, heteroaryl, or heterocyclyl;

wherein each cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from oxo, -NO_2, -N_3, -OR^a, halo, cyano, -C_{1-6} alkyl, -C_{1-6} haloalkyl, -C_{2-6}alkenyl, -C_{2-6} alkynyl, -O-C_{1-6} haloalkyl, NR^aR^b, -C(O)R^a, -C(O)OR^a, -OC_{1-6} alkylCN, -C(O)NR^aR^b, -NR^aC(O)R^a, -NR^aC(O)OR^a, -NR^aC(O)OR^a, -C(O)N(R^a)OR^b, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$NR^aS(O)_2R^b$, -$NR^aS(O)_2NR^aR^b$, -C(O)$NR^aS(O)_2NR^aR^b$, -C_{3-8}cycloalkyl, heteroaryl, and -C_{1-6}alkylC_{3-8} cycloalkyl; and

wherein the alkyl, alkenyl, or alkynyl group is optionally independently substituted with -OR^a, halo, cyano, -NR^aR^b or -C_{3-8} cycloalkyl;

each t is independently 0, 1 or 2;

each R^1 is independently selected from hydrogen, -C_{1-8} alkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, -C_{3-6} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, -C_{1-6} alkylheterocyclyl, -C_{1-6} alkylC(O)OR^a, -C_{2-6} alkenylC(O)OR^a, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -C(O)$NR^aS(O)_2R^a$, and -C_{1-6} alkylC_{3-8}cycloalkyl;

wherein each alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from -OR^a, cyano, halo, C_{1-6}alkyl, -C_{1-6} alkylOR^a, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, C_{3-8} cycloalkyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -C(O)R^a, -C_{1-6} alkylC(O)R^a, -C(O)OR^a, -C_{1-6} alkylC(O)OR^a, -NR^aR^b, -OC(O)NR^aR^b, -NR^aC(O)OR^b, -C_{1-6} alkylNR^aR^b, -C(O)NR^aR^b, -C_{1-6} alkylC(O)NR^aR^b, -SO_2R^a, -C_{1-6} alkylSO_2R^a, -$SO_2NR^aR^b$, -C_{1-6} alkyl$SO_2NR^aR^b$, -C(O)$NR^aSO_2R^b$, -C_{1-6} alkylC(O)$NR^aSO_2R^b$, -NR^aC(O)R^b, and -C_{1-6}alkylNR^aC(O)R^b;

each R^2 is independently selected from hydrogen, -C_{1-6} alkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, -C_{3-6} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, -C_{1-6} alkylheterocyclyl, -C_{2-6} alkyl-OR^a, -C_{1-6} alkylC(O)OR^a, and -C_{2-6} alkenylC(O)OR^a;

wherein each alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from -OR^a, cyano, halo, C_{1-6} alkyl, -C_{1-6} alkylOR^a, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, -C_{3-8} cycloalkyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -C(O)R^a, -C_{1-6} alkylC(O)R^a, -C(O)OR^a, -C_{1-6} alkylC(O)OR^a, -NR^aR^b, -C_{1-6} alkylNR^aR^b, -C(O)NR^aR^b, C_{1-6} alkylC(O)NR^aR^b, -$S(O)_2R^a$, -C_{1-6} alkyl$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -C_{1-6} alkyl$S(O)_2NR^aR^b$, -C(O)$NR^aS(O)_2R^b$ and -NR^aC(O)R^b;

or R^1 and R^2 combine to form a heterocyclyl optionally substituted with 1 to 3 groups independently selected from oxo, -C_{1-6} alkyl, -C_{3-8} cycloalkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, -OR^a, -$C(O)OR^a$, -C_{1-6} cyanoalkyl, -C_{1-6} alkylOR^a, -C_{1-6} haloalkyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -$C(O)R^a$, -C_{1-6} alkyl$C(O)R^a$, -C_{1-6} alkyl$C(O)OR^a$, -NR^aR^b, -C_{1-6}alkylNR^aR^b, -$C(O)NR^aR^b$, -C_{1-6} alkyl$C(O)NR^aR^b$, -$S(O)_2R^a$, -C_{1-6} alkyl$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)N{=}S(O)R^aNR^aR^b$, -$C(O)N{=}S(O)R^aNR^aC(O)R^b$, and -$C_{1-6}$ alkyl$S(O)_2NR^aR^b$;

each R^3 is independently hydrogen, -C_{1-6} alkyl, -C_{2-6} alkenyl, -C_{3-6} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, -C_{1-6} alkylheterocyclyl, -C_{2-6} alkyl-OR^a, -C_{1-6} alkyl$C(O)OR^a$, or -C_{2-6} alkenyl$C(O)OR^a$;

each R^a is independently selected from hydrogen, -C_{1-6} alkyl, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6}alkylheterocyclyl;

each R^b is independently selected from hydrogen, -C_{1-6} alkyl, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6} alkylheterocyclyl;

or R^a and R^b may combine together to form a heterocyclyl optionally substituted with 1 to 4 groups independently selected from -OR^f, cyano, halo, -C_{1-6} alkylOR^f, -C_{1-6} cyanoalkyl, -C_{1-6} haloalkyl, -C_{3-8} cycloalkyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -$C(O)R^f$, -C_{1-6} alkyl$C(O)R^f$, -$C(O)OR^f$, -C_{1-6} alkyl$C(O)OR^f$, -NR^fR^g, -C_{1-6} alkylNR^fR^g, -$C(O)NR^fR^g$, -C_{1-6} alkyl$C(O)NR^fR^g$, -$S(O)_2R^f$, -C_{1-6} alkyl$S(O)_2R^f$, -$S(O)_2NR^fR^g$, -C_{1-6} alkyl$S(O)_2NR^fR^g$, -$C(O)NR^fS(O)_2R^g$ and -$NR^fC(O)R^g$;

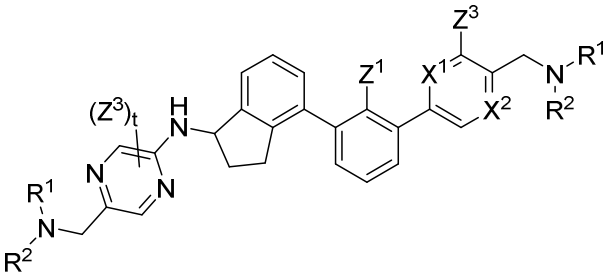
each R^c is independently selected from hydrogen, -OH, -C_{1-6} alkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8} cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6} alkylheterocyclyl;

R^d is independently selected from hydrogen, -C_{1-6} alkyl, -C_3-C_8cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6} alkylheterocyclyl;

each R^f is independently selected from hydrogen, -C_{1-6} alkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8} cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6} alkylheterocyclyl; and

each R^g is independently selected from hydrogen, -C_{1-6} alkyl, -C_{3-8} cycloalkyl, aryl, heteroaryl, heterocyclyl, -C_{1-3} alkylC_{3-8} cycloalkyl, -C_{1-6} alkylaryl, -C_{1-6} alkylheteroaryl, and -C_{1-6} alkylheterocyclyl.

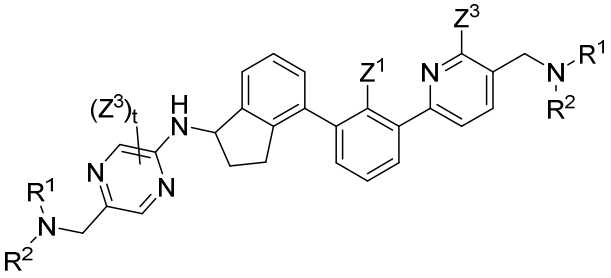
6. The compound of claim 1, wherein the compound is of formula (VIA):



(VIA)

or a pharmaceutically acceptable salt thereof.

7. The compound of claim 1, wherein the compound is of formula (VIC):



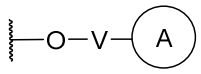
(VIC)

or a pharmaceutically acceptable salt thereof.

8. The compound of any one of the preceding claims, wherein each Z^1 is independently halo.

9. The compound of any one of the preceding claims, wherein at least one Z^3 is halo, -C_{1-6} alkyl, C_{1-6} haloalkyl, -O-cyanoalkyl, -O-C_{1-6} haloalkyl, or C_{1-6} alkoxy.

10. The compound of any one of the preceding claims, wherein at least one Z^3 is of the formula:



V is independently selected from a bond, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl;

wherein each alkyl, alkenyl, or alkynyl is optionally independently substituted with -OR^a, halo, cyano, -NR^aR^b or -C_{3-8} cycloalkyl;

ring A is independently cycloalkyl, aryl, heteroaryl, or heterocyclyl;

wherein each cycloalkyl, aryl, heteroaryl, or heterocyclyl is optionally substituted with 1 to 4 groups independently selected from oxo, -NO_2, -N_3, -OR^a, halo, cyano, -C_{1-6} alkyl, -C_{1-6} haloalkyl, -C_{2-6}alkenyl, -C_{2-6} alkynyl, -O-C_{1-6} haloalkyl, NR^aR^b, -$C(O)R^a$, -$C(O)OR^a$, -OC_{1-6} alkylCN, -$C(O)NR^aR^b$, -$NR^aC(O)R^a$, $NR^aC(O)OR^a$, -$NR^aC(O)OR^a$, -$C(O)N(R^a)OR^b$, -$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$NR^aS(O)_2R^b$, -$NR^aS(O)_2NR^aR^b$, -$C(O)NR^aS(O)_2NR^aR^b$, -C_{3-8} cycloalkyl, heteroaryl, and -C_{1-6}alkylC_{3-8} cycloalkyl.

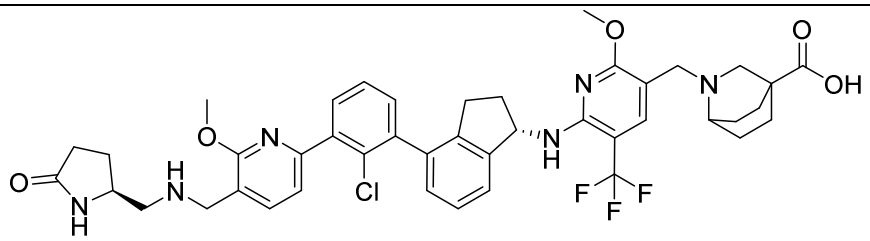
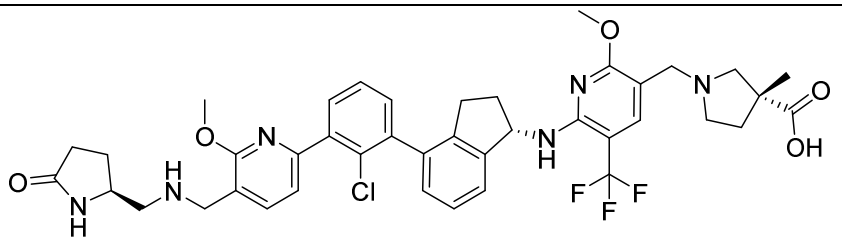
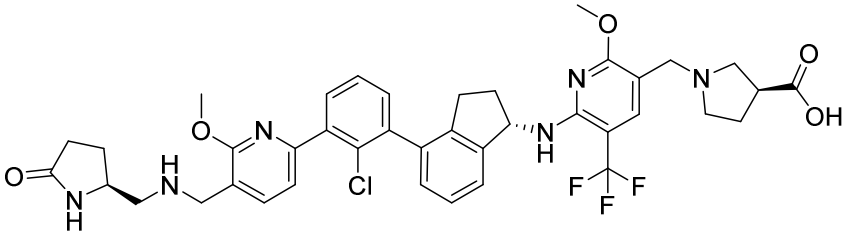
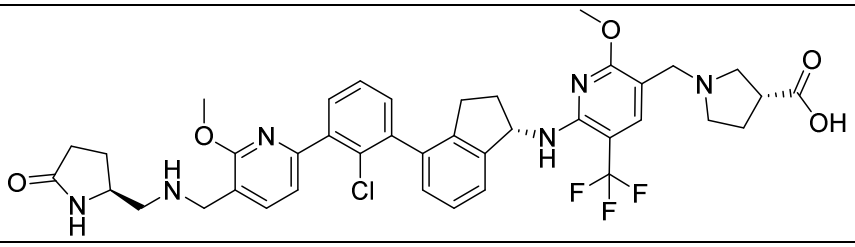
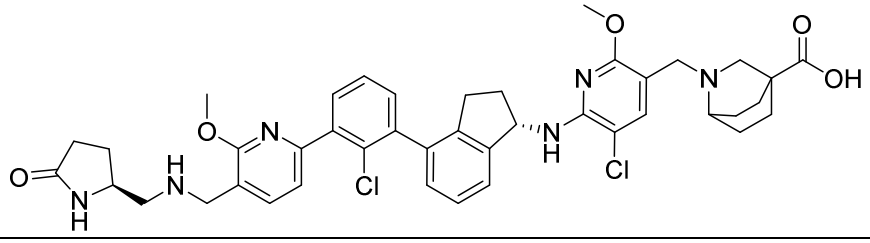
11. The compound of any one of the preceding claims, wherein R^1 and R^2 combine to form a heterocyclyl optionally substituted with 1 to 3 groups independently selected from oxo, -C_{1-6} alkyl, -C_{3-8}

cycloalkyl, -C_{2-6} alkenyl, -C_{2-6} alkynyl, -OR^a, -$C(O)OR^a$, -C_{1-6} cyanoalkyl, -C_{1-6} alkylOR^a, -C_{1-6} haloalkyl, -C_{1-3} alkylC_{3-8}cycloalkyl, -$C(O)R^a$, -C_{1-6} alkyl$C(O)R^a$, -C_{1-6} alkyl$C(O)OR^a$, -NR^aR^b, -C_{1-6}alkylNR^aR^b, -$C(O)NR^aR^b$, -C_{1-6} alkyl$C(O)NR^aR^b$, -$S(O)_2R^a$, -C_{1-6} alkyl$S(O)_2R^a$, -$S(O)_2NR^aR^b$, -$C(O)N{=}S(O)R^aNR^aR^b$, -$C(O)N{=}S(O)R^aNR^aC(O)R^b$, and -$C_{1-6}$ alkyl$S(O)_2NR^aR^b$.

12. The compound of any one of claims 1 to 10, wherein at least one of R^1 and R^2 is -C_{1-6} alkylheteroaryl or -C_{1-6} alkylheteocyclyl.

13. A compound selected from Table 1A, or a pharmaceutically acceptable salt thereof or a compound selected from Table 1B, or a pharmaceutically acceptable salt thereof:

Table 1A

No.	Structure
A-1	
A-2	
A-3	
A-4	
A-5	

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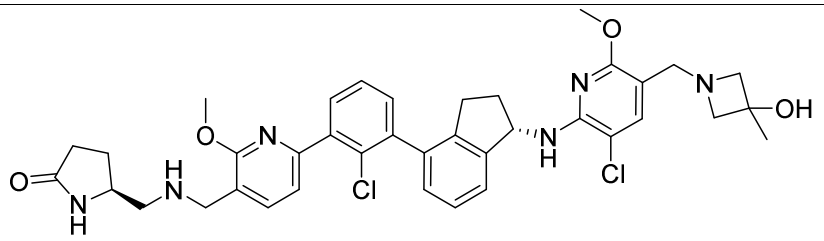
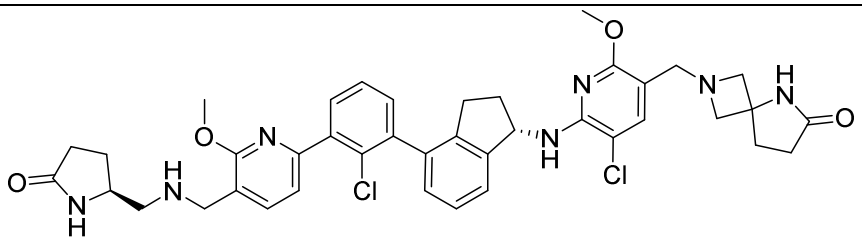
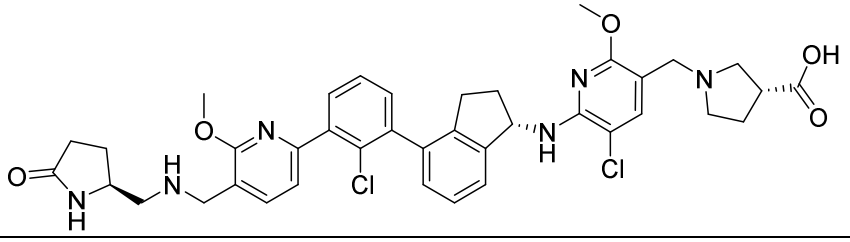
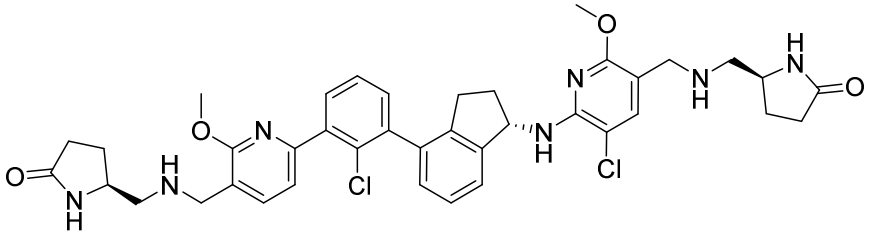
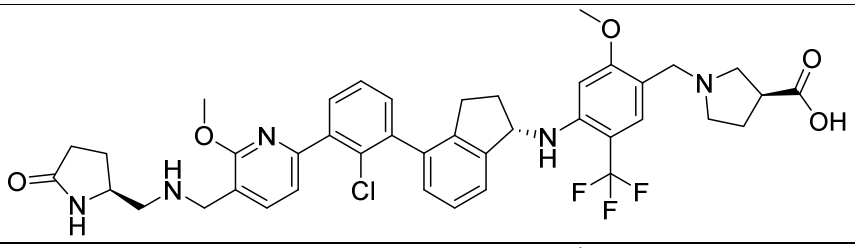
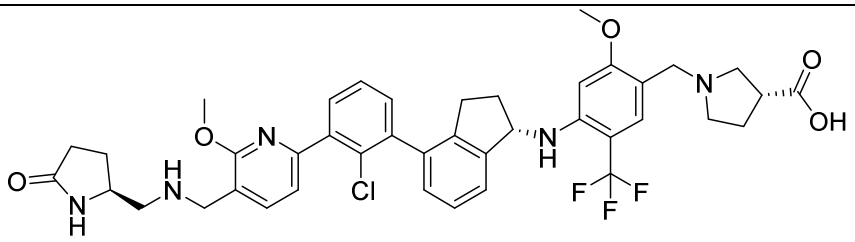
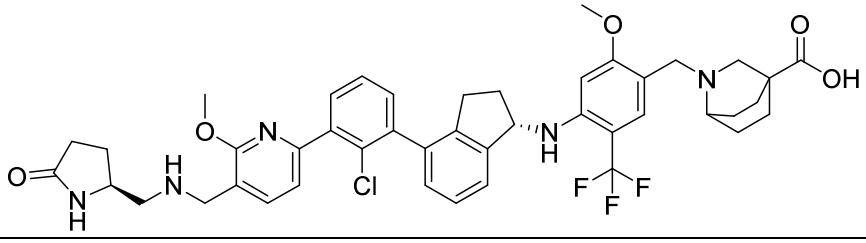
A-6	
A-7	
A-8	
A-9	
A-10	
A-11	
A-12	

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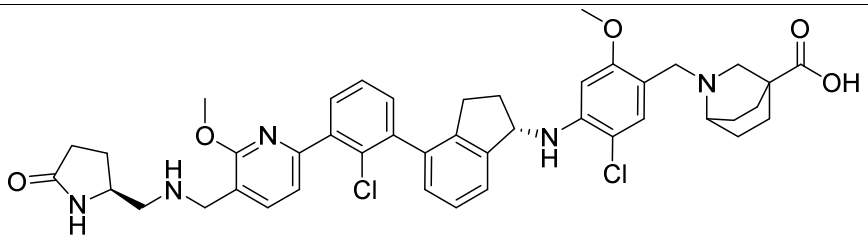
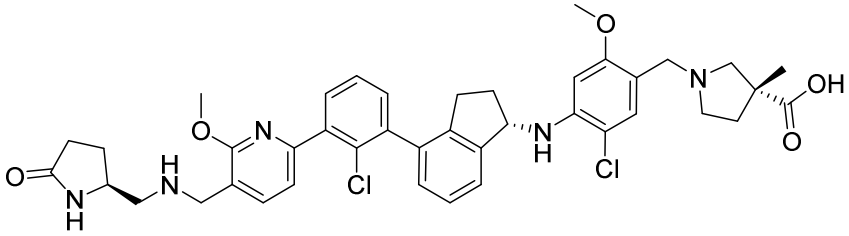
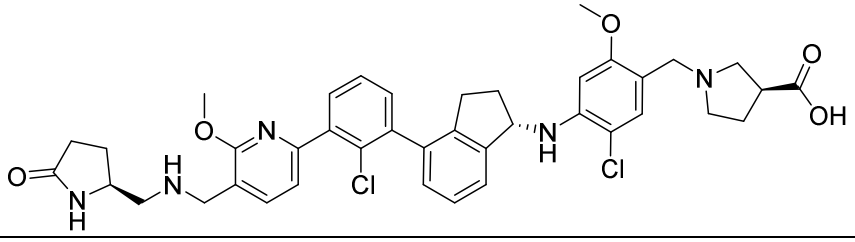
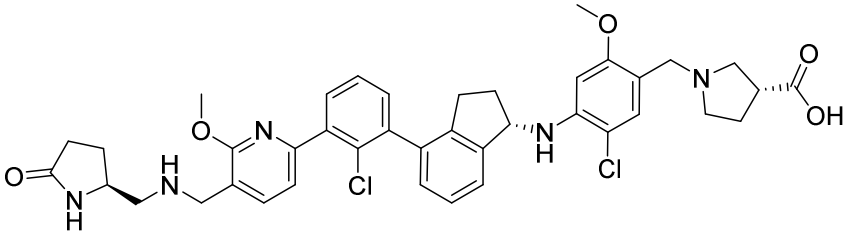
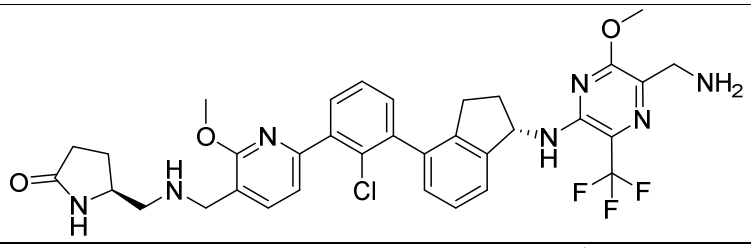
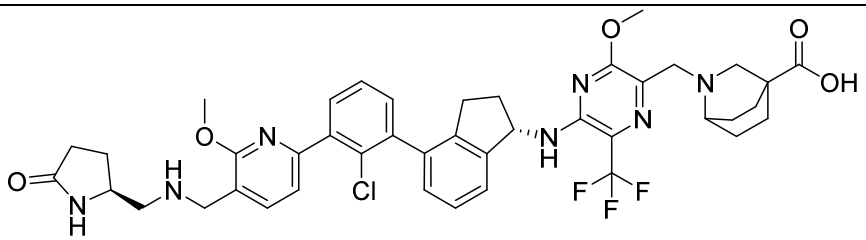
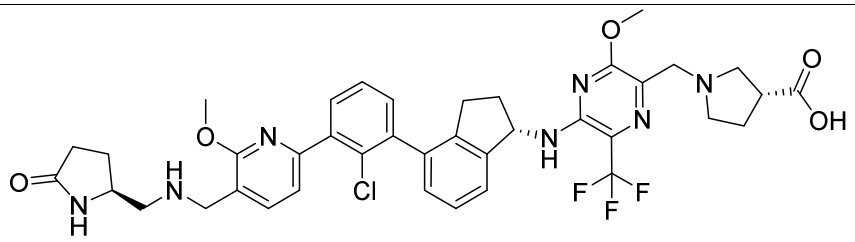
A-13	
A-14	
A-15	
A-16	
A-17	
A-18	
A-19	

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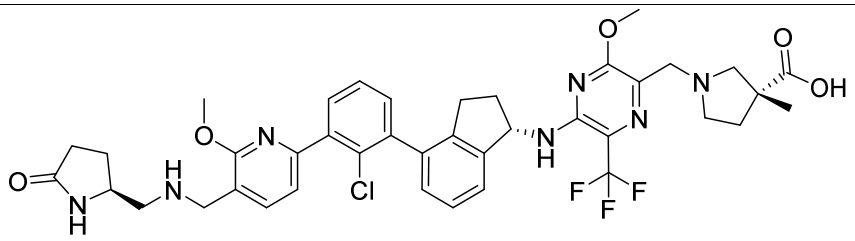
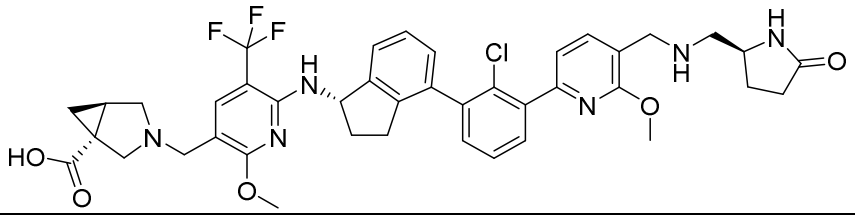
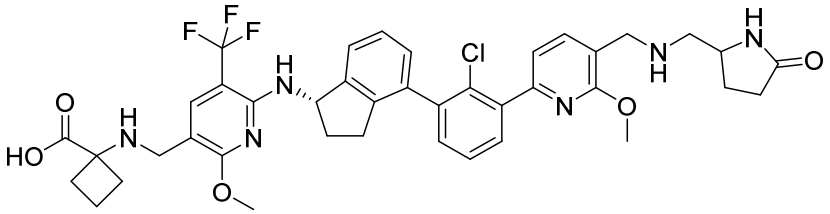
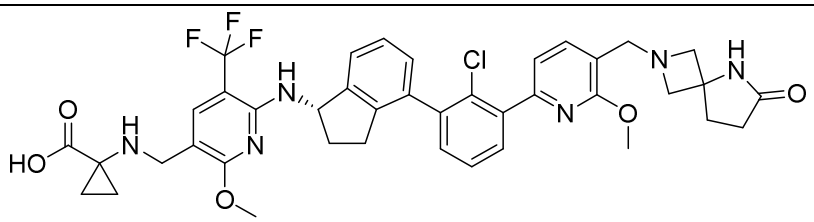
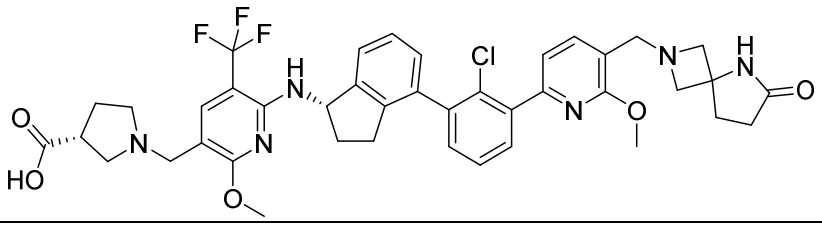
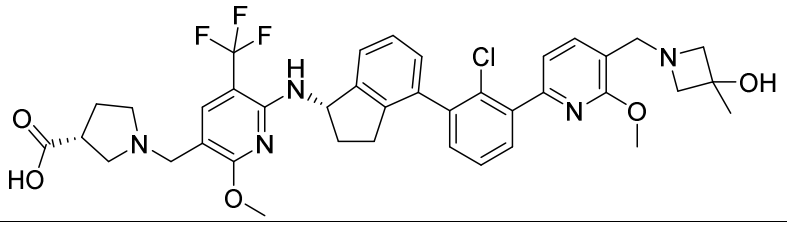
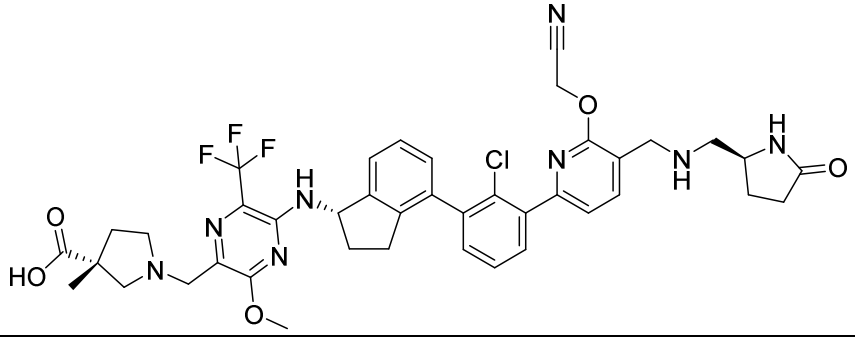
A-20	
A-21	
A-22	
A-23	
A-24	
A-25	
A-26	

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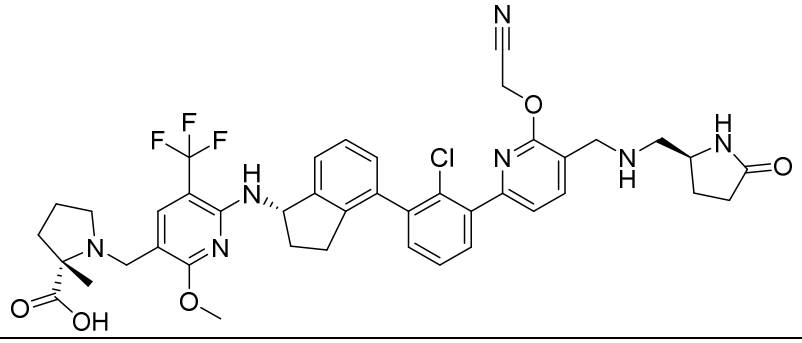
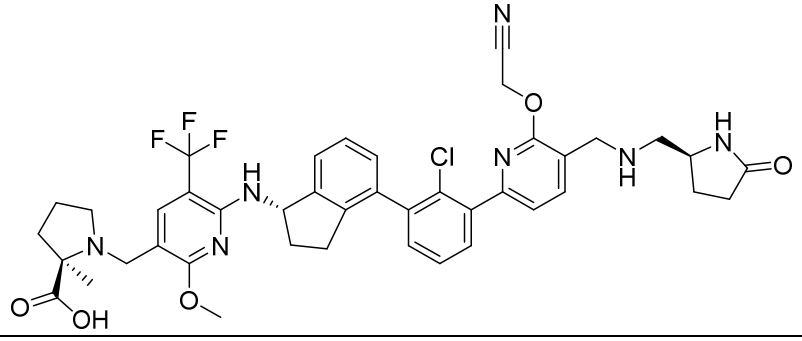
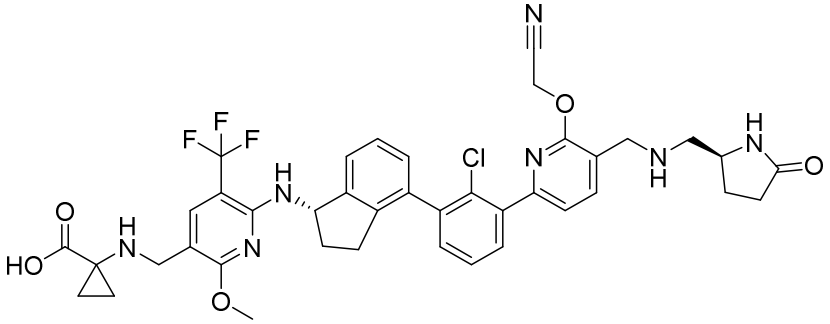
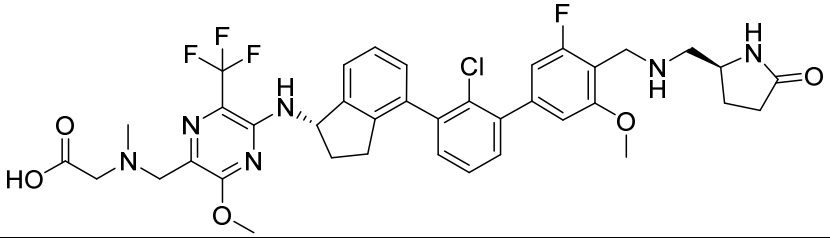
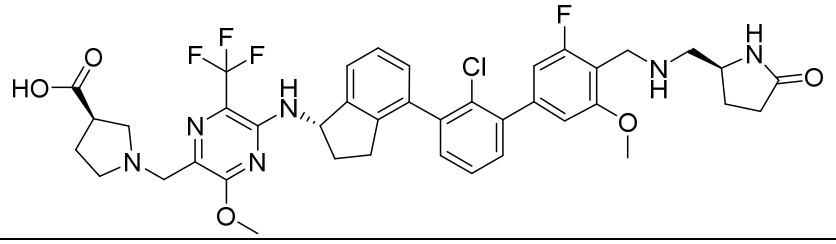
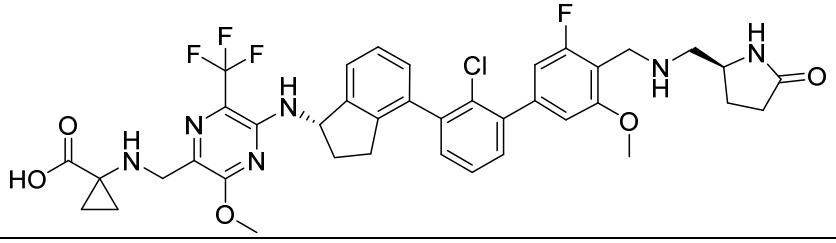
A-27	
A-28	
A-29	
A-30	
A-31	
A-32	

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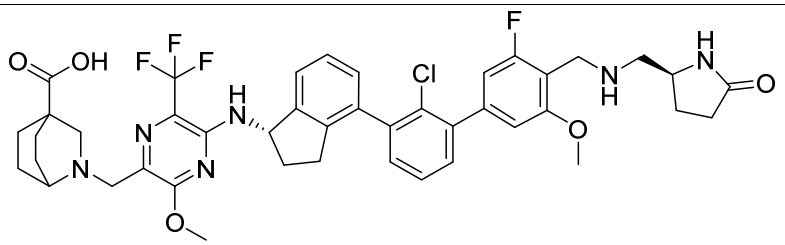
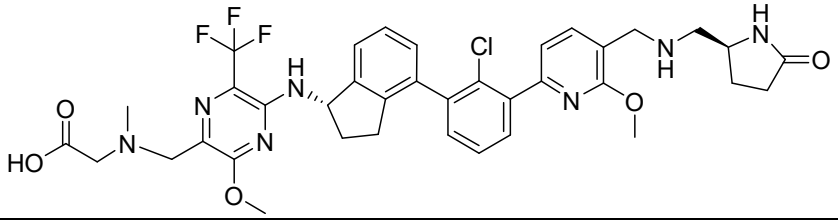
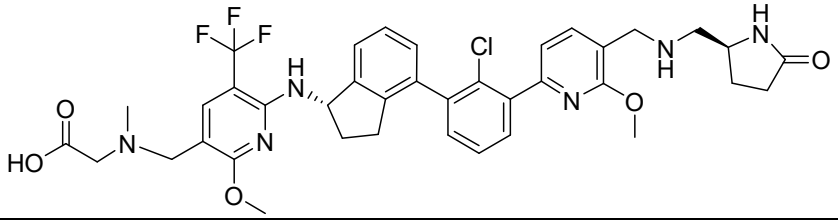
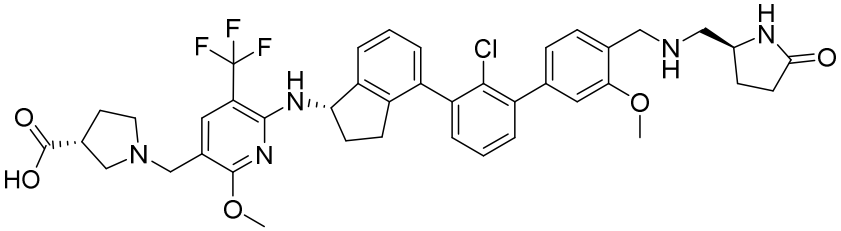
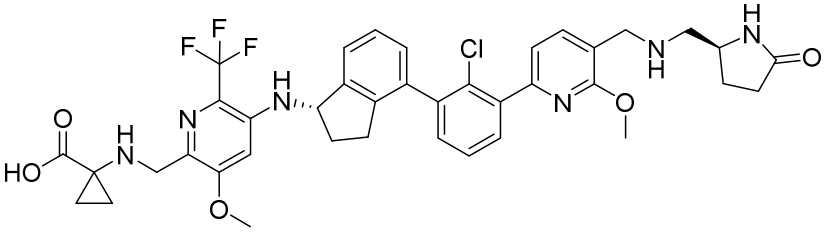
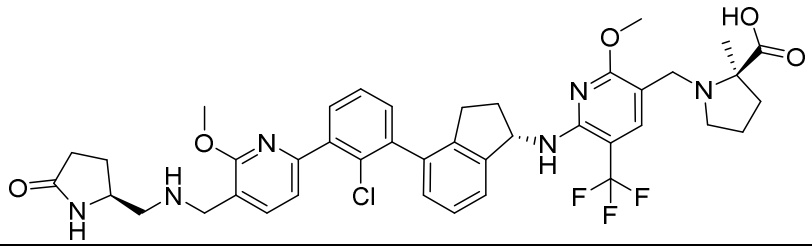
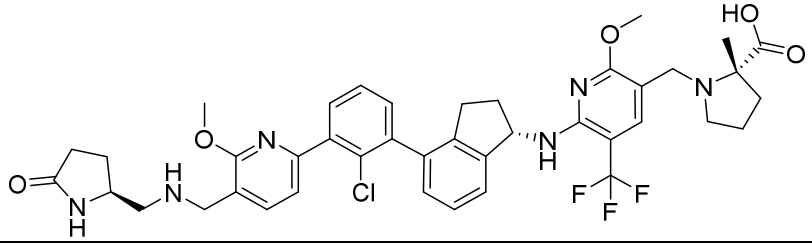
A-33	
A-34	
A-35	
A-36	
A-37	
A-38	
A-39	

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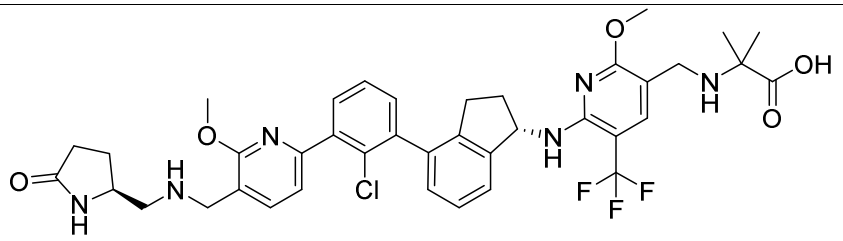
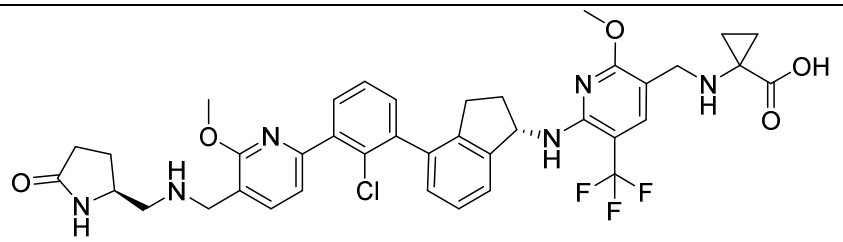
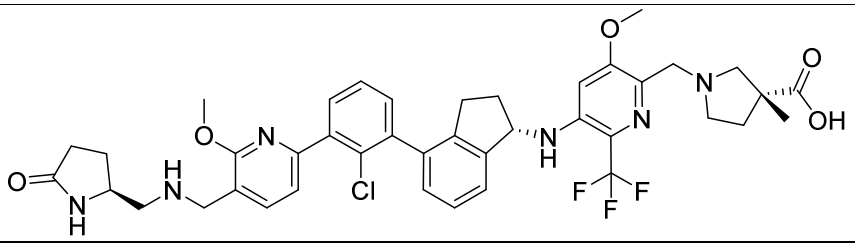
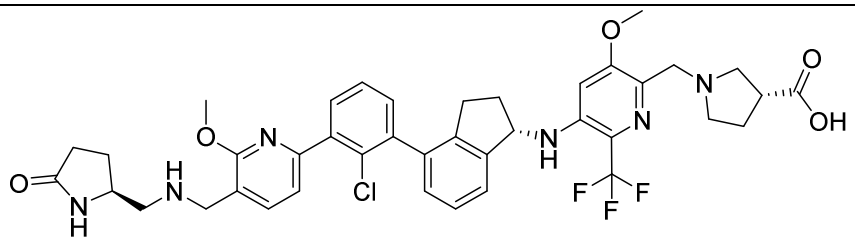
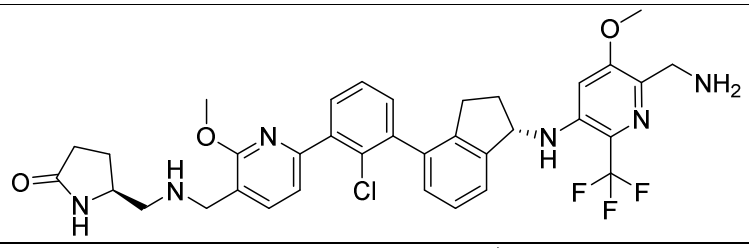
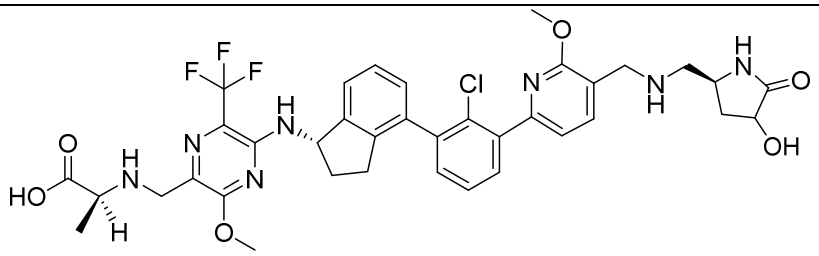
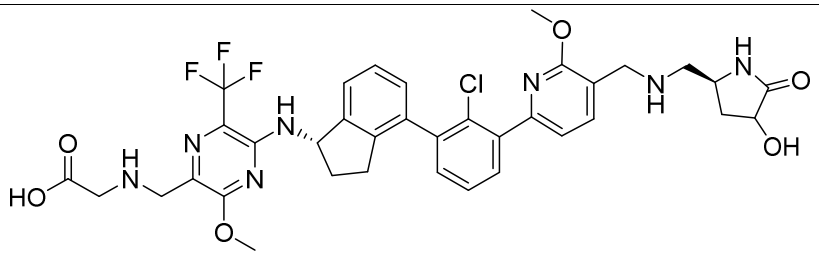
A-40	
A-41	
A-42	
A-43	
A-44	
A-45	
A-46	

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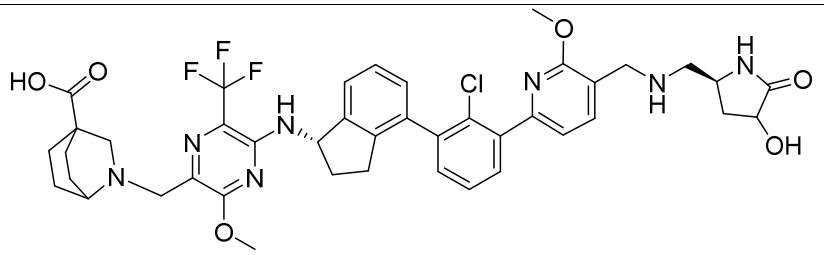
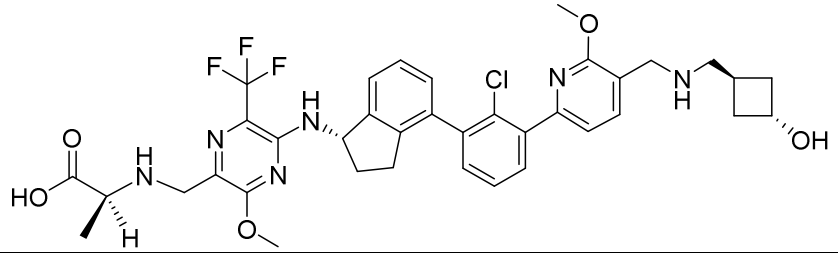
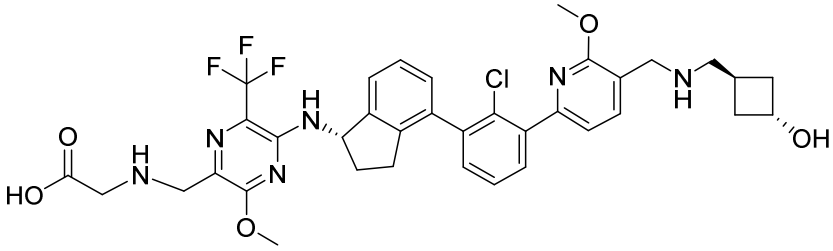
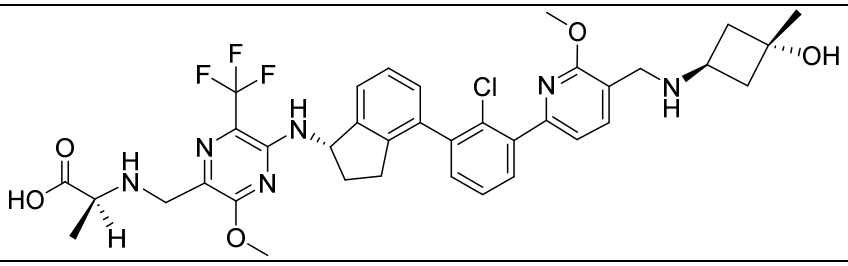
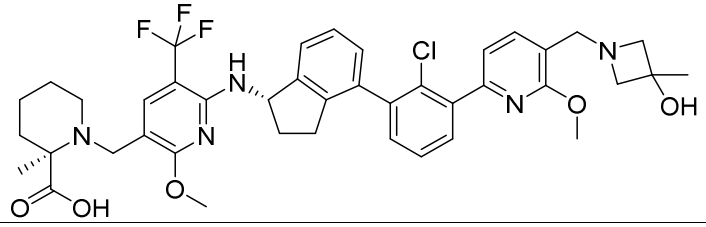
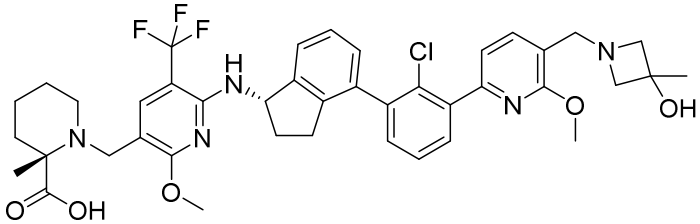
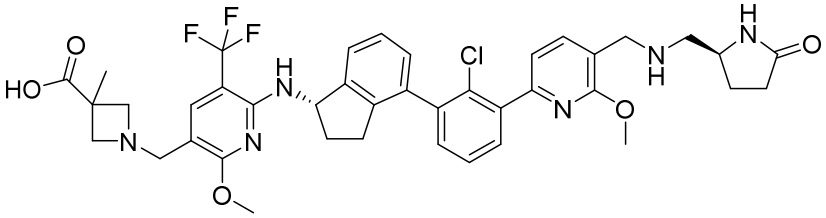
A-47	
A-48	
A-49	
A-50	
A-51	
A-52	
A-53	

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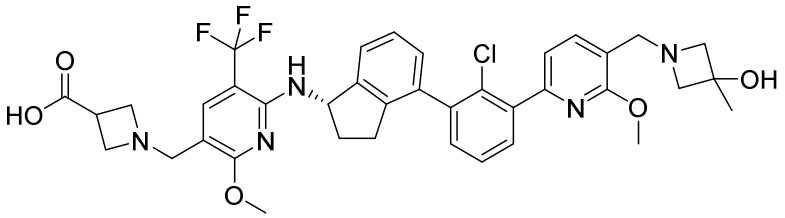
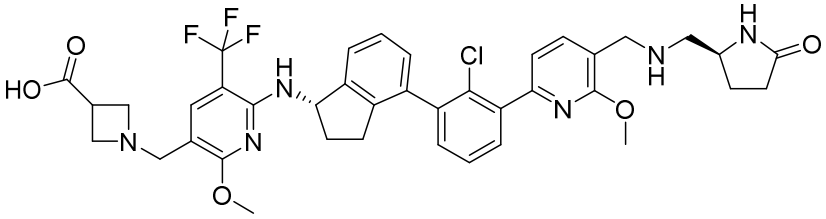
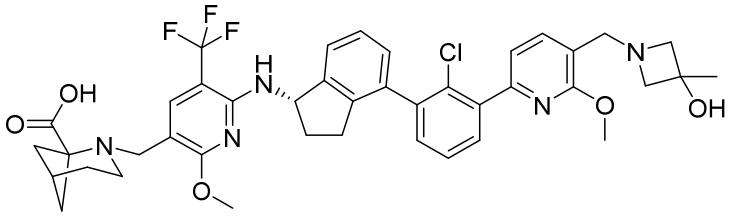
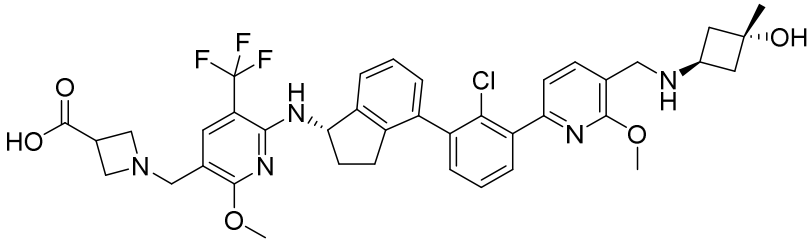
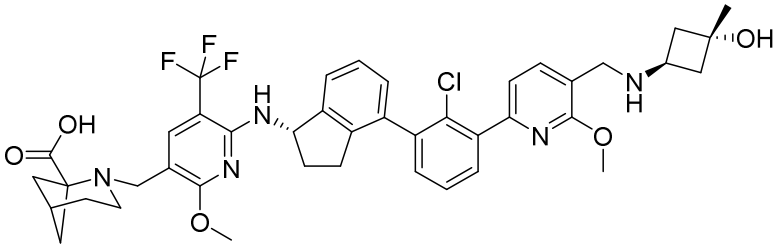
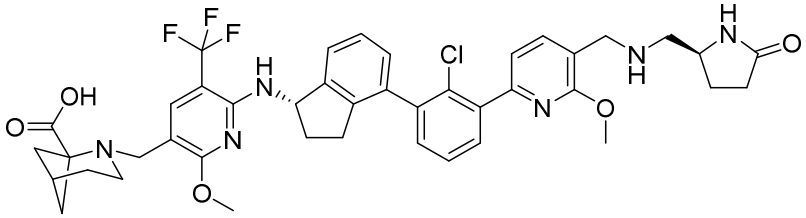
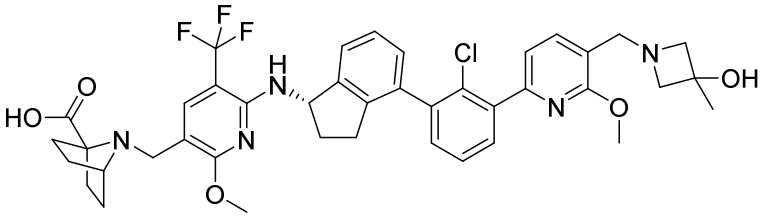
A-54	
A-55	
A-56	
A-57	
A-58	
A-59	
A-60	

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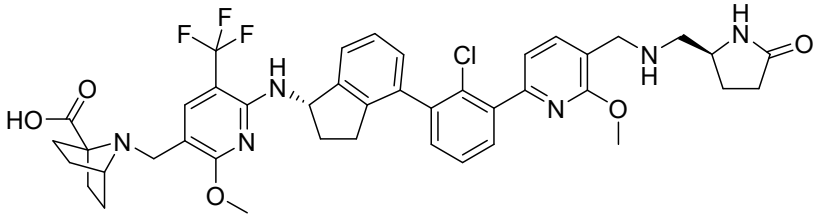
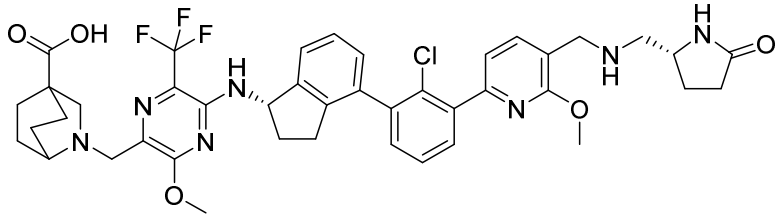
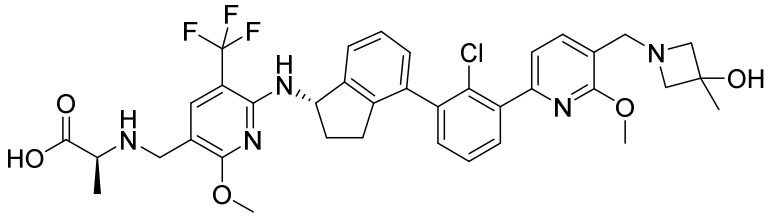
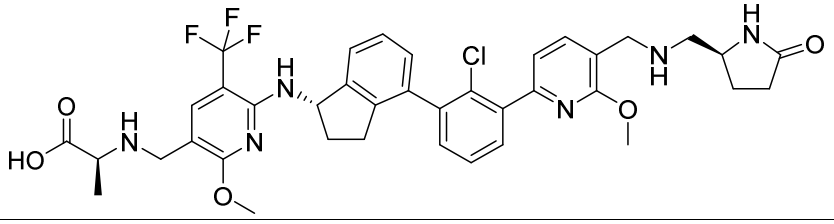
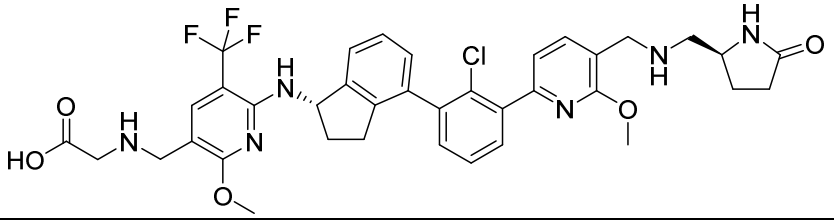
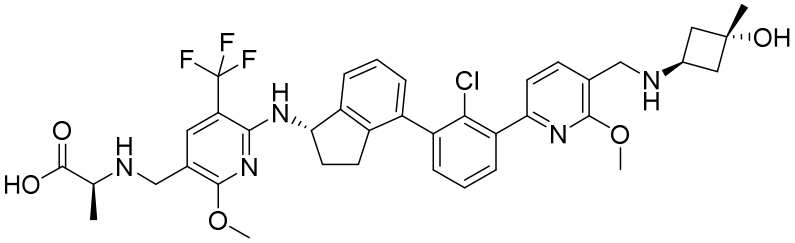
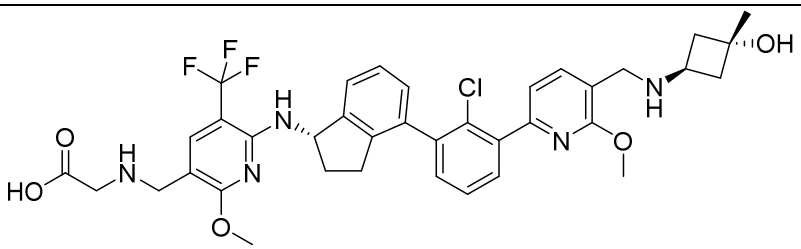
A-61	
A-62	
A-63	
A-64	
A-65	
A-66	
A-67	

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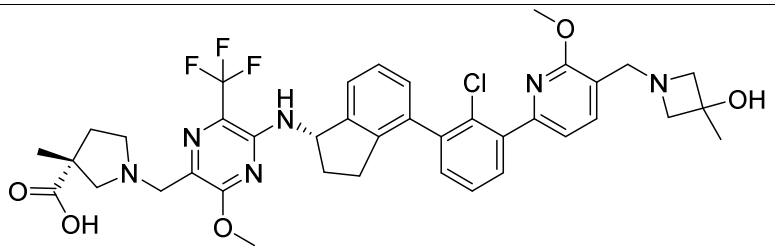
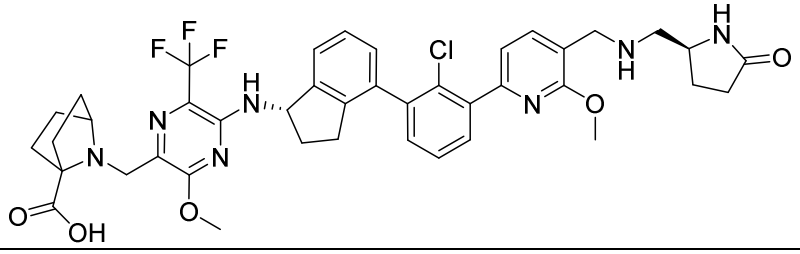
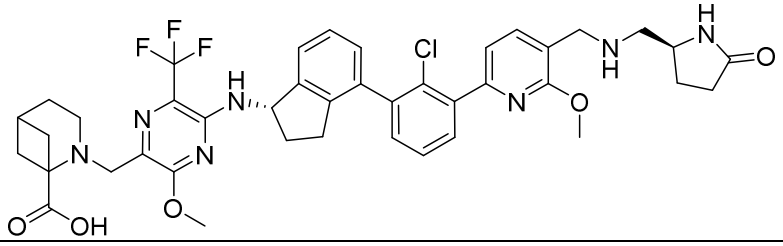
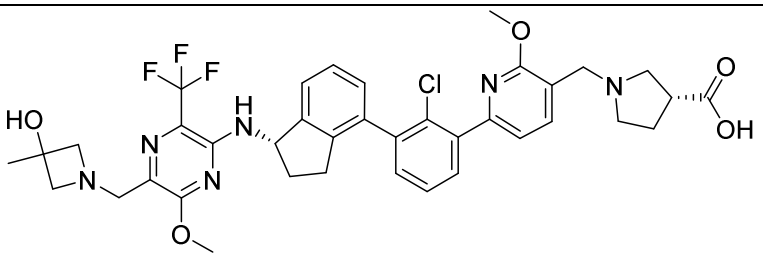
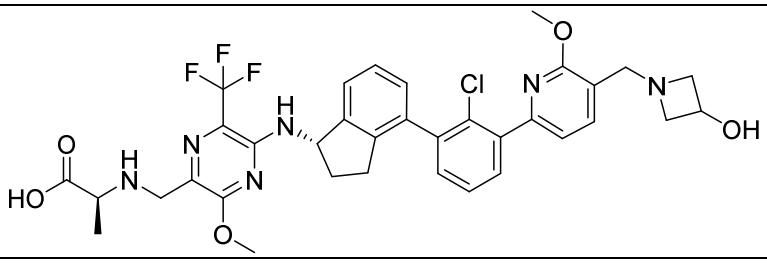
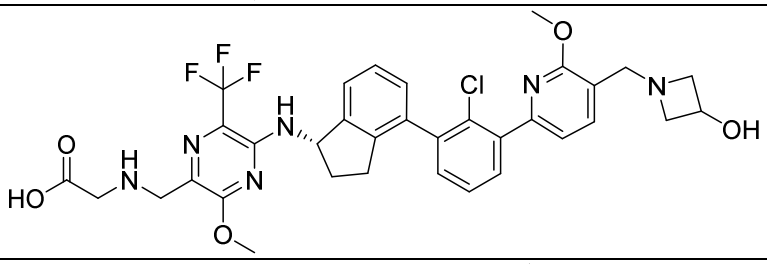
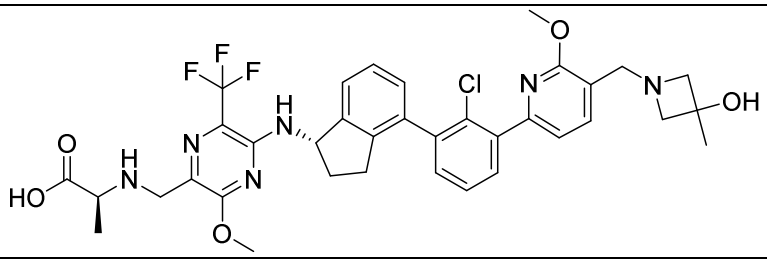
A-68	
A-69	
A-70	
A-71	
A-72	
A-73	
A-74	

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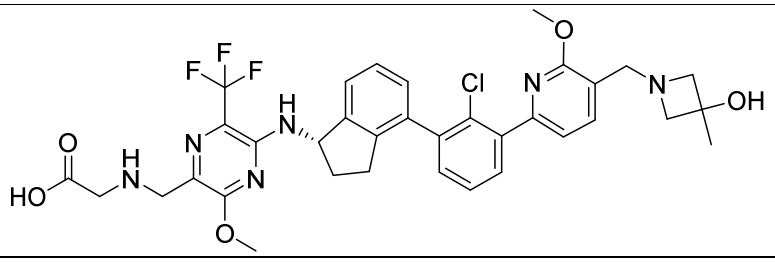
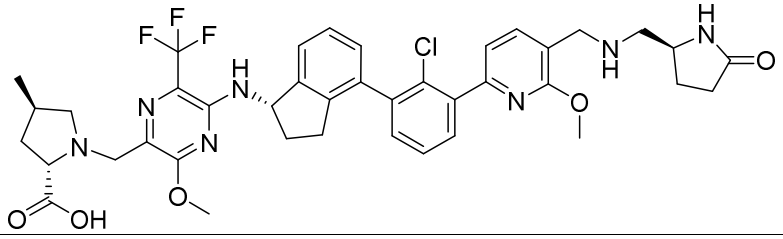
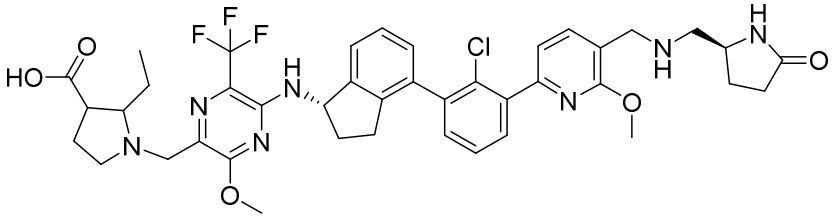
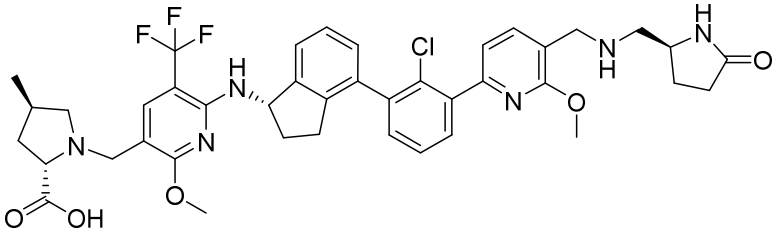
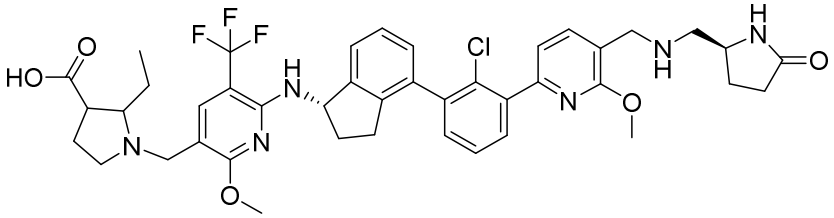
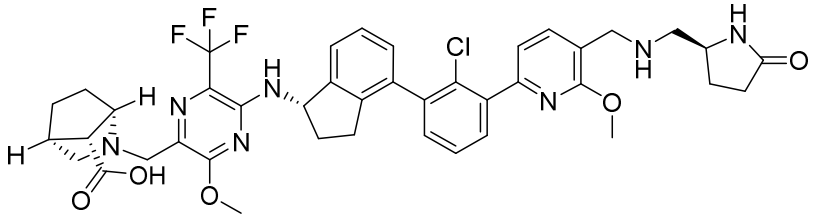
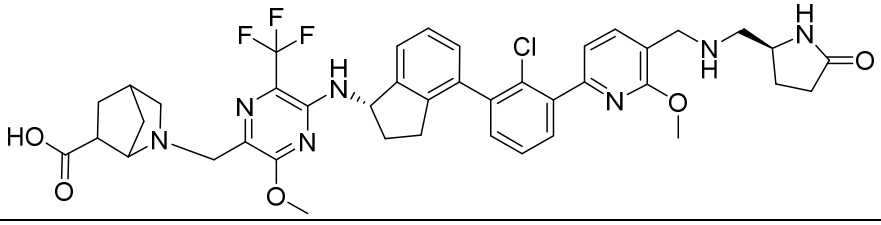
A-75	
A-76	
A-77	
A-78	
A-79	
A-80	
A-81	

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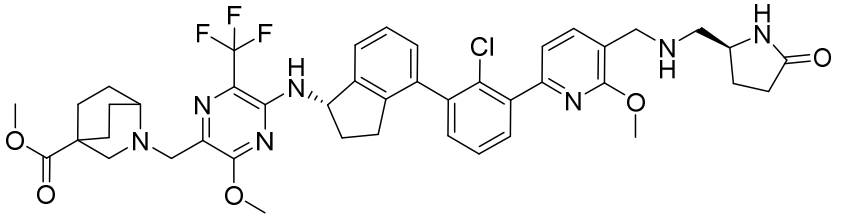
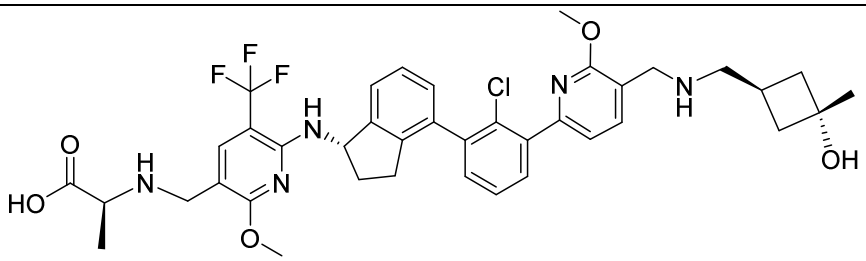
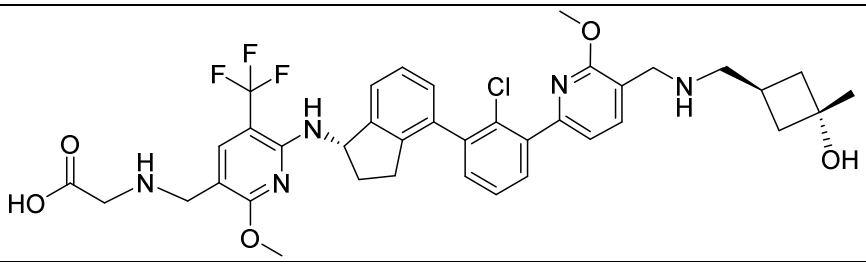
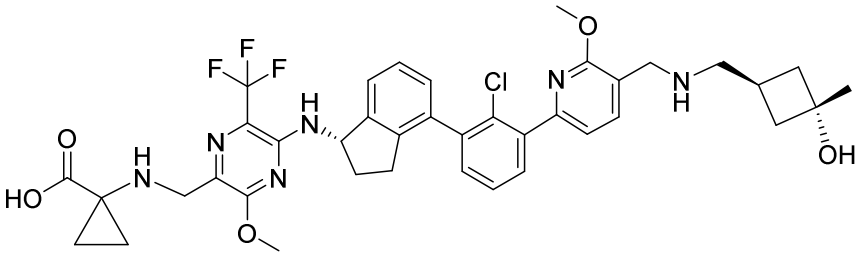
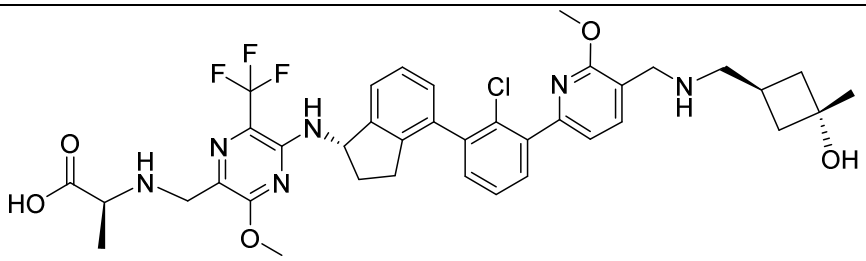
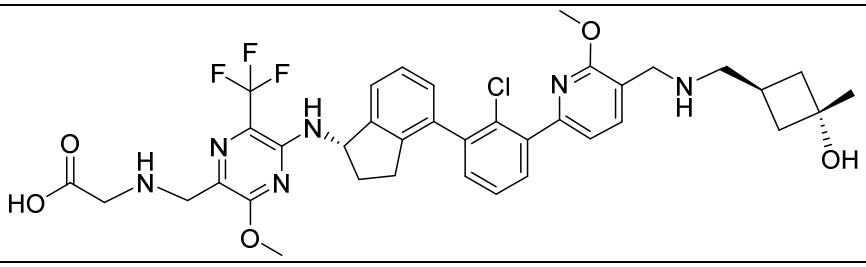
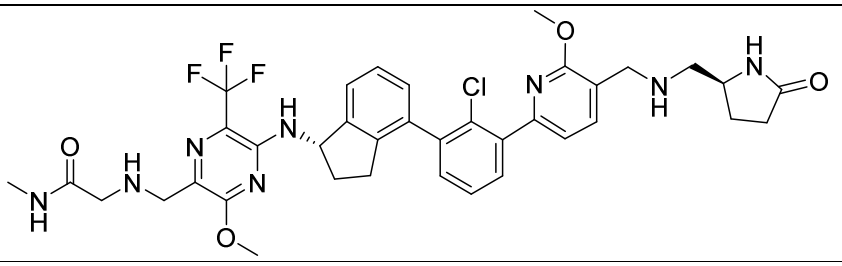
A-82	
A-83	
A-84	
A-85	
A-86	
A-87	
A-88	

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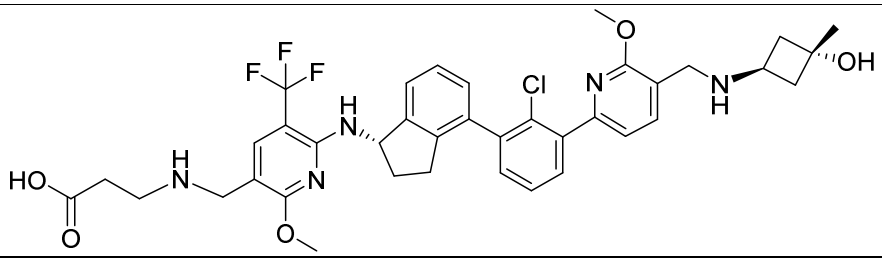
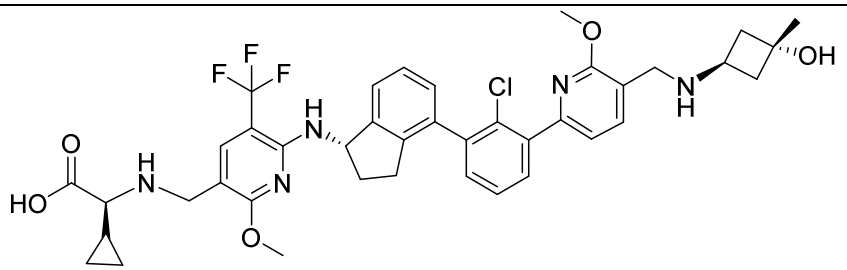
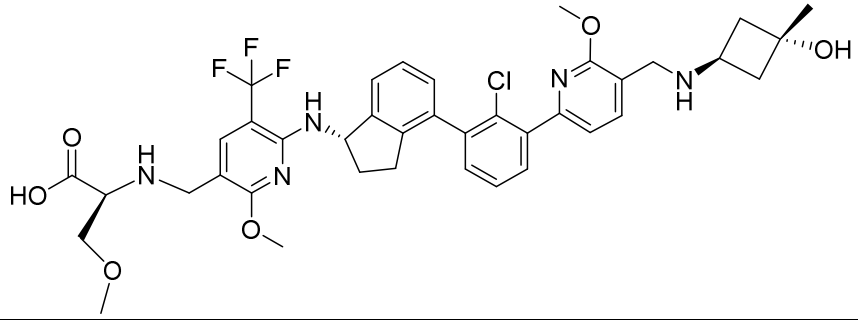
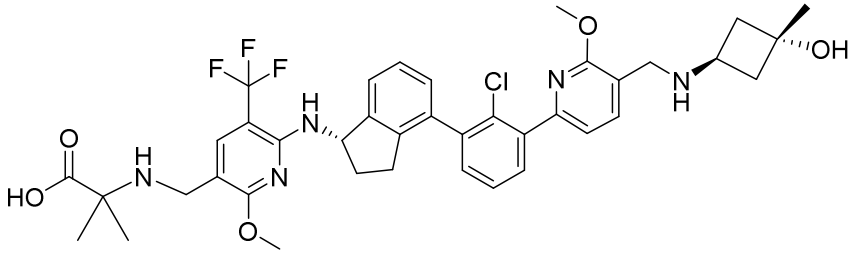
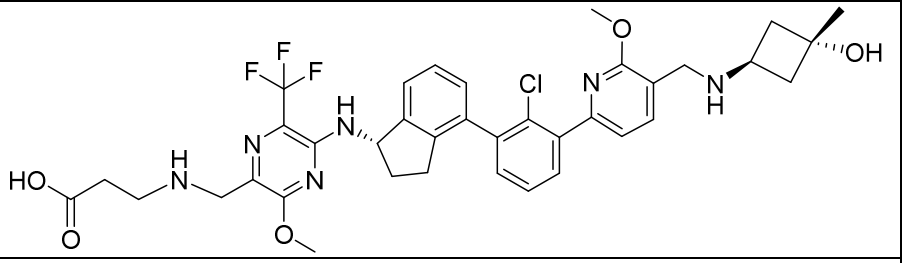
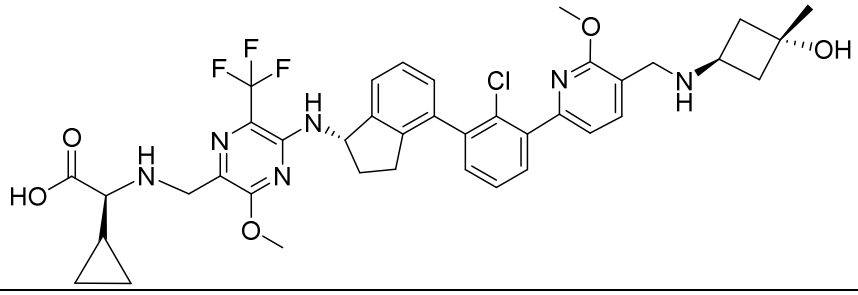
A-89	
A-90	
A-91	
A-92	
A-93	
A-94	

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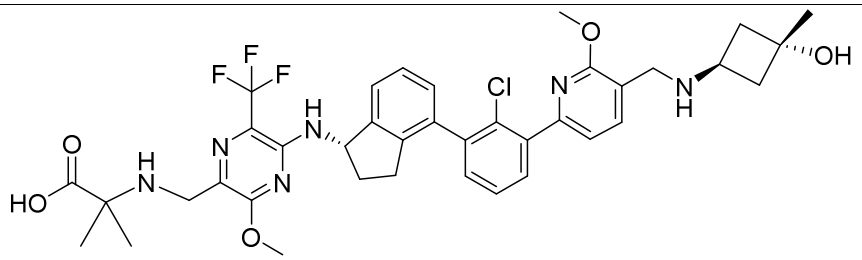
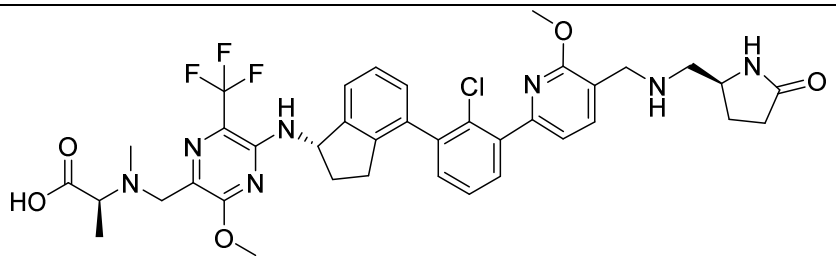
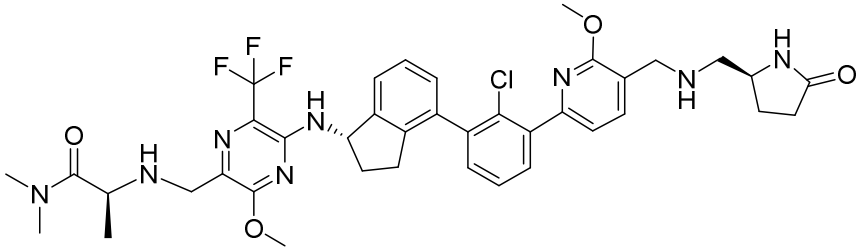
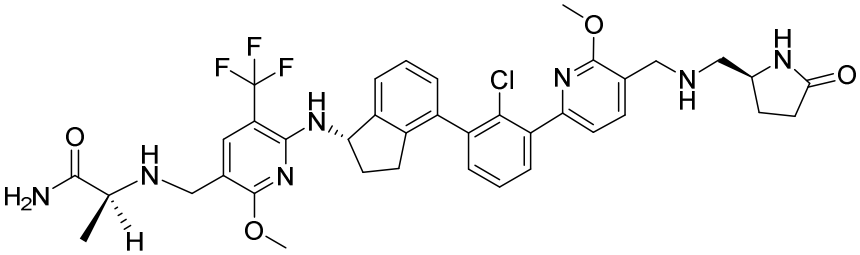
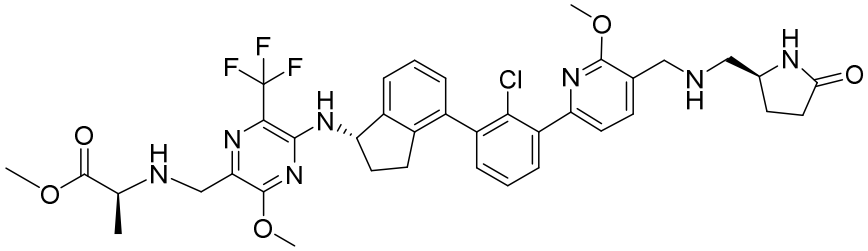
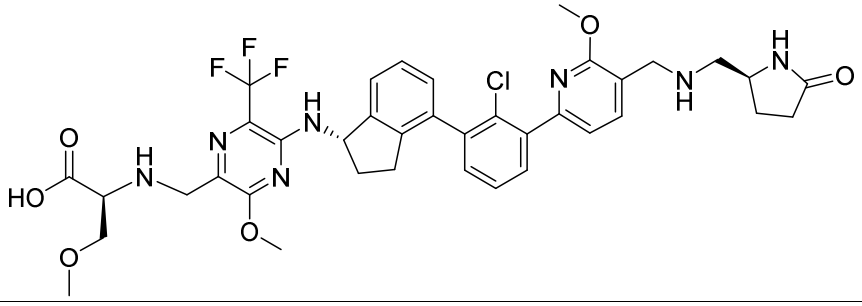
A-95	
A-96	
A-97	
A-98	
A-99	
A-100	

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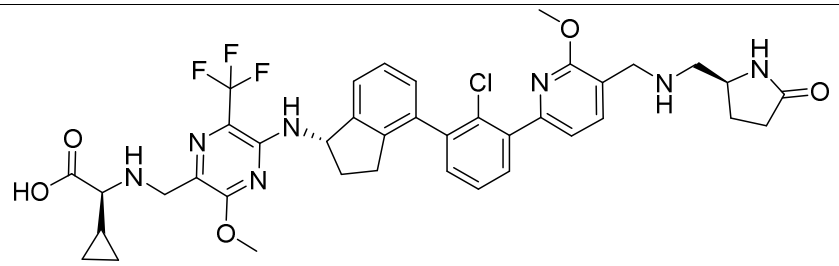
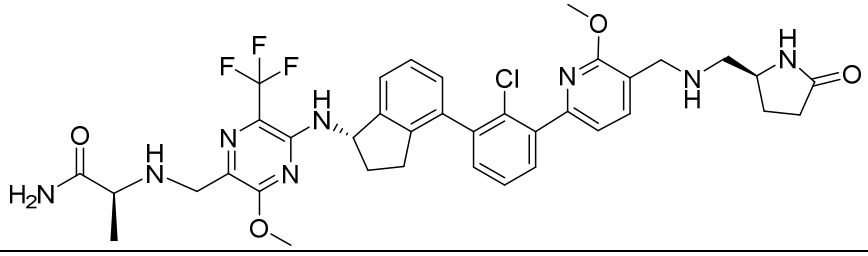
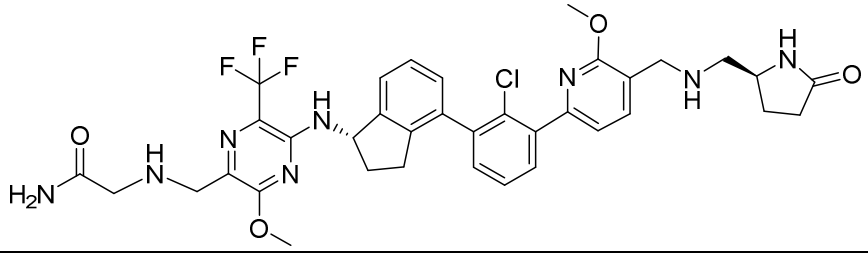
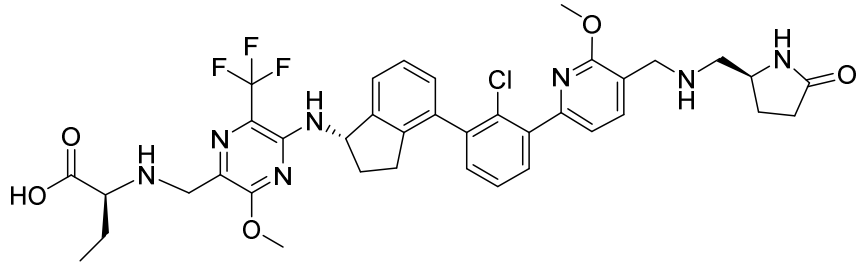
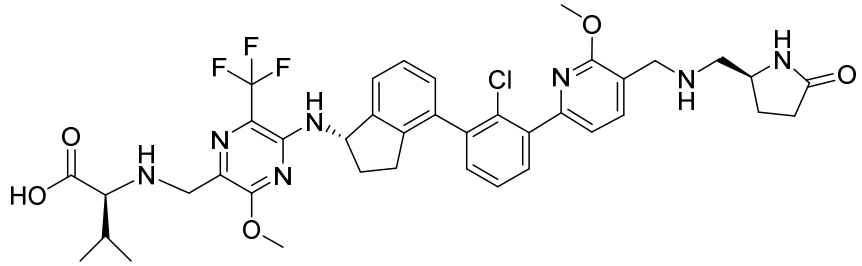
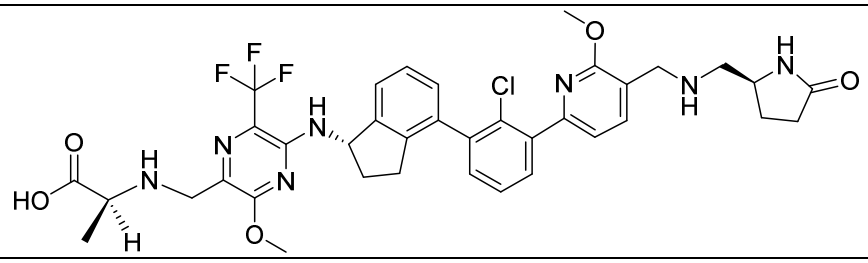
A-101	
A-102	
A-103	
A-104	
A-105	
A-106	

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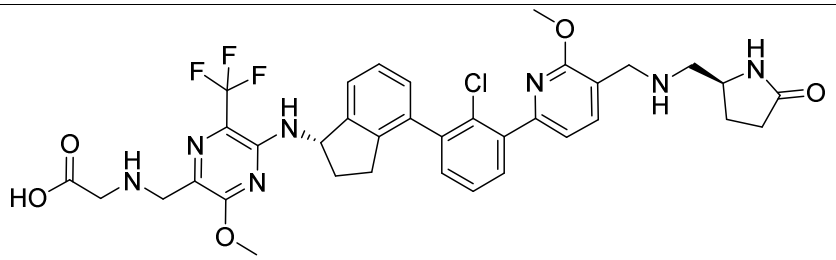
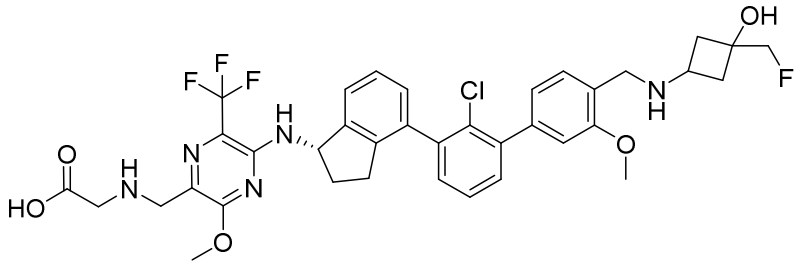
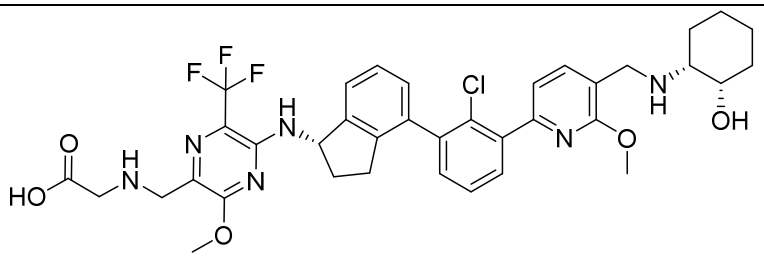
A-107	
A-108	
A-109	

Table 1B

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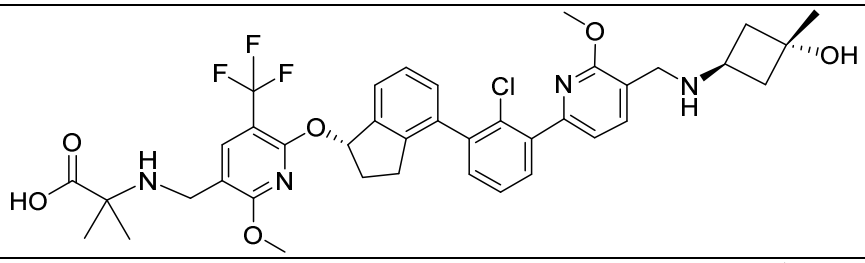
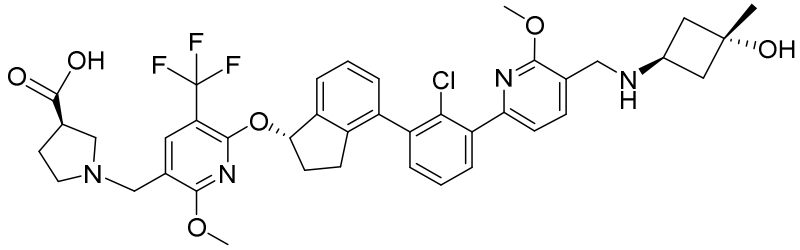
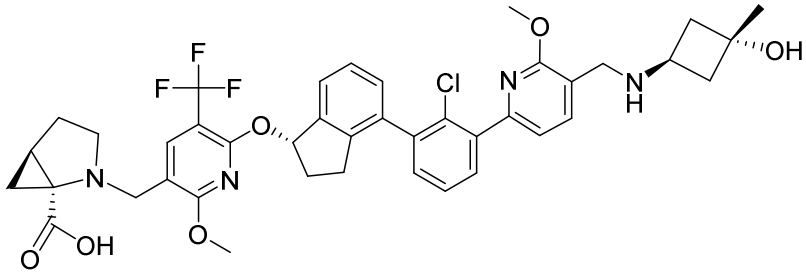
B-1	
B-2	
B-3	

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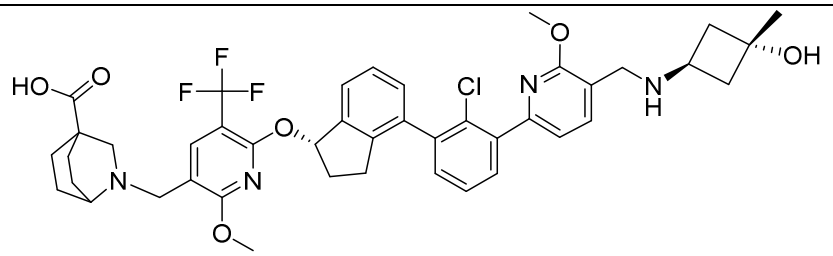
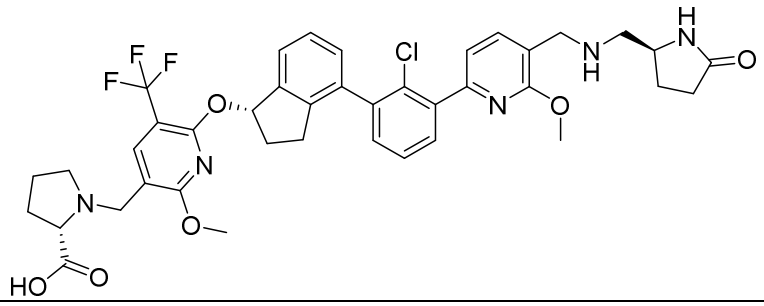
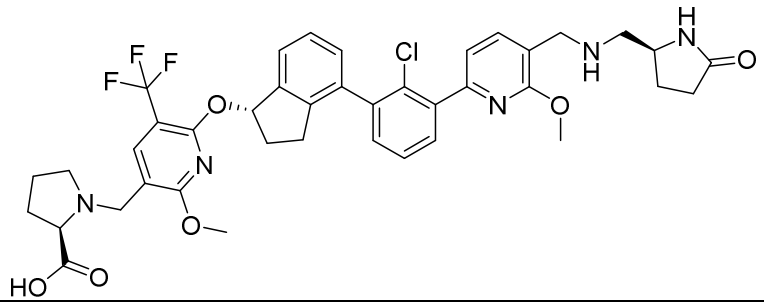
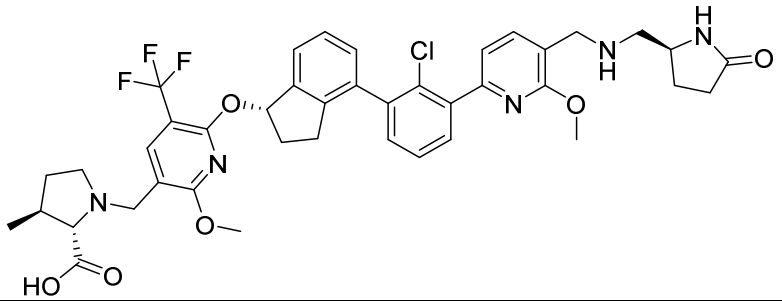
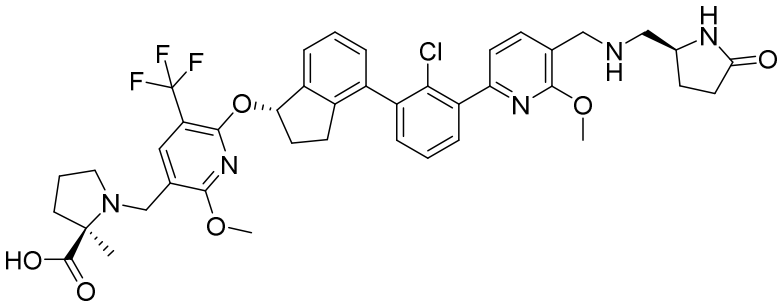
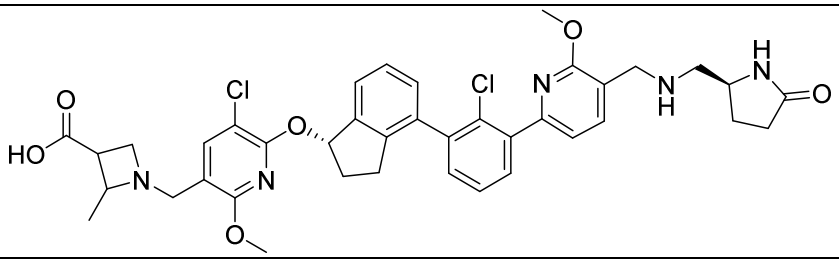
B-4	
B-5	
B-6	
B-7	
B-8	
B-9	

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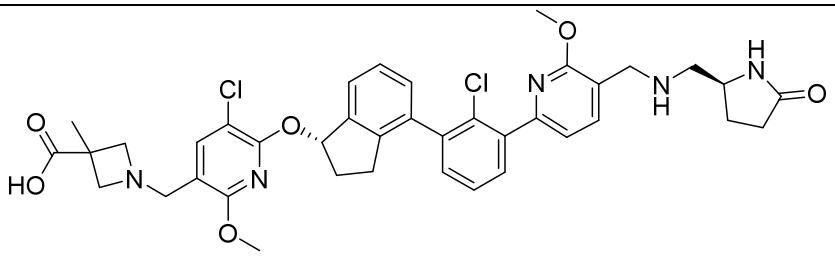
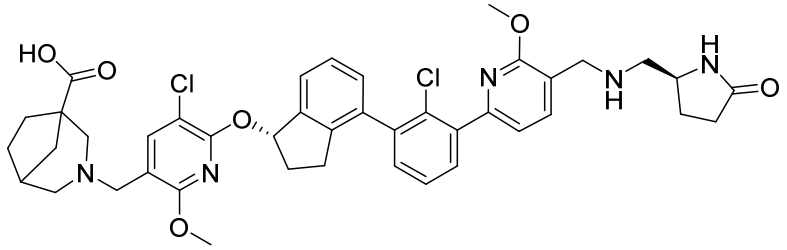
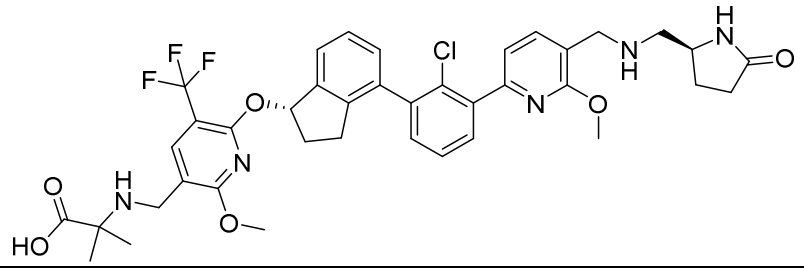
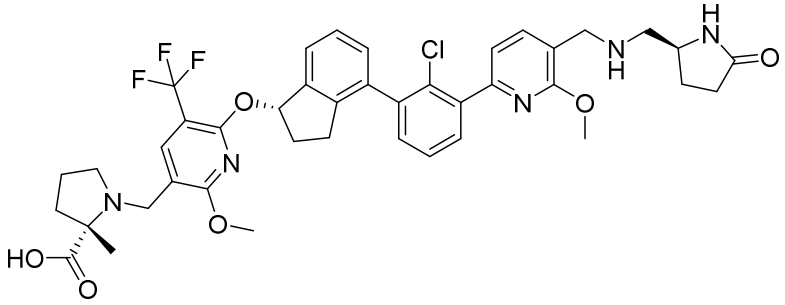
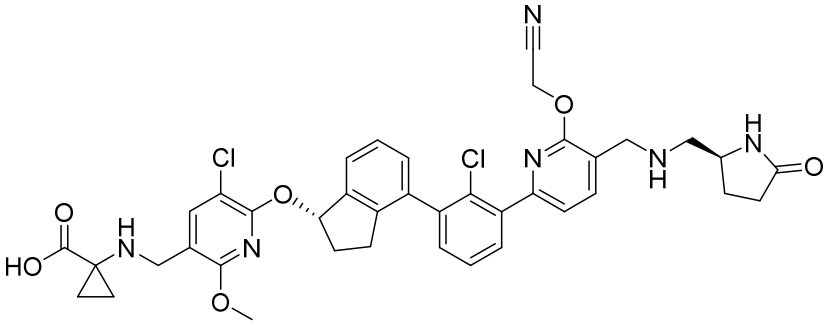
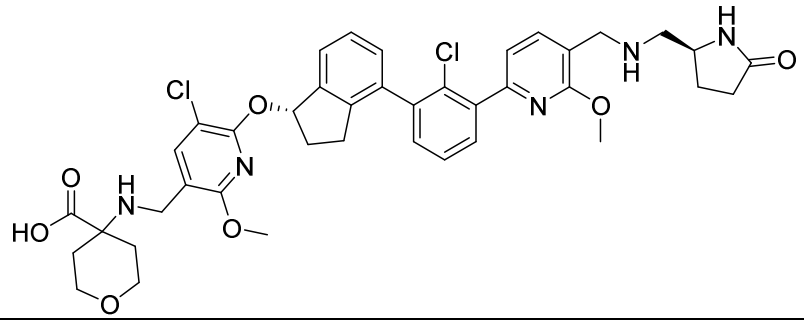
B-10	
B-11	
B-12	
B-13	
B-14	
B-15	

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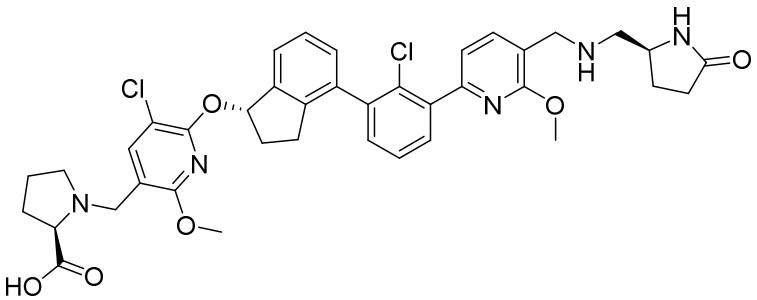
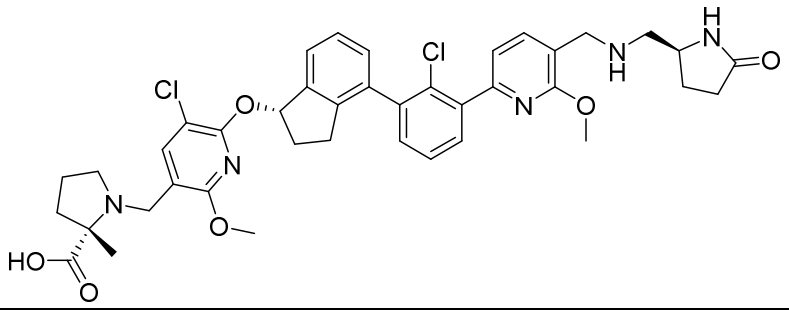
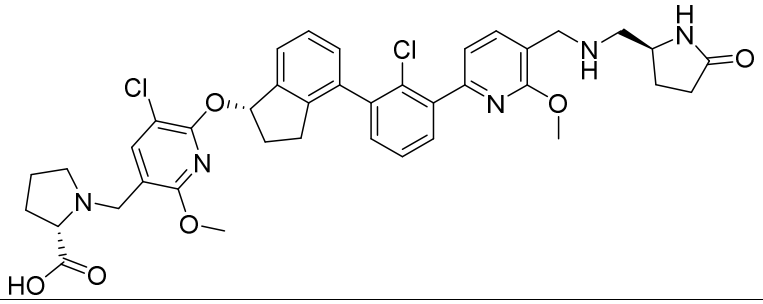
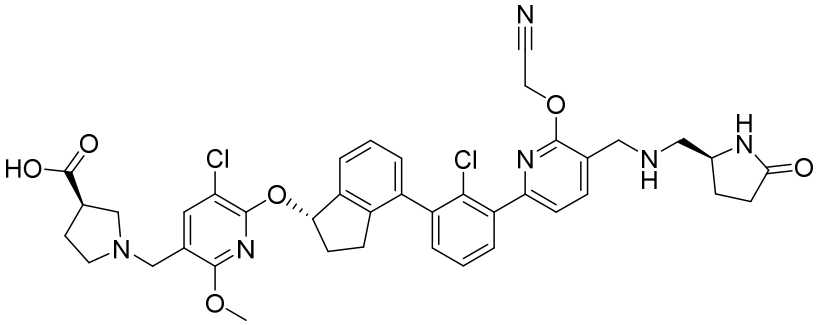
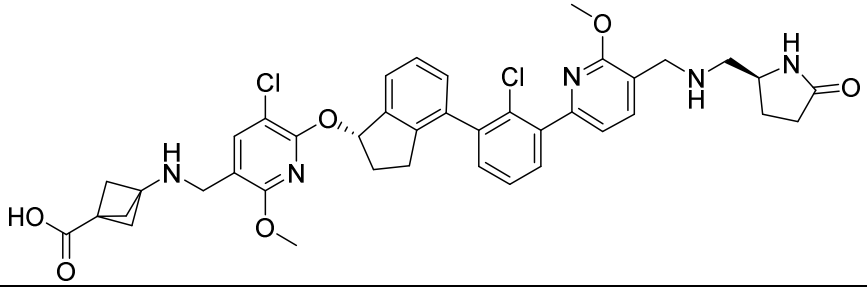
B-16	
B-17	
B-18	
B-19	
B-20	

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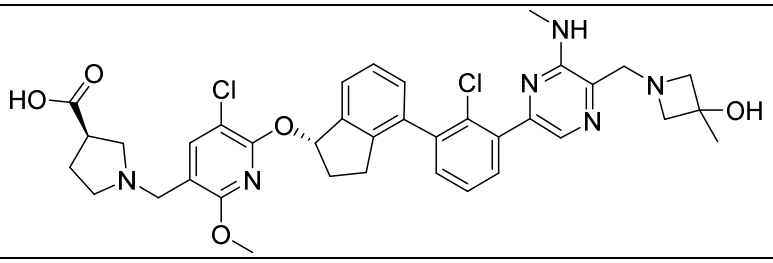
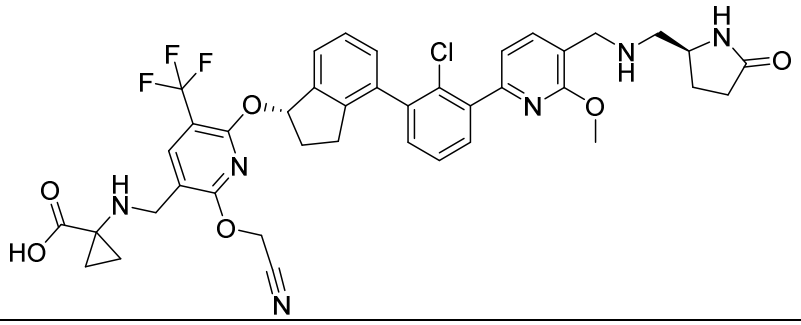
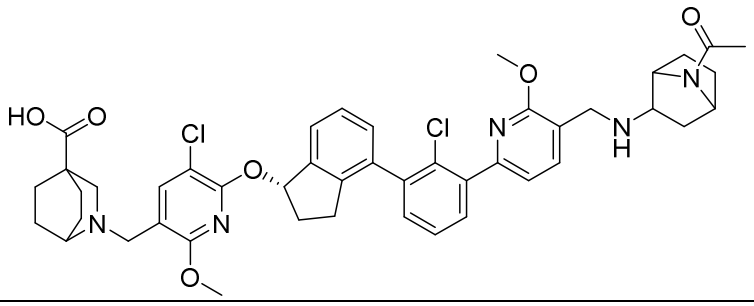
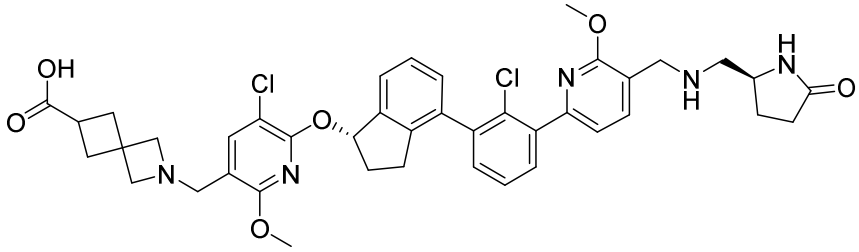
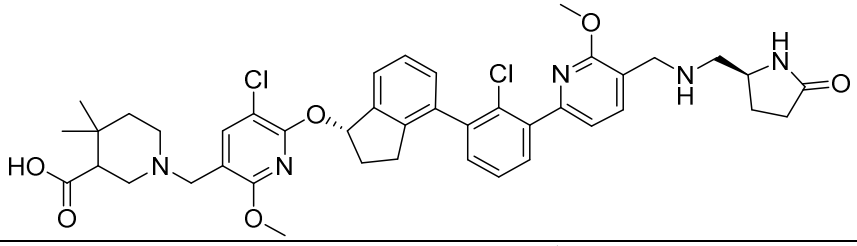
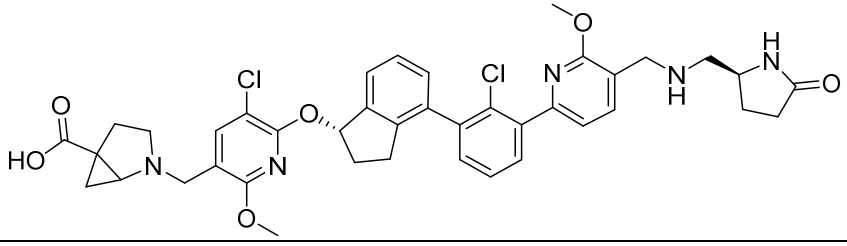
B-21	
B-22	
B-23	
B-24	
B-25	
B-26	

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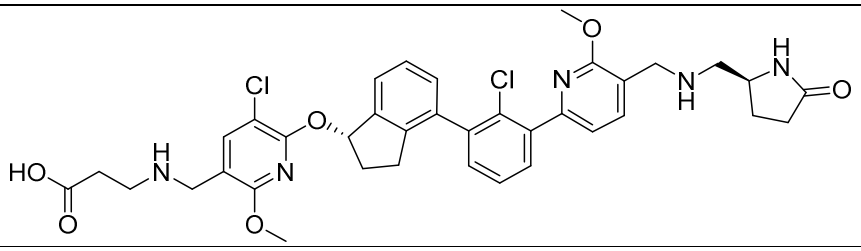
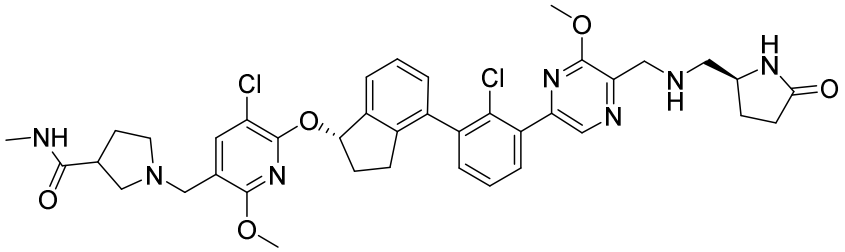
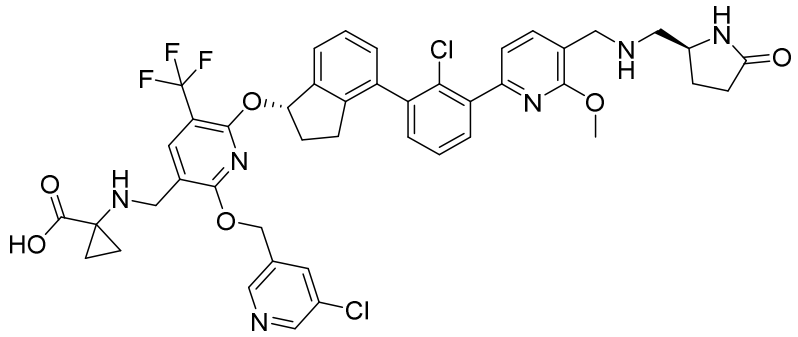
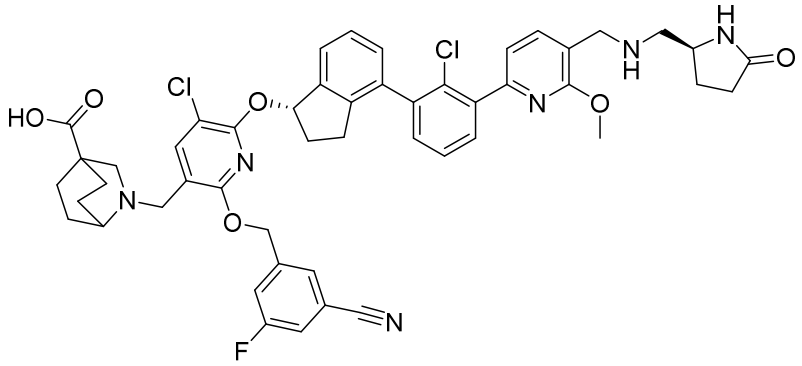
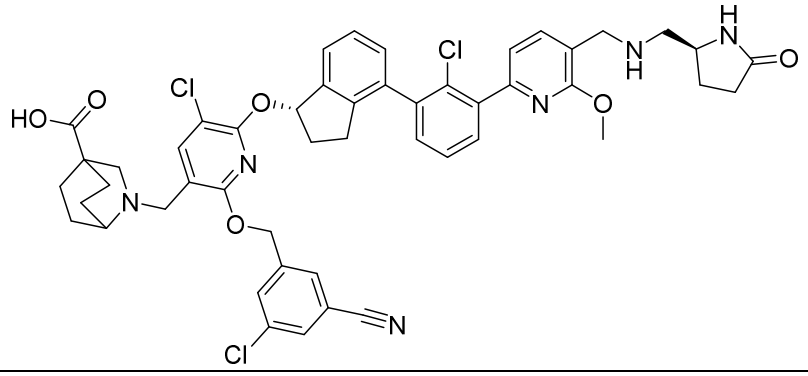
B-27	
B-28	
B-29	
B-30	
B-31	

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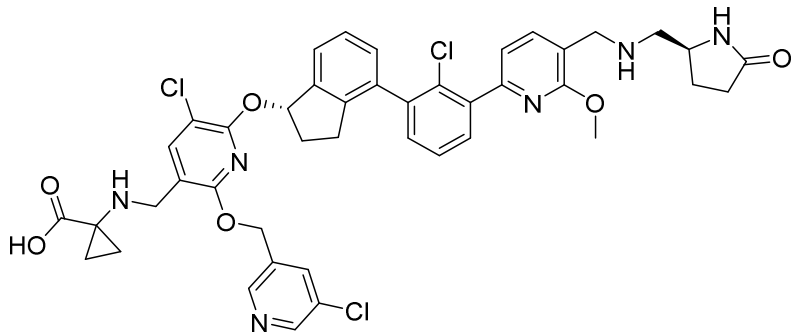
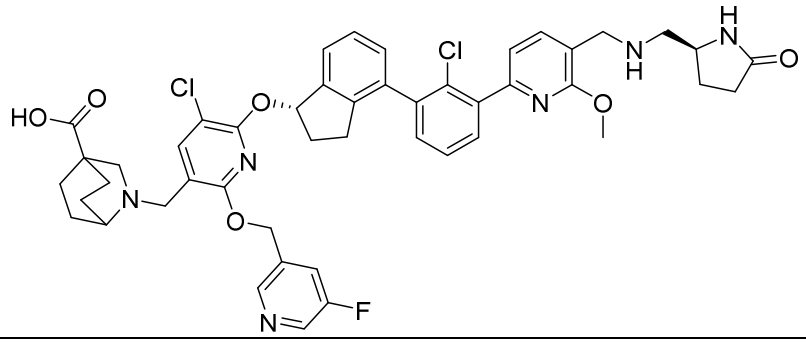
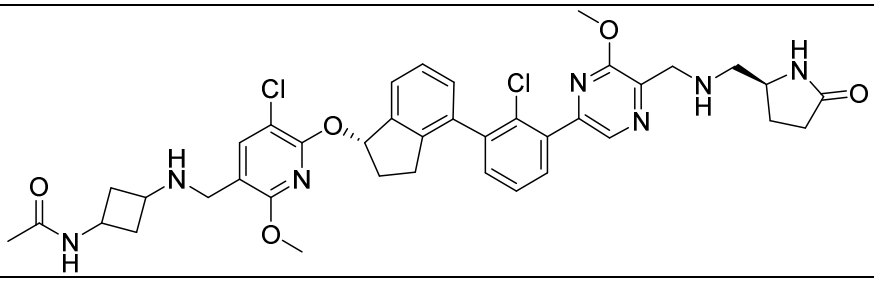
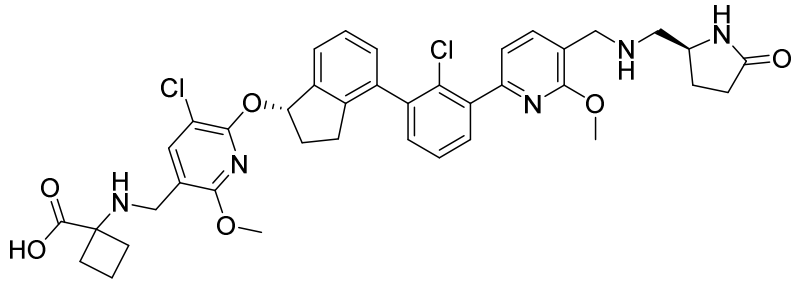
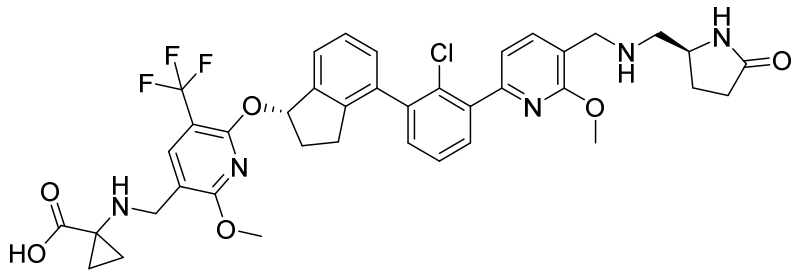
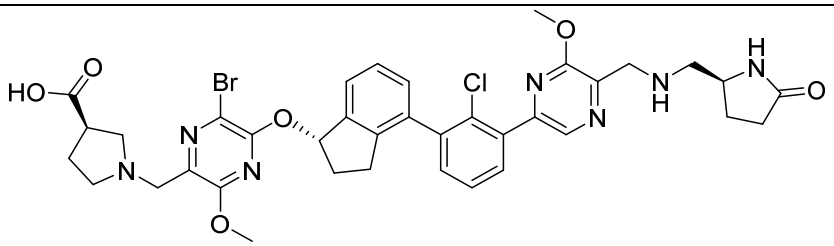
B-32	
B-33	
B-34	
B-35	
B-36	
B-37	

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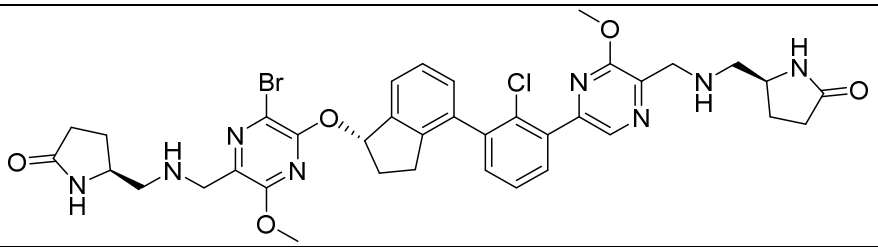
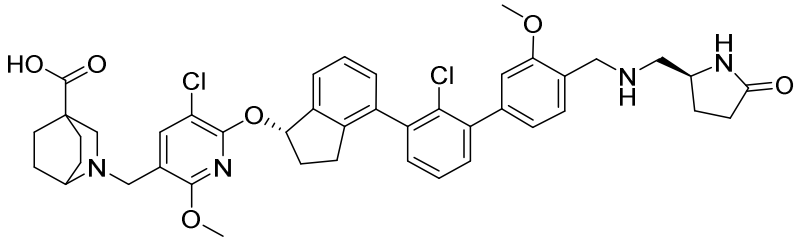
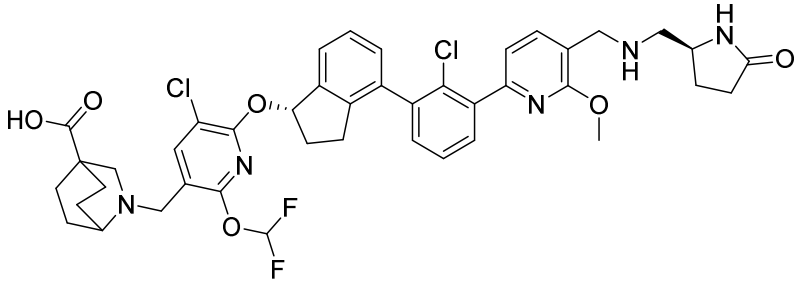
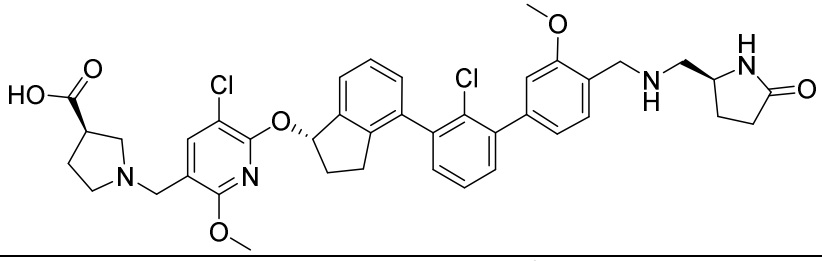
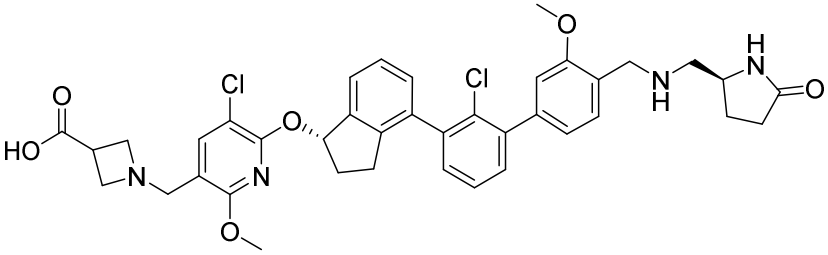
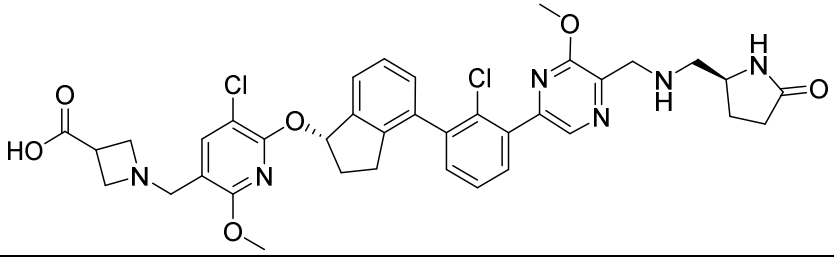
B-38	
B-39	
B-40	
B-41	
B-42	
B-43	

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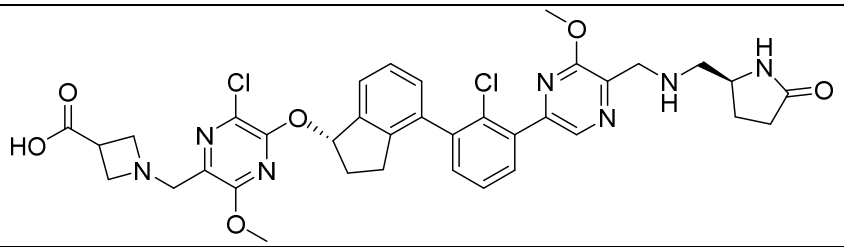
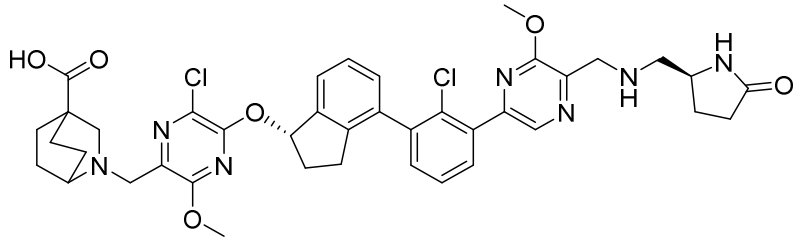
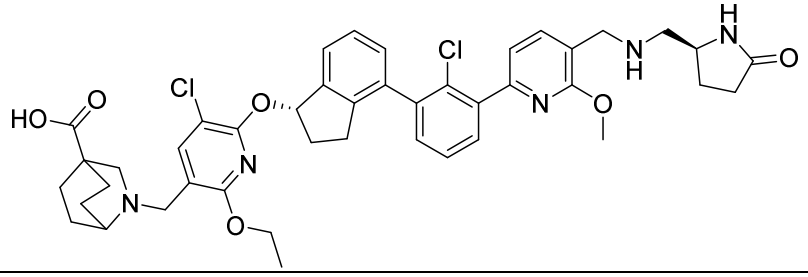
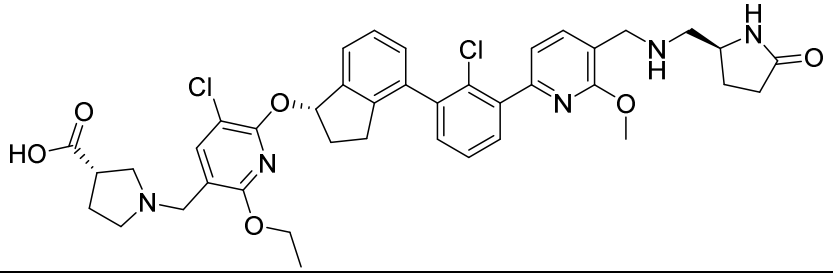
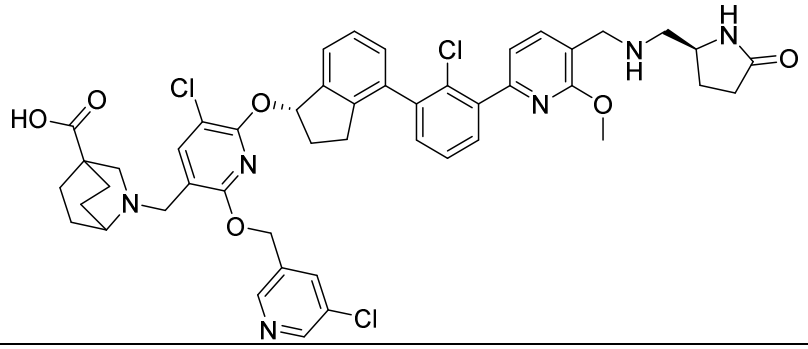
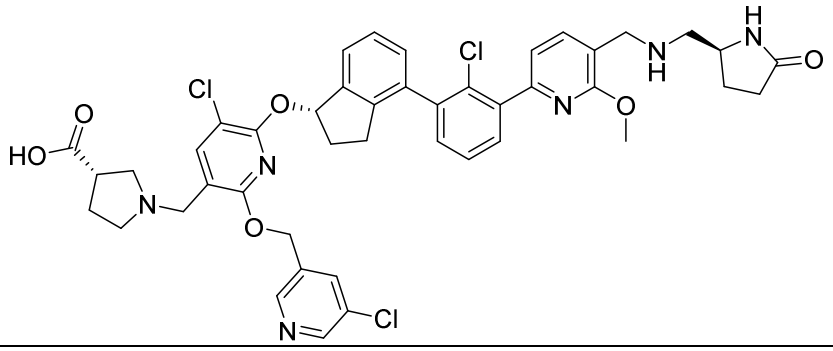
B-44	
B-45	
B-46	
B-47	
B-48	
B-49	

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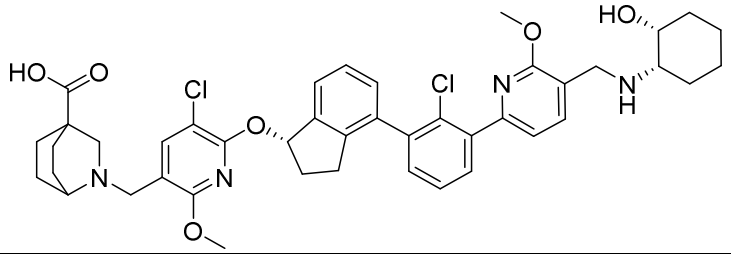
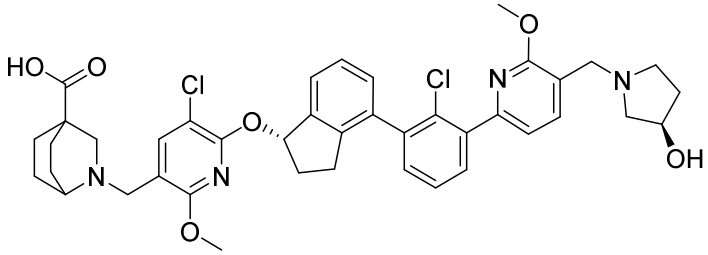
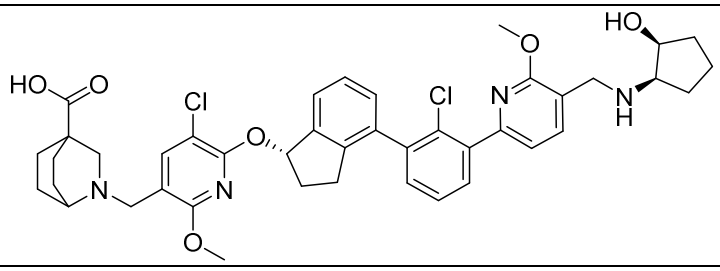
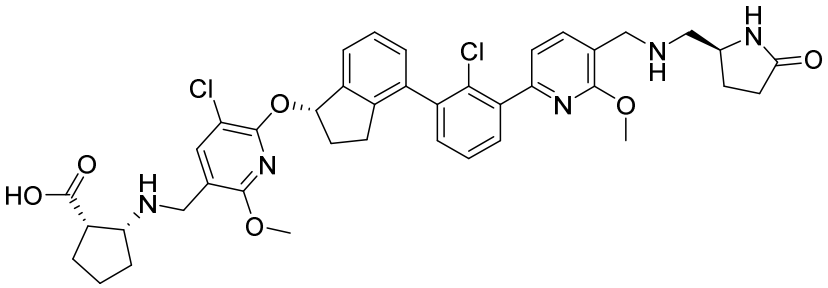
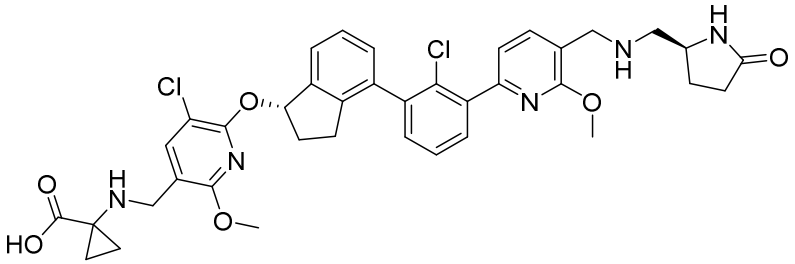
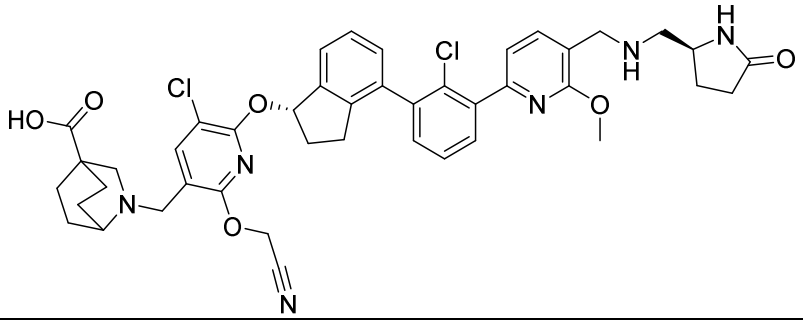
B-50	
B-51	
B-52	
B-53	
B-54	
B-55	

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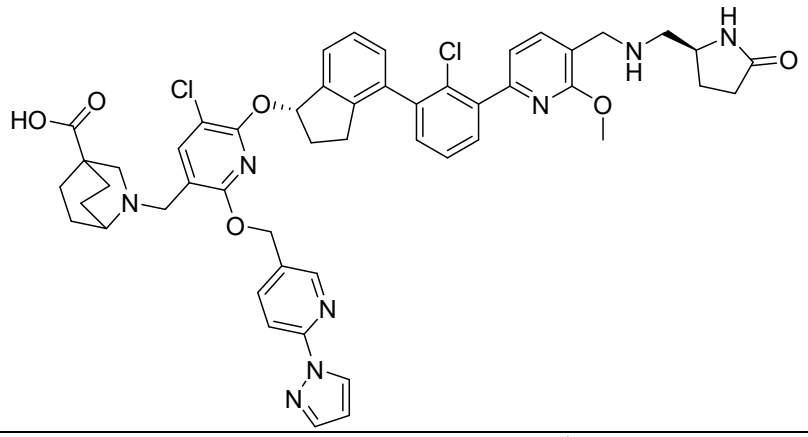
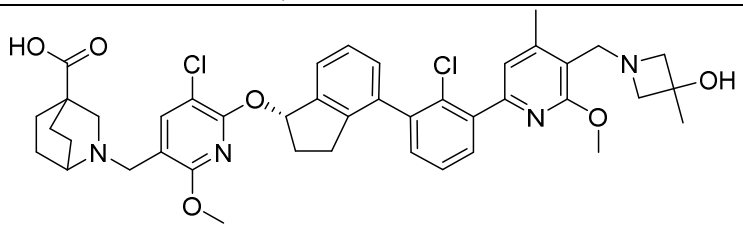
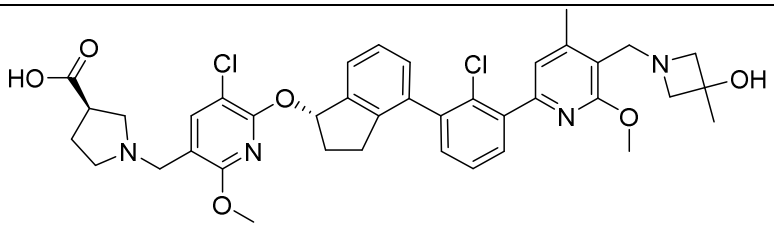
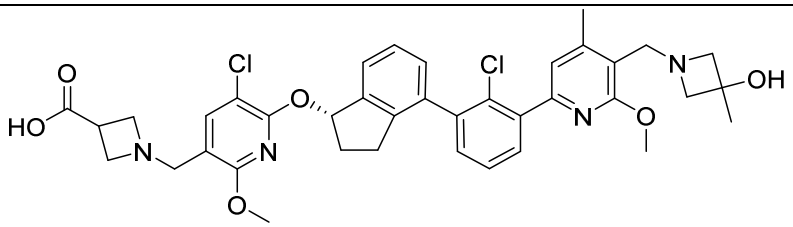
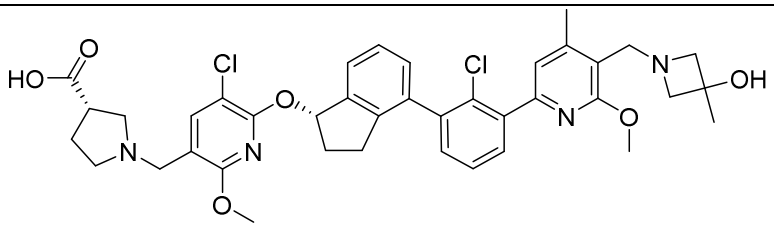
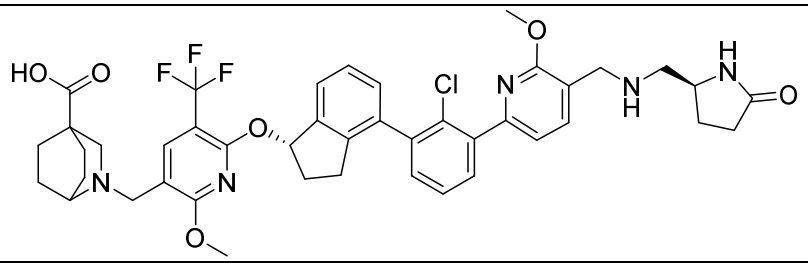
B-56	
B-57	
B-58	
B-59	
B-60	
B-61	

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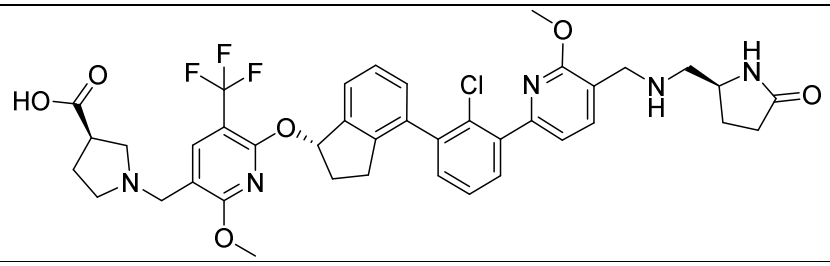
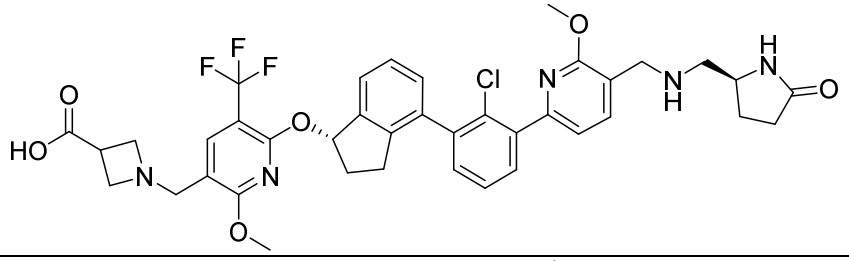
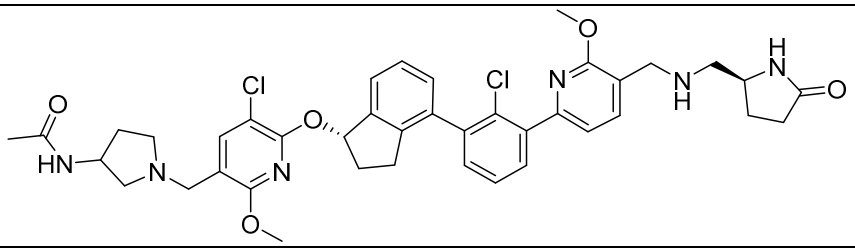
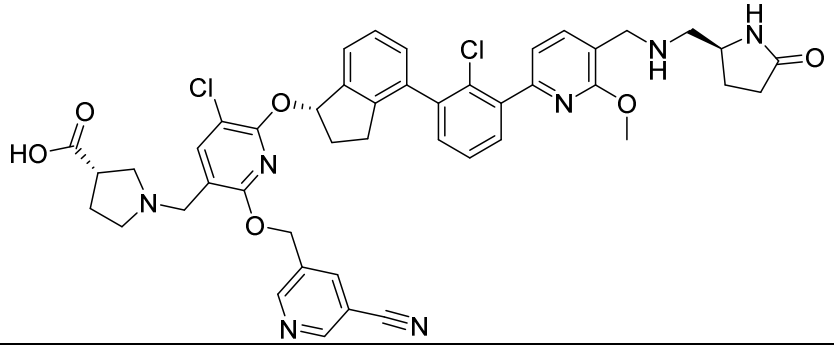
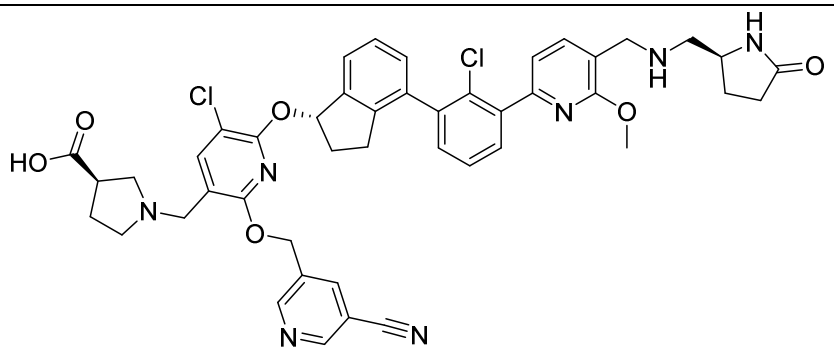
B-62	
B-63	
B-64	
B-65	
B-66	

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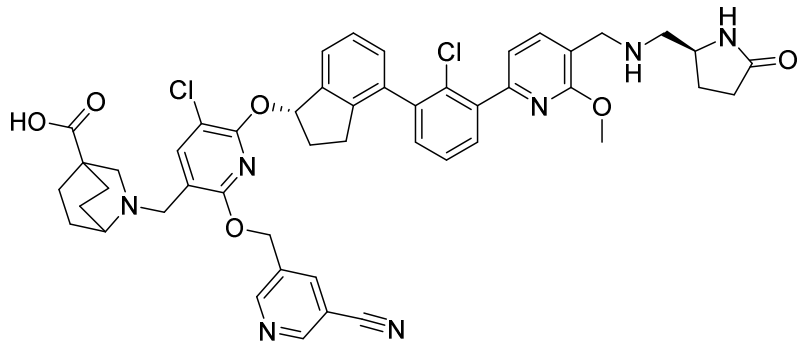
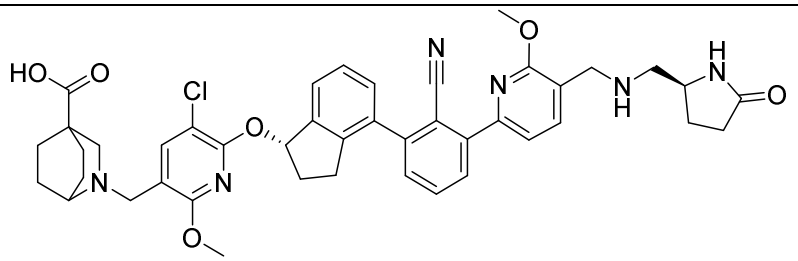
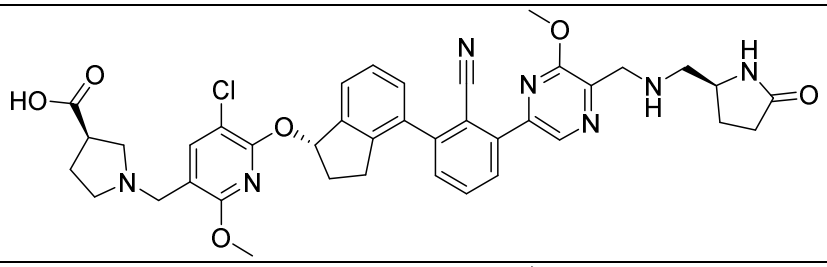
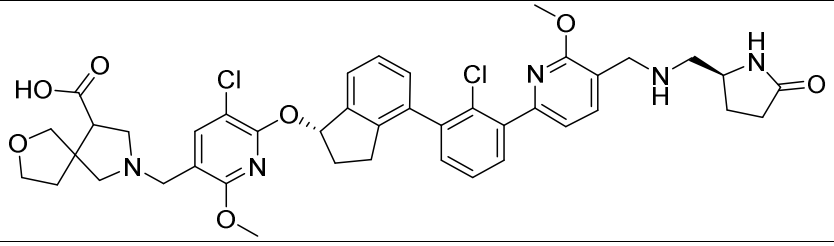
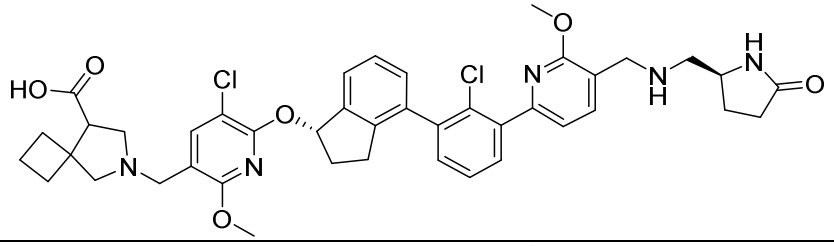
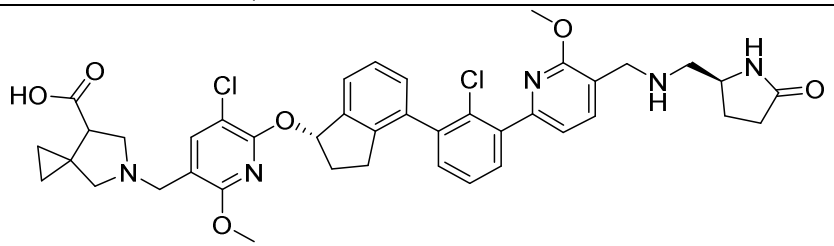
B-67	
B-68	
B-69	
B-70	
B-71	
B-72	

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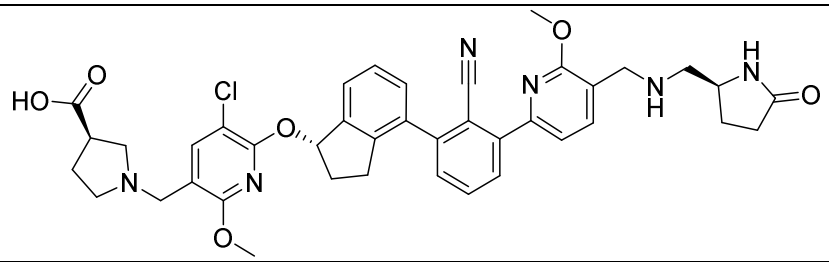
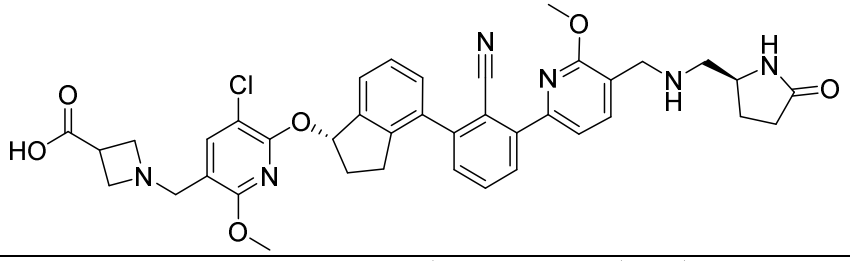
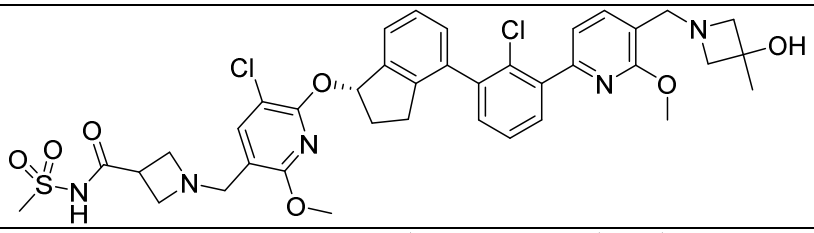
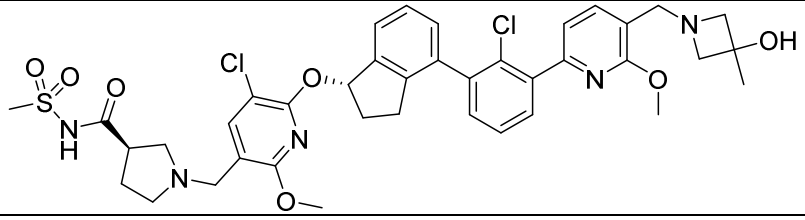
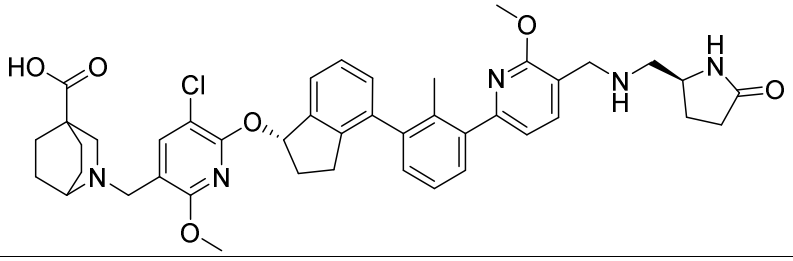
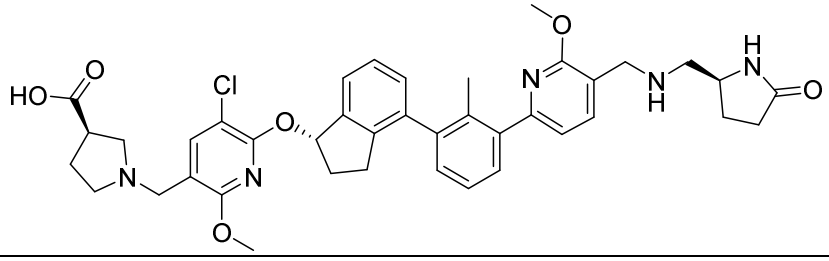
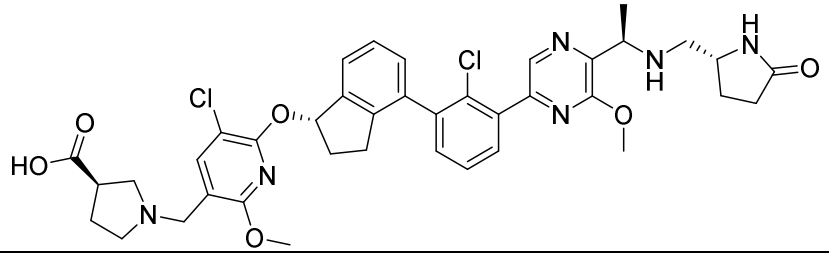
B-73	
B-74	
B-75	
B-76	
B-77	
B-78	
B-79	

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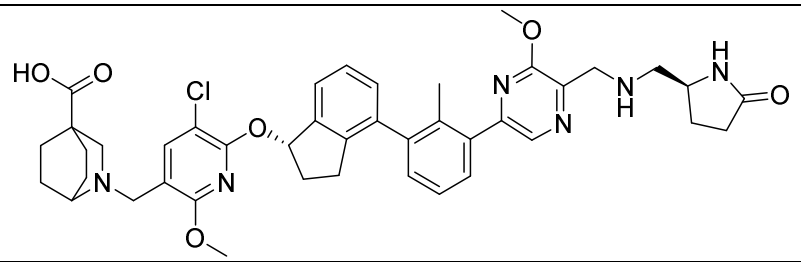
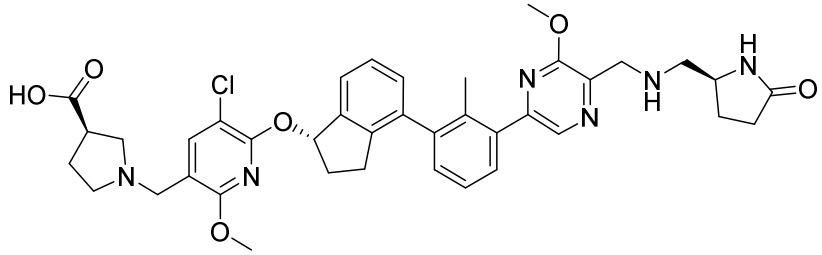
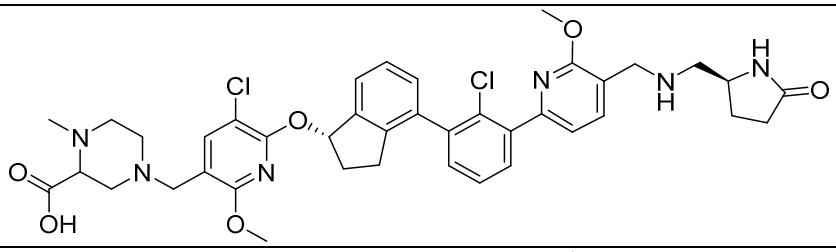
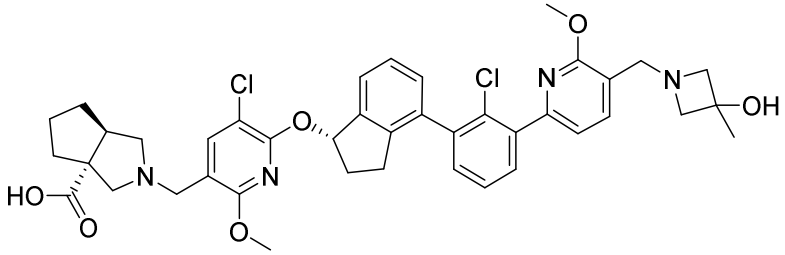
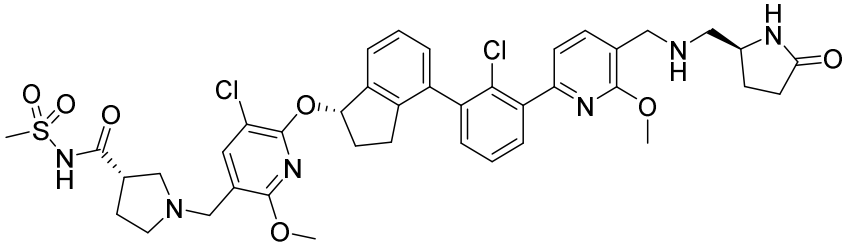
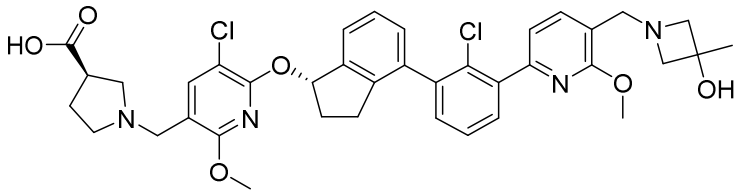
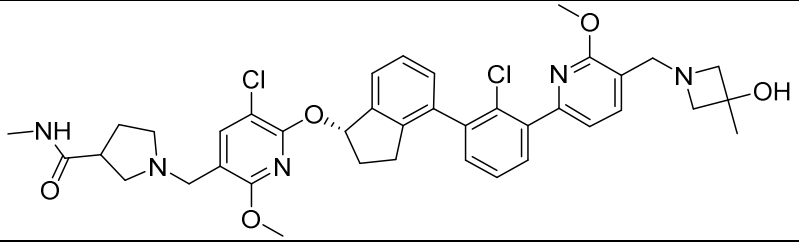
B-80	
B-81	
B-82	
B-83	
B-84	
B-85	
B-86	

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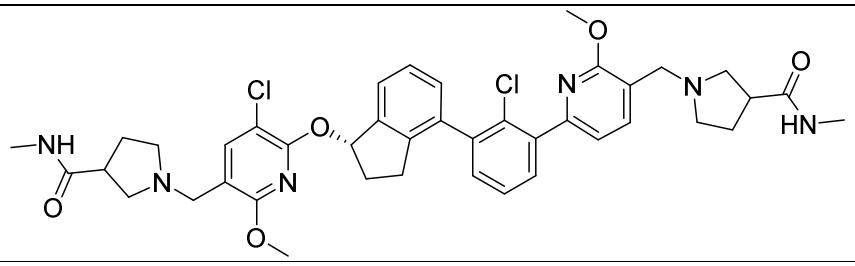
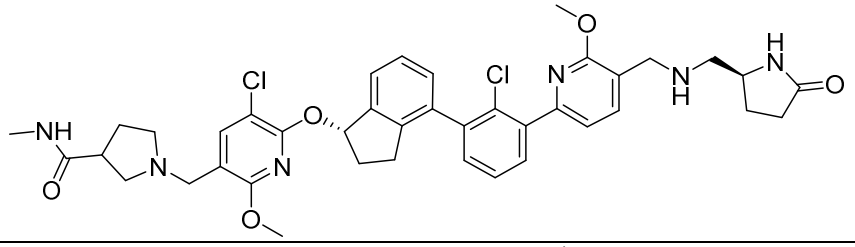
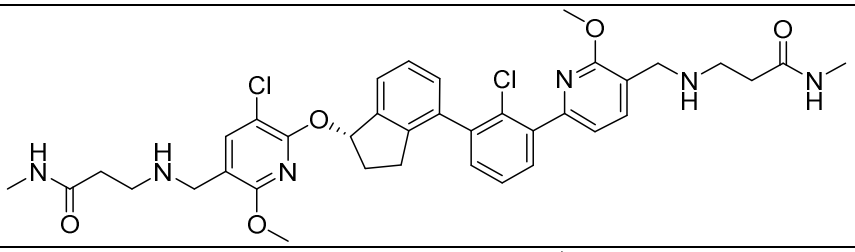
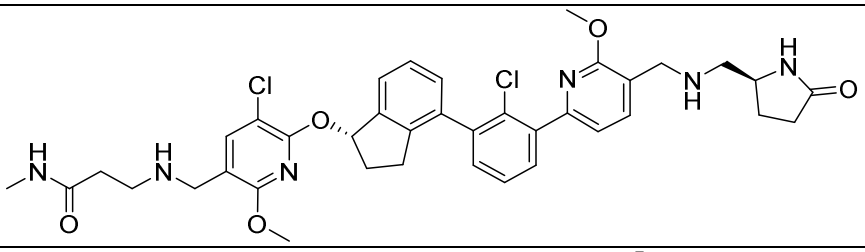
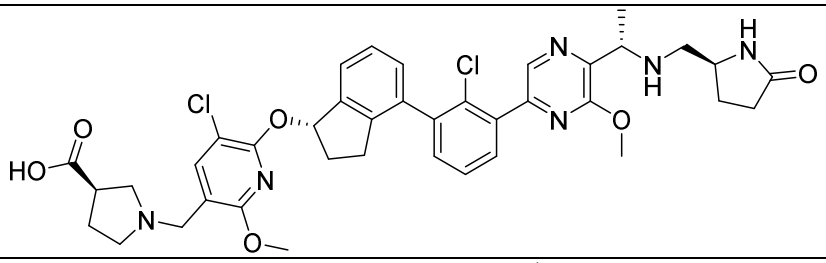
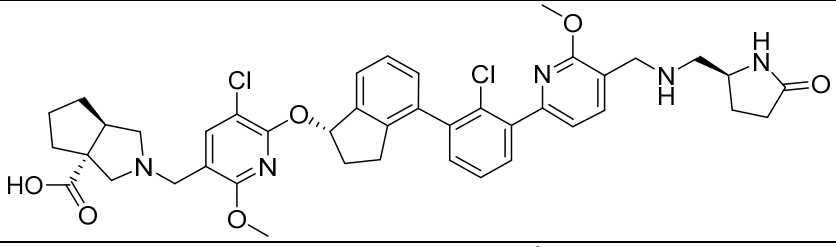
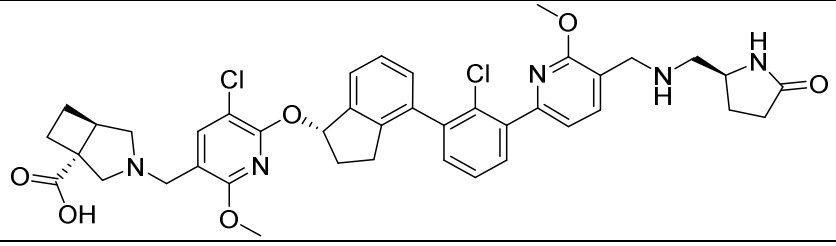
B-87	
B-88	
B-89	
B-90	
B-91	
B-92	
B-93	

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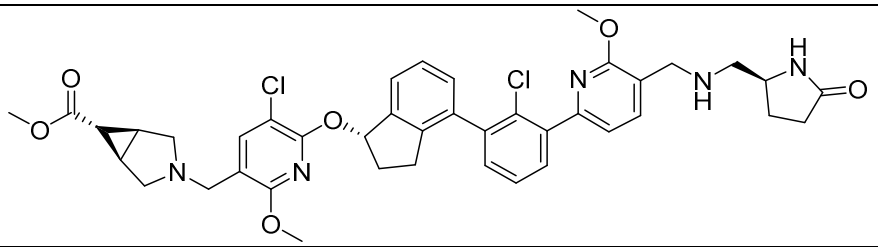
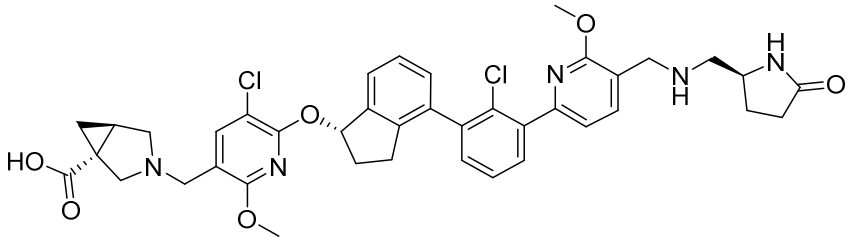
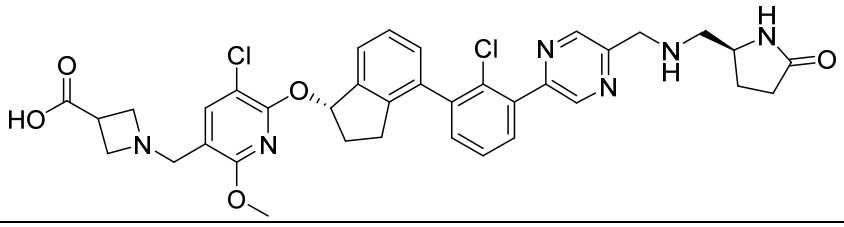
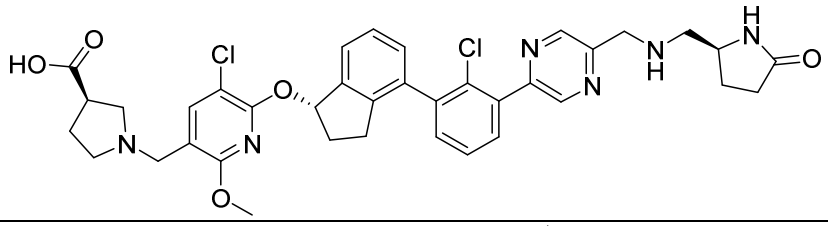
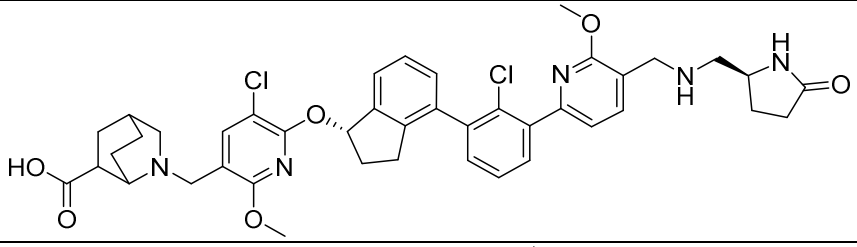
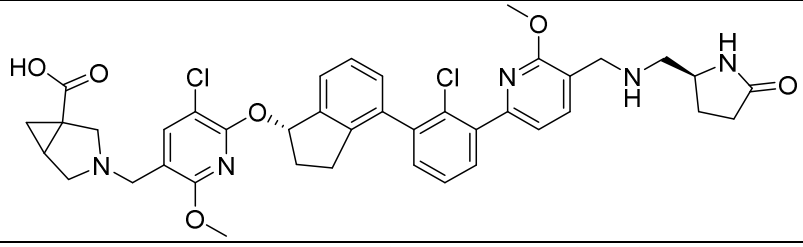
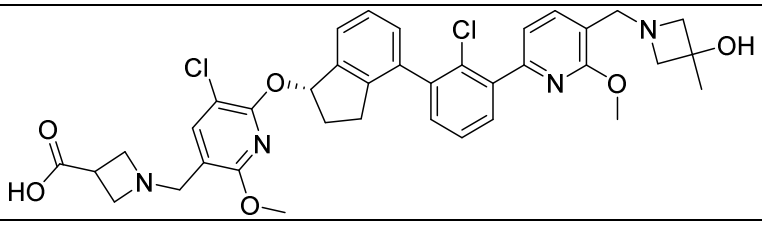
B-94	
B-95	
B-96	
B-97	
B-98	
B-99	
B-100	

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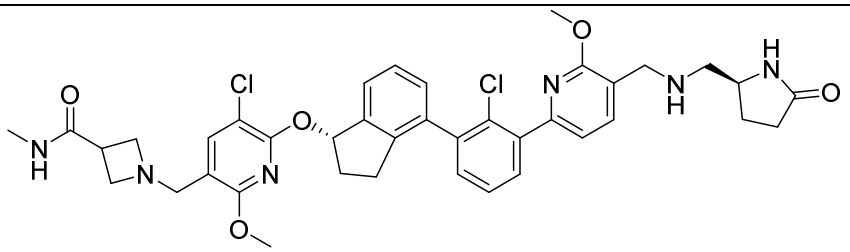
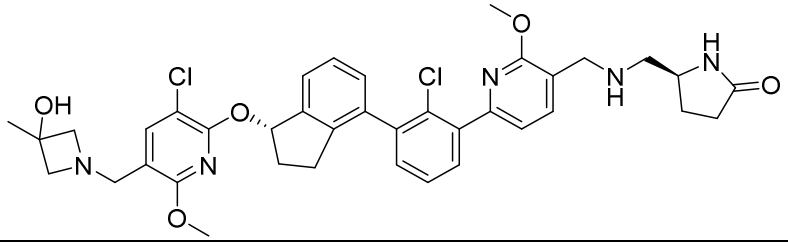
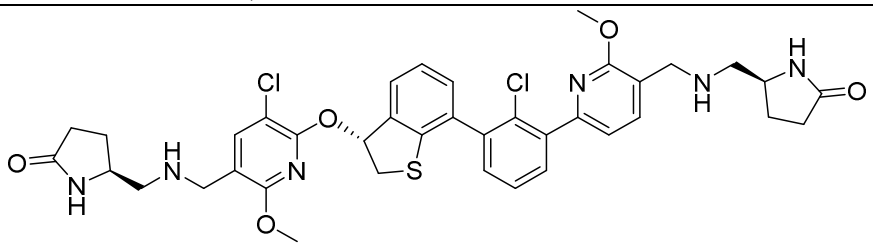
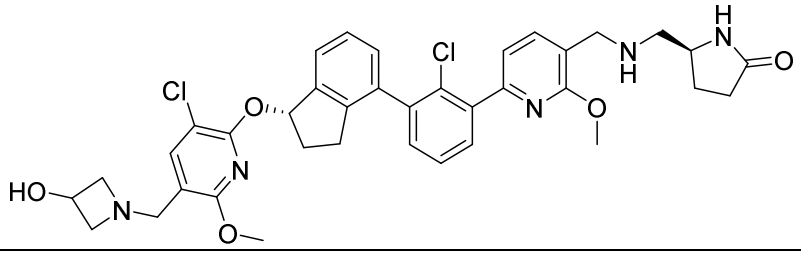
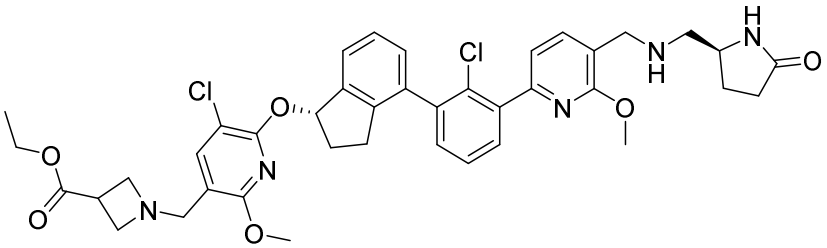
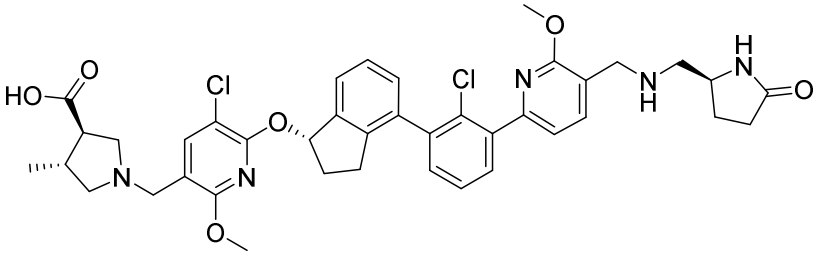
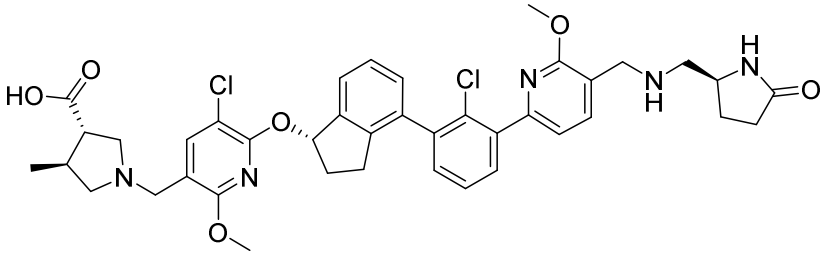
B-101	
B-102	
B-103	
B-104	
B-105	
B-106	
B-107	

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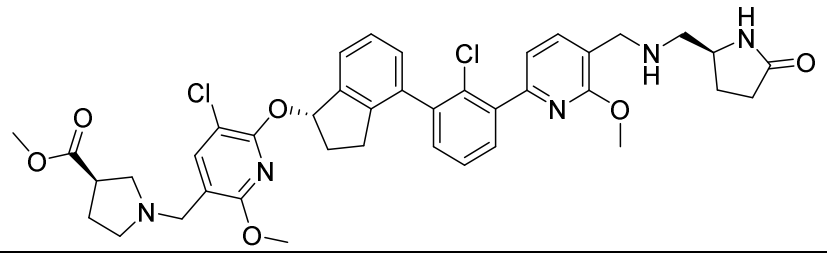
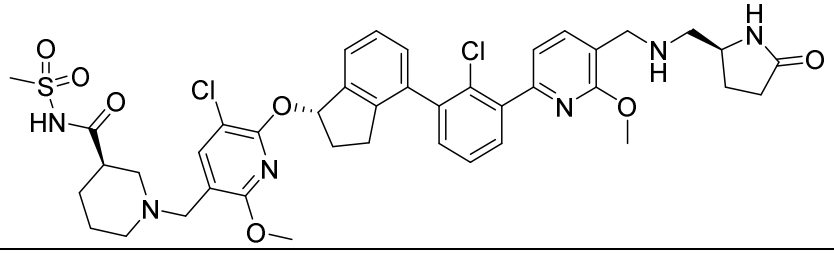
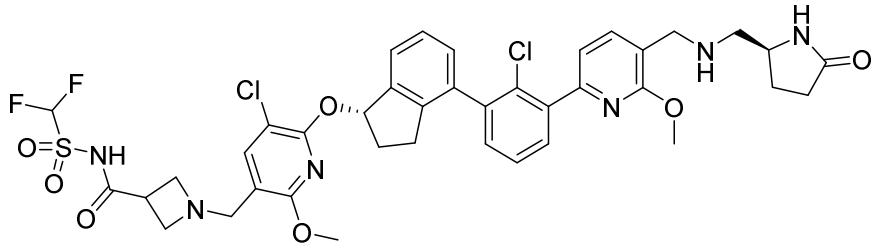
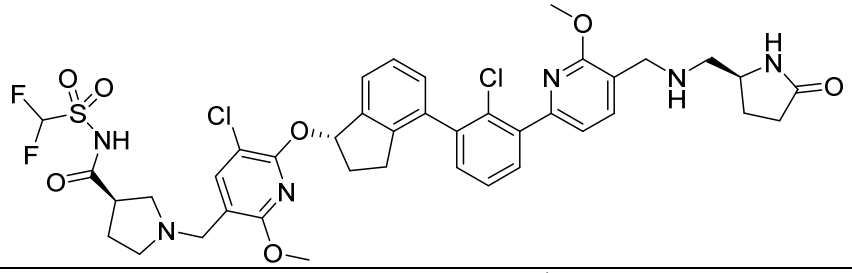
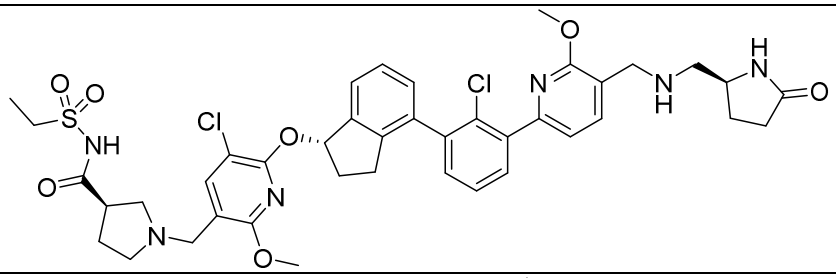
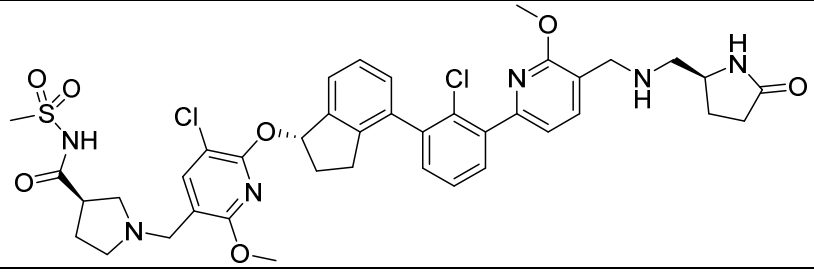
B-108	
B-109	
B-110	
B-111	
B-112	
B-113	

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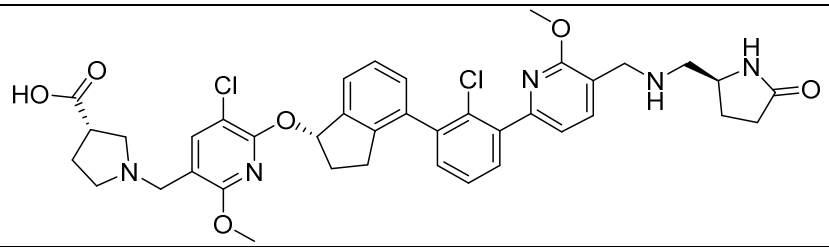
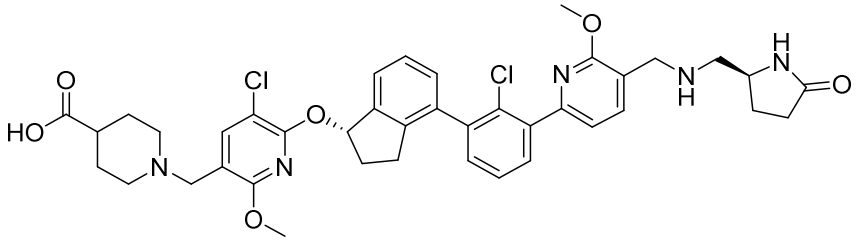
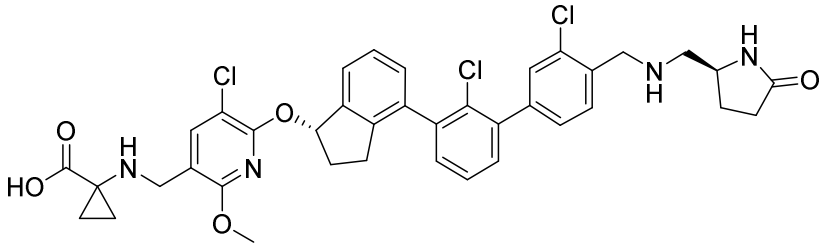
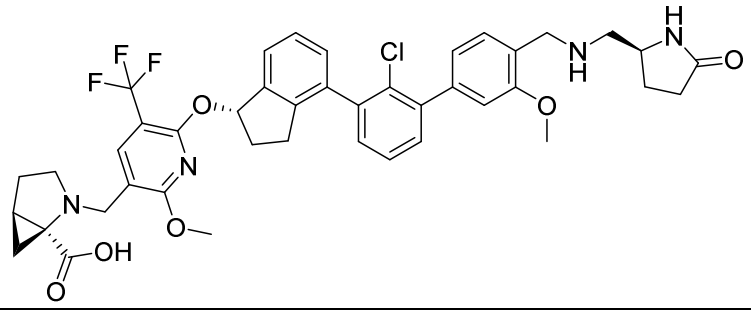
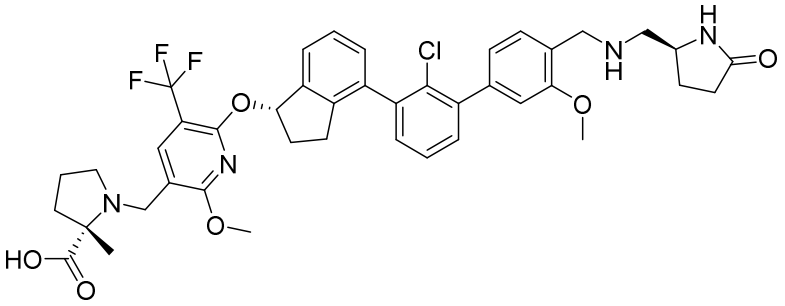
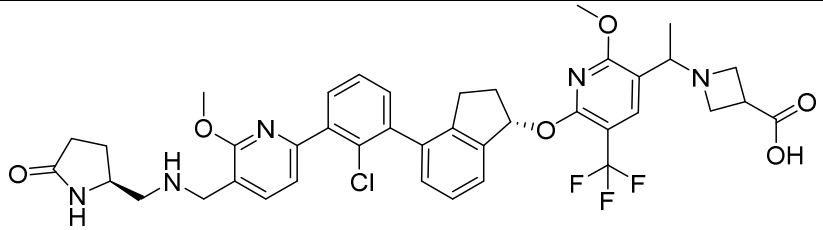
B-114	
B-115	
B-116	
B-117	
B-118	
B-119	

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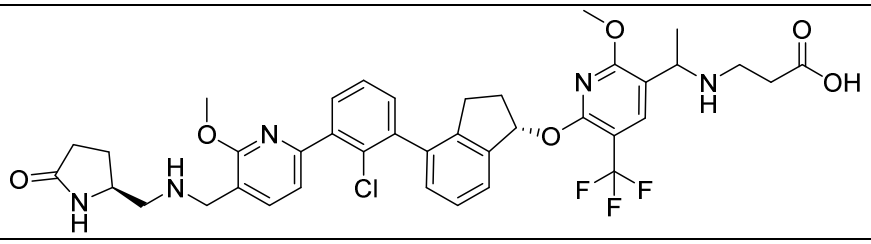
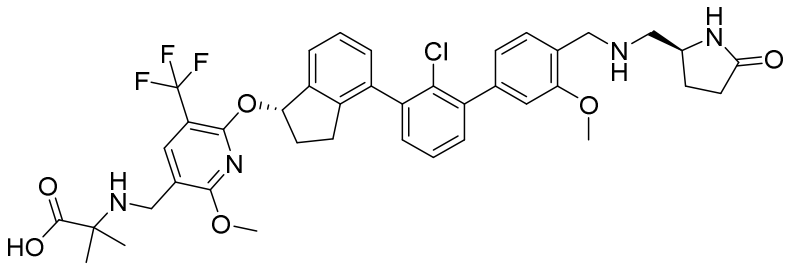
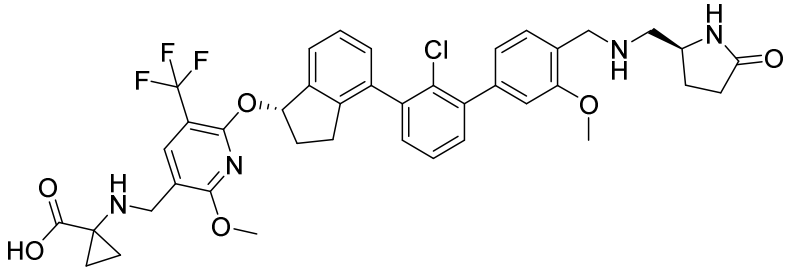
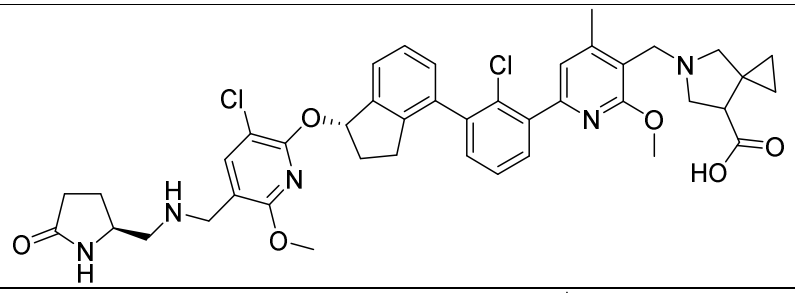
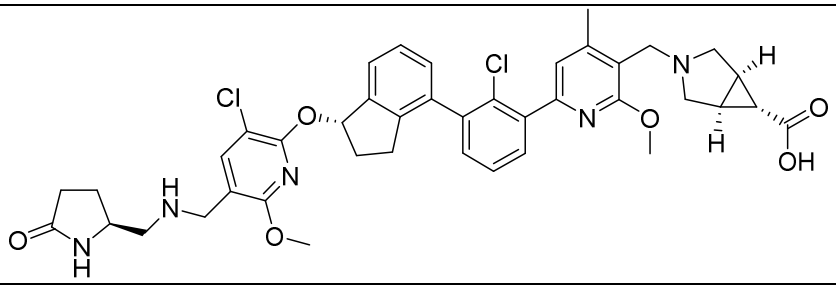
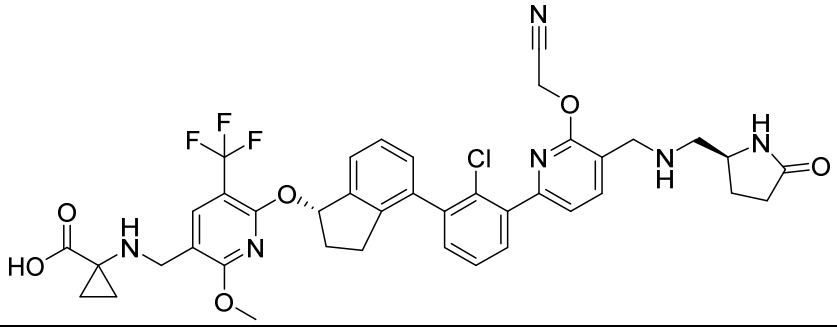
B-120	
B-121	
B-122	
B-123	
B-124	
B-125	

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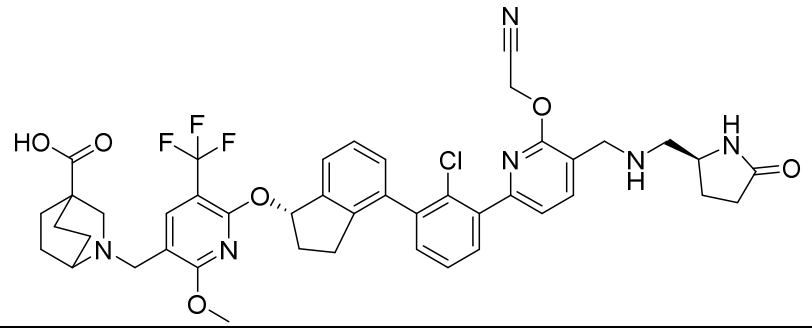
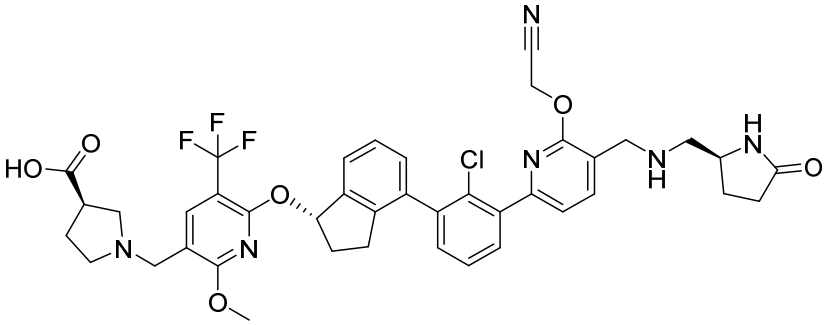
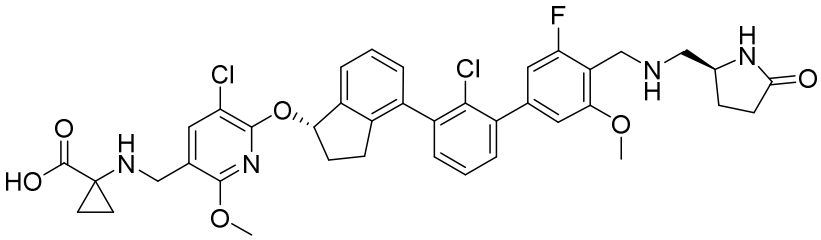
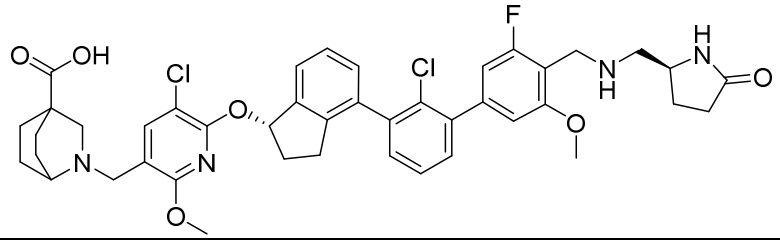
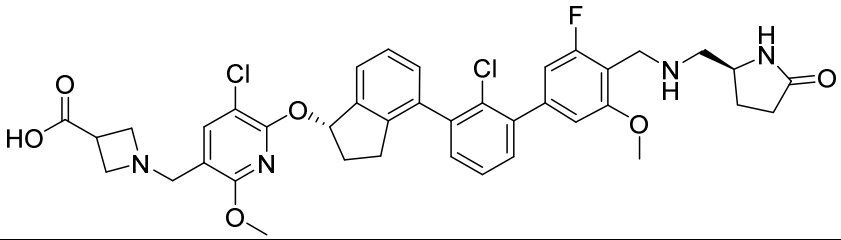
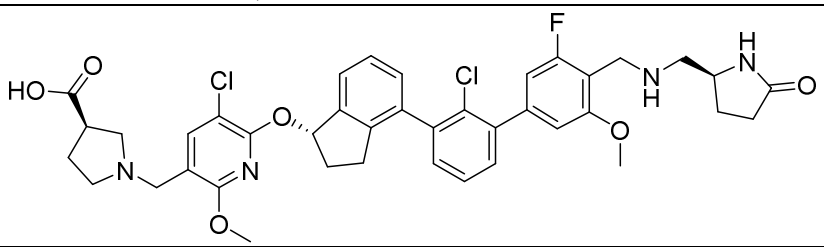
B-126	
B-127	
B-128	
B-129	
B-130	
B-131	

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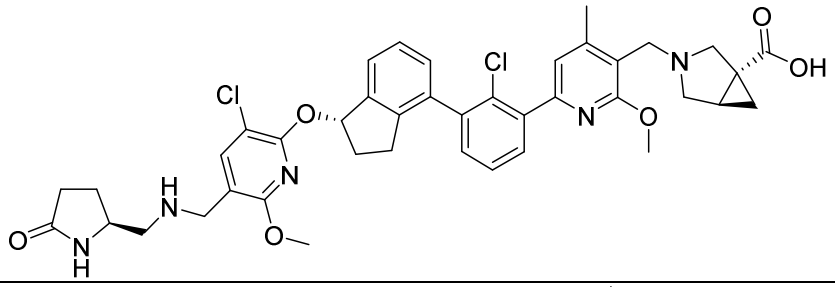
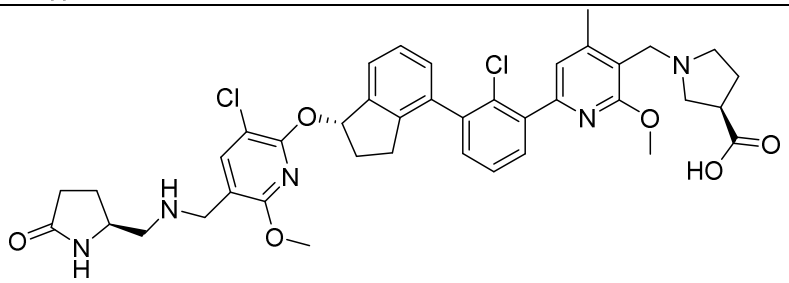
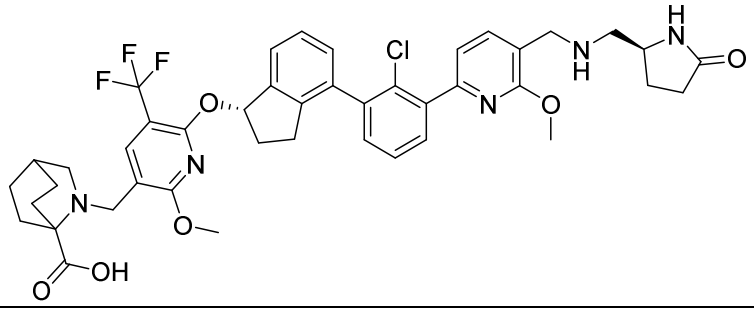
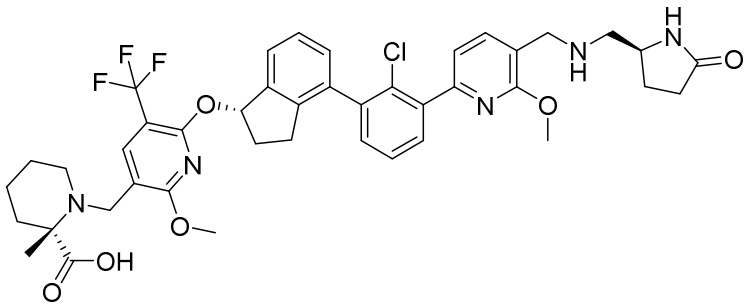
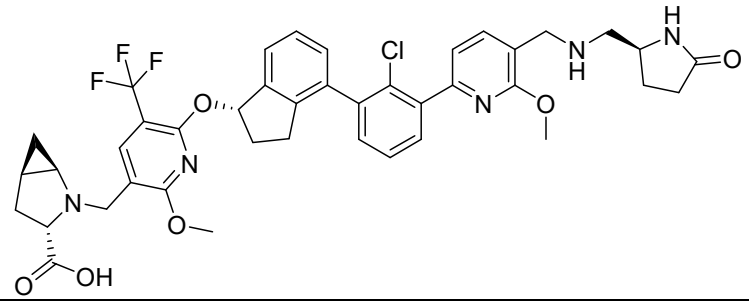
B-132	
B-133	
B-134	
B-135	
B-136	

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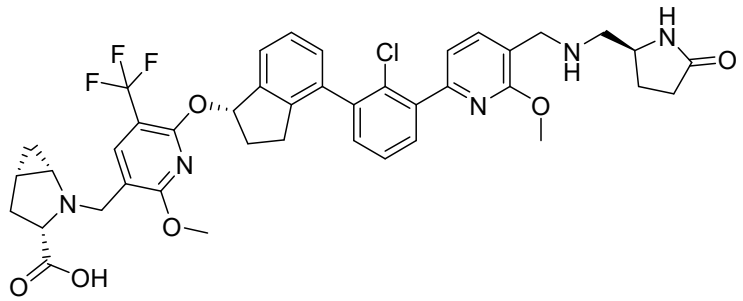
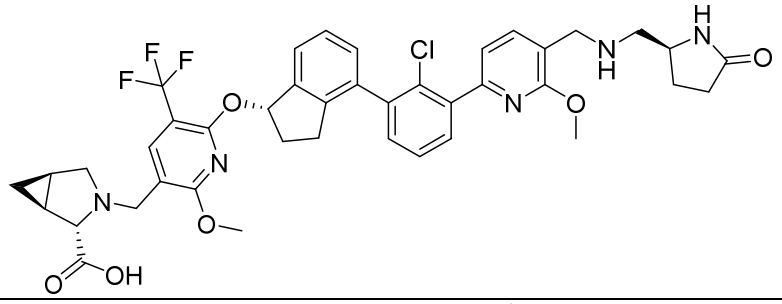
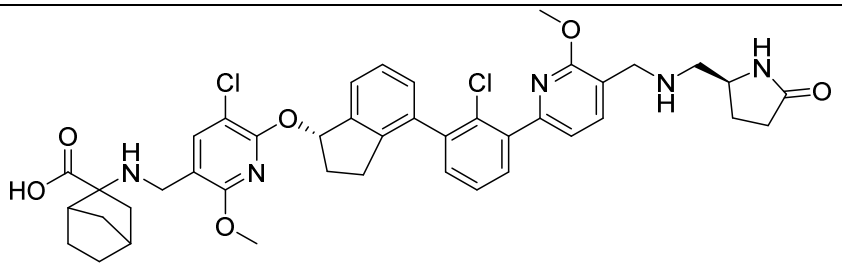
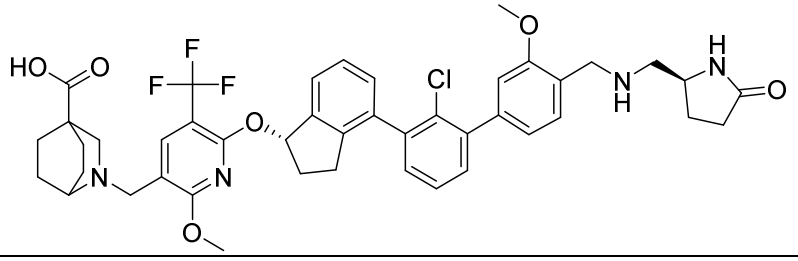
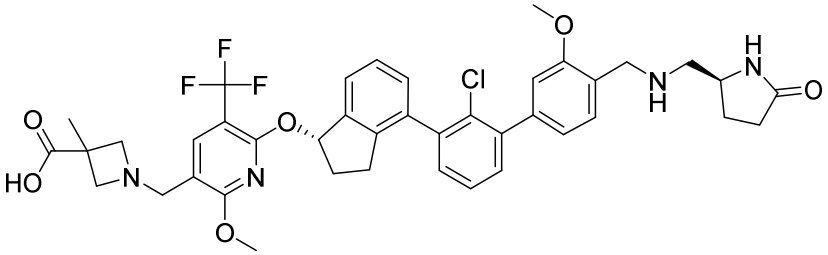
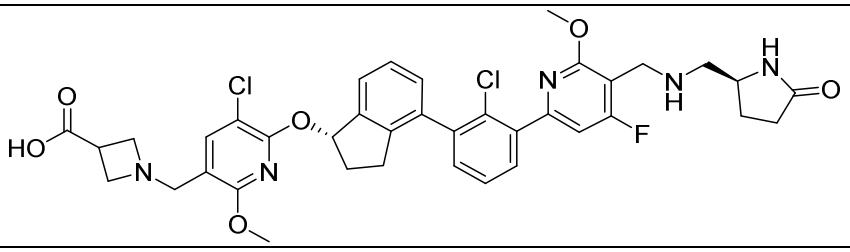
B-137	
B-138	
B-139	
B-140	
B-141	
B-142	

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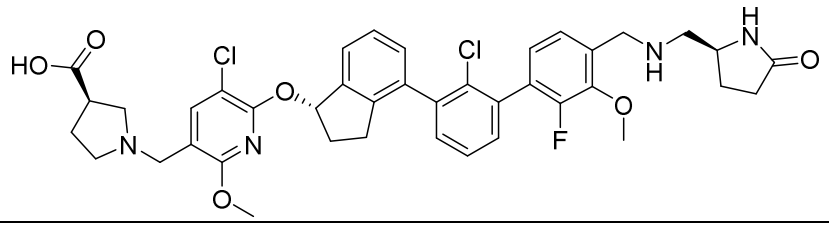
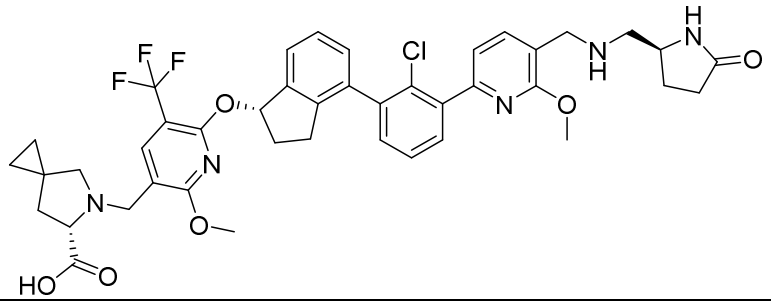
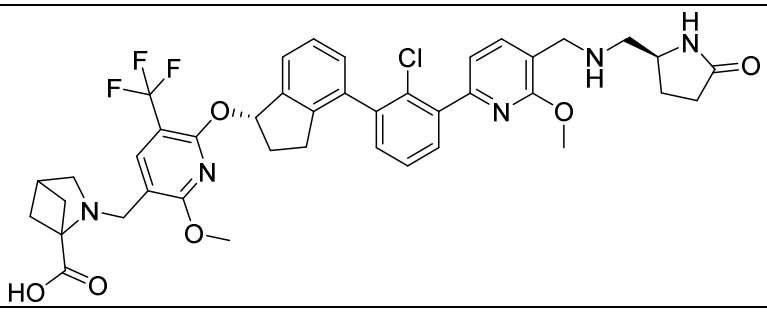
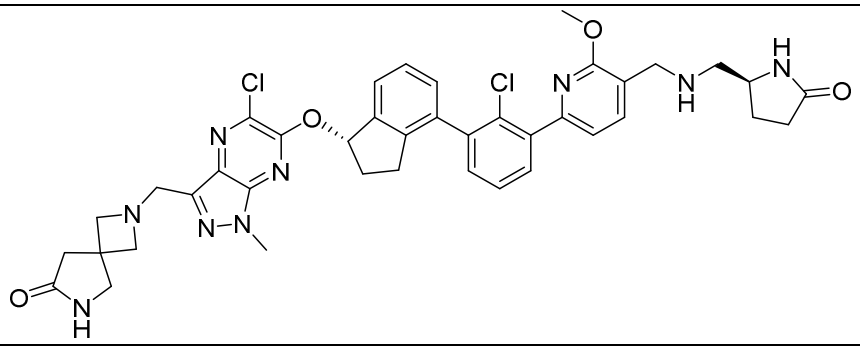
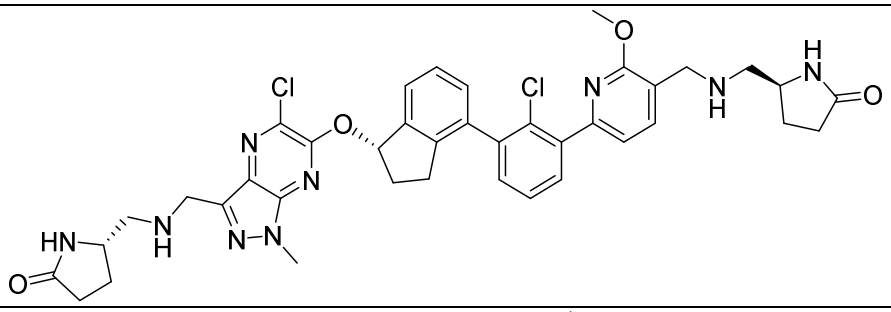
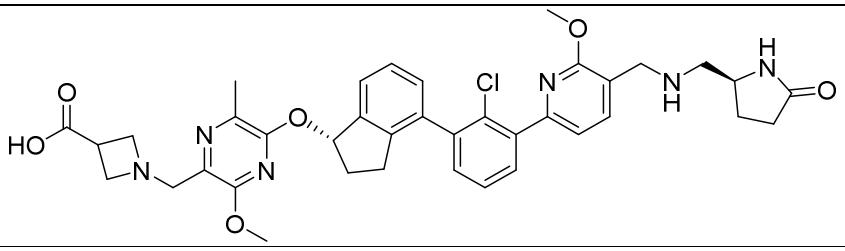
B-143	
B-144	
B-145	
B-146	
B-147	
B-148	

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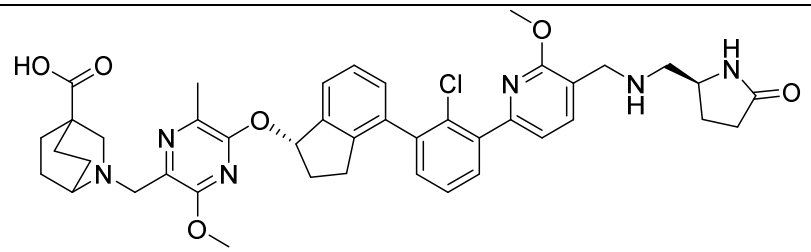
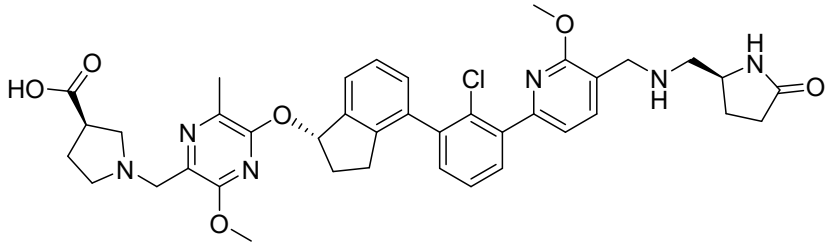
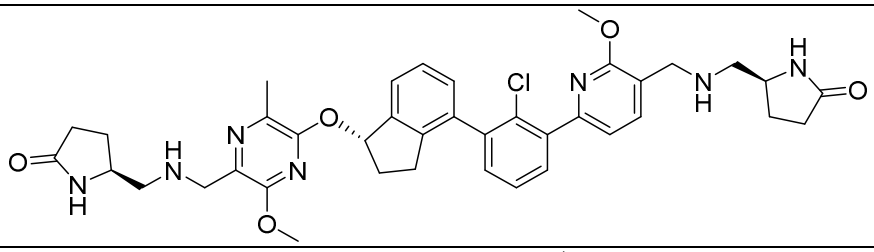
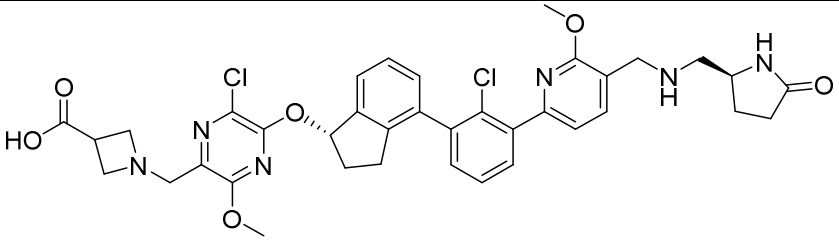
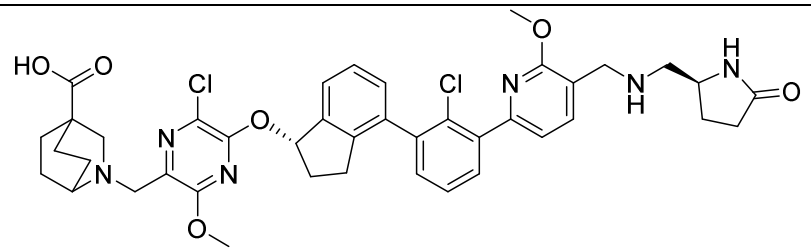
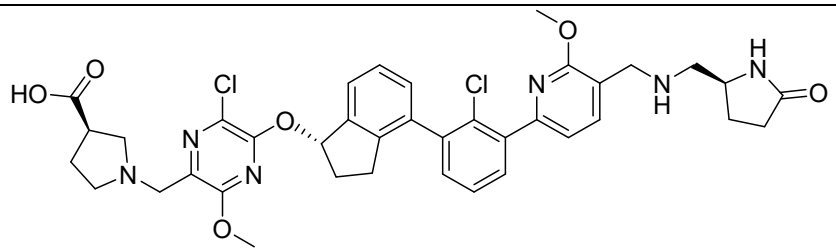
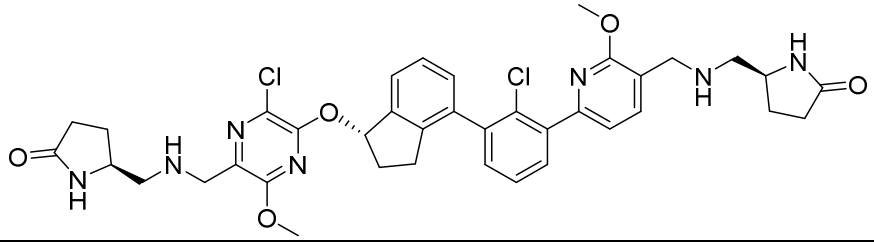
B-149	
B-150	
B-151	
B-152	
B-153	
B-154	
B-155	

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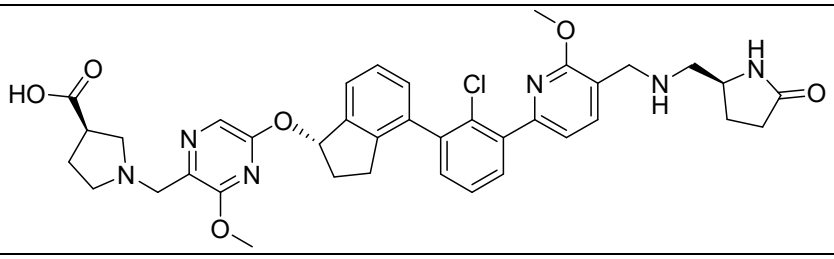
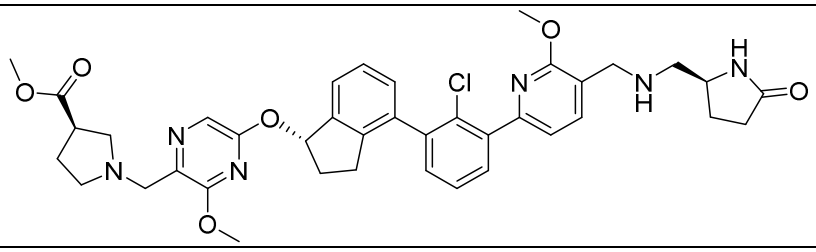
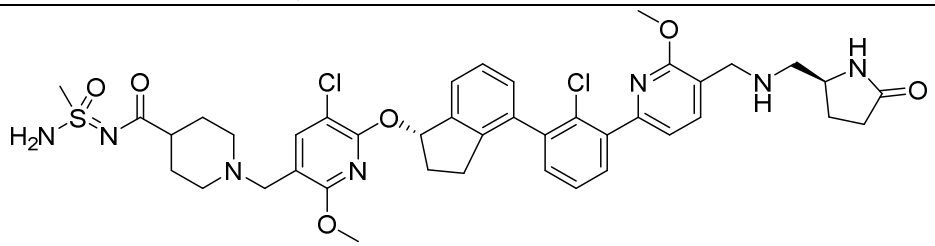
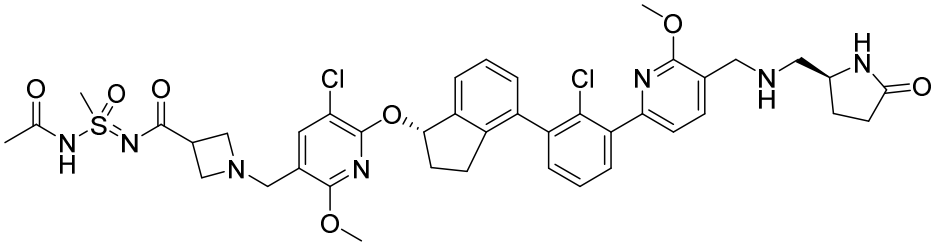
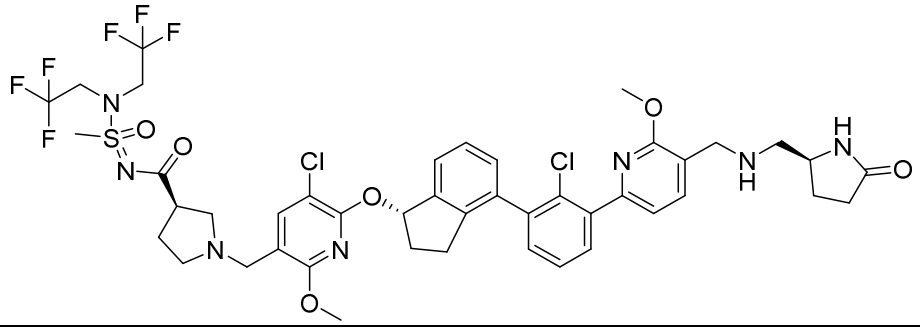
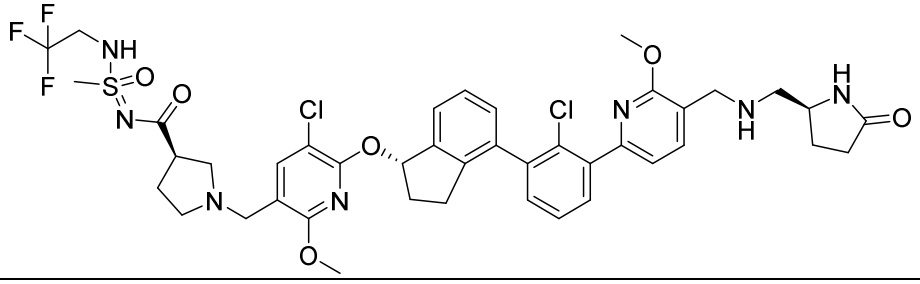
B-156	
B-157	
B-158	
B-159	
B-160	
B-161	

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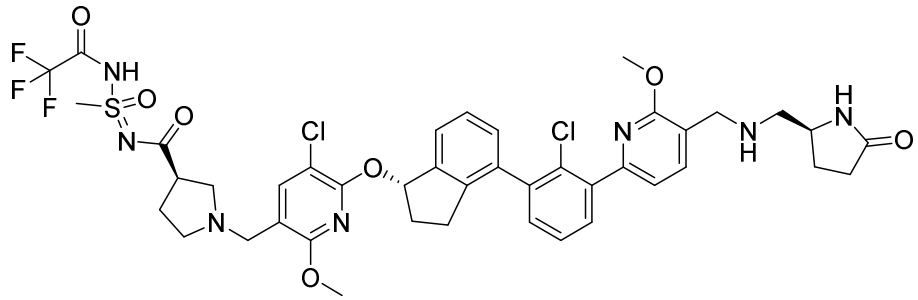
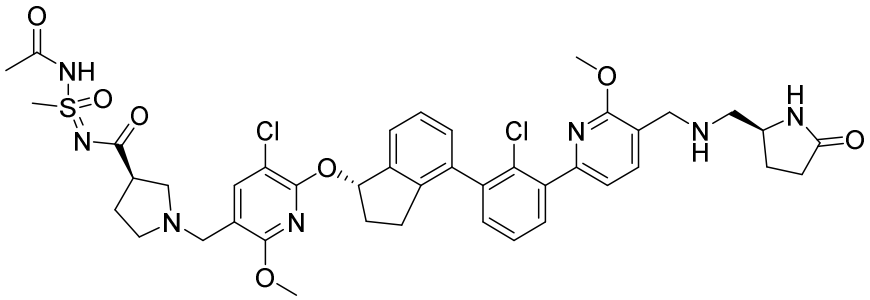
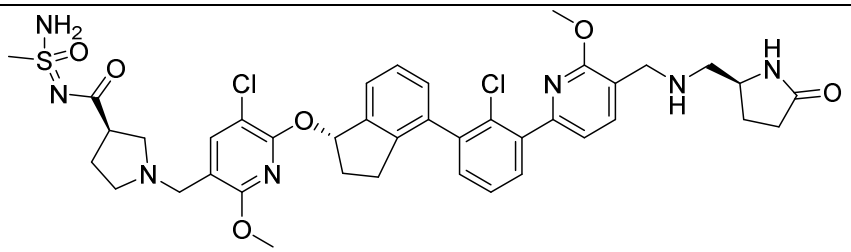
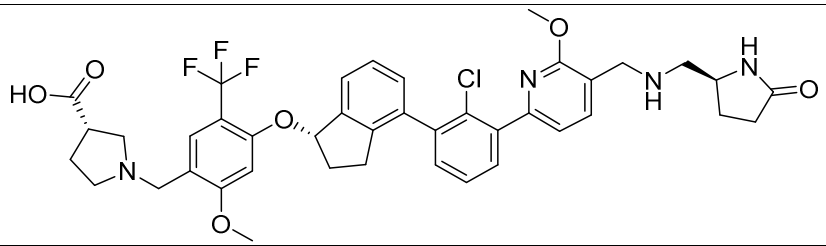
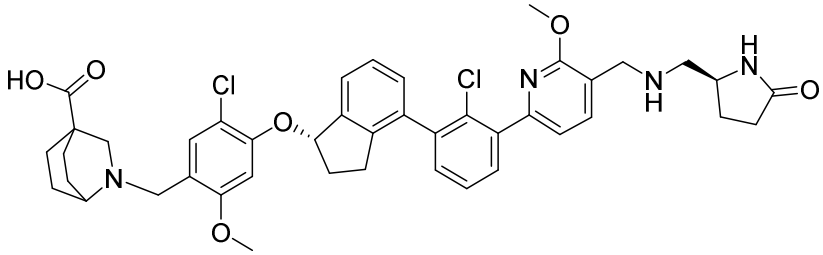
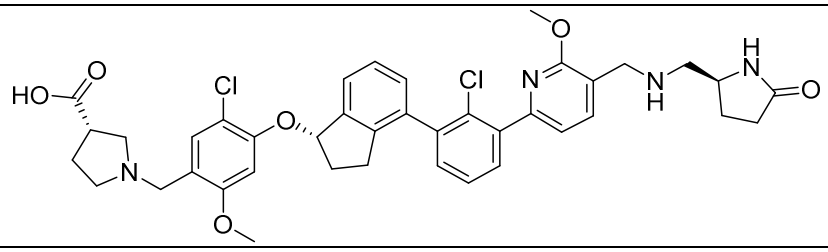
B-162	
B-163	
B-164	
B-165	
B-166	
B-167	

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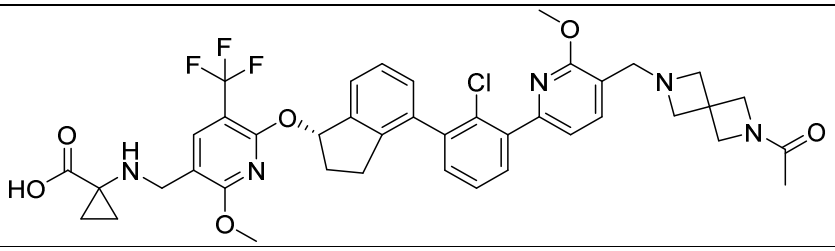
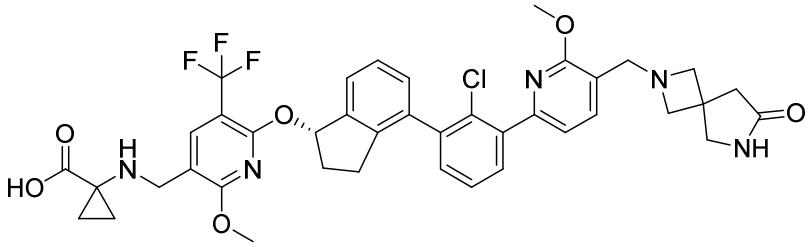
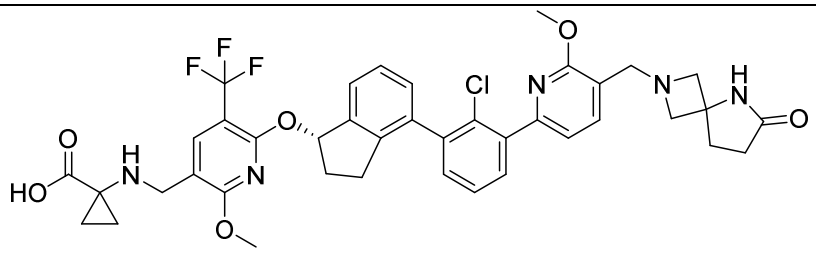
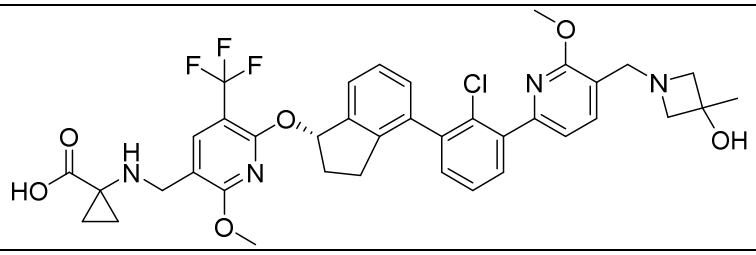
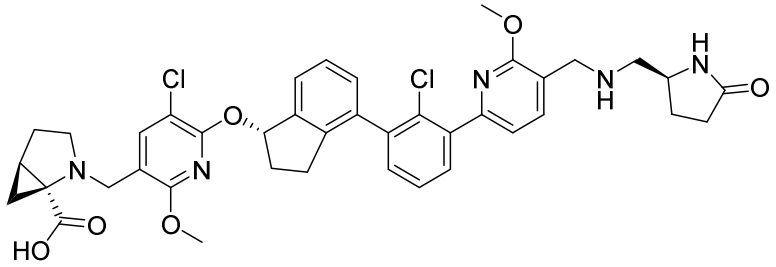
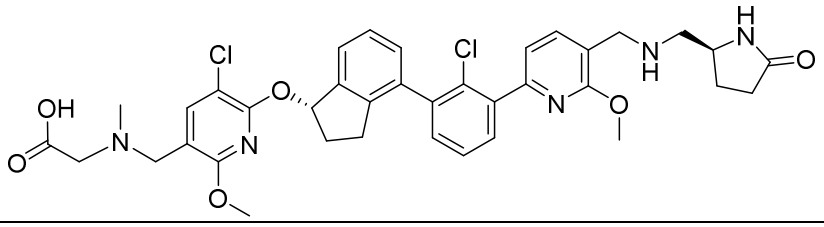
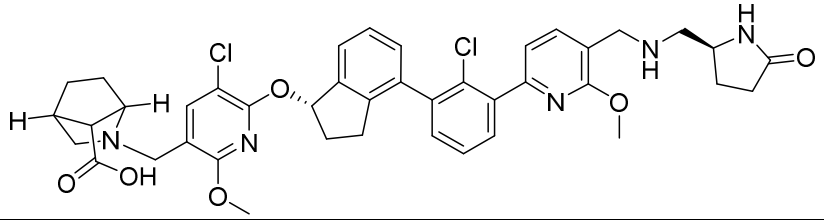
B-168	
B-169	
B-170	
B-171	
B-172	
B-173	
B-174	

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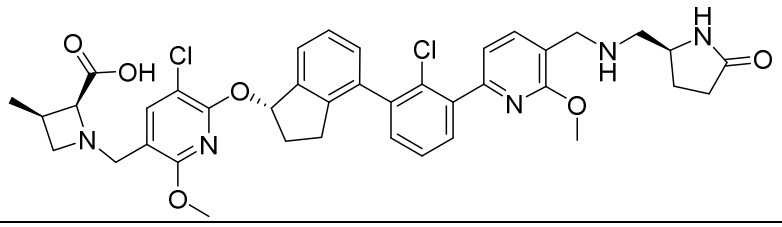
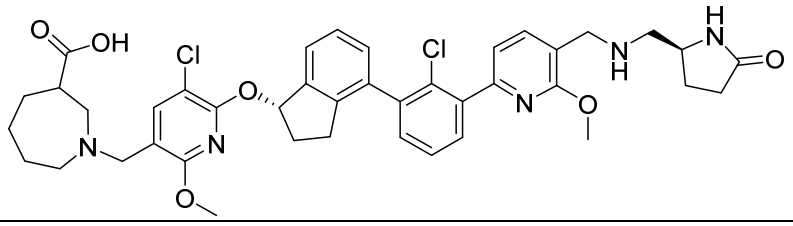
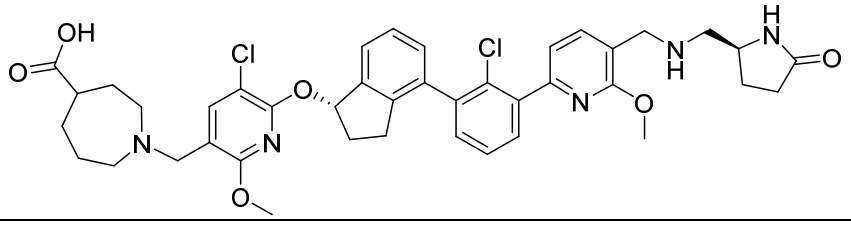
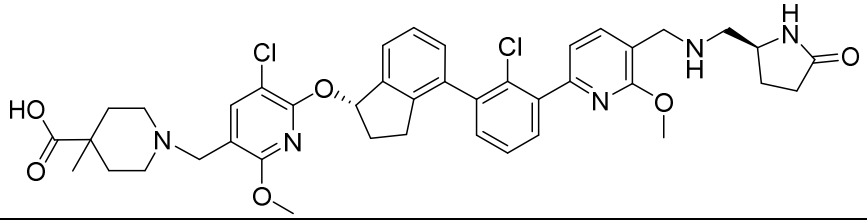
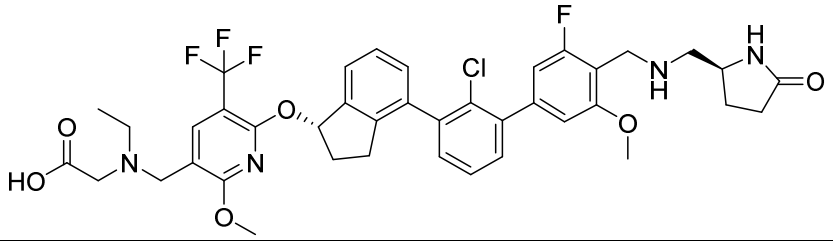
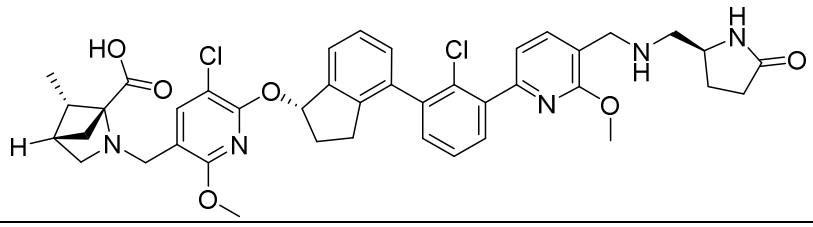
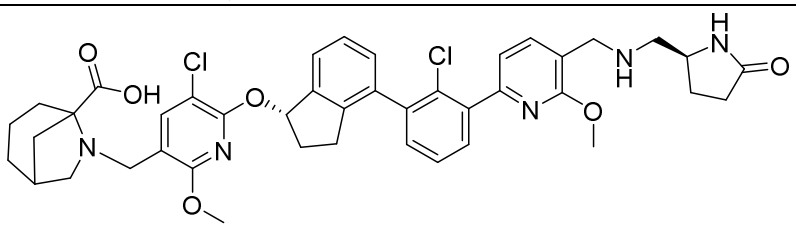
B-175	
B-176	
B-177	
B-178	
B-179	
B-180	
B-181	

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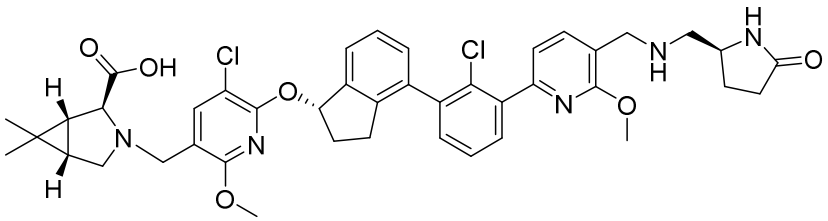
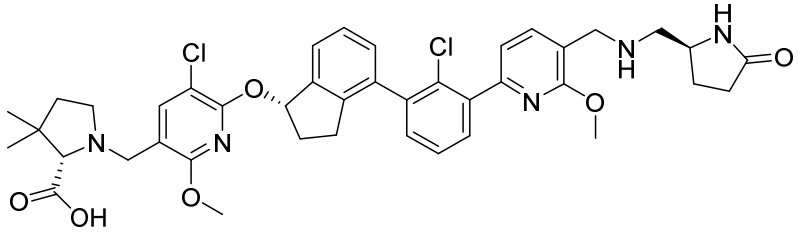
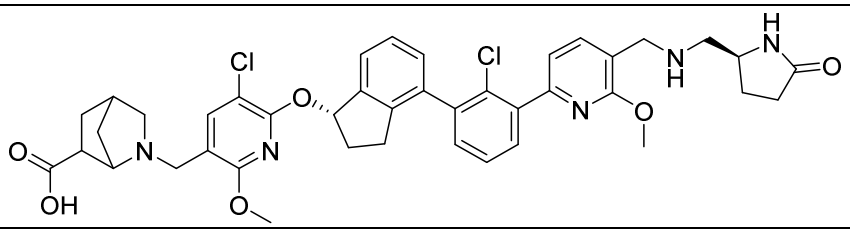
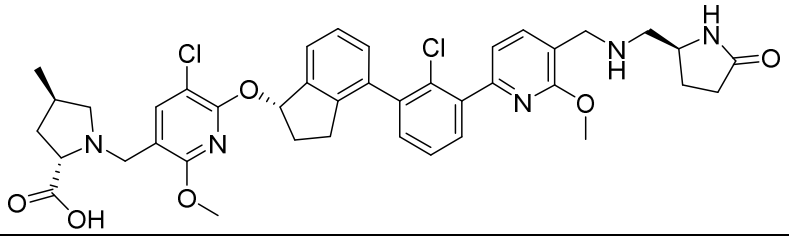
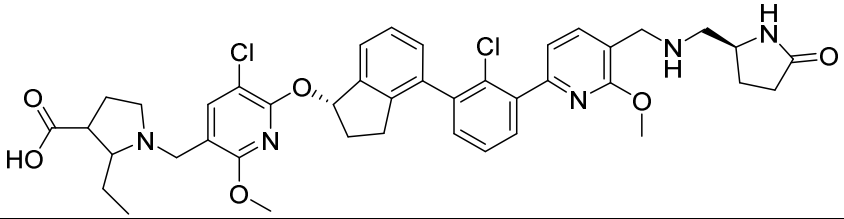
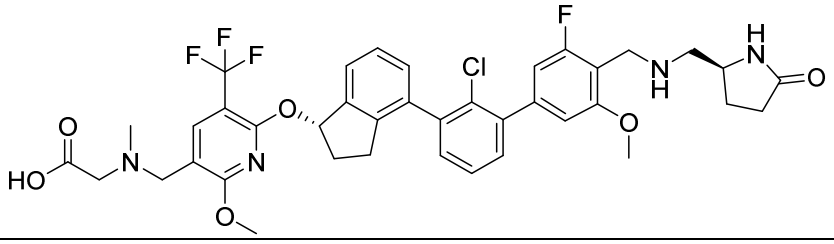
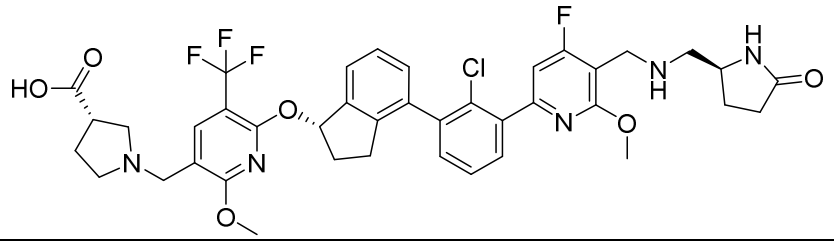
B-182	
B-183	
B-184	
B-185	
B-186	
B-187	
B-188	

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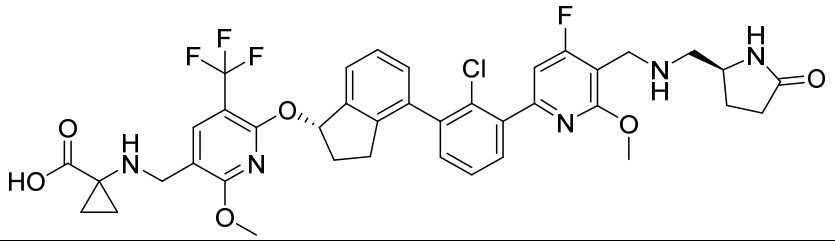
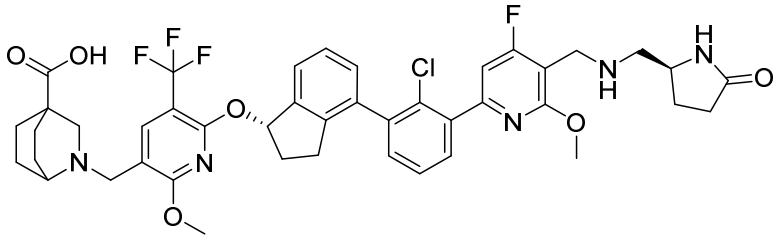
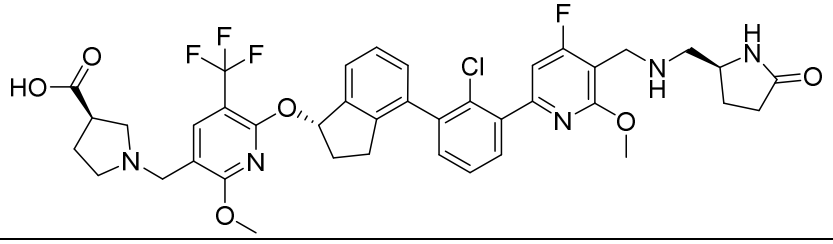
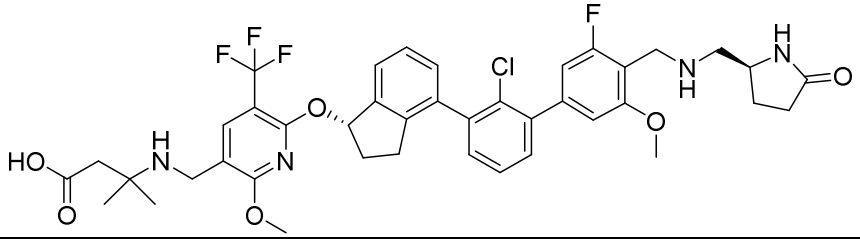
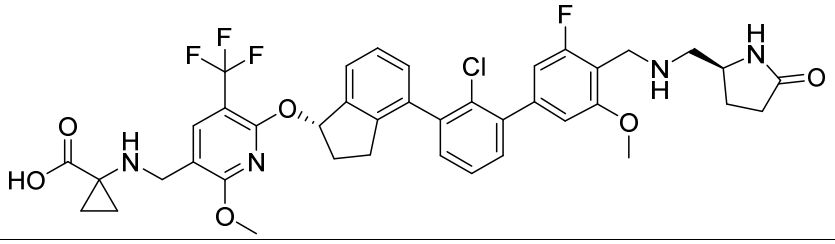
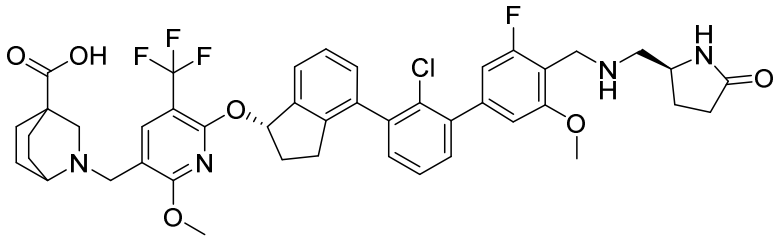
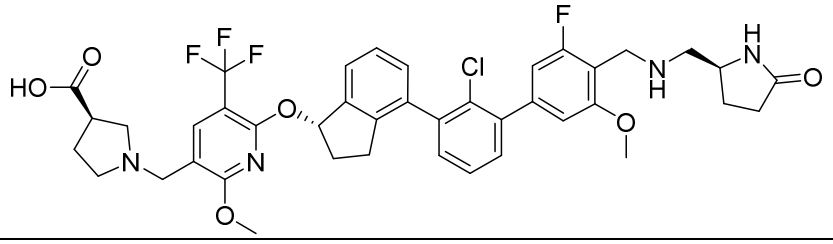
B-189	
B-190	
B-191	
B-192	
B-193	
B-194	
B-195	

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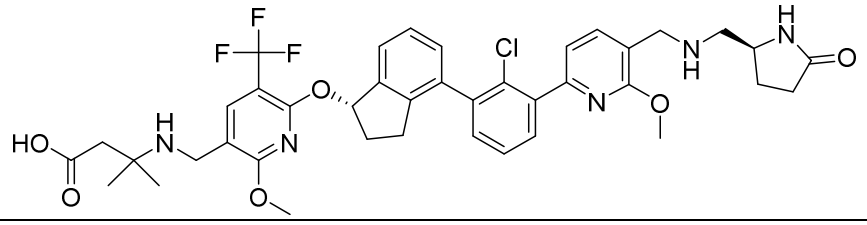
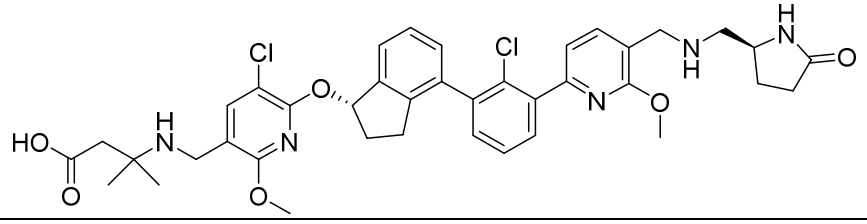
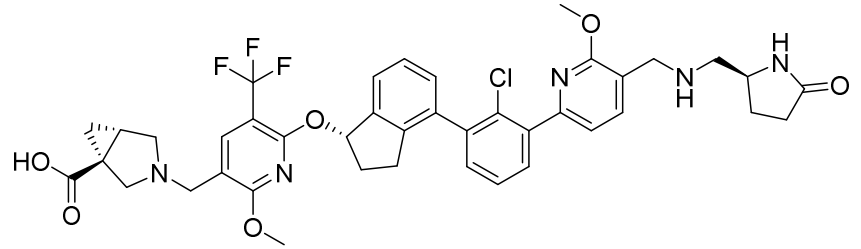
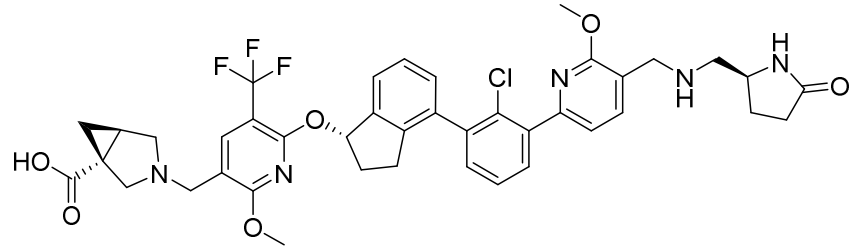
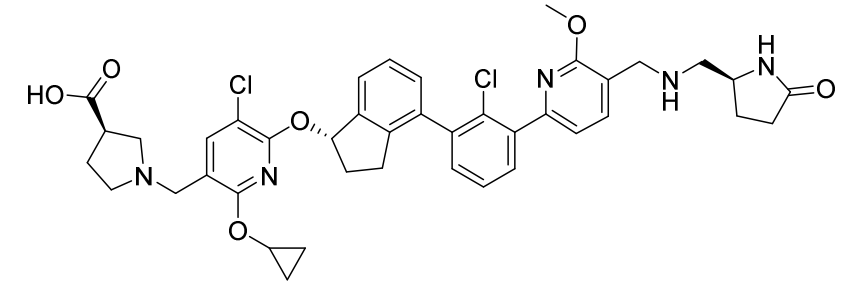
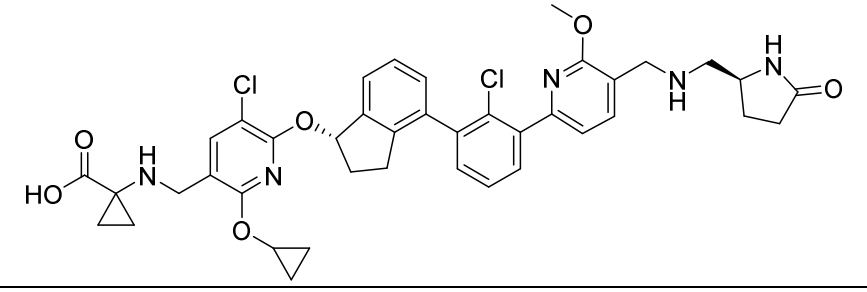
B-196	
B-197	
B-198	
B-199	
B-200	
B-201	

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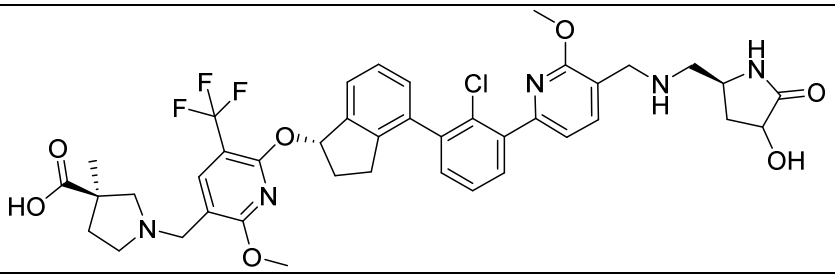
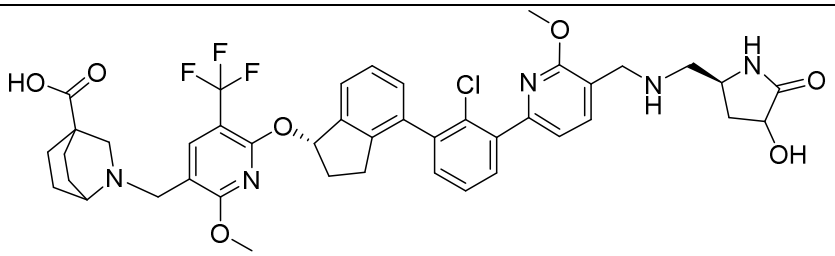
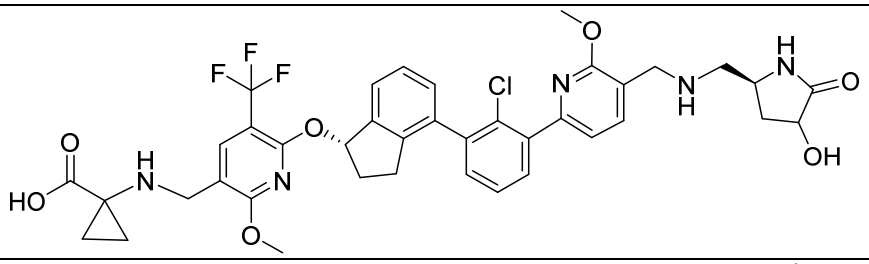
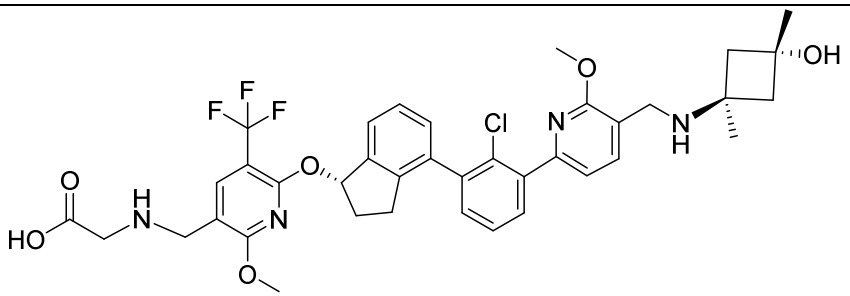
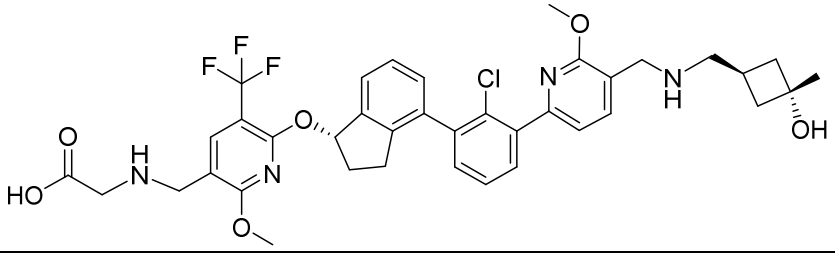
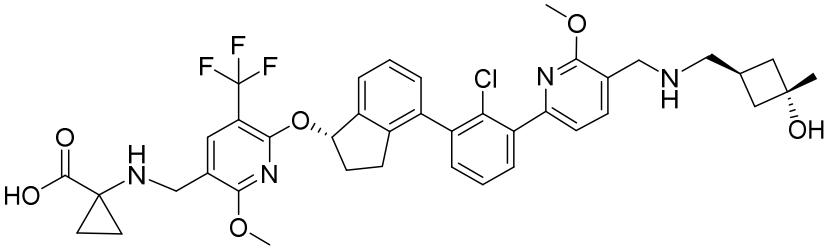
B-202	
B-203	
B-204	
B-205	
B-206	
B-207	

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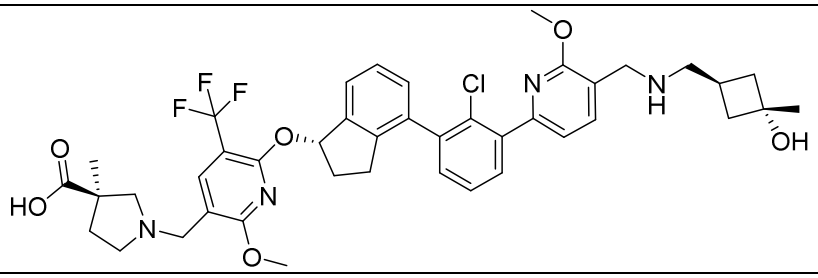
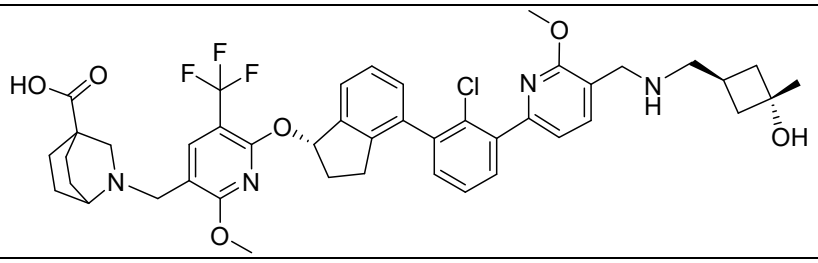
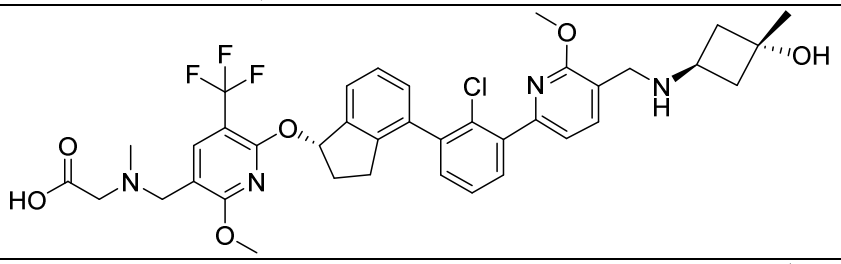
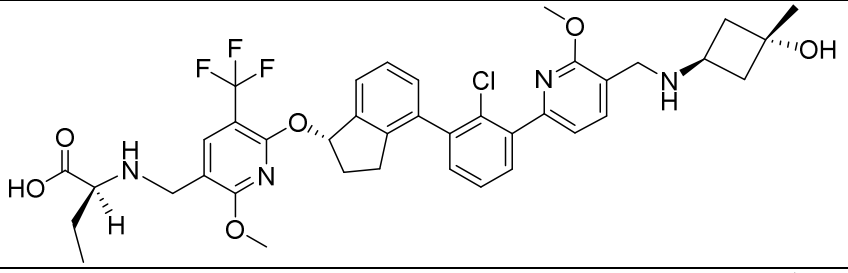
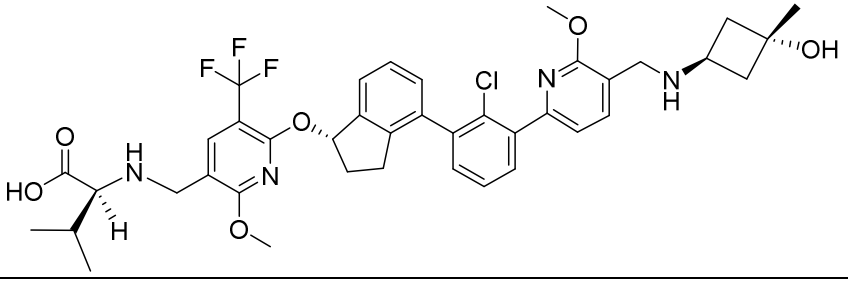
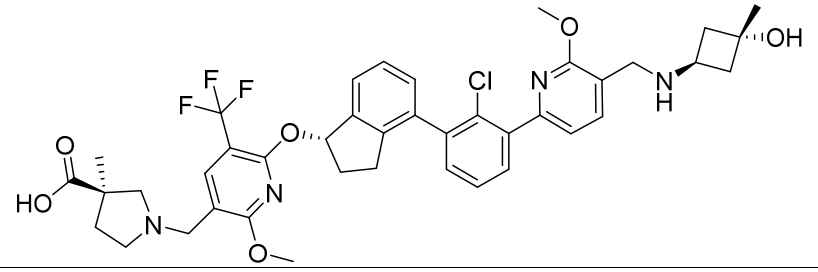
B-208	
B-209	
B-210	
B-211	
B-212	
B-213	

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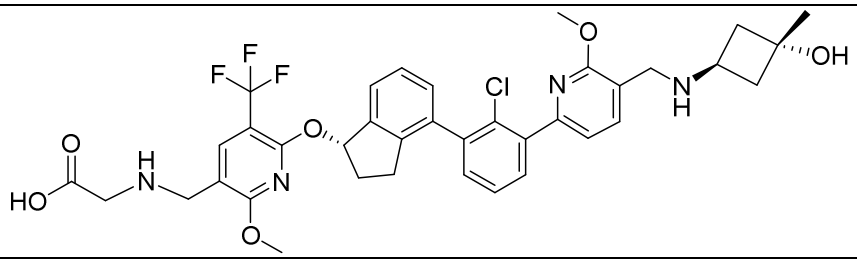
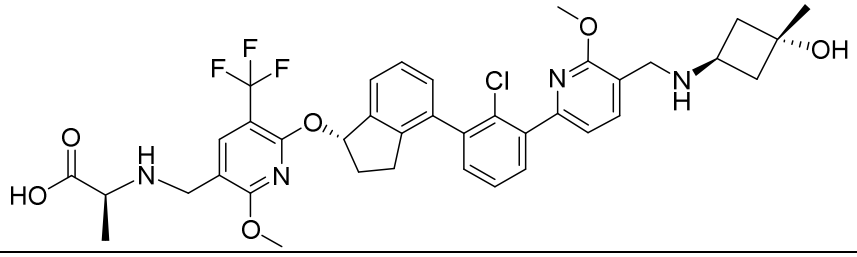
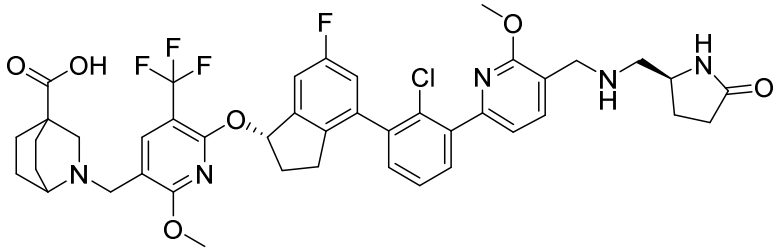
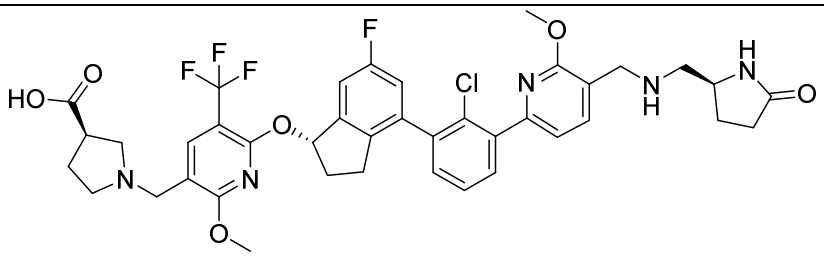
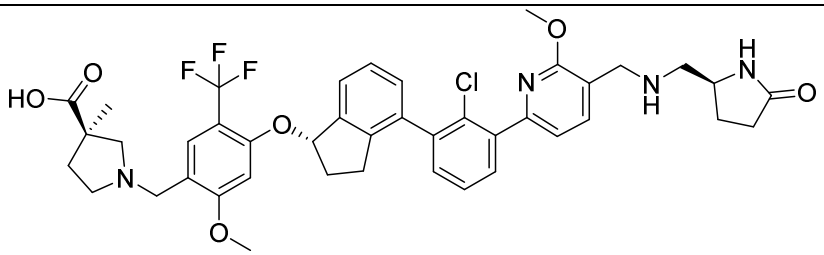
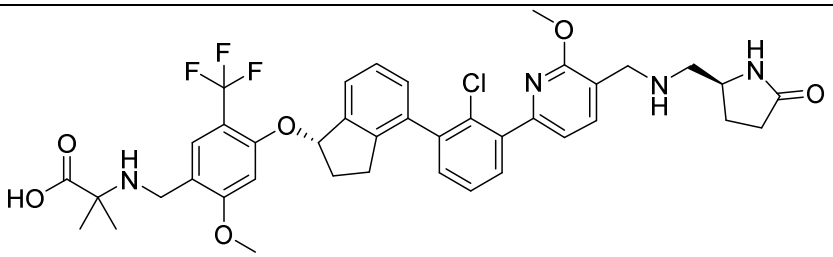
B-214	
B-215	
B-216	
B-217	
B-218	
B-219	

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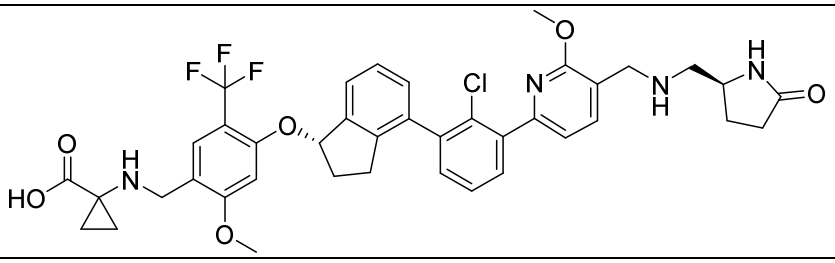
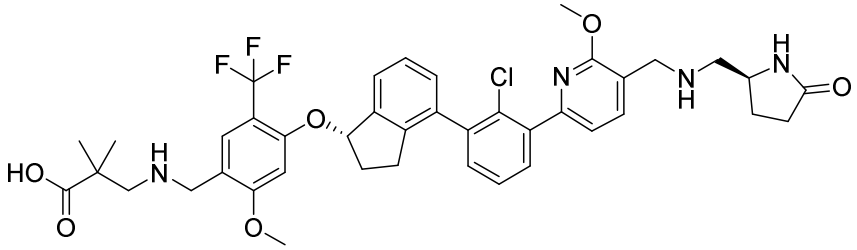
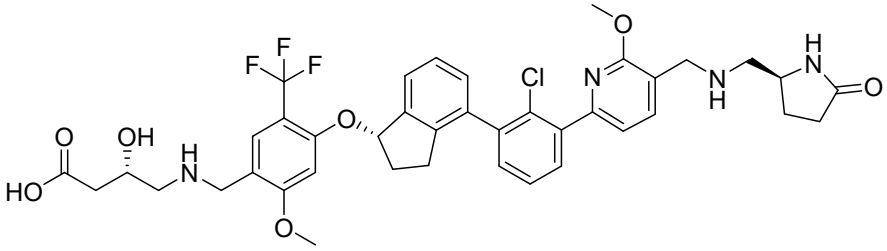
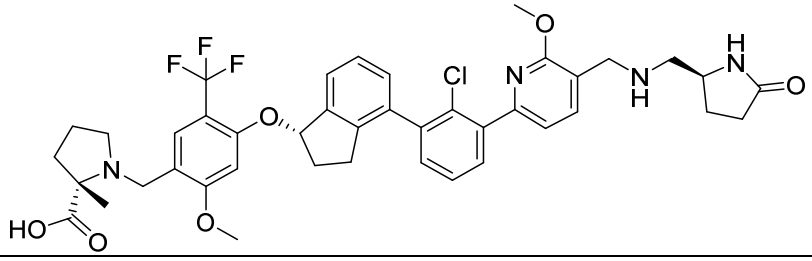
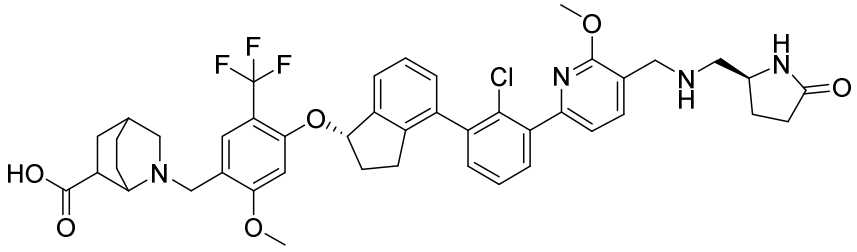
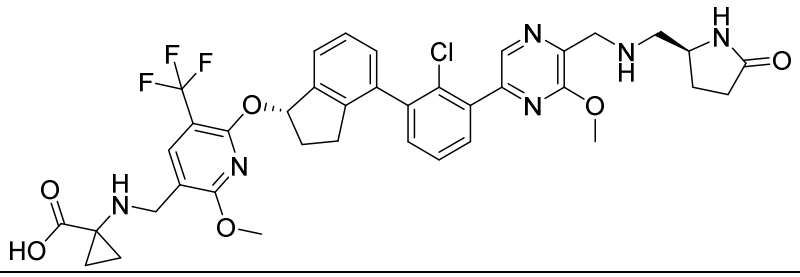
B-220	
B-221	
B-222	
B-223	
B-224	
B-225	

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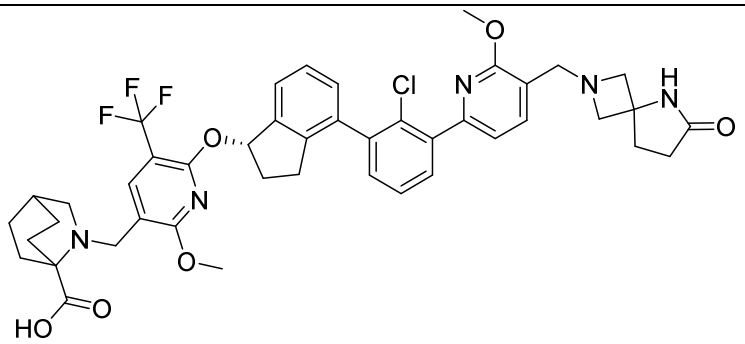
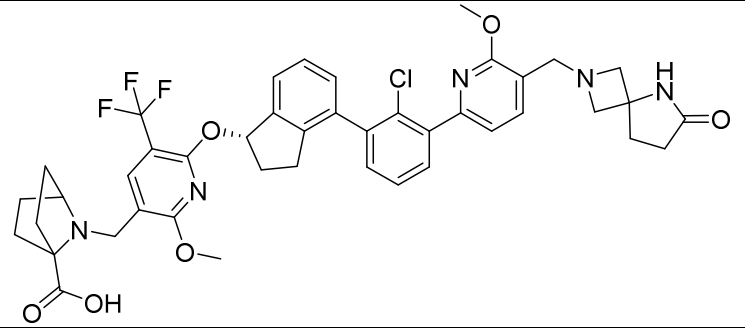
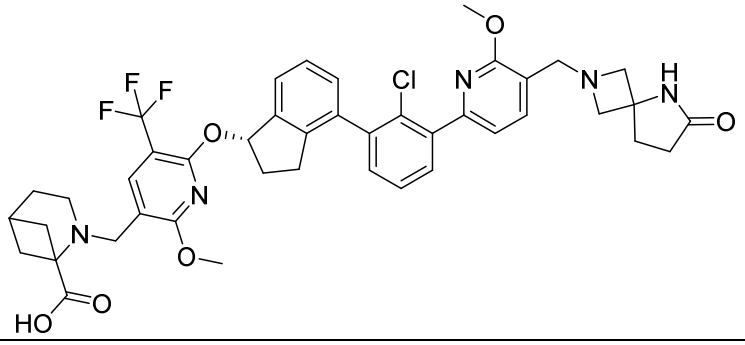
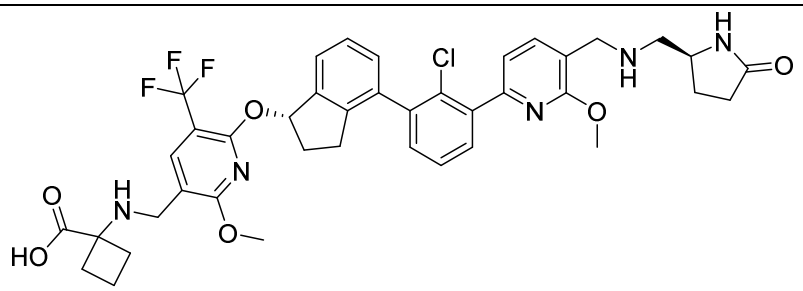
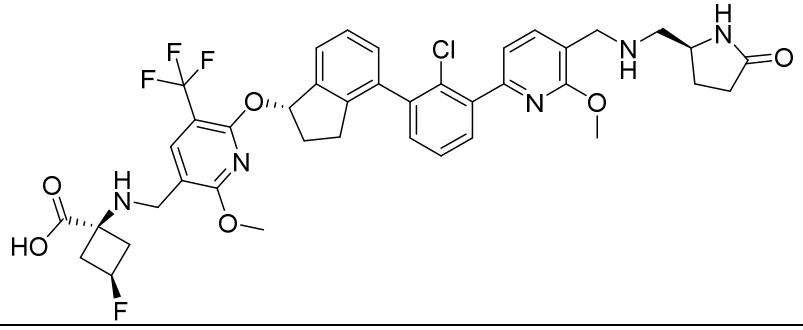
B-226	
B-227	
B-228	
B-229	
B-230	

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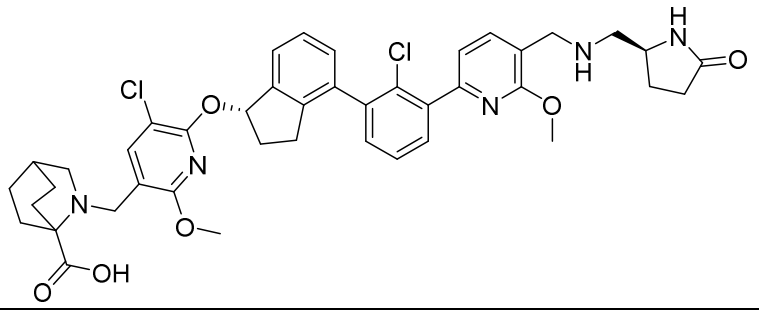
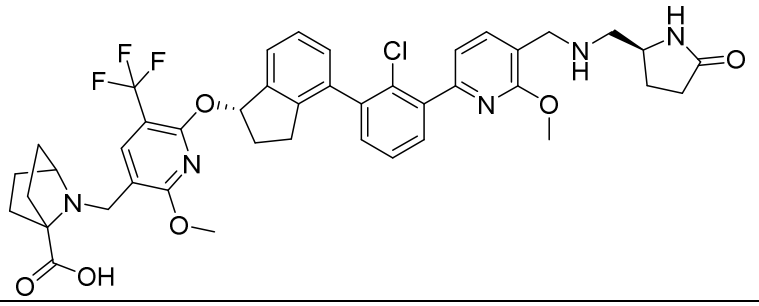
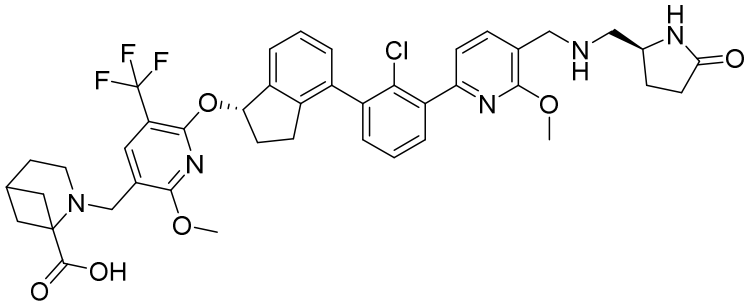
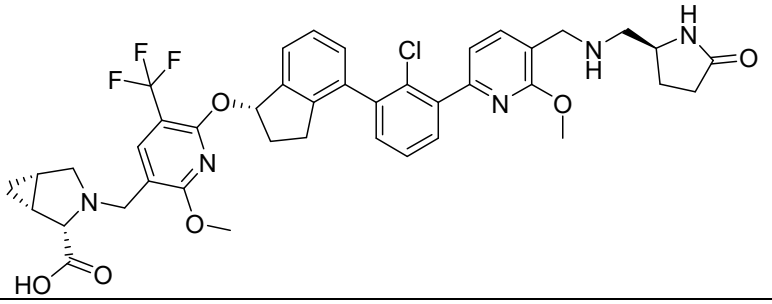
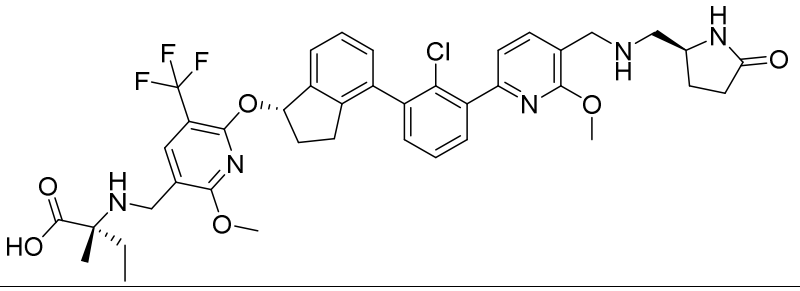
B-231	
B-232	
B-233	
B-234	
B-235	

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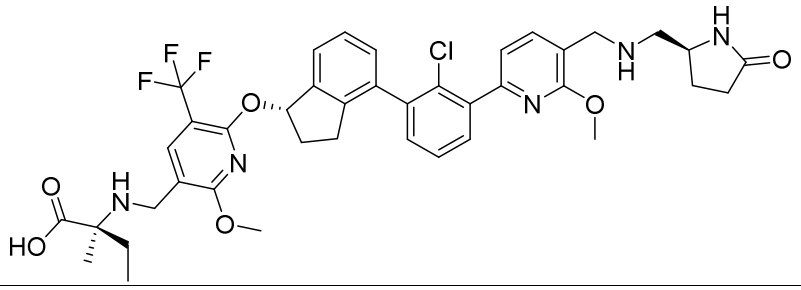
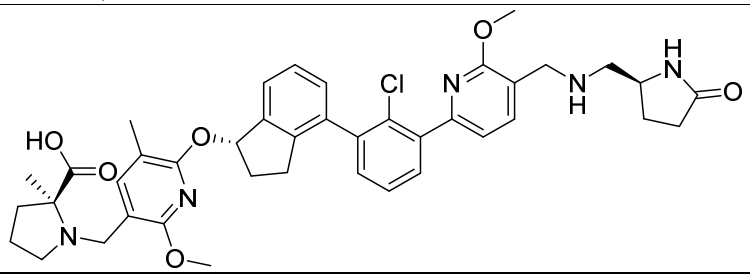
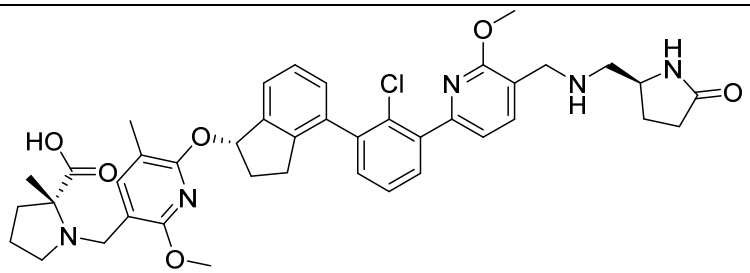
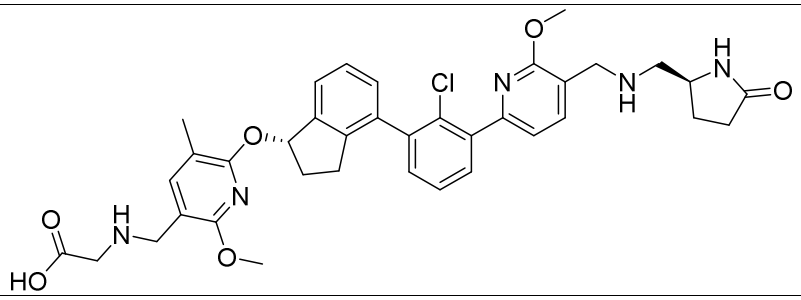
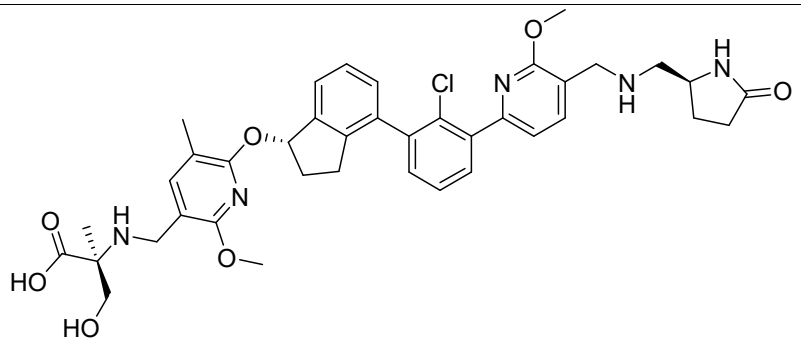
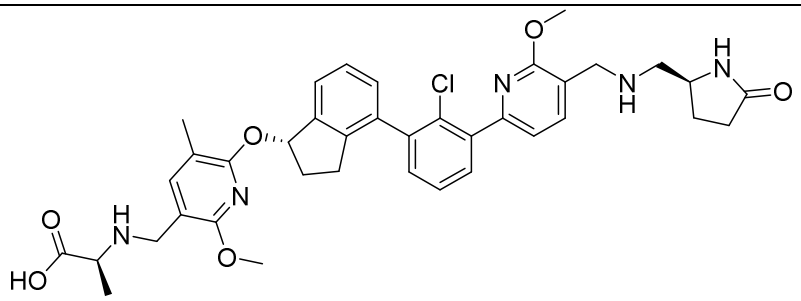
B-236	
B-237	
B-238	
B-239	
B-240	
B-241	

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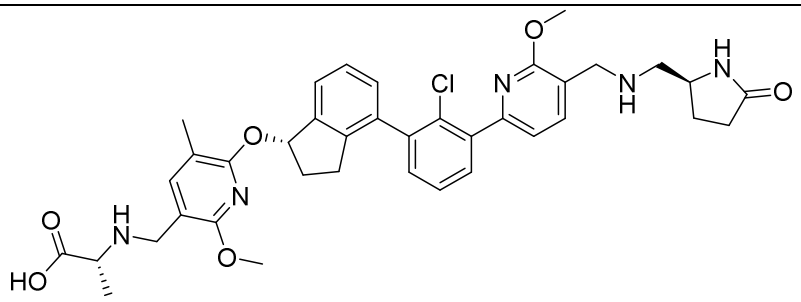
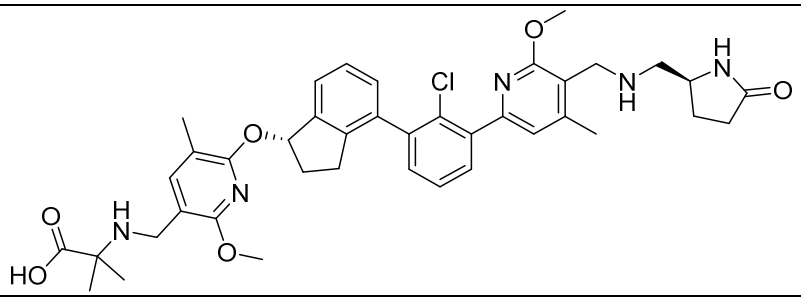
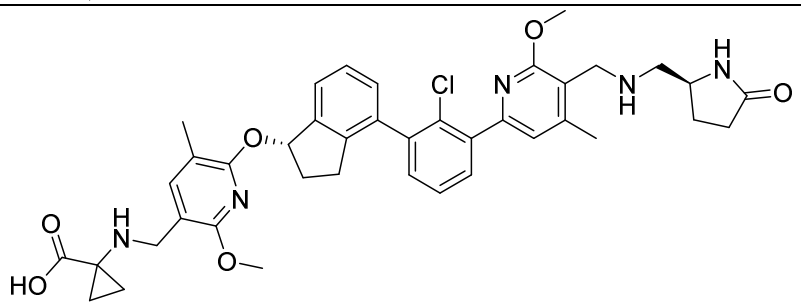
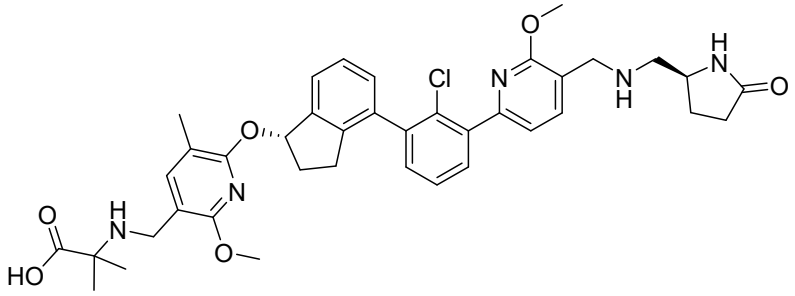
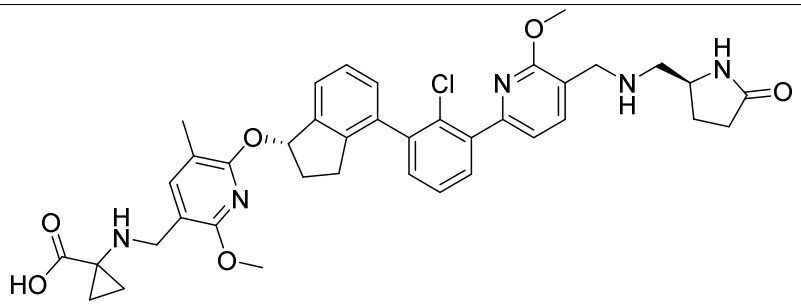
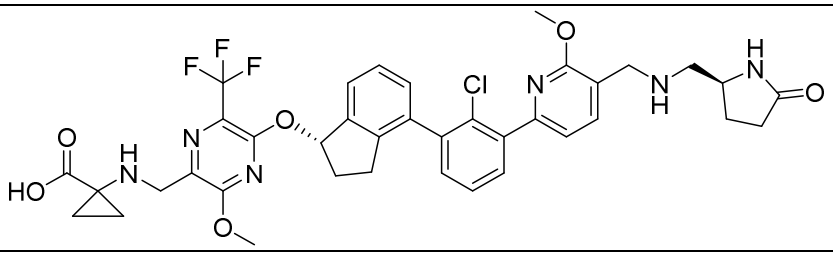
B-242	
B-243	
B-244	
B-245	
B-246	
B-247	

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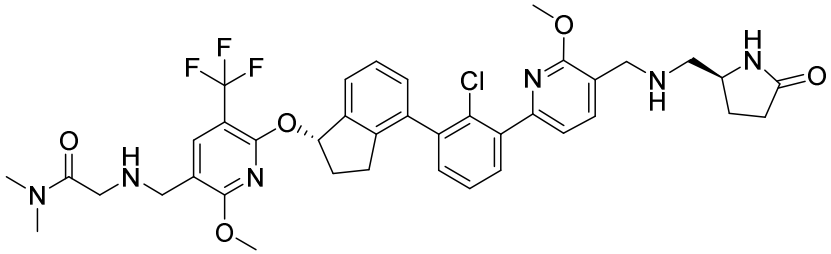
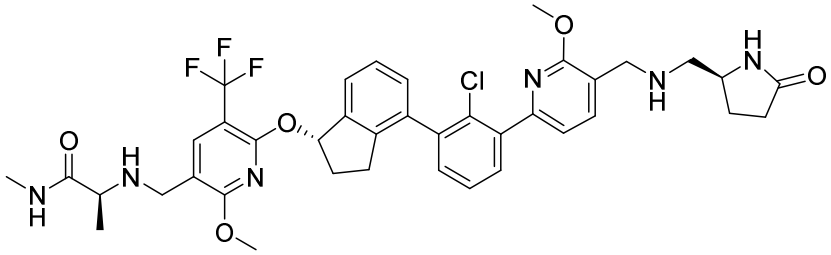
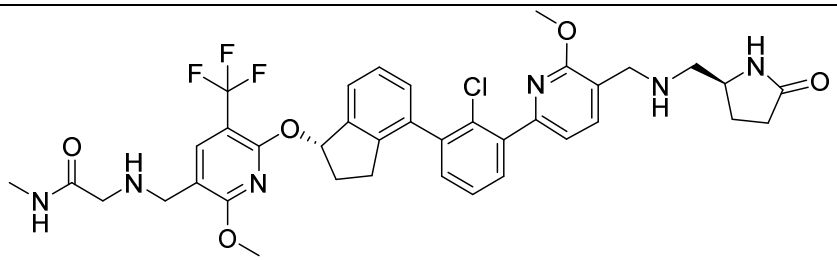
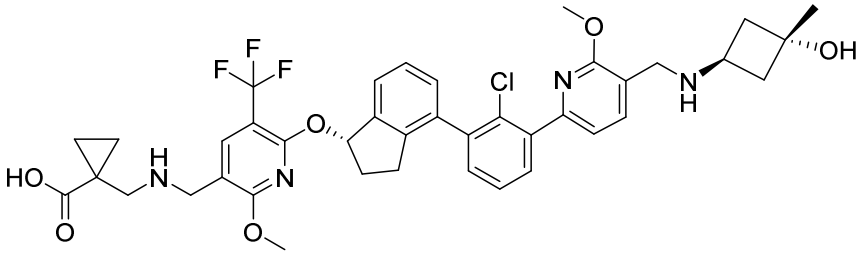
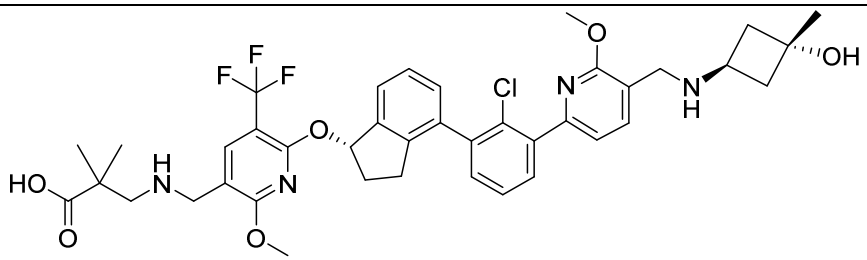
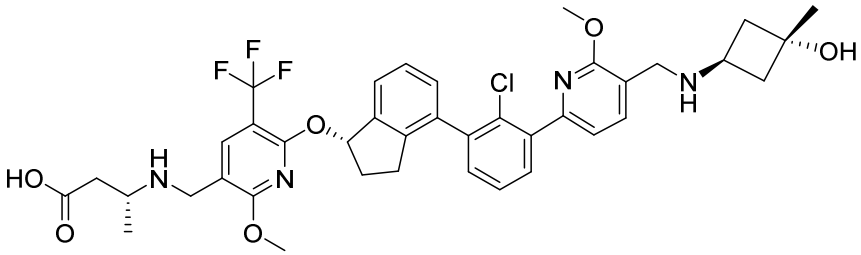
B-248	
B-249	
B-250	
B-251	
B-252	
B-253	

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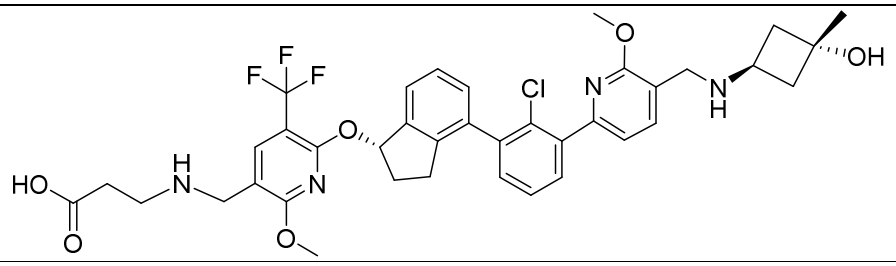
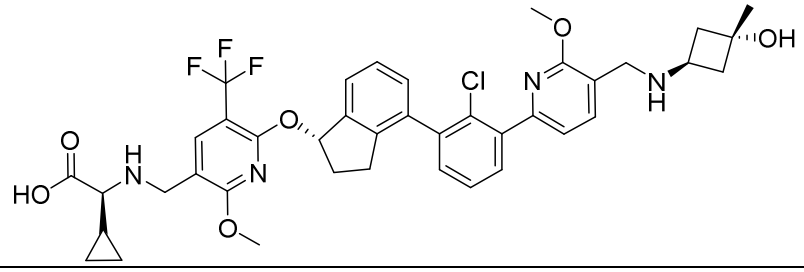
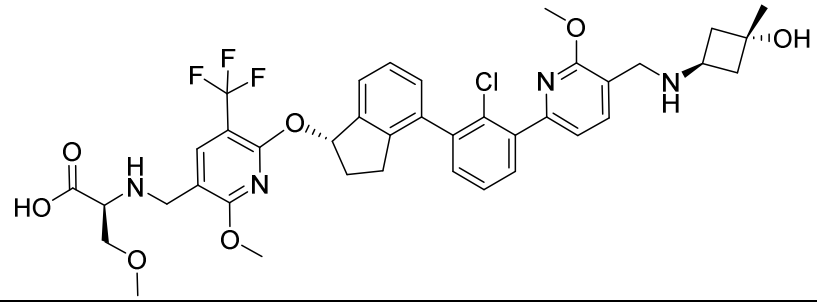
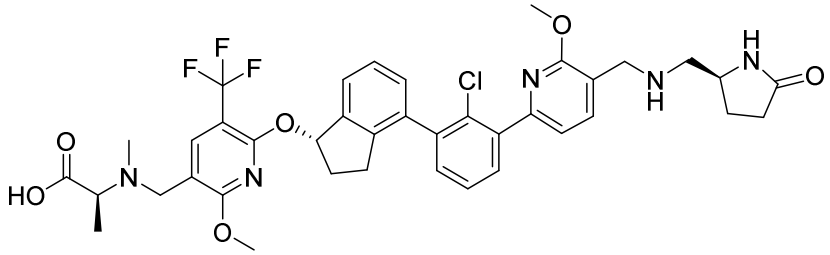
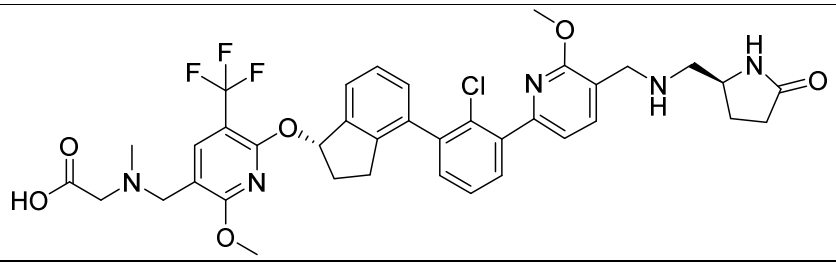
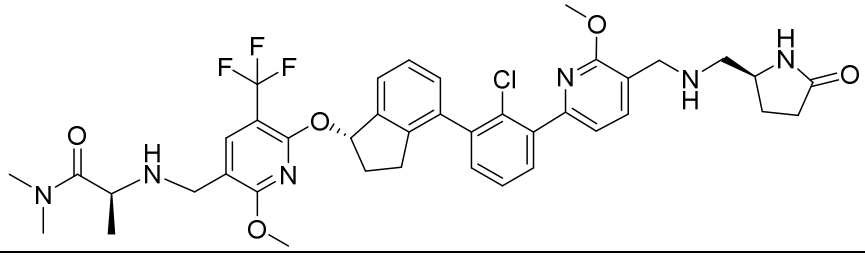
B-254	
B-255	
B-256	
B-257	
B-258	
B-259	

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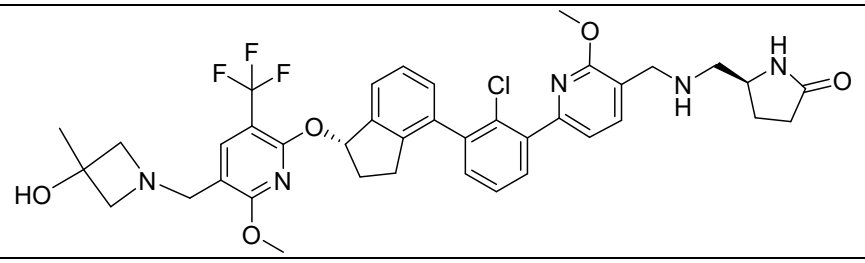
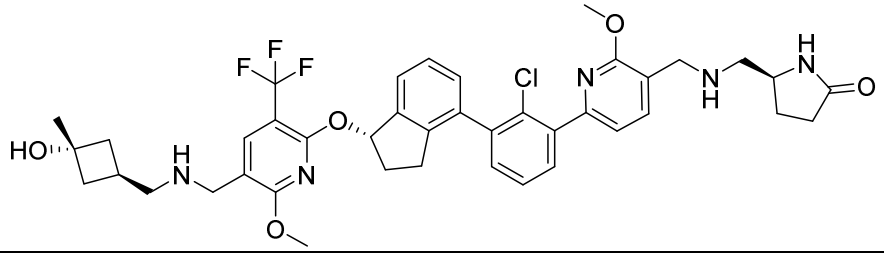
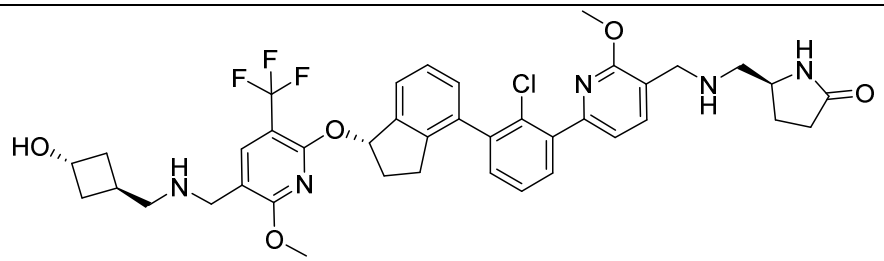
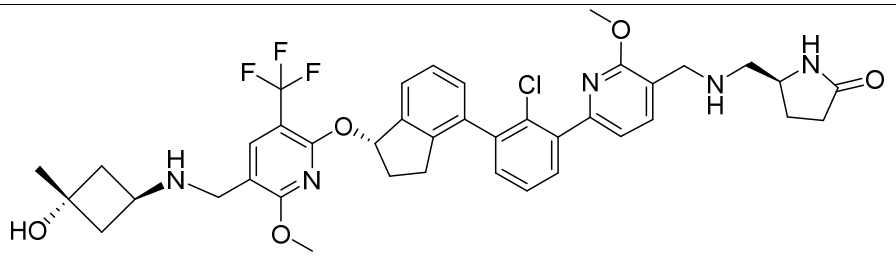
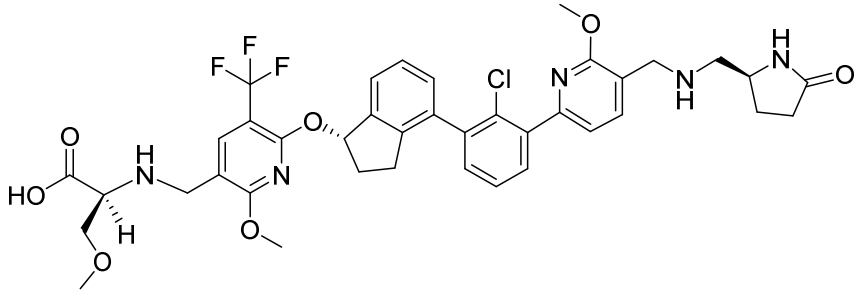
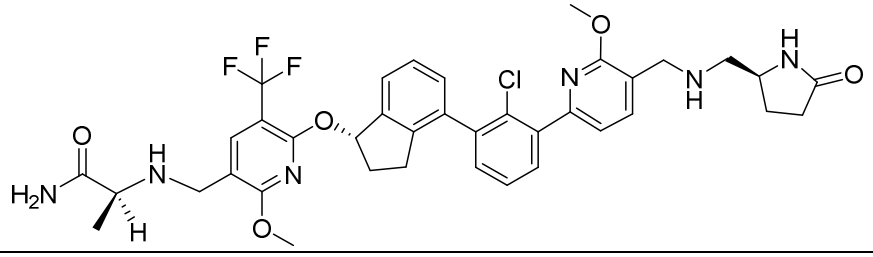
B-260	
B-261	
B-262	
B-263	
B-264	
B-265	

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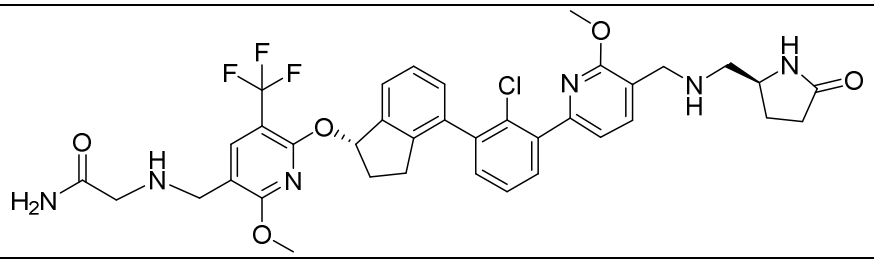
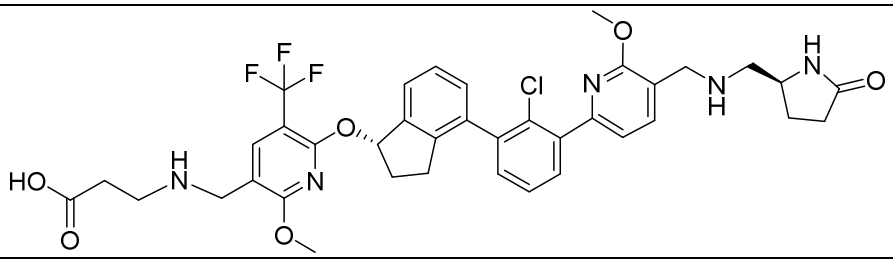
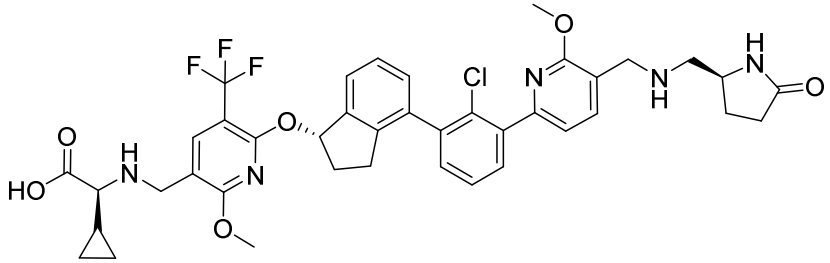
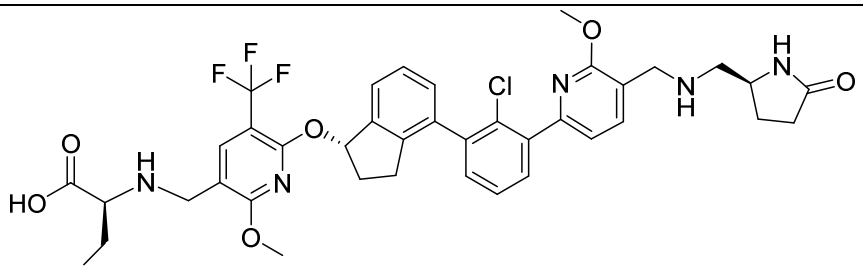
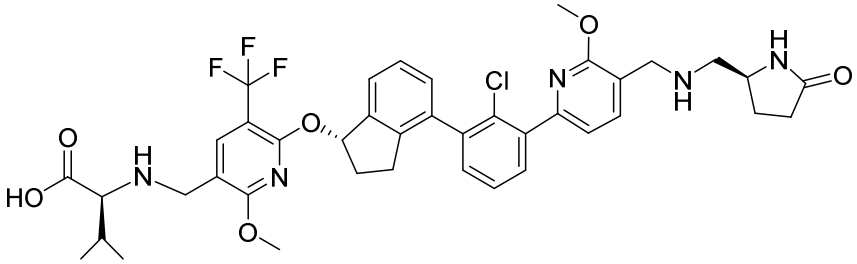
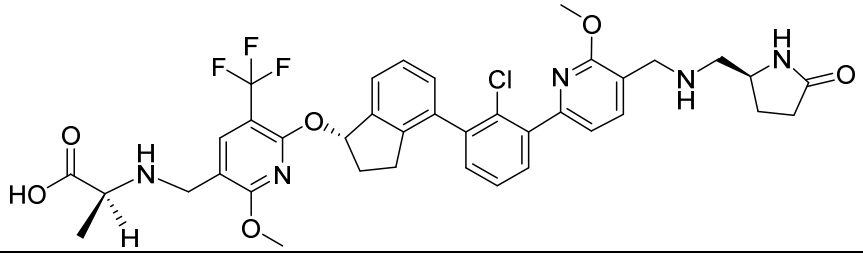
B-266	
B-267	
B-268	
B-269	
B-270	
B-271	

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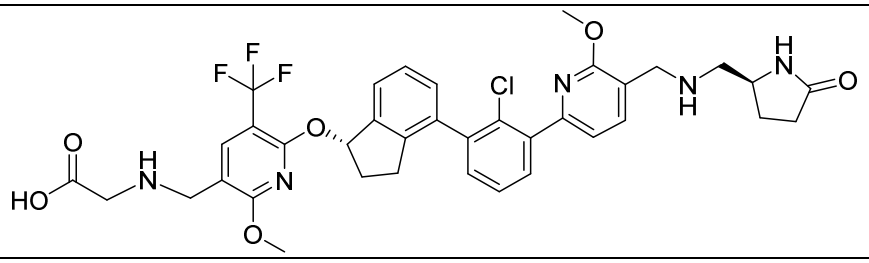
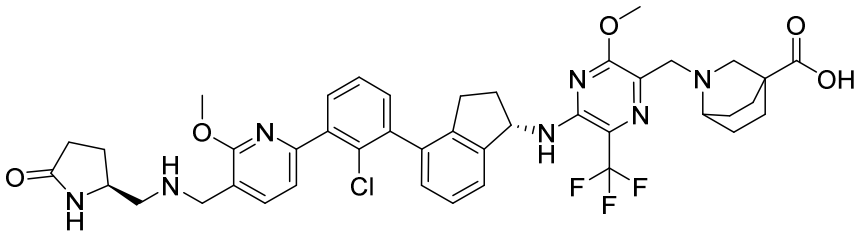
B-272	

14. A compound which is:


;

or a pharmaceutically acceptable salt thereof.

15. A pharmaceutical composition comprising a compound according to any one of claims 1-14 or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

16. The pharmaceutical composition according to claim 15, further comprising at least one additional anticancer agent or therapy selected from rituxan, doxorubicin, gemcitabine, nivolumab, pembrolizumab, ipilimumab, and atezolizumab, and at least one pharmaceutically acceptable excipient.

17. Use of a compound according to any one of claims 1-14 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer in a patient in need thereof.