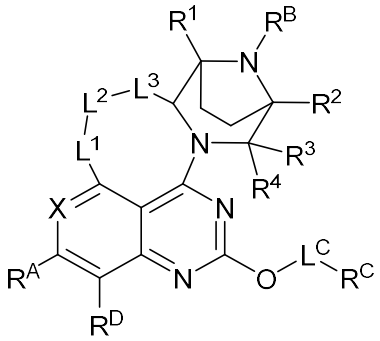
CLAIMS

1. A compound of Formula I:



Formula I,

or a pharmaceutically acceptable salt thereof,

wherein

X is N, CH, or CR^x;

R^x is $(CH_2)_mCN$ or halo;

m is 0, 1, 2 or 3;

R^1, R^2, R^3, and R^4 are each independently H or C_1-C_3 alkyl;

L^1 is O, S, or $CR^{1a}R^{1b}$;

R^{1a} and R^{1b} are each independently H, C_1-C_3 alkyl, C_1-C_3 alkoxy, halo, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, -CN, C_1-C_3 cyanoalkyl, or C_3-C_6 cycloalkyl;

alternatively, R^{1a} and R^{1b} can combine with the atom to which they are attached to form a C_3-C_6 cycloalkyl;

L^2 is $CR^{2a}R^{2b}$;

alternatively, L^2 is O or S, and L^1 is $CR^{1a}R^{1b}$;

R^{2a} and R^{2b} are each independently H, C_1-C_3 alkyl, C_1-C_3 alkoxy, halo, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, -CN, C_1-C_3 cyanoalkyl, or C_3-C_6 cycloalkyl;

alternatively, R^{2a} and R^{2b} can combine with the atom to which they are attached to form a C_3-C_6 cycloalkyl;

alternatively, R^{1b} and R^{2b} can combine with the atoms to which they are attached to form a C_3-C_6 cycloalkyl;

L^3 is a bond or $CR^{3a}R^{3b}$;

R^{3a} and R^{3b} are each independently H, C_1-C_3 alkyl, C_1-C_3 alkoxy, halo, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, -CN, C_1-C_3 cyanoalkyl, or C_3-C_6 cycloalkyl;

alternatively, R^{3a} and R^{3b} can combine with the atom to which they are attached to form a C_3-C_6 cycloalkyl;

alternatively, R^{2b} and R^{3b} can combine with the atoms to which they are attached to form a C_3-C_6 cycloalkyl;

R^A is phenyl or naphthyl, wherein R^A is substituted with 0, 1, 2, 3, 4, or 5 R^{A2};

each R^{A2} is independently -OH, C_1-C_{10} alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_{10} alkoxy, C_1-C_{10} hydroxyalkyl, C_2-C_{10} alkoxyalkyl, C_1-C_6 alkyl-$N(R^{A2a})(R^{A2b})$, C_1-C_{10} thioalkyl, halo, C_1-C_6 haloalkyl, -CN, $-C(O)R^{A2a}$, $-C(O)OR^{A2a}$, $-OC(O)R^{A2a}$, $-OC(O)OR^{A2a}$, $-C(O)N(R^{A2a})(R^{A2b})$, $-N(R^{A2a})C(O)(R^{A2b})$, $-OC(O)N(R^{A2a})(R^{A2b})$, $-N(R^{A2a})C(O)(OR^{A2b})$, oxo, $-OR^{A2a}$, $-SR^{A2a}$, $-S(O)_2R^{A2a}$, $-S(O)_2OR^{A2a}$, $-N(R^{A2a})(R^{A2b})$, -(C_0-C_3 alkyl)-SF_5, $-OP(O)(OR^{A2a})(OR^{A2b})$, C_3-C_8 cycloalkyl, -(C_1-C_6 alkyl)-(C_3-C_8 cycloalkyl), 3- to 14-membered heterocyclyl, -(C_1-C_6 alkyl)-(3- to 14-membered heterocyclyl), C_6-C_{14} aryl, -(C_1-C_6 alkyl)-(C_6-C_{14} aryl), 5- to 14-membered heteroaryl, or -(C_1-C_6 alkyl)-(5- to 14-membered heteroaryl), wherein each alkyl, alkenyl, alkynyl, alkoxy, hydroxyalkyl, and haloalkyl is substituted with 0, 1, 2, or 3 R^{A3}, and wherein each cycloalkyl, alkyl-cycloalkyl, heterocyclyl, alkyl-heterocyclyl, aryl, alkyl-aryl, heteroaryl, and alkyl-heteroaryl is substituted with 0, 1, 2, or 3 R^{A4};

each R^{A2a} and R^{A2b} is independently H, C_1-C_{10} alkyl, C_1-C_6 haloalkyl, or C_3-C_8 cycloalkyl;

each R^{A3} is independently halo, -CN, -OR^{A3a}, -SR^{A3a}, -$N(R^{A3a})(R^{A3b})$, C_3-C_8 cycloalkyl, or 5- to 14-membered heteroaryl;

each R^{A3a} and R^{A3b} is independently H, C_1-C_{10} alkyl, C_1-C_6 haloalkyl, or C_3-C_8 cycloalkyl;

each R^{A4} is independently C_1-C_6 alkoxy, C_1-C_6 hydroxyalkyl, C_2-C_6 alkoxyalkyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, C_1-C_6 haloalkylthio, C_3-C_8 cycloalkyl, -(C_1-C_6 alkyl)-(C_6-C_{10} aryl), halo, -CN, -OH, or -$N(R^{A4a})(R^{A4b})$;

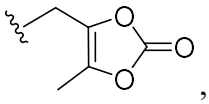
each R^{A4a} and R^{A4b} is independently H or C_1-C_6 alkyl;

alternatively, two R^{A2} can combine to form a C_3-C_{10} cycloalkyl, C_6-C_{10} aryl, a 3- to 10-membered heterocyclyl, or 5- to 14-membered heteroaryl on two adjacent atoms on R^A;

R^B is H, -$C(O)R^{B1}$, or -$C(O)OR^{B2}$;

R^{B1} is C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, C_6-C_{14} aryl, or 5- to 14-membered heteroaryl, wherein the C_3-C_8 cycloalkyl, C_6-C_{14} aryl or 5- to 14-membered heteroaryl are substituted with 0, 1, 2, or 3 R^{B1a};

R^{B2} is C_1-C_6 alkyl, C_1-C_6 haloalkyl, (C_1-C_6 alkyl)-$OC(O)R^{B3}$, C_3-C_8 cycloalkyl, C_6-C_{14} aryl, 5- to 14-membered heteroaryl, or

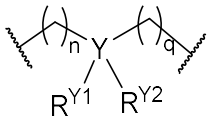

,

wherein the C_3-C_8 cycloalkyl, C_6-C_{14} aryl or 5- to 14-membered heteroaryl are substituted with 0, 1, 2, or 3 R^{B2a};

R^{B3} is C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, C_6-C_{14} aryl, or 5- to 14-membered heteroaryl, wherein the C_3-C_8 cycloalkyl, C_6-C_{14} aryl or 5- to 14-membered heteroaryl are substituted with 0, 1, 2, or 3 R^{B3a};

each R^{B1a}, R^{B2a} and R^{B3a} is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkoxyalkyl, halo, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, oxo, -OH, -CN, or C_3-C_{10} cycloalkyl;

L^C is a bond or



;

Y is C or Si;

n is 0, 1, 2, or 3;

q is 0, 1, 2, or 3;

R^{Y1} is H or C_1-C_3 alkyl;

R^{Y2} is H or C_1-C_3 alkyl;

alternatively, R^{Y1} and R^{Y2} combine to form a C_3-C_{10} cycloalkyl or a 3- to 10-membered heterocyclyl;

R^C is H, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 hydroxyalkyl, C_2-C_6 alkoxyalkyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, $-NH_2$, $-NHR^{C1}$, $-N(R^{C1})_2$, C_3-C_8 cycloalkyl, 3- to 14-membered heterocyclyl, C_6-C_{14} aryl, or 5- to 14-membered heteroaryl, wherein each C_3-C_8 cycloalkyl, 3- to 14-membered heterocyclyl, C_6-C_{14} aryl, and 3- to 14-membered heteroaryl, is substituted with 0, 1, 2, 3, or 4 R^{C3};

each R^{C1} is independently selected from C_1-C_6 alkyl;

each R^{C3} is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_8 alkynyl, C_1-C_6 alkoxyalkyl, C_1-C_6 hydroxyalkyl, halo, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, -(C_1-C_6 alkyl)-$N(R^{C3a})(R^{C3b})$, -CN, $-C(O)R^{C3a}$, $-C(O)OR^{C3a}$, $-C(O)N(R^{C3a})(R^{C3b})$, $-N(R^{C3a})C(O)(R^{C3b})$, $-OC(O)N(R^{C3a})(R^{C3b})$, $-N(R^{C3a})C(O)(OR^{C3b})$, $=CH_2$, $=CF_2$, oxo, $-OR^{C3a}$, $-SR^{C3a}$, $-N(R^{C3a})(R^{C3b})$, $-N_3$, SF_5, C_3-C_8 cycloalkyl, -(C_1-C_6 alkyl)-(C_3-C_8 cycloalkyl), 3- to 10-membered heterocyclyl, -(C_1-C_6 alkyl)-(3- to 10-membered heterocyclyl), C_6-C_{10} aryl, -(C_1-C_6 alkyl)-(C_6-C_{10} aryl), 5- to 10-membered heteroaryl, or -(C_1-C_6 alkyl)-(5- to 10-membered heteroaryl),
wherein each alkyl is substituted with 0, 1, 2, or 3 -CN, $-C(O)OR^{C3a1}$, $-C(O)N(R^{C3a1})(R^{C3a2})$, $-N(R^{C3a1})C(O)(R^{C3a2})$, $-OC(O)N(R^{C3a1})(R^{C3a2})$, $-OR^{C3a1}$, $-SR^{C3a1}$, N_3, SF_5, or 3- to 10-membered heterocyclyl substituted with 0, 1, 2, or 3 R^{C3a2},

each cycloalkyl, alkyl-cycloalkyl, heterocyclyl, alkyl-heterocyclyl, aryl, alkyl-aryl, heteroaryl, and alkyl-heteroaryl is substituted with 0, 1, 2, or 3 halo, -CN, or R^{C3a2}, each alkenyl is substituted with 0, 1, 2, or 3 halo, and each alkoxyalkyl and alkynyl is substituted with 0, 1, 2, or 3 C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl substituted with 0 or 1 C_1-C_6 haloalkyl, C_6-C_{10} aryl, or 5- to 10-membered heteroaryl;

each R^{C3a} and R^{C3b} is independently H, C_1-C_{10} alkyl, C_1-C_6 haloalkyl, C_6-C_{10} aryl, C_3-C_6 cycloalkyl, 3- to 6-membered heterocyclyl, or 5- to 10-membered heteroaryl, wherein each aryl and heteroaryl is substituted with 0, 1, 2, or 3 halo, -CN, or R^{C3a2};

alternatively, R^{C3a} and R^{C3b} together with the N to which they are attached form a 3- to 8-membered heterocycle;

each R^{C3a1} and R^{C3a2} is independently C_1-C_3 alkyl, halo, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, -(C_1-C_3 alkyl)-(C_3-C_8 cycloalkyl), 3- to 10-membered heterocyclyl, -(C_1-C_3 alkyl)-(3- to 10-membered heterocyclyl), C_6-C_{10} aryl, -(C_1-C_3 alkyl)-(C_6-C_{10} aryl), -(C_2-C_4 alkynyl)-(C_6-C_{10} aryl), 5- to 10-membered heteroaryl, -(C_1-C_3 alkyl)-(5- to 10-membered heteroaryl), or SF_5, wherein each cycloalkyl, alkyl-cycloalkyl, heterocyclyl, alkyl-heterocyclyl, aryl, alkyl-aryl, alkynyl-aryl, heteroaryl, and alkyl-heteroaryl is substituted with 0, 1, 2, or 3 halo, C_1-C_3 haloalkyl, C_1-C_3 haloalkoxy, or SF_5;

alternatively, R^{C3a1} and R^{C3a2} together with the N to which they are attached form a 3- to 8-membered heterocycle;

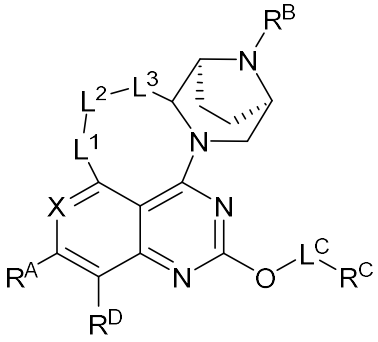
R^D is halo;

each heterocyclyl has 1, 2, 3, or 4 heteroatoms selected from N, O, S, and Si; and

each heteroaryl has 1, 2, 3, or 4 heteroatoms selected from N, O, and S.

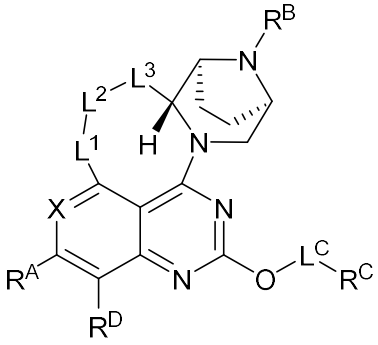
2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^1, R^2, R^3, and R^4 are each H; R^B is H; and R^D is F.

3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, having the structure of Formula (I-1):



(I-1).

4. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, having the structure of Formula (I-2):

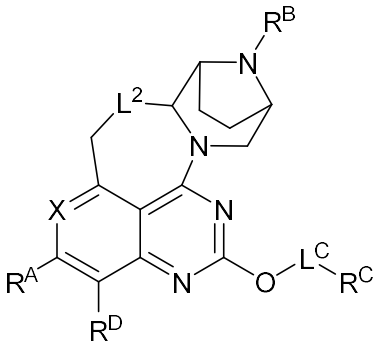


(I-2).

5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein X is N, CH, or C-Cl.

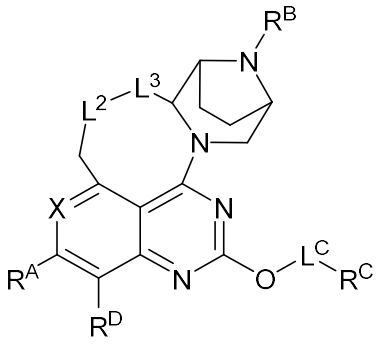
6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein L^1 is CHR^{1b}.

7. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, having the structure of Formula (IIb):



(IIb).

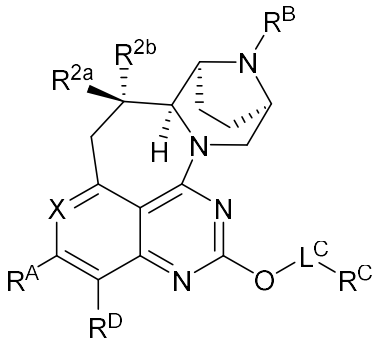
8. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, having the structure of Formula (Ib):



(Ib).

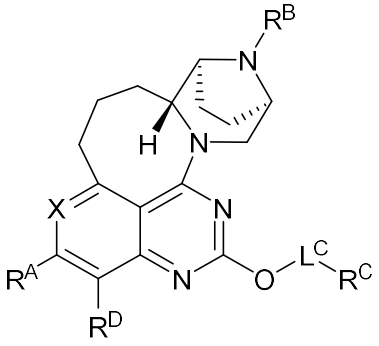
9. The compound of any one of claims 1 to 6 and 8, or a pharmaceutically acceptable salt thereof, wherein L^3 is $CR^{3a}R^{3b}$.

10. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, having the structure of Formula (IIb-2):



(IIb-2).

11. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, having the structure of Formula (Ib-2):

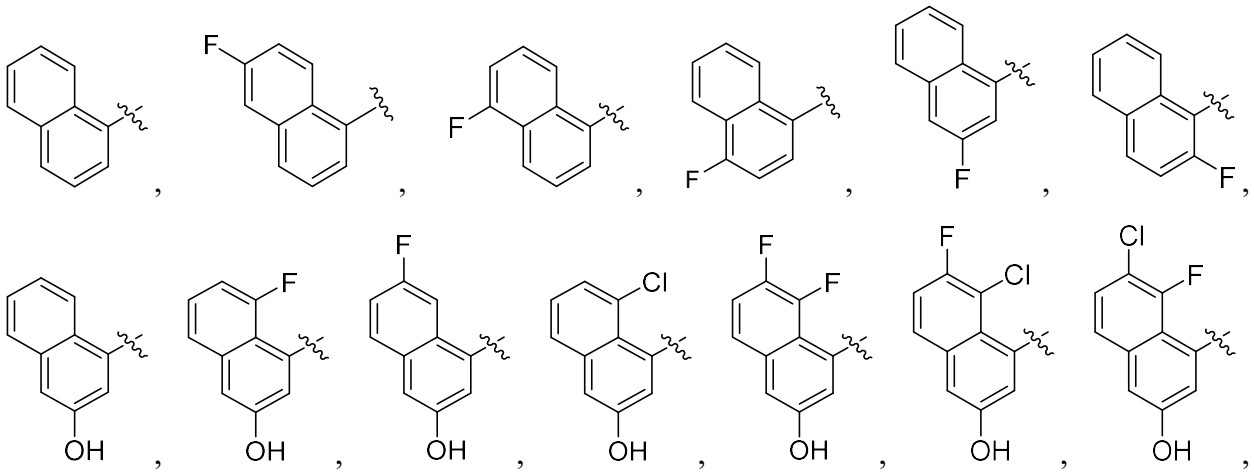


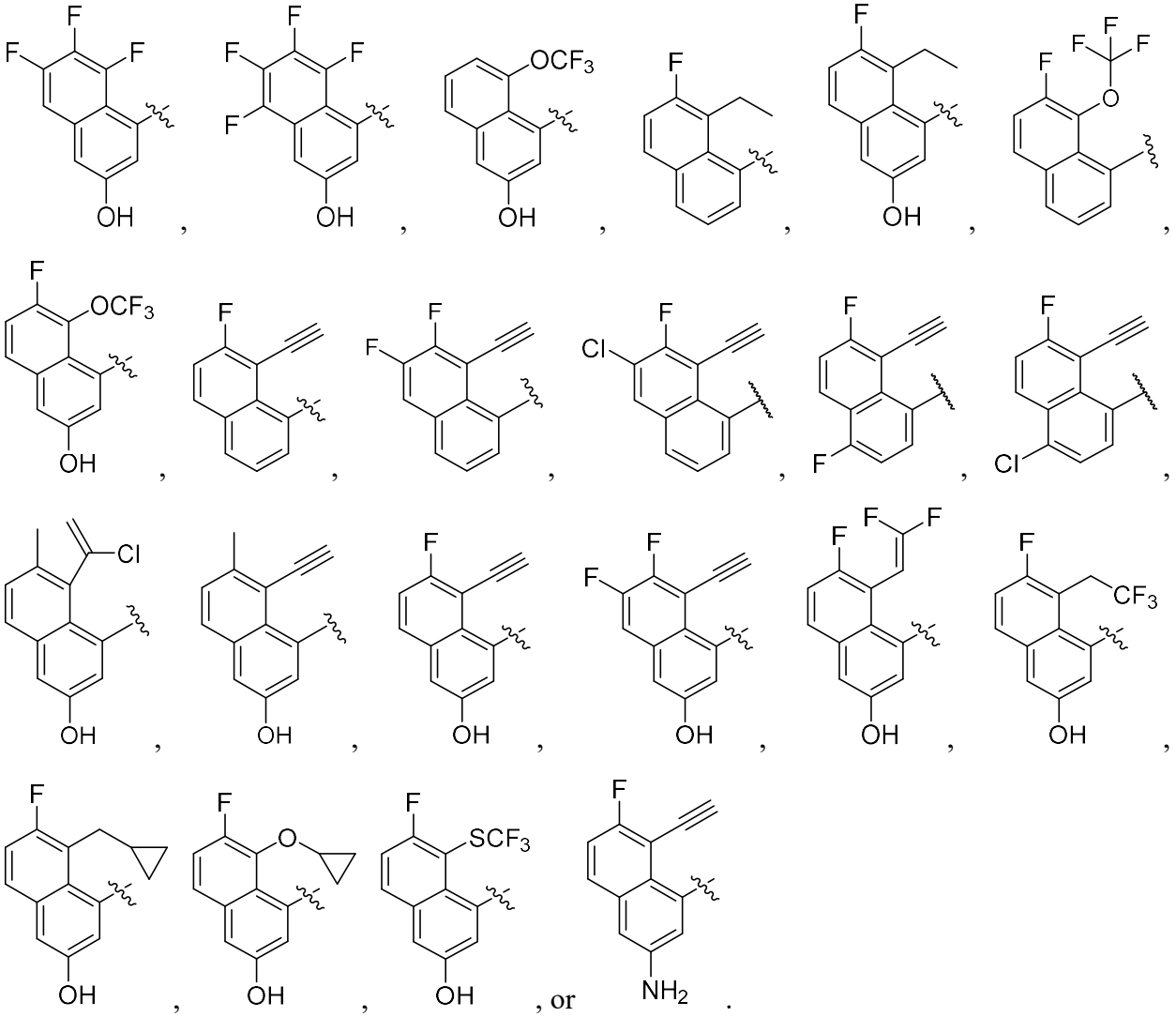
(Ib-2).

12. The compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, wherein R^A is naphthyl substituted with 0, 1, 2, 3, 4, or 5 R^{A2}.

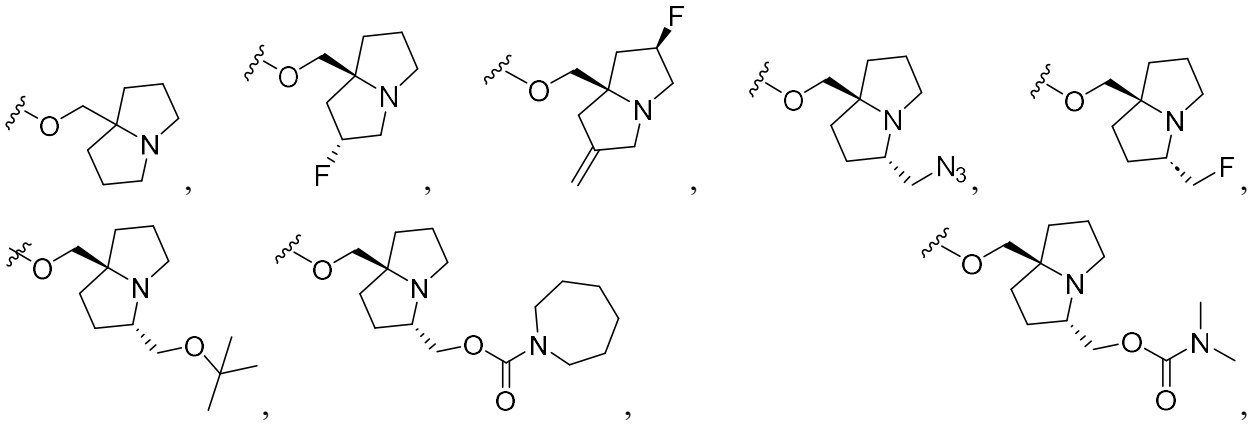
13. The compound of claim 12, or a pharmaceutically acceptable salt thereof, wherein each R^{A2} is independently Me, -OH, -C(Cl)=CH_2, -CH=CHF_2, -C≡CH, F, Cl, -CH_2CF_3, -OCF_3, -O-cyclopropyl, -SCF_3, or –CH_2-cyclopropyl.

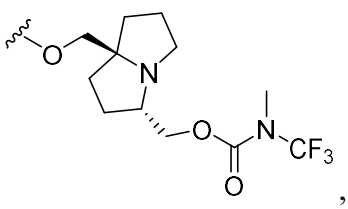
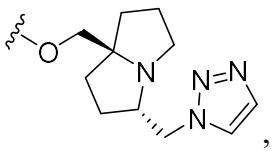
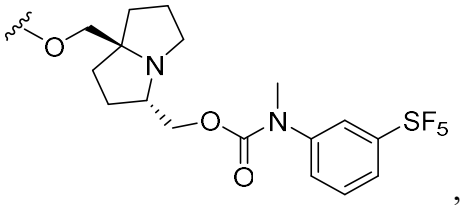
14. The compound of any one of claims 1 to 12, or a pharmaceutically acceptable salt thereof, wherein R^A is

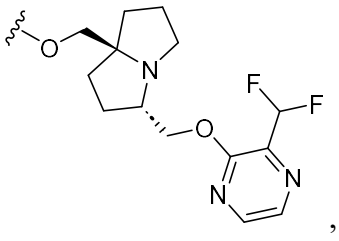
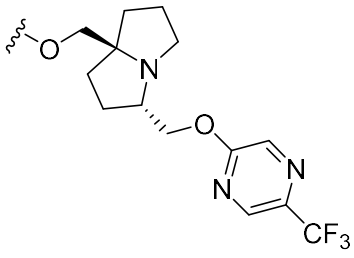
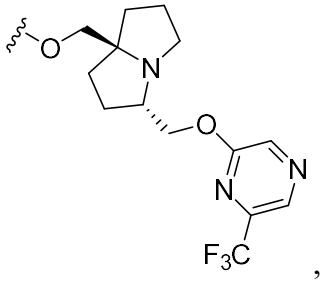
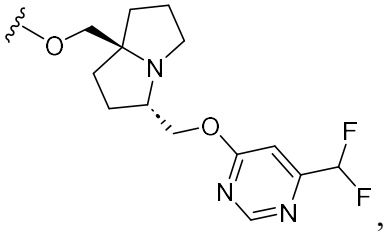
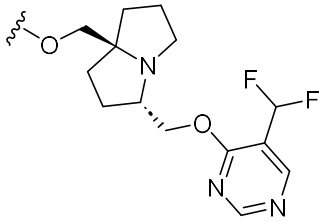
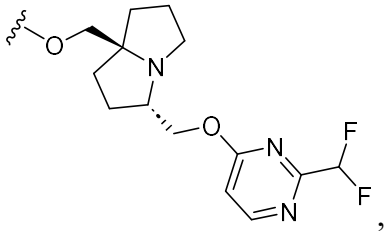
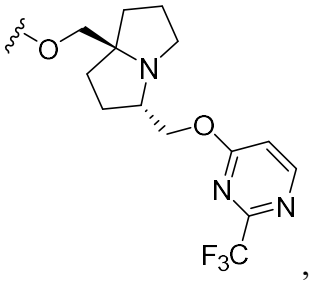
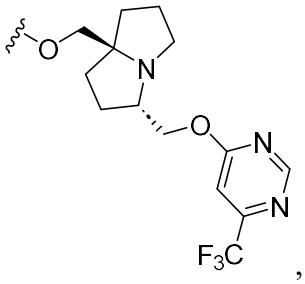
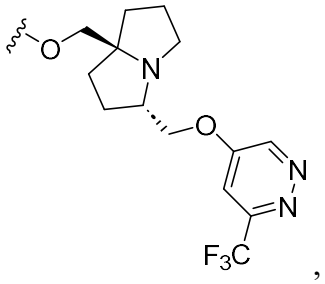
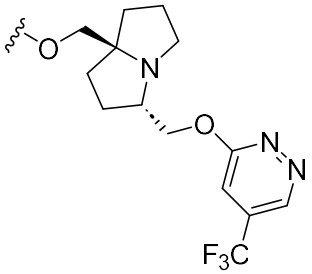
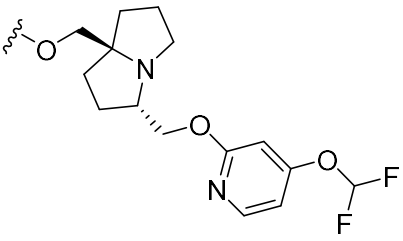
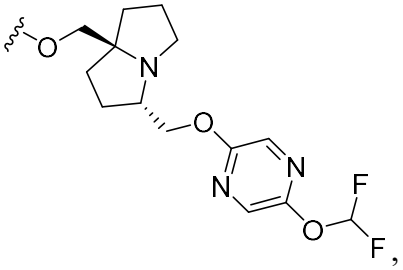
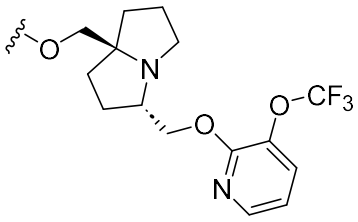
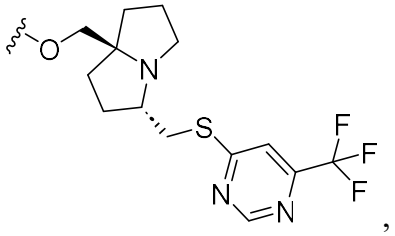
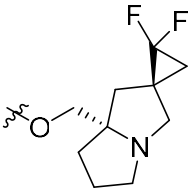
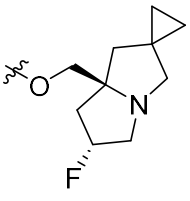
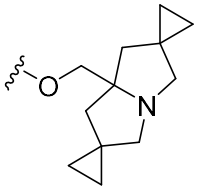


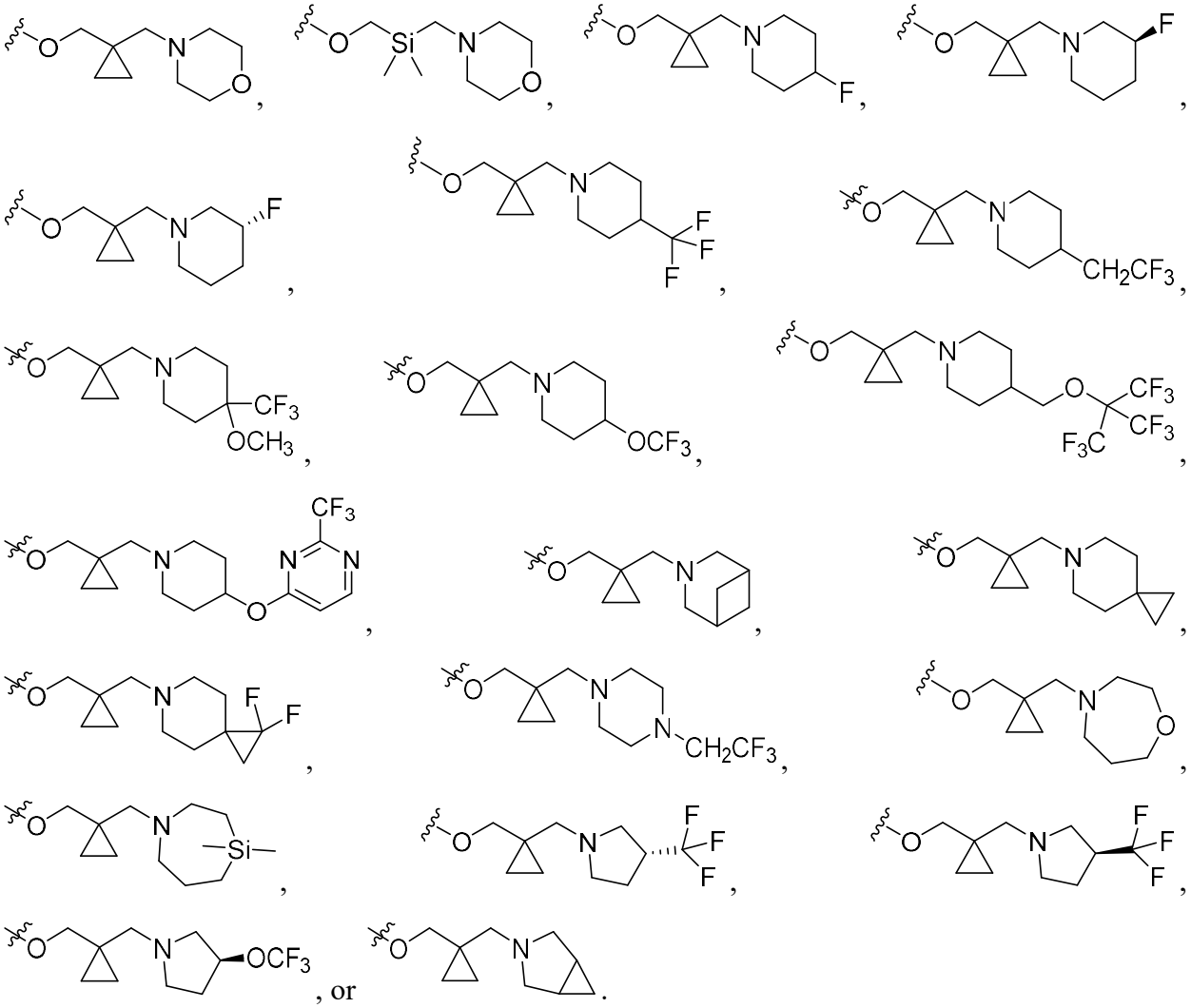


15. The compound of any one of claims 1 to 14, or a pharmaceutically acceptable salt thereof, wherein the –O-L^C-R^C moiety is




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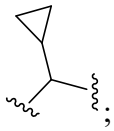


16. The compound of any one of claims 1, 3, and 4, or a pharmaceutically acceptable salt thereof, wherein

X is N, CH, or C-Cl;

L^1 is CH_2, $CHCH_3$, $CHCH_2CH_3$, CHF, or CF_2;

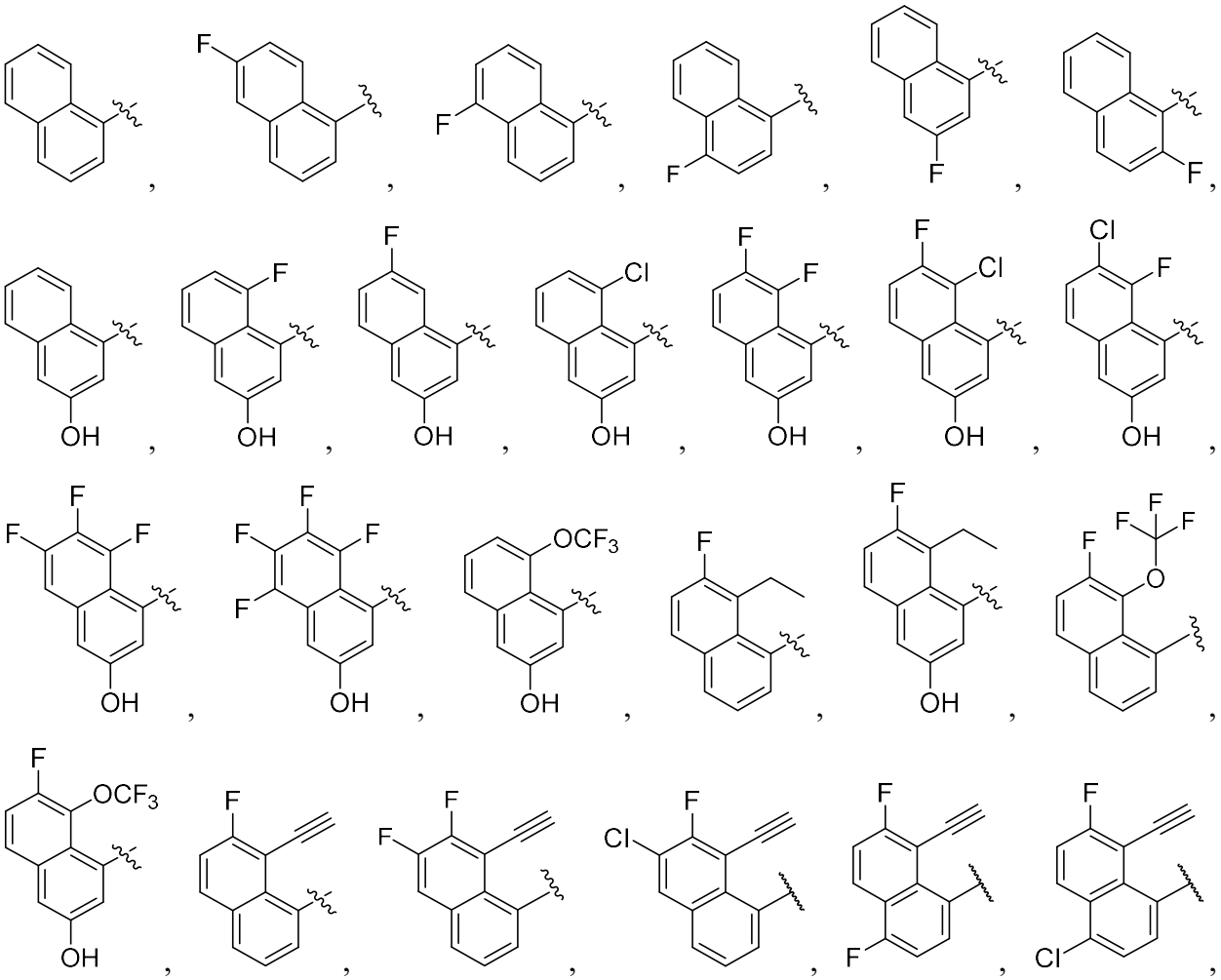
L^2 is CH_2, $CHCH_3$, $CHCH_2CH_3$, $CHCHF_2$, or

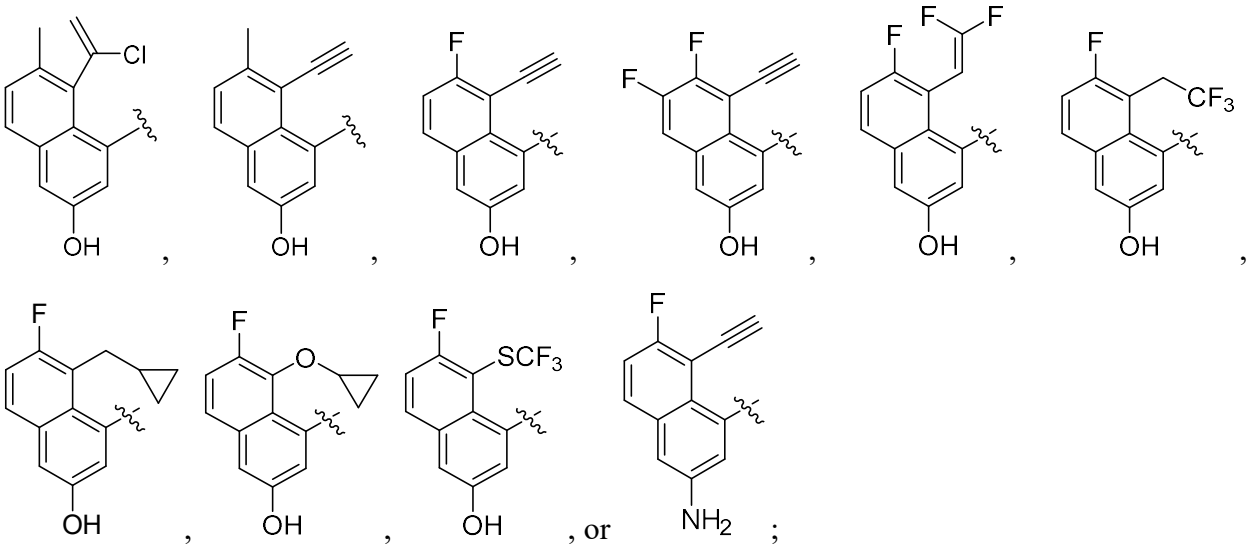


L^3 is a bond, CH_2, or $CHCH_3$;

R^1, R^2, R^3, and R^4 are each H;

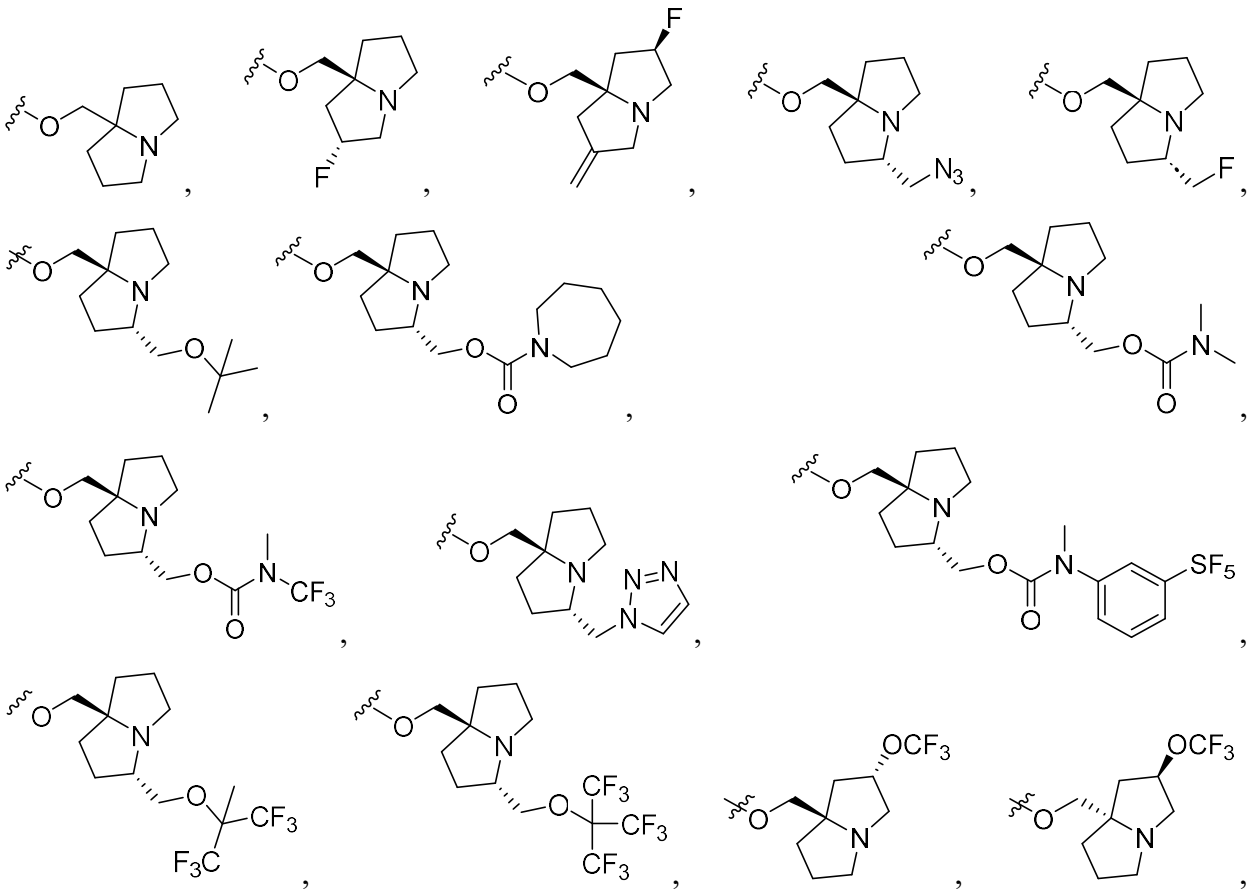
R^A is

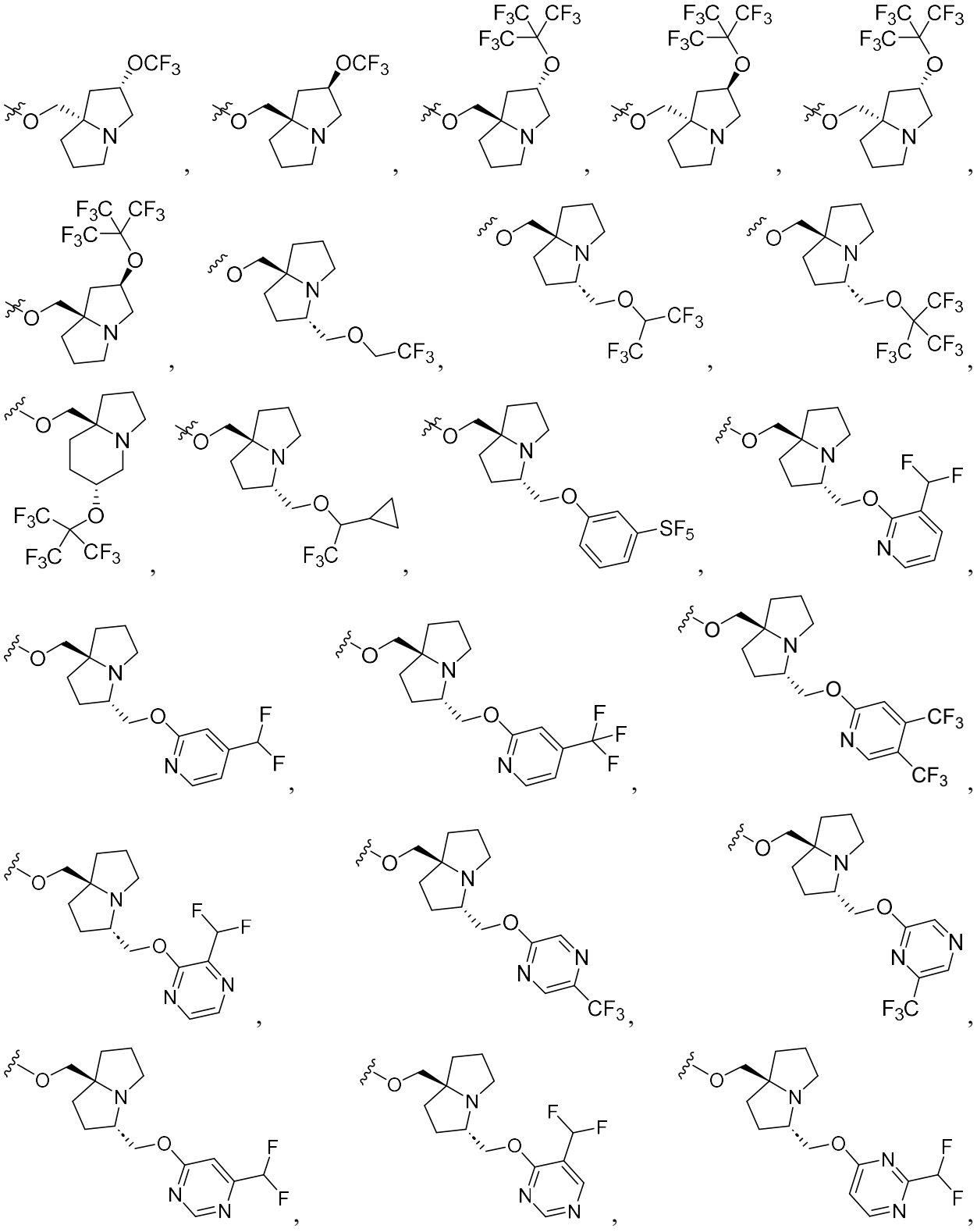


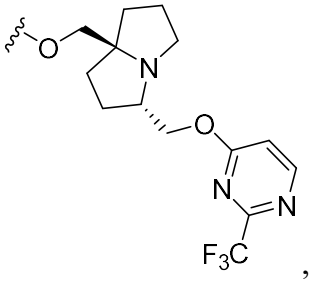
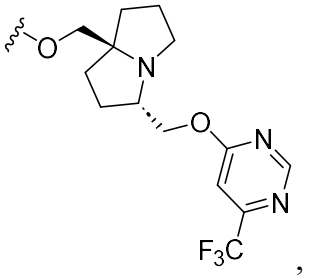
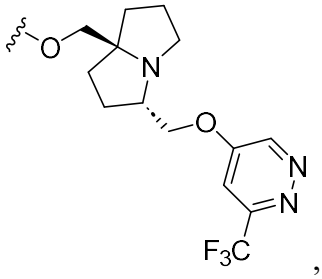
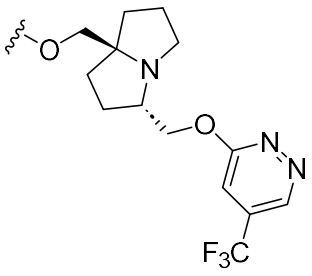
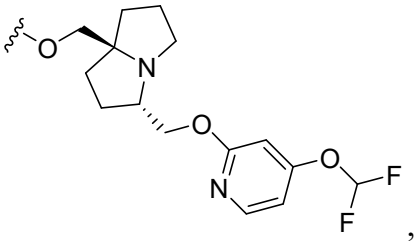
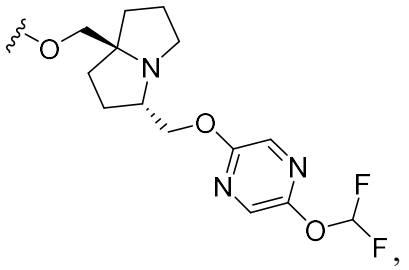
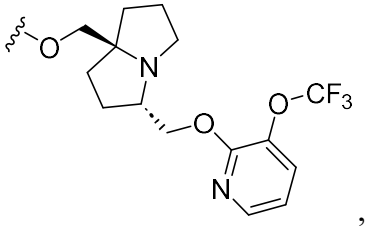
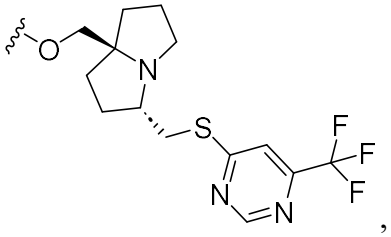
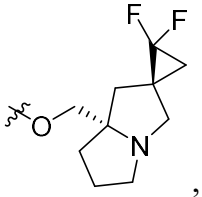
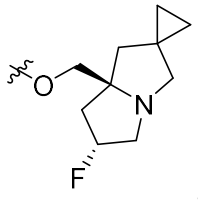
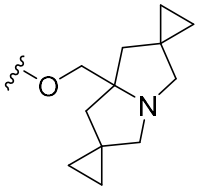
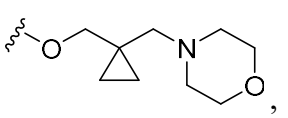
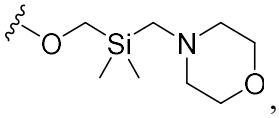
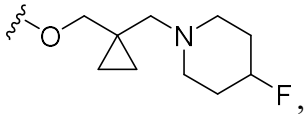
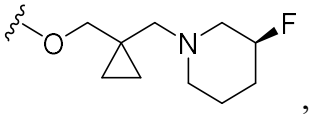
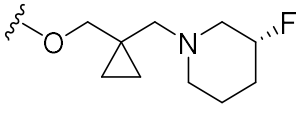
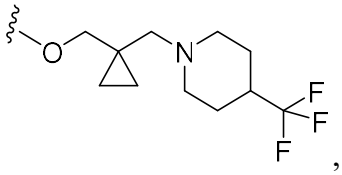
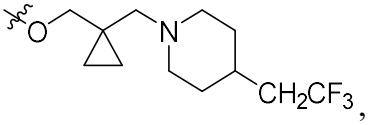
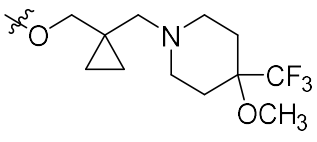
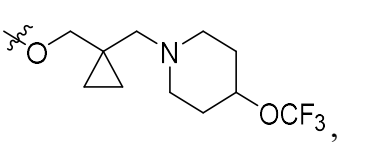
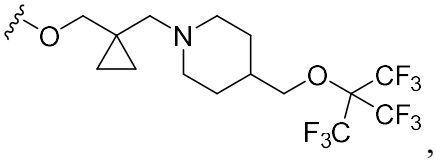


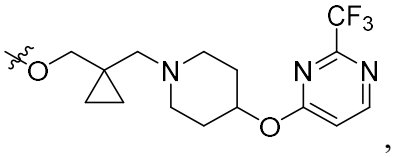
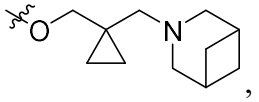
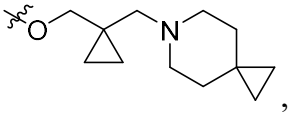
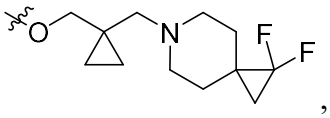
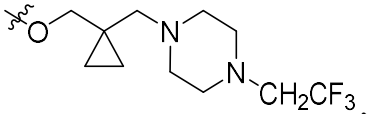
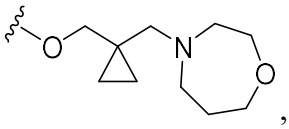
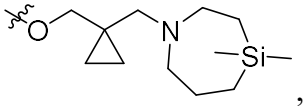
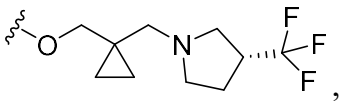
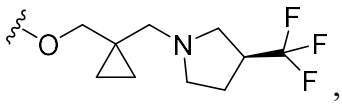
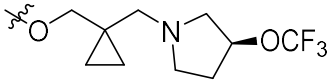
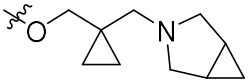
R^B is H;

the $-O-L^C-R^C$ moiety is



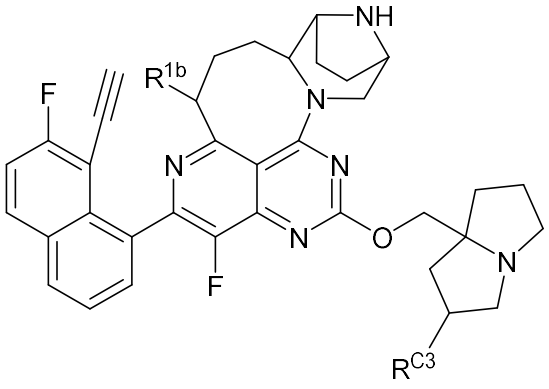


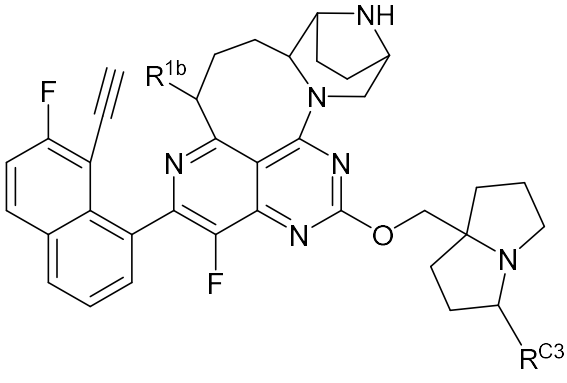

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R^D is F.

17. The compound of claim 1, or a pharmaceutically acceptable salt thereof, having the structure of Formula (Ib-5) or Formula (Ib-6):


(Ib-5),


(Ib-6),

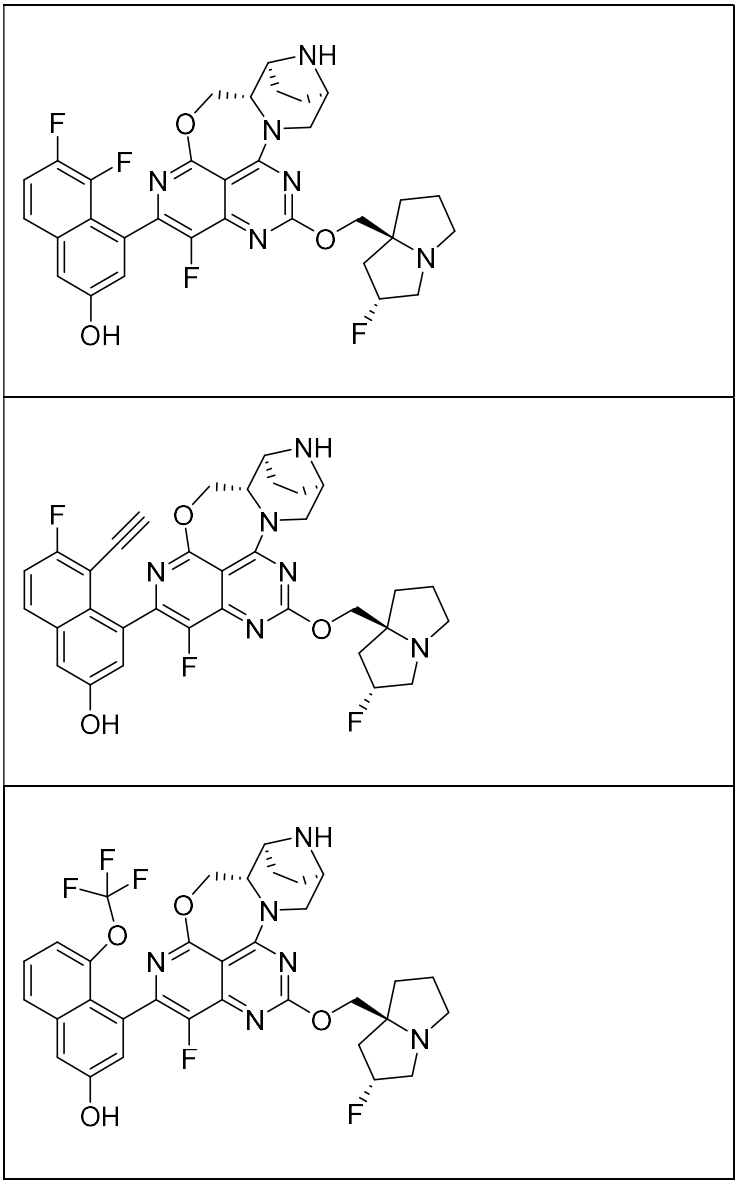
wherein

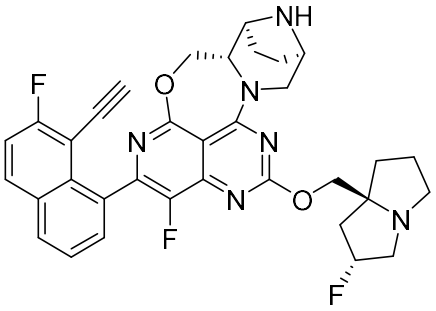
R^{1b} is H or methyl;

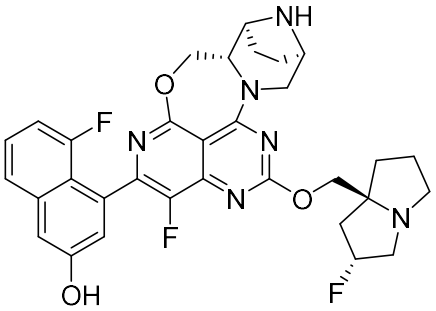
R^{C3} is $-CH_2OR^{C3a1}$ or F; and

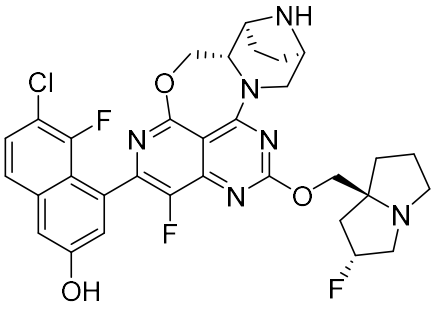
R^{C3a1} is 5- to 6-membered heteroaryl substituted with one halo or C_1-C_2 haloalkyl.

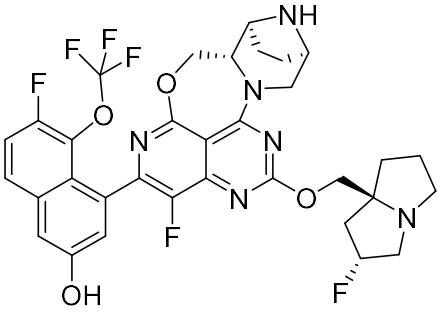
18. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound has the structure:

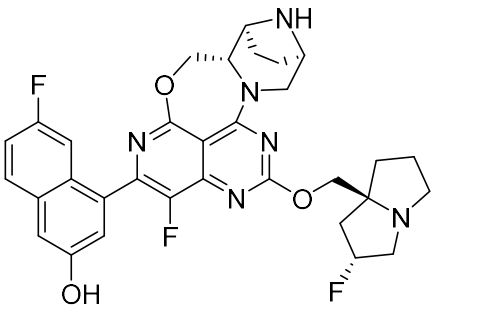


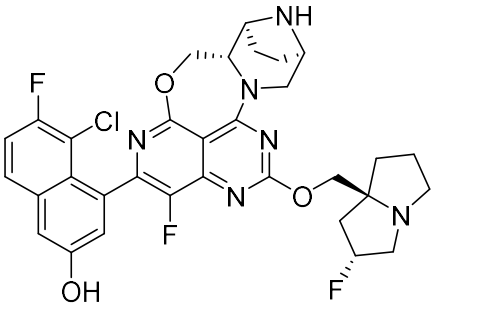


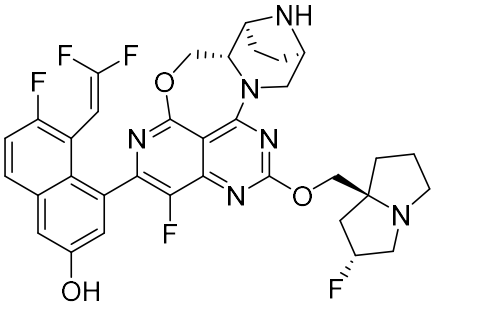


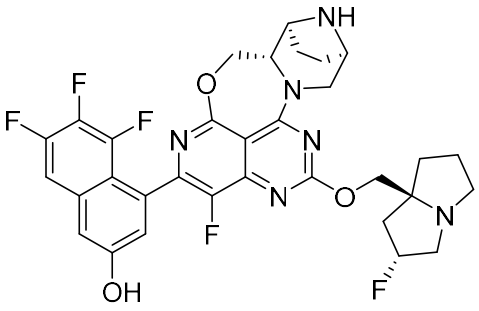


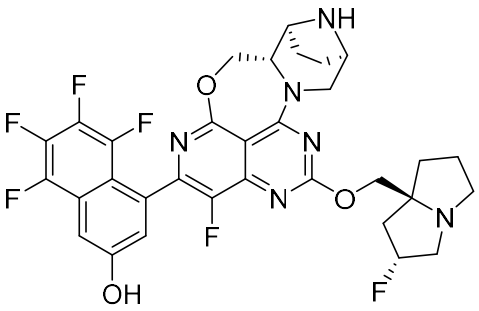


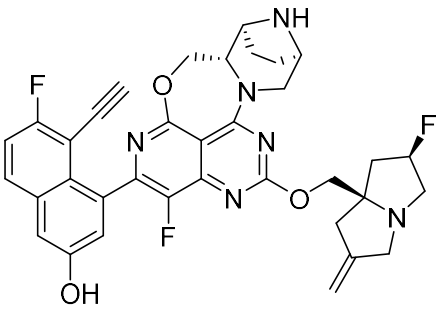


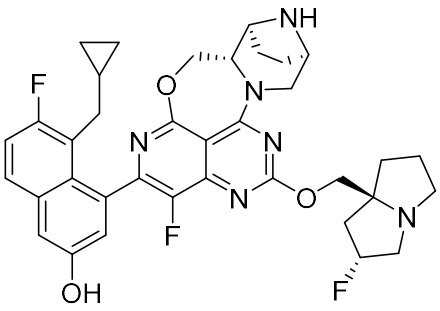


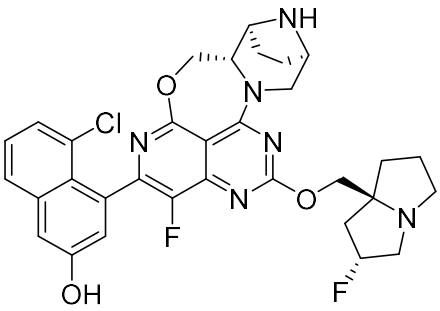


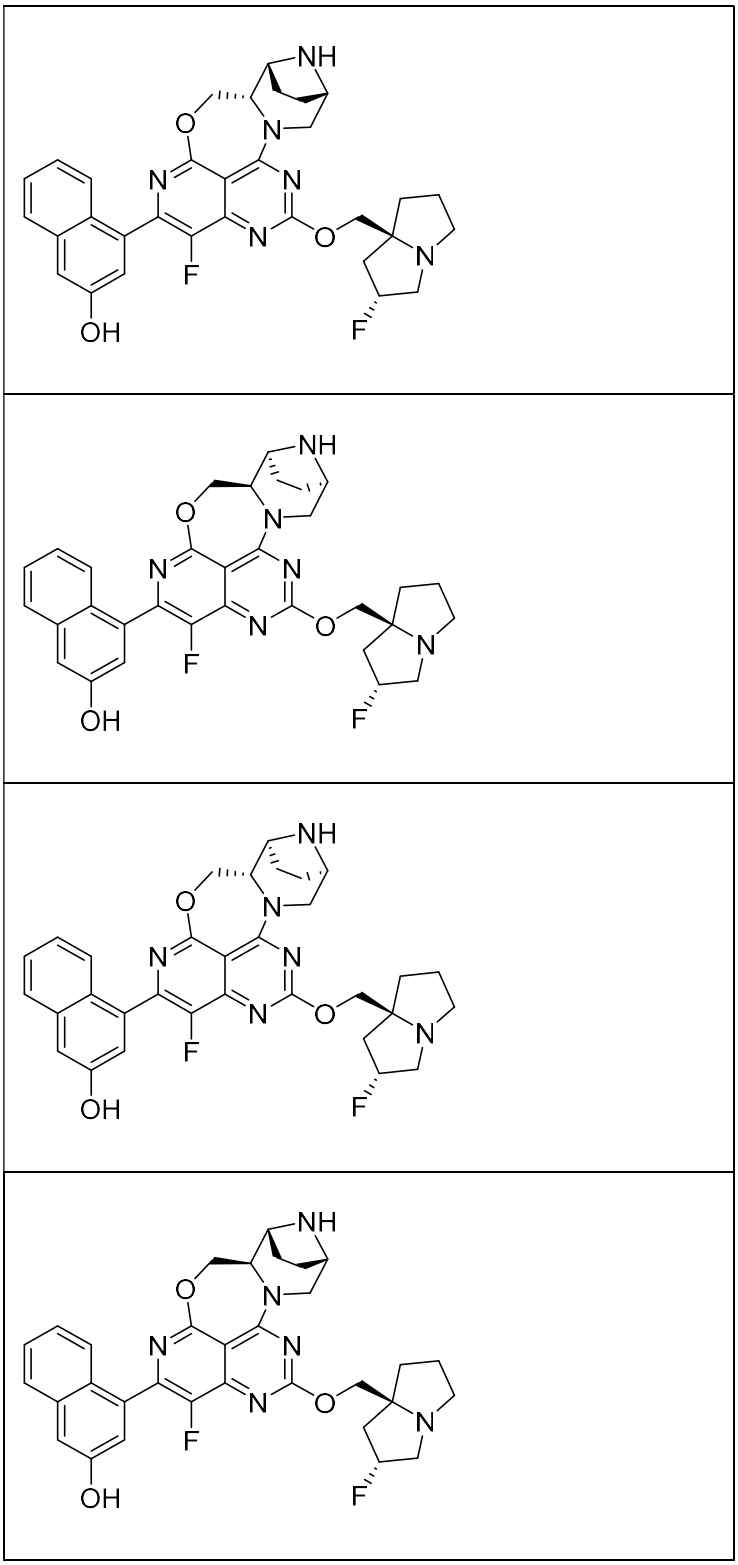


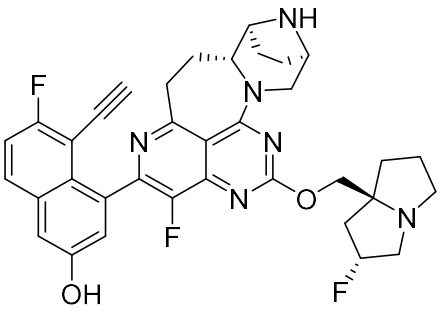


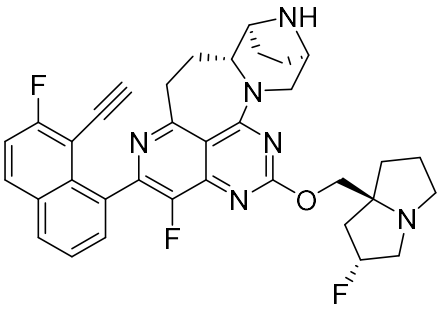


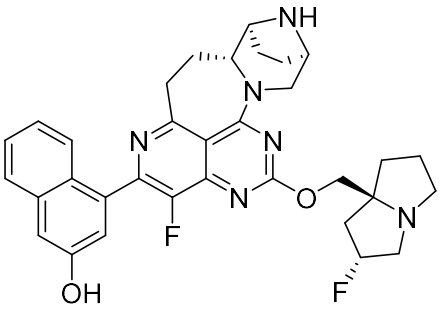


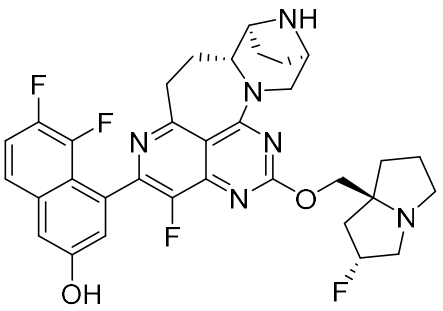


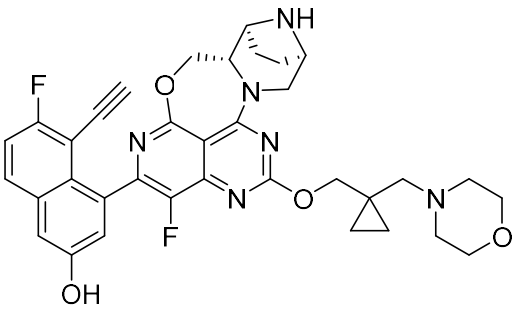


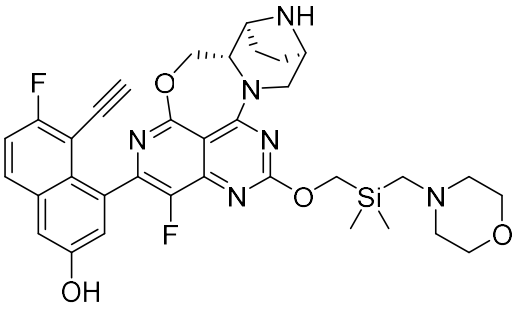


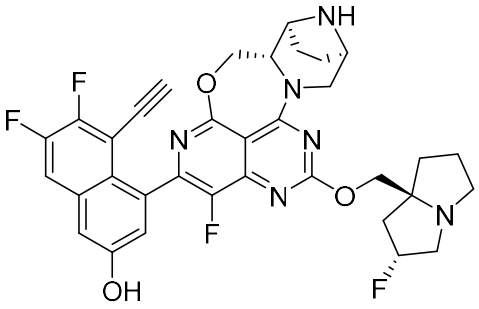


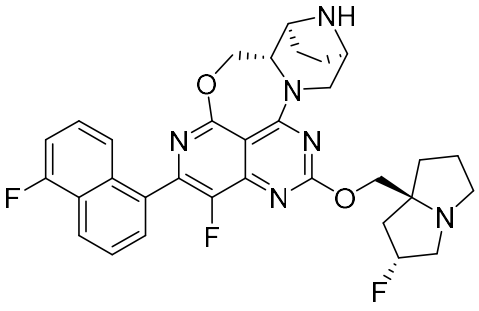


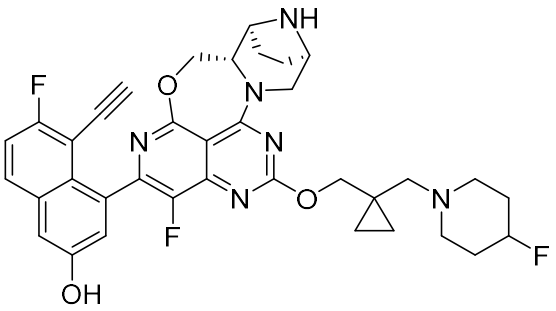


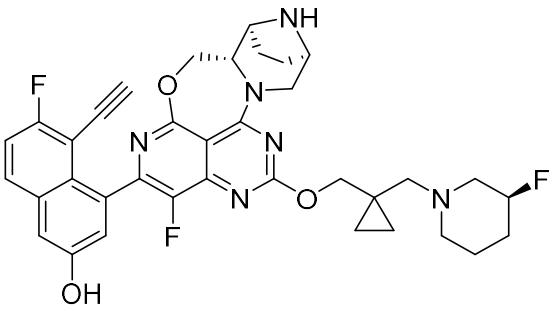


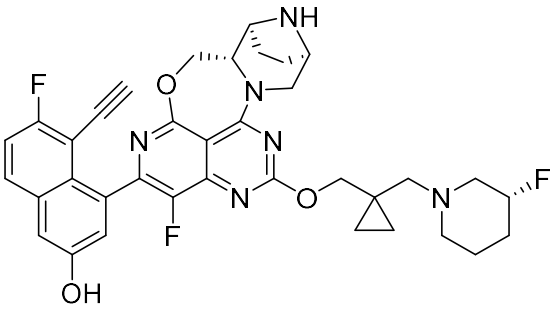


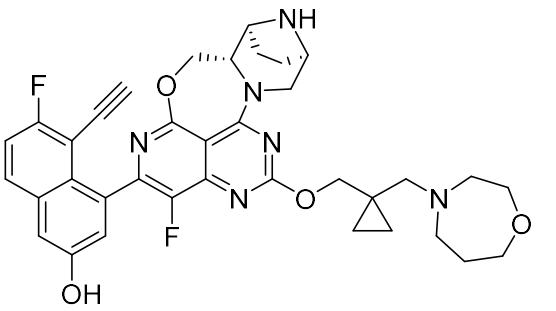


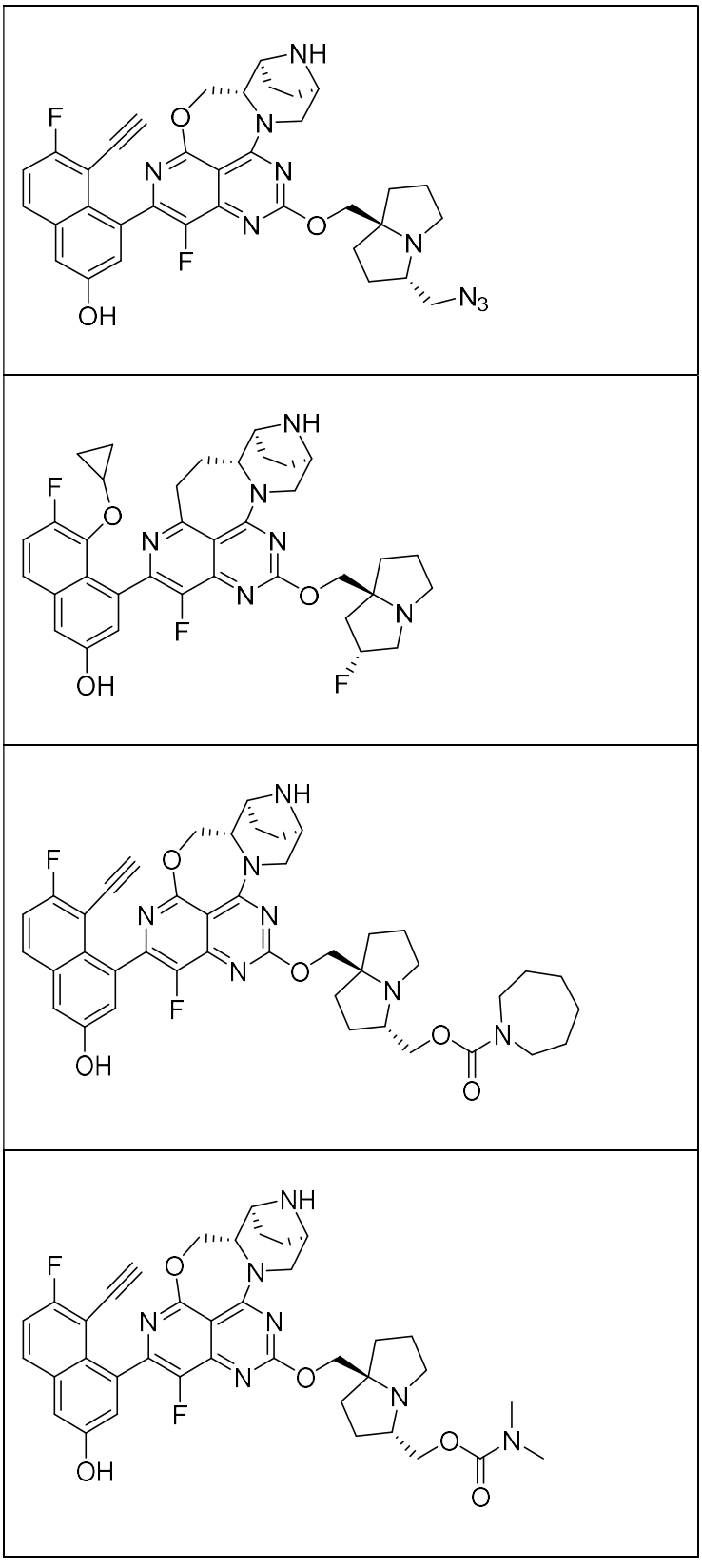


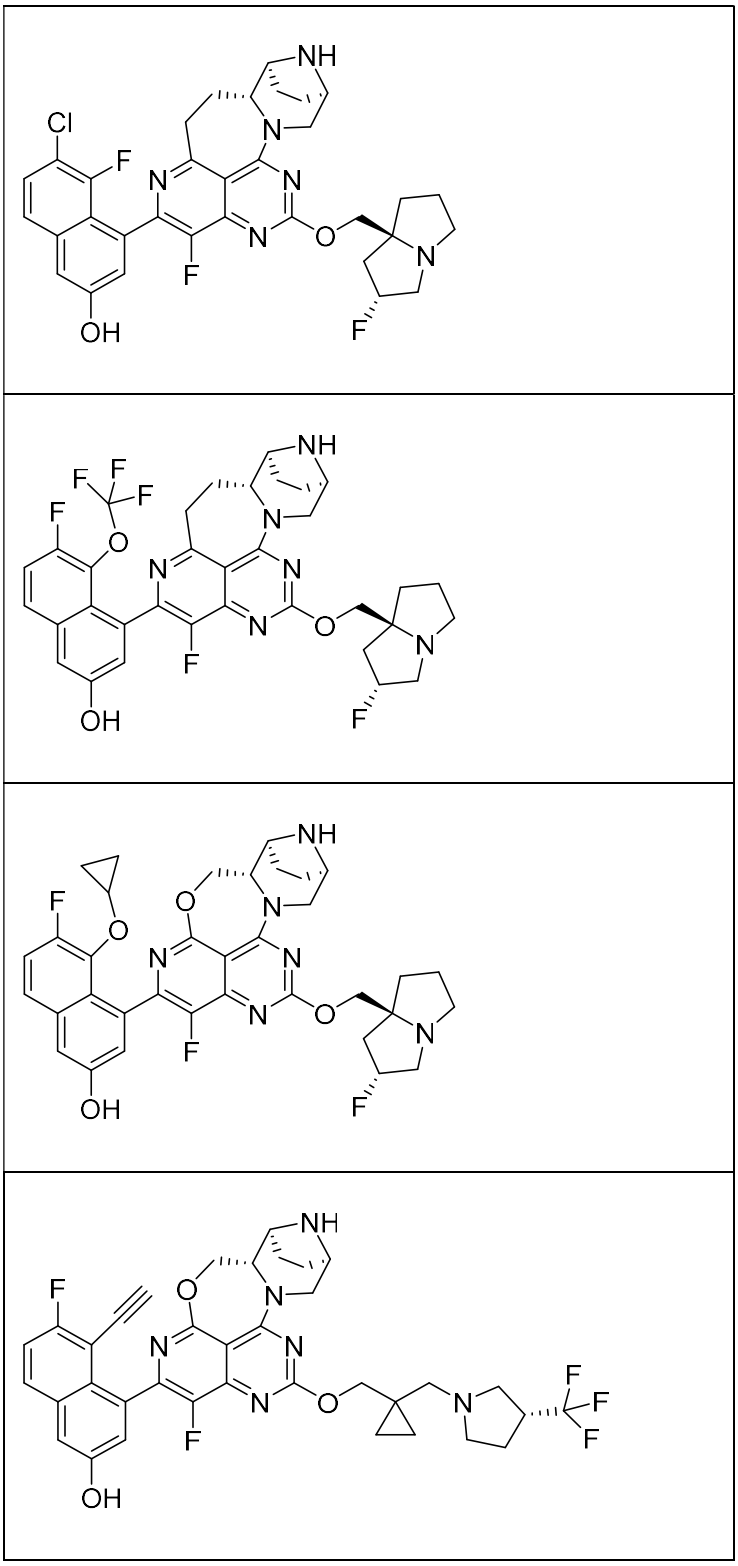


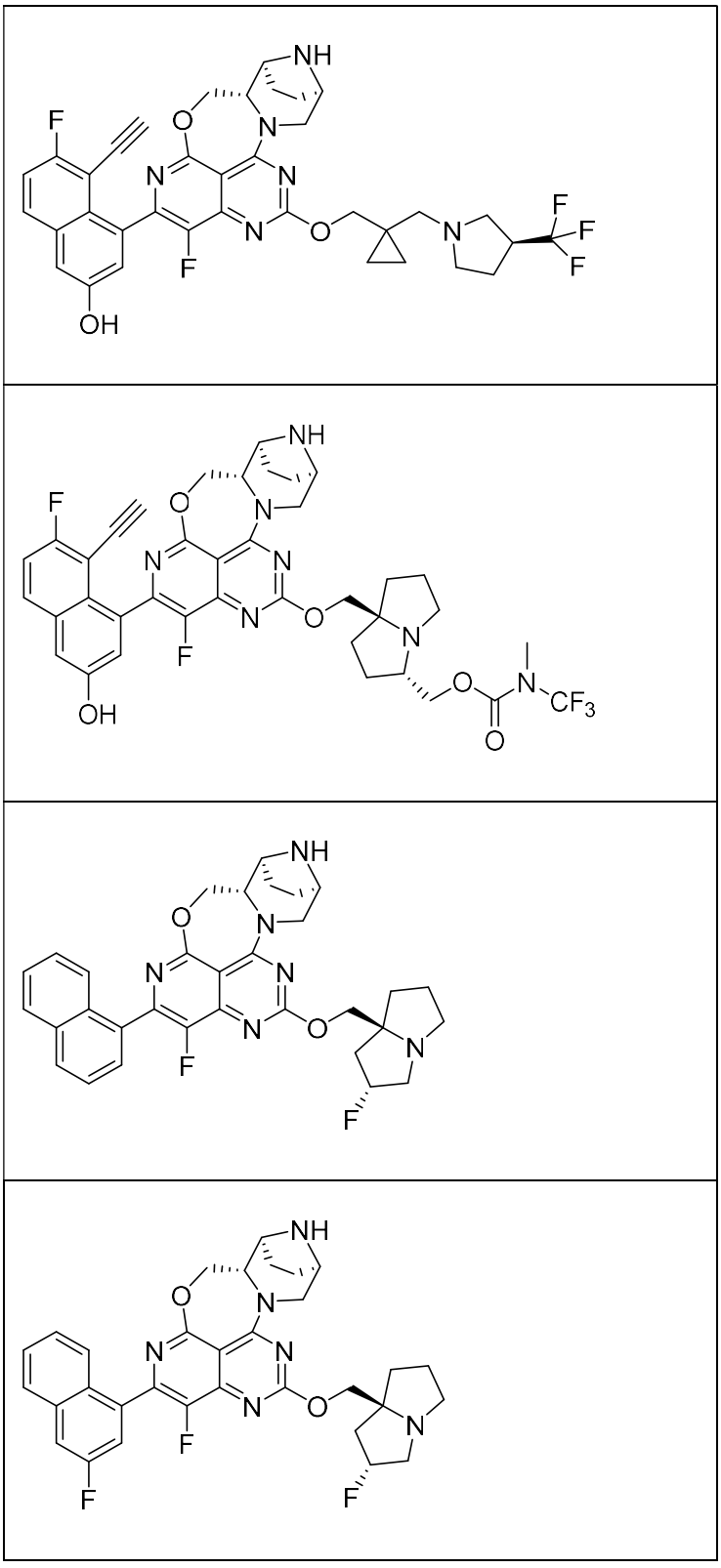


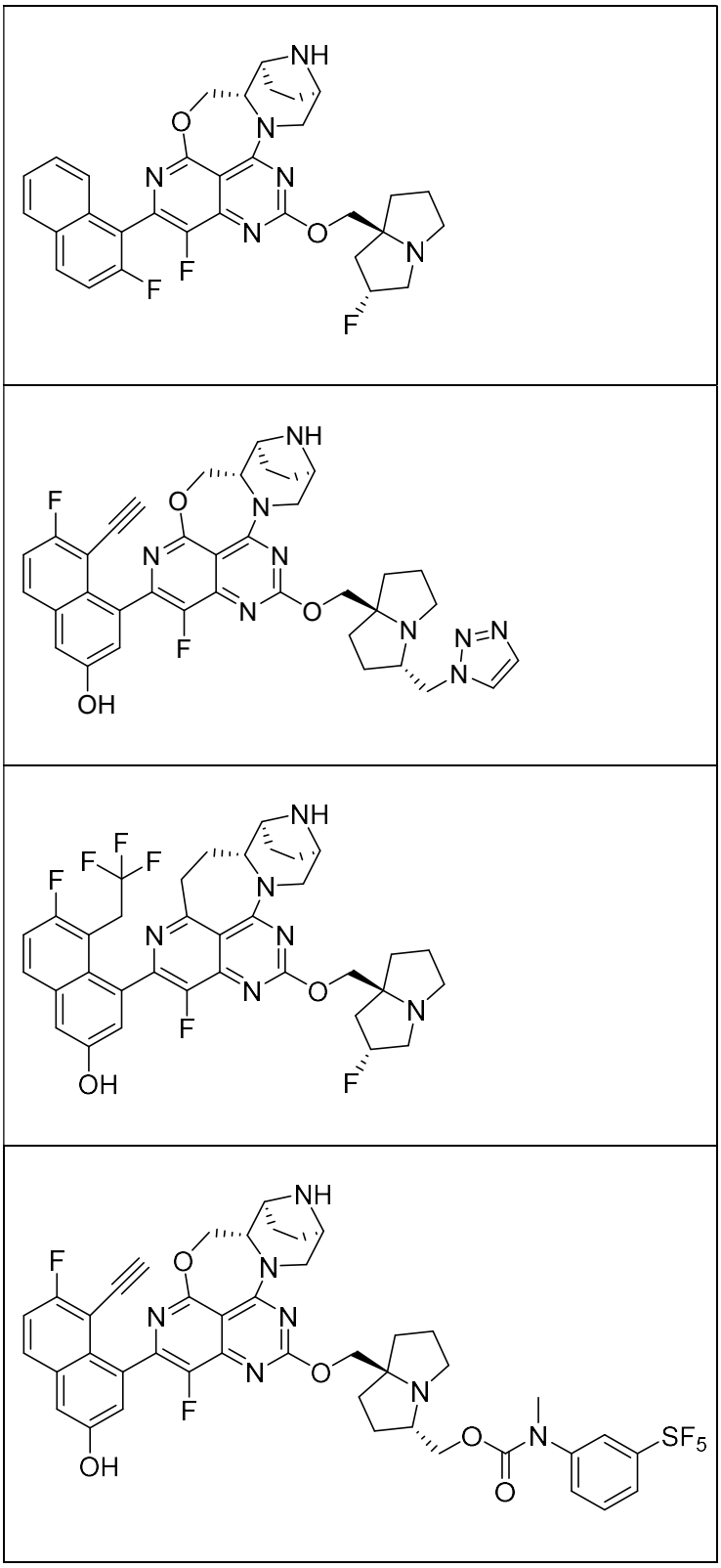


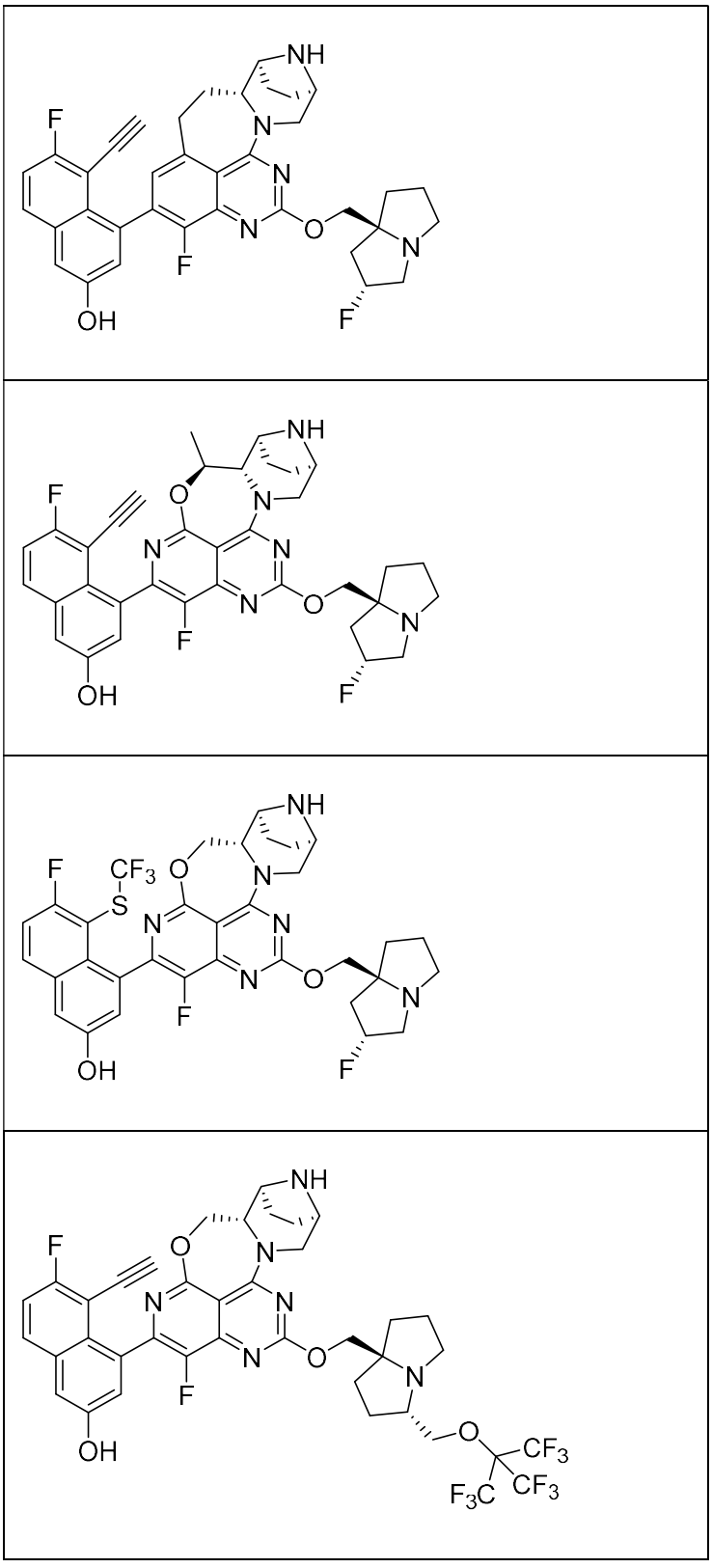


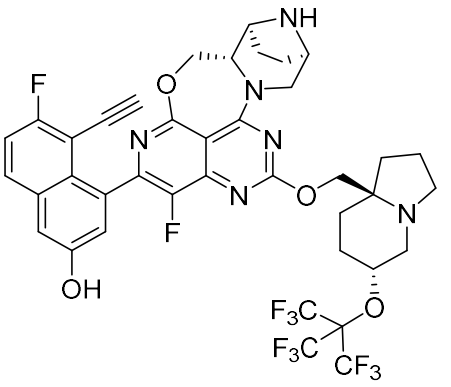


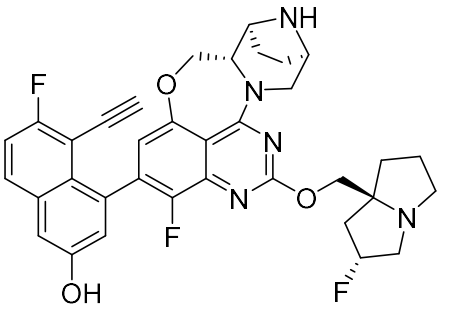


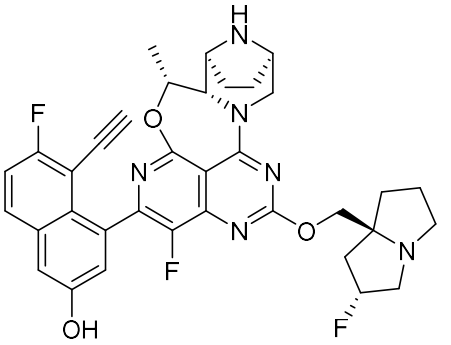


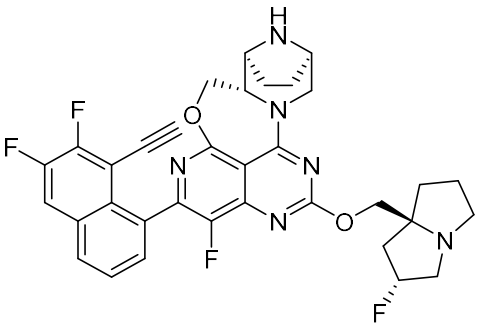


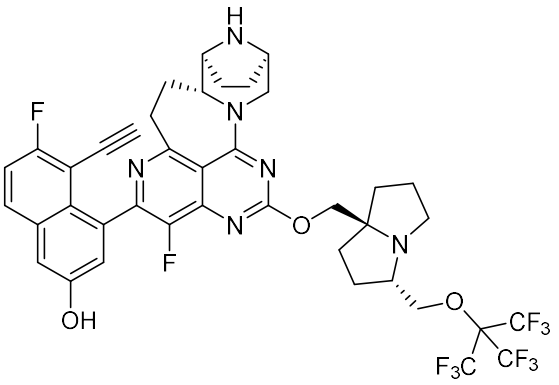


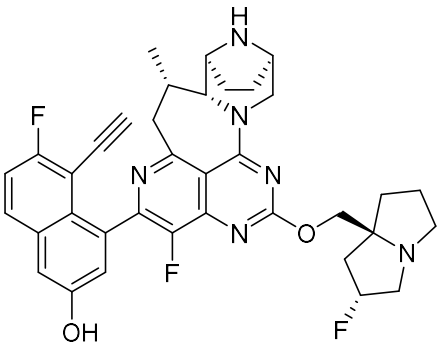


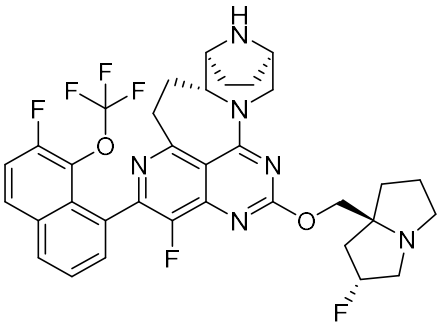


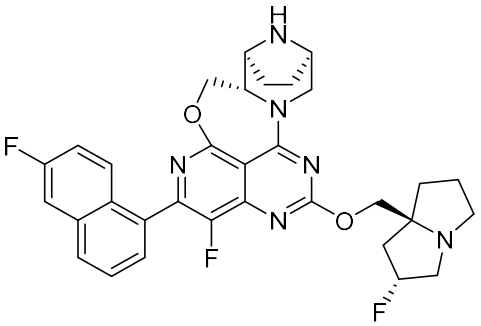


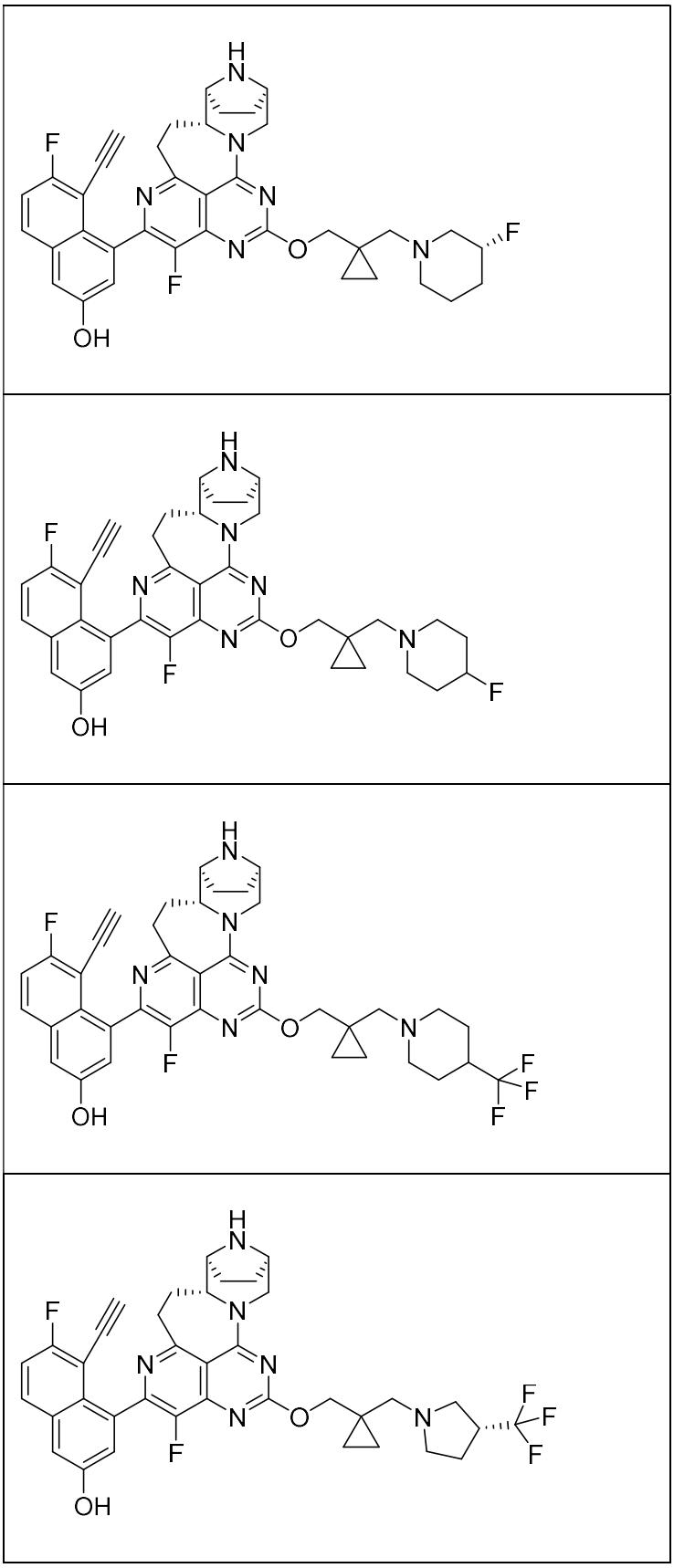


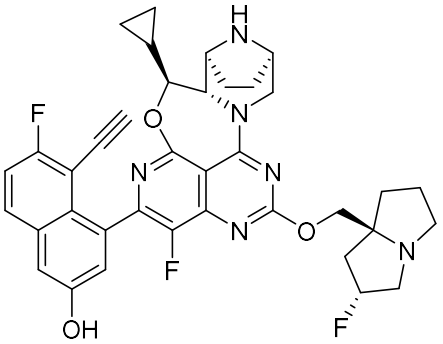


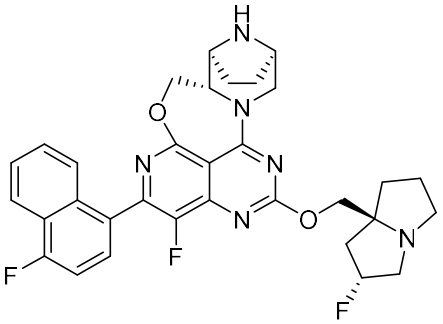


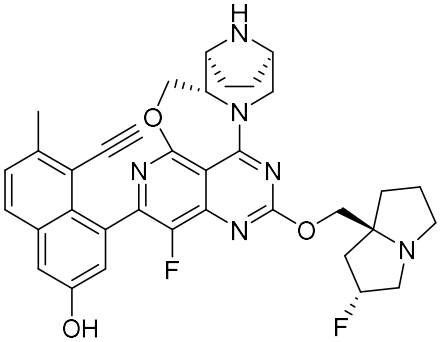


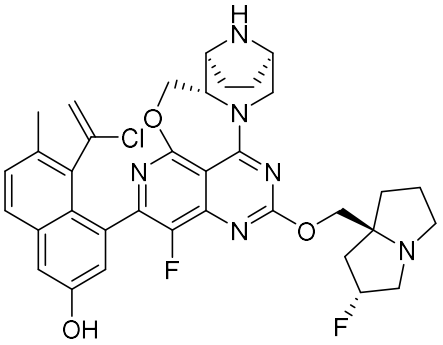


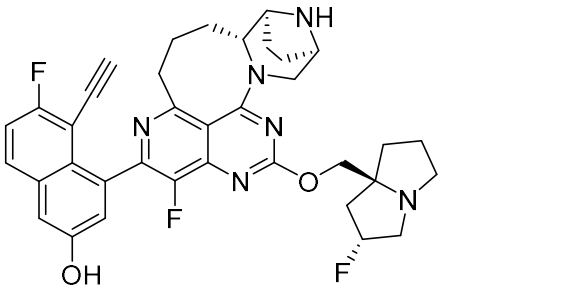


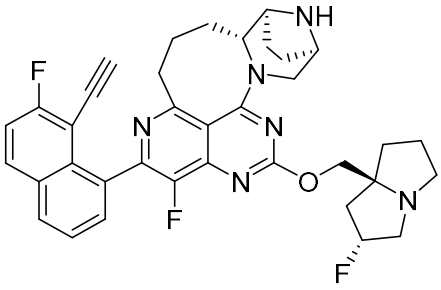


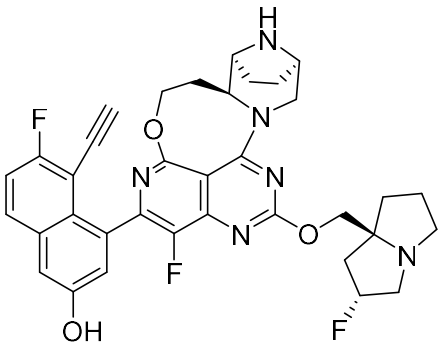


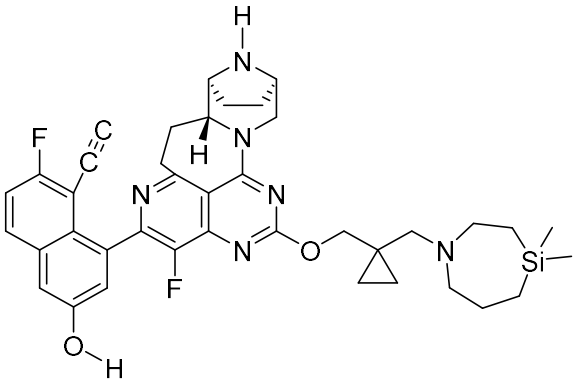


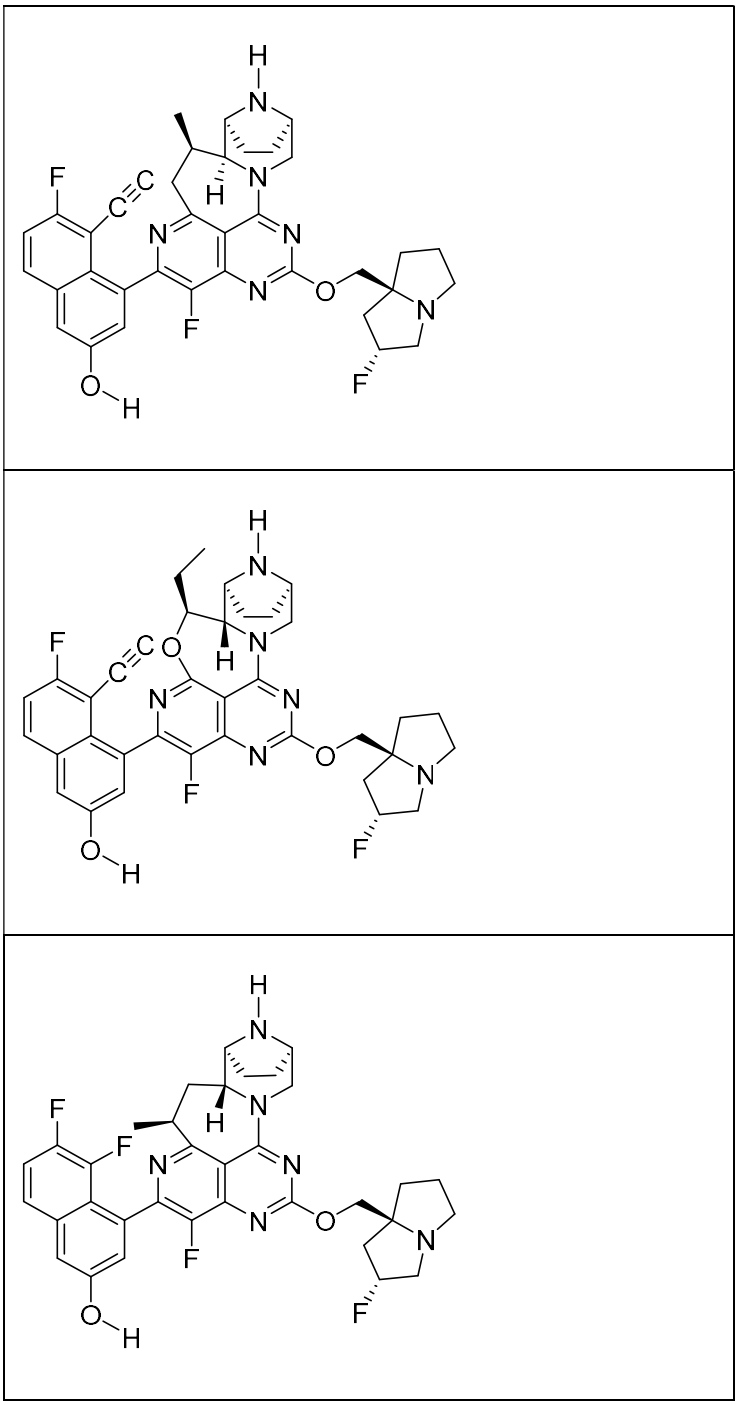


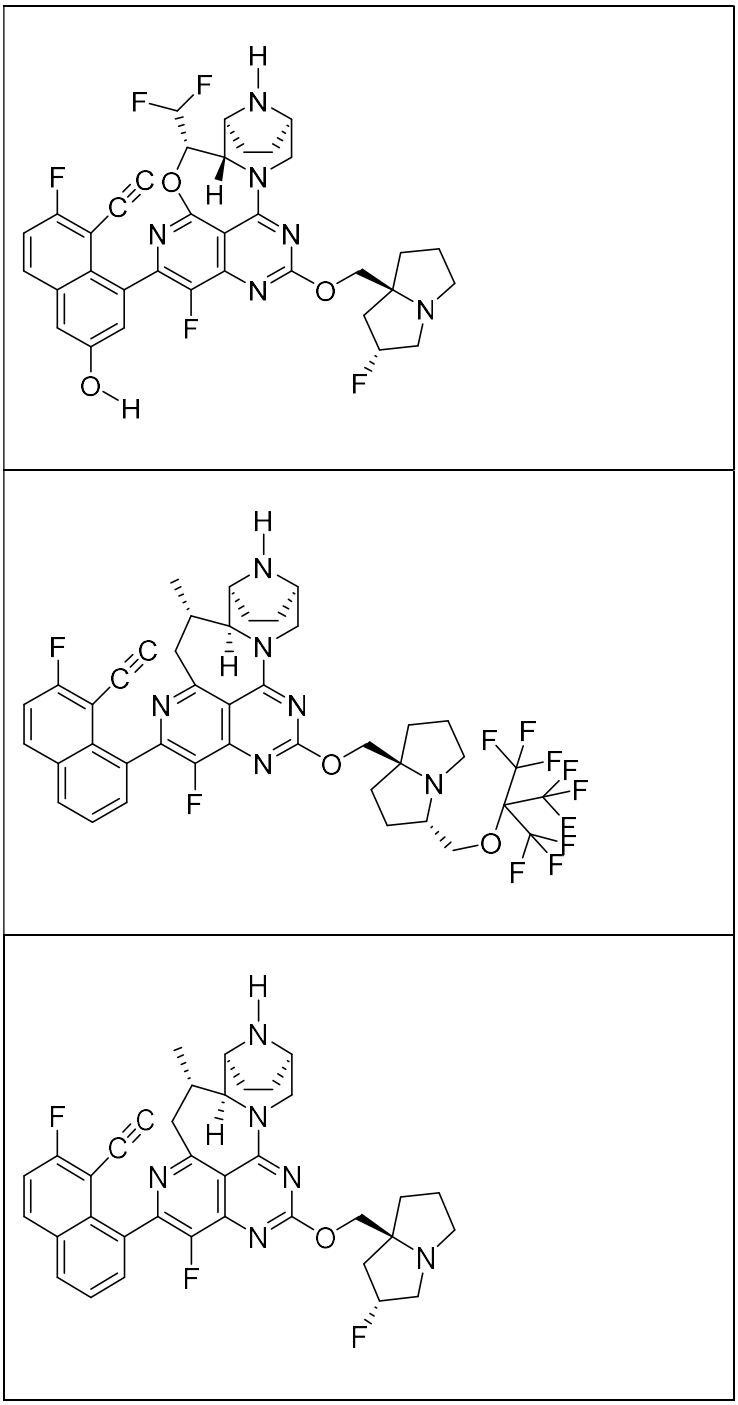


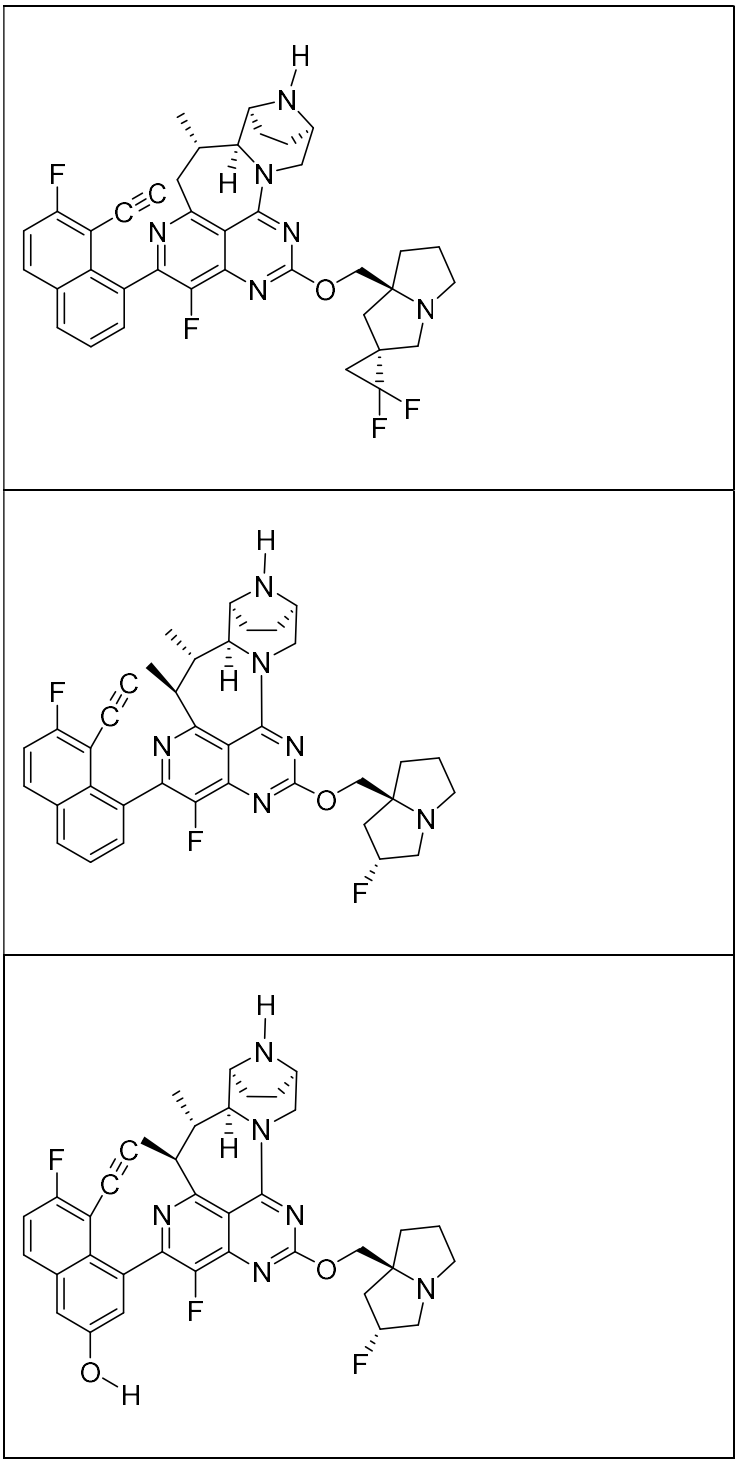


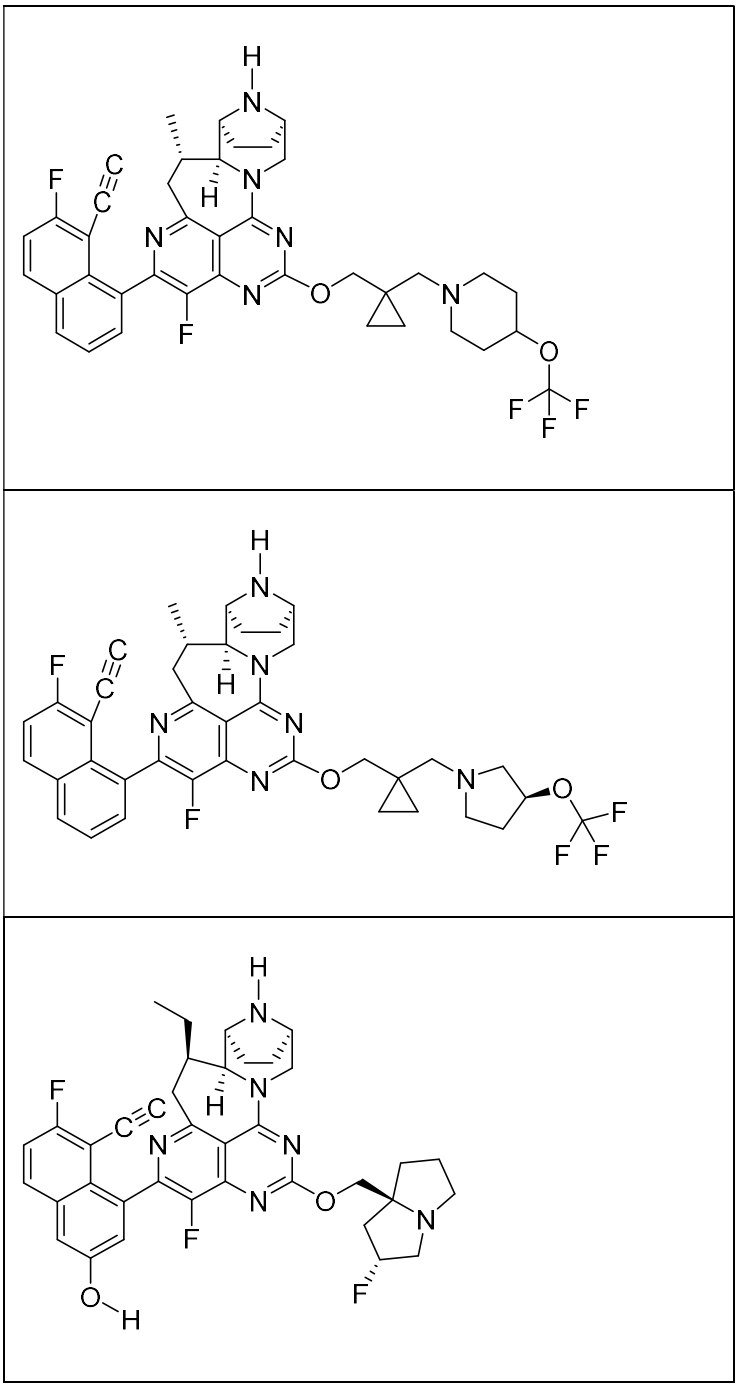


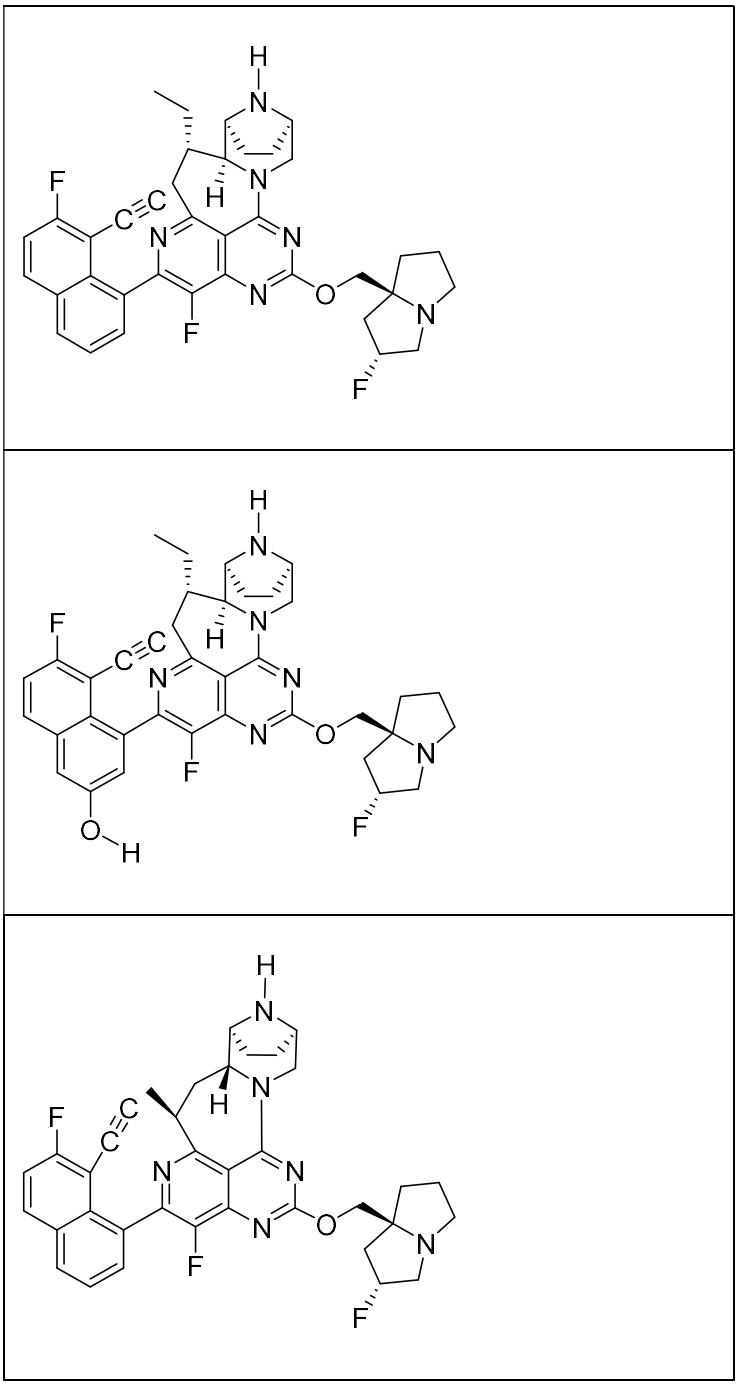


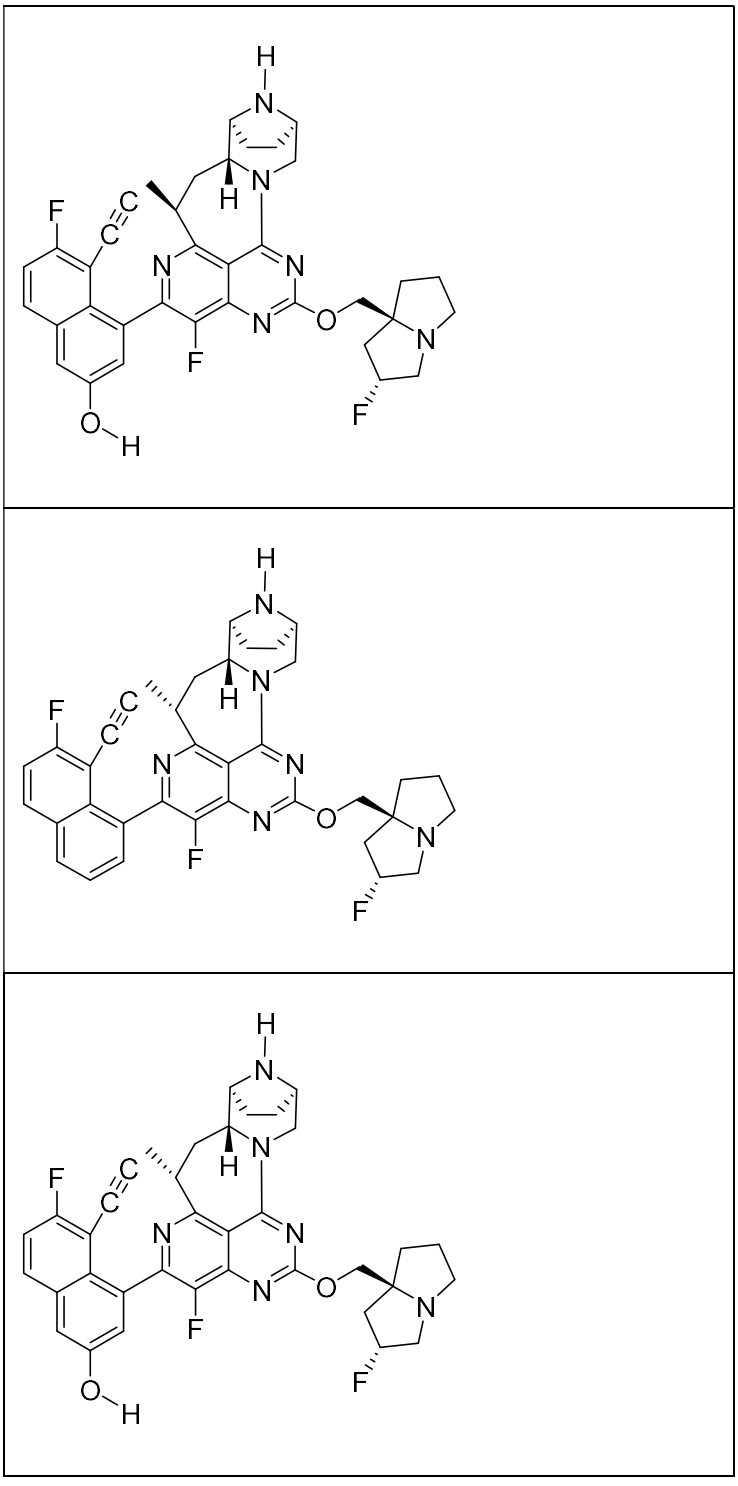


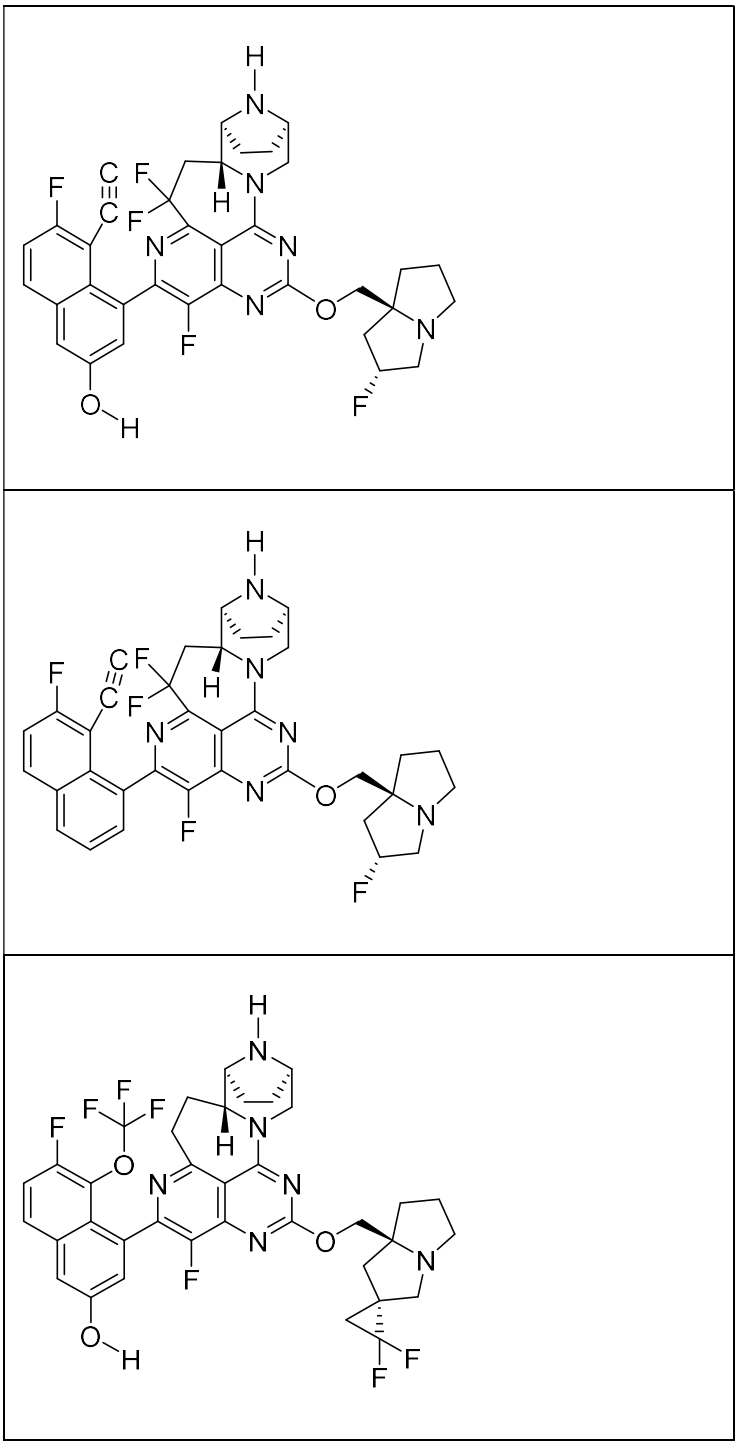


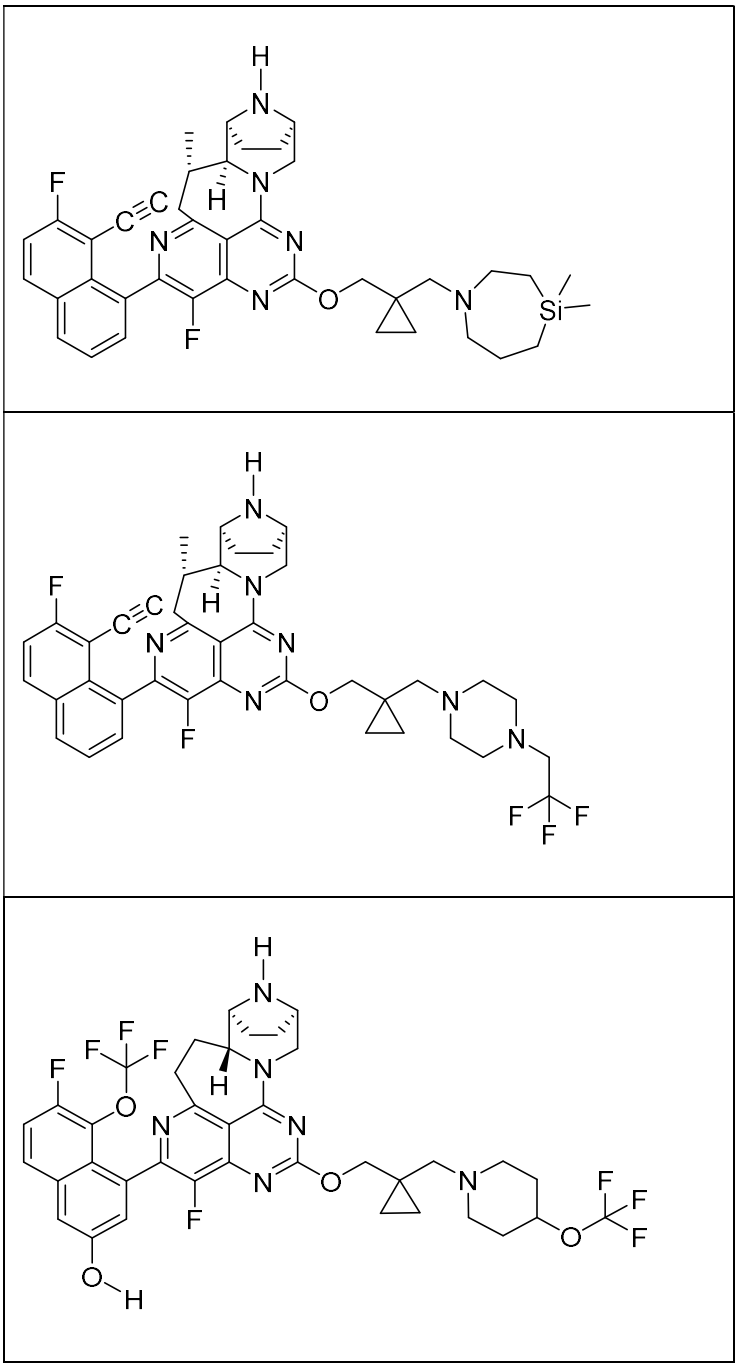


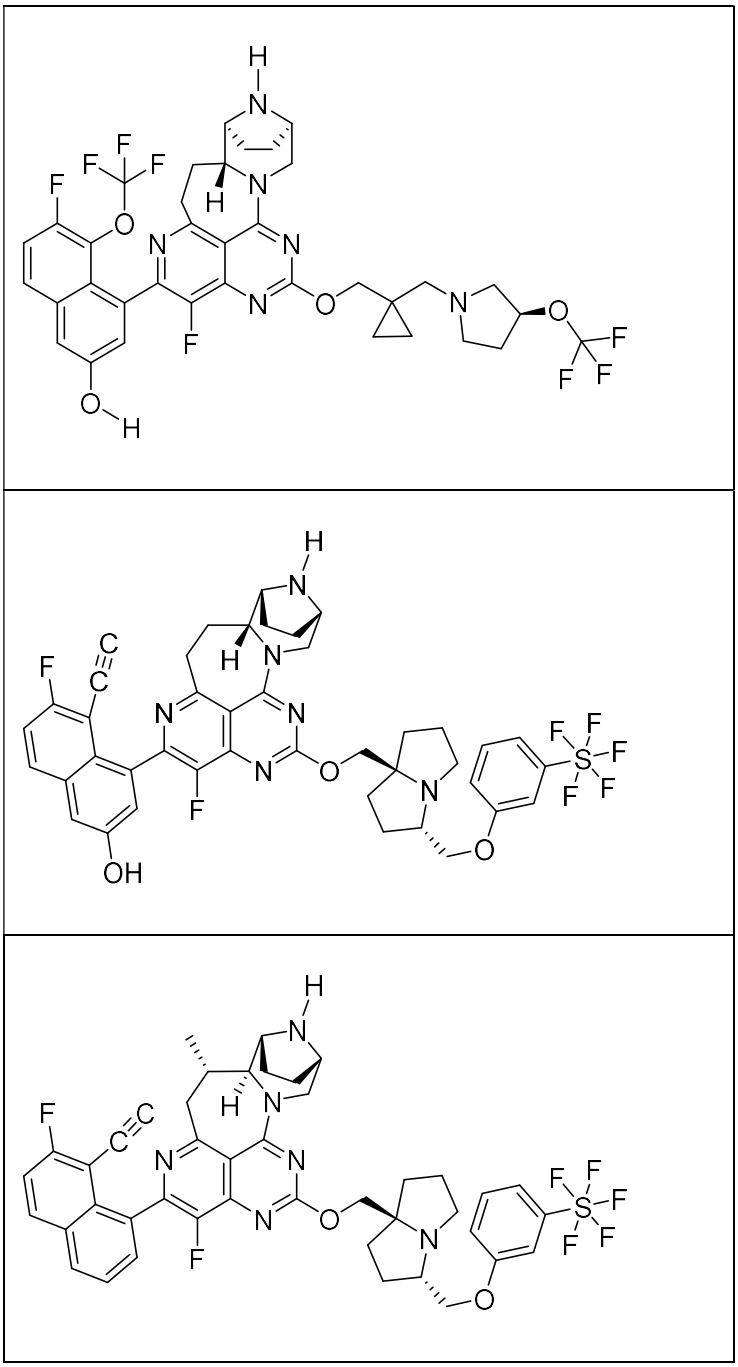


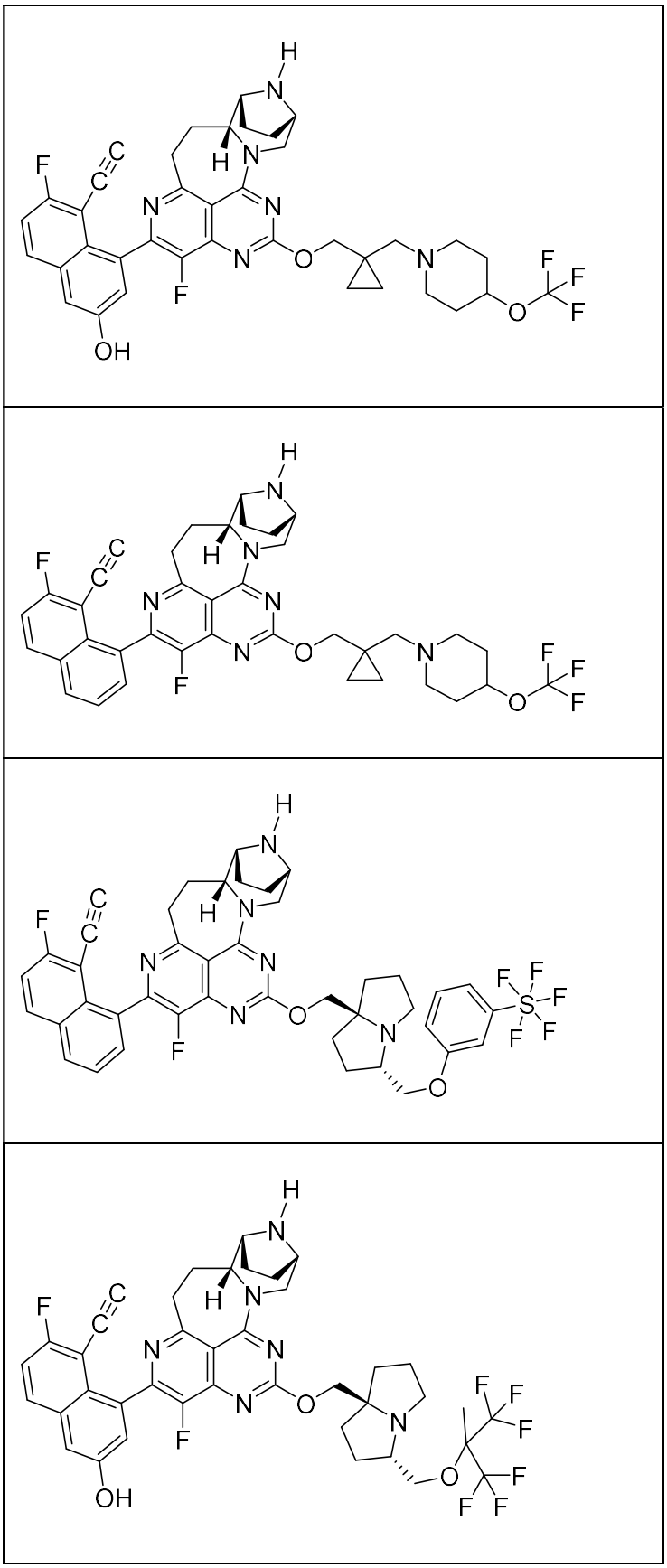


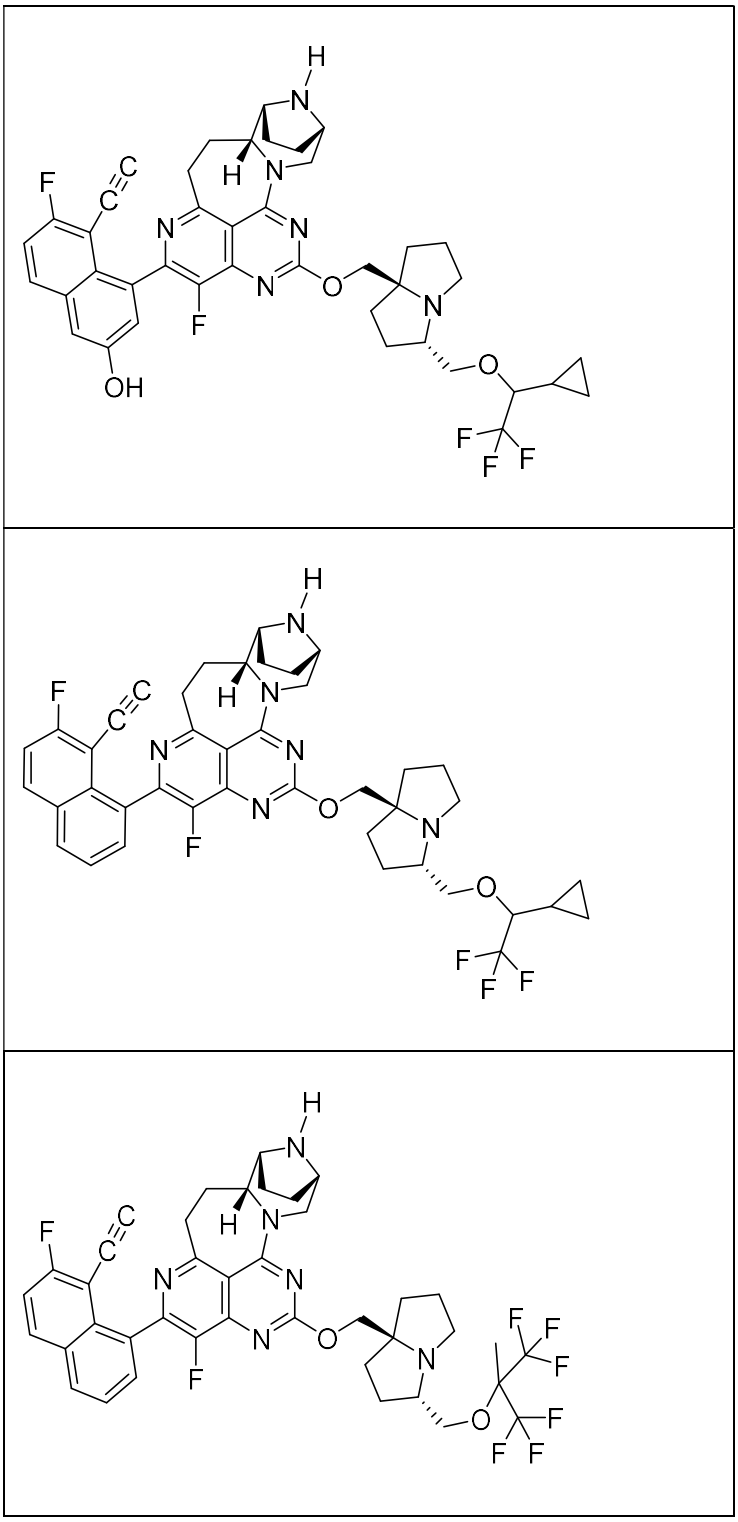


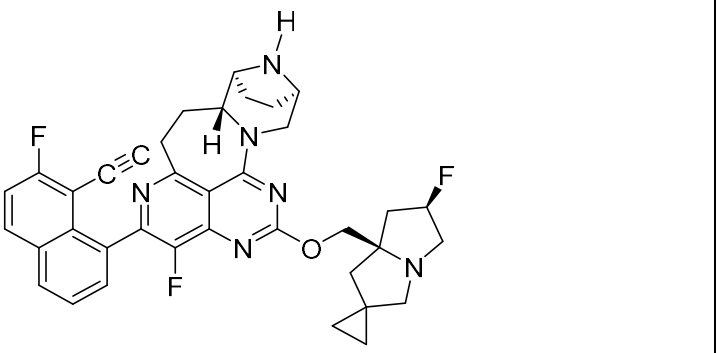


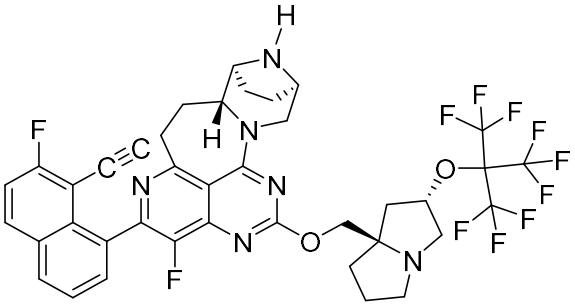


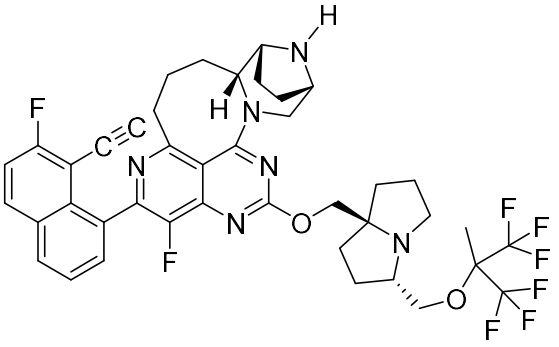


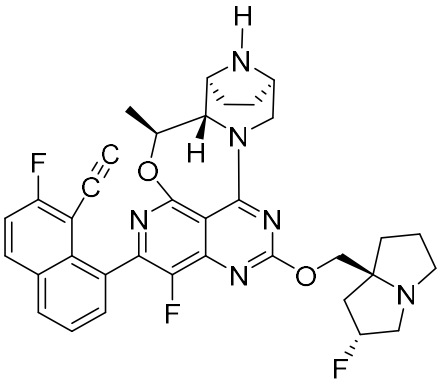


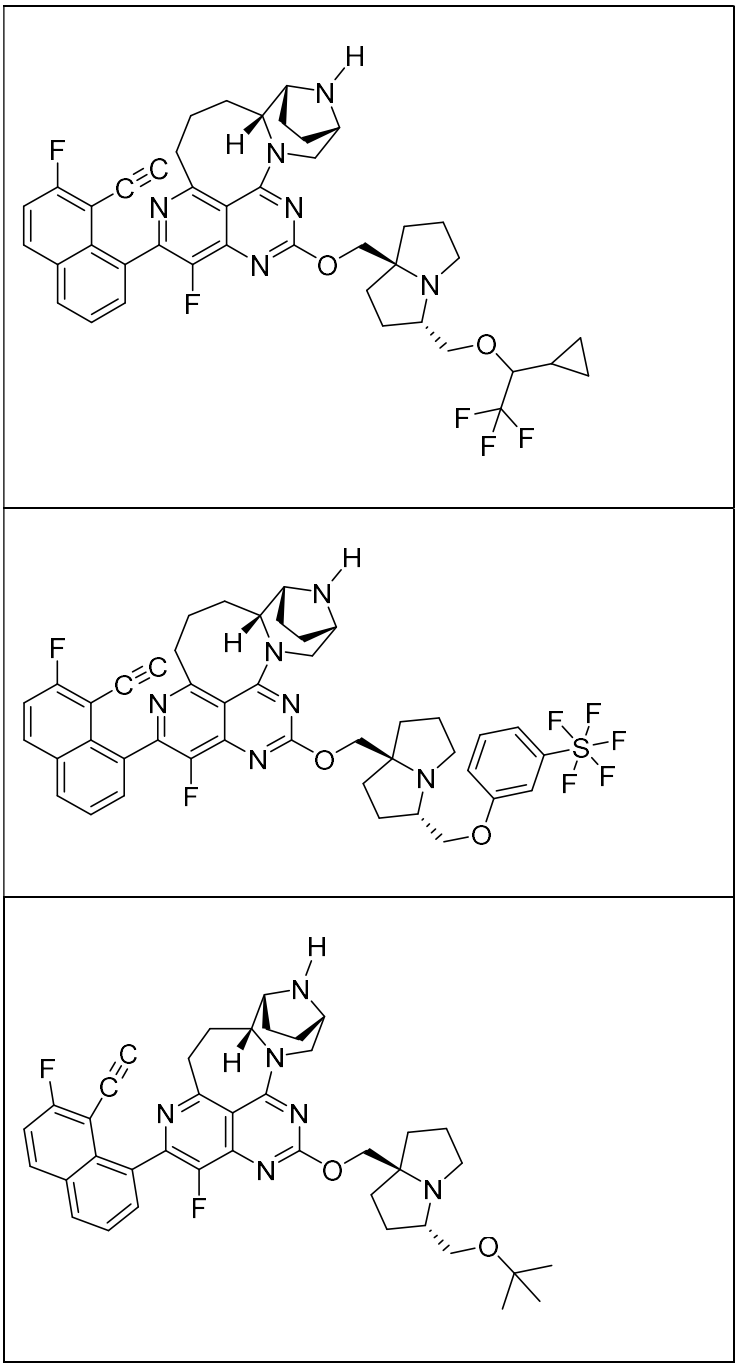


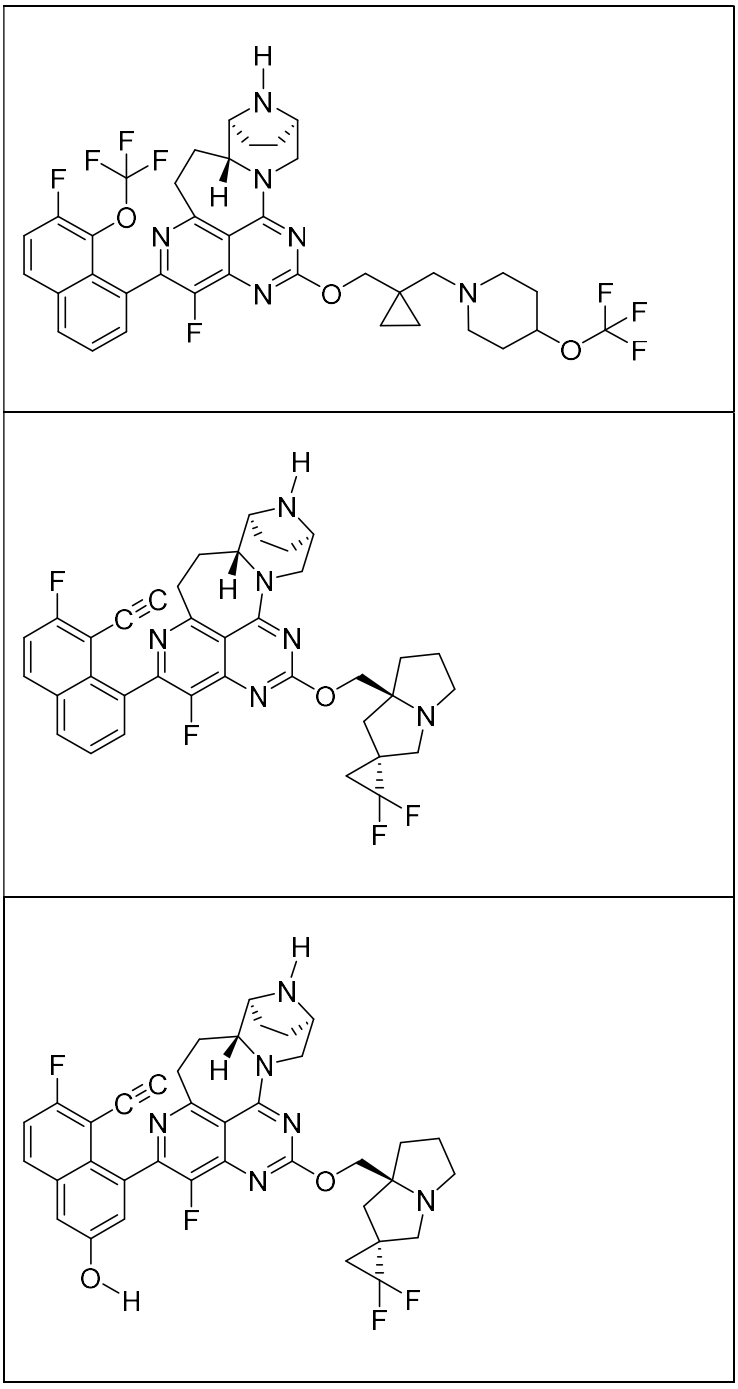


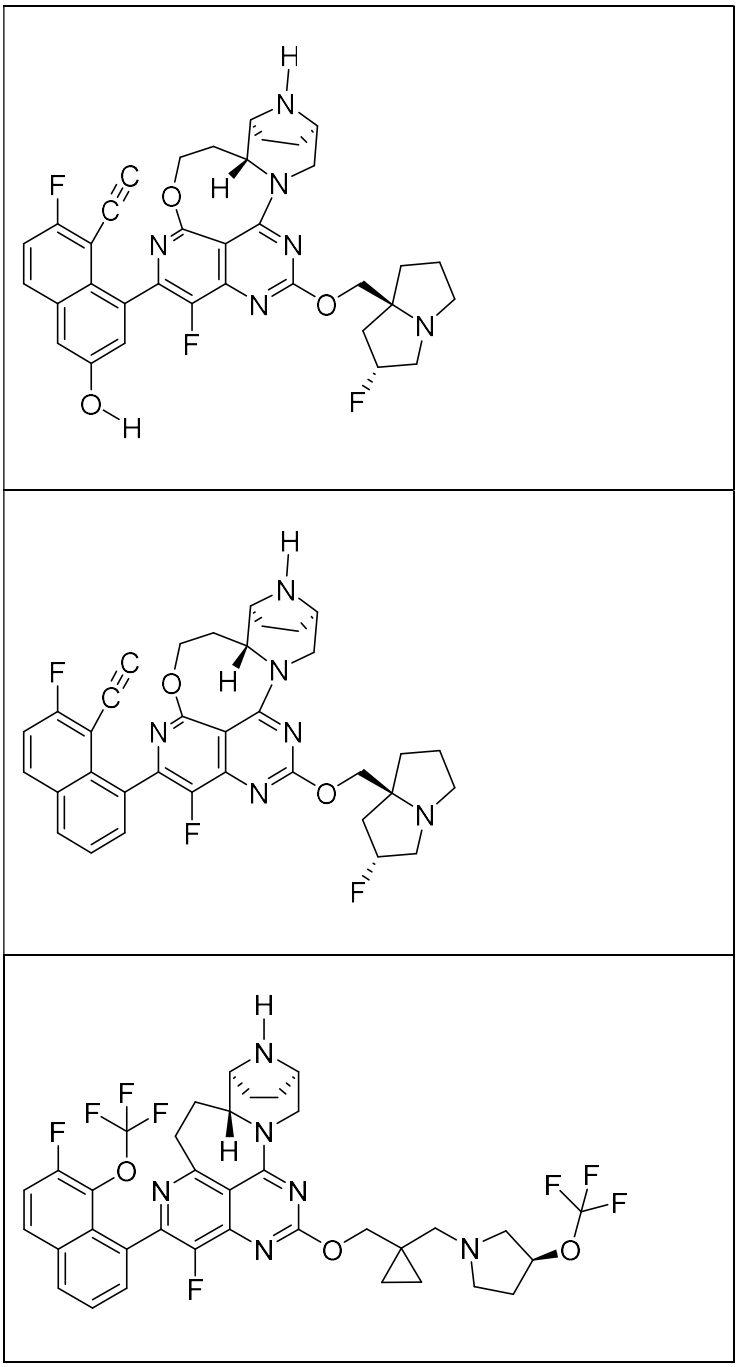


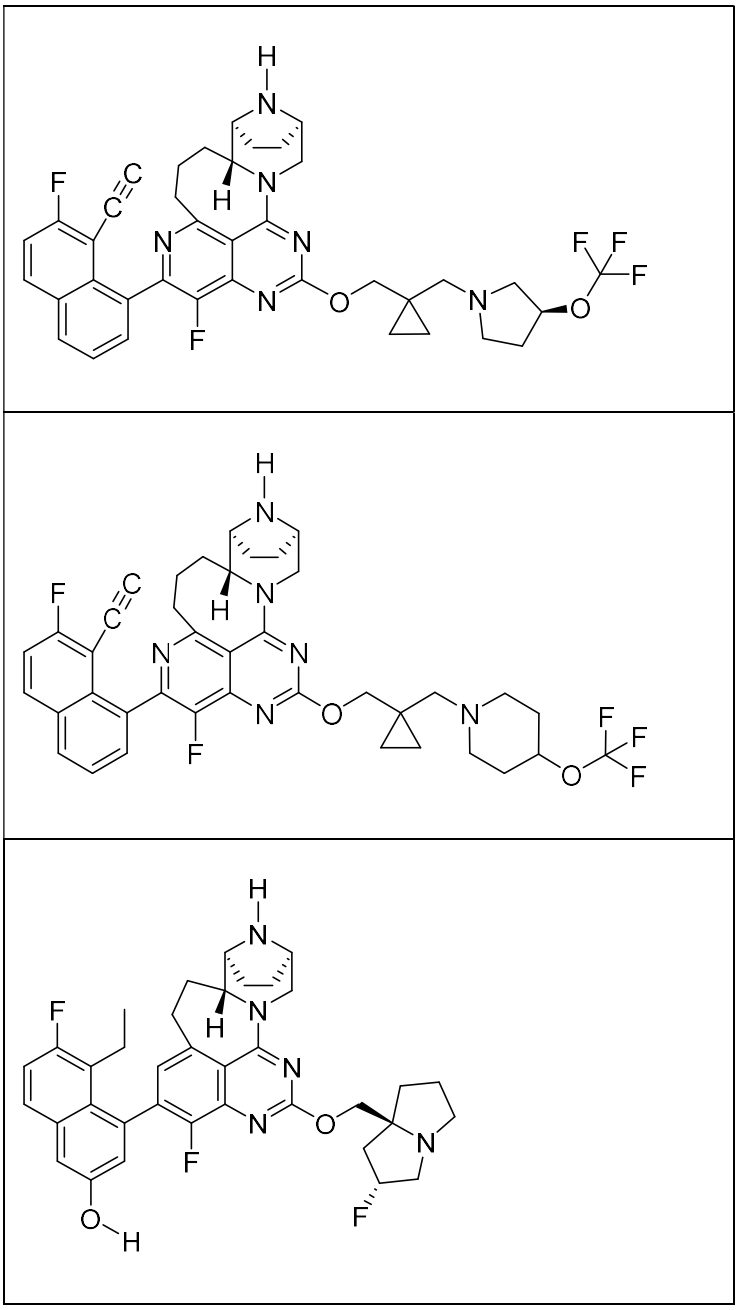


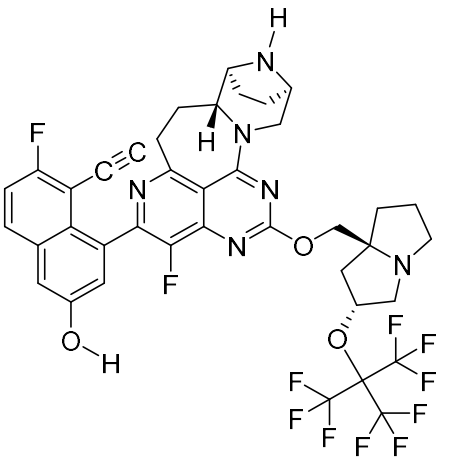


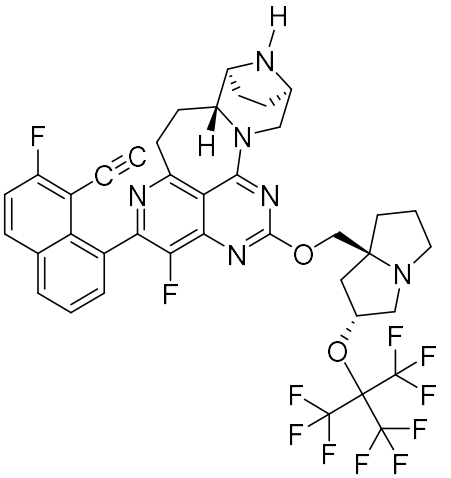


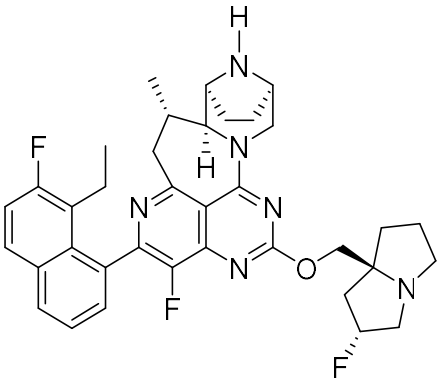


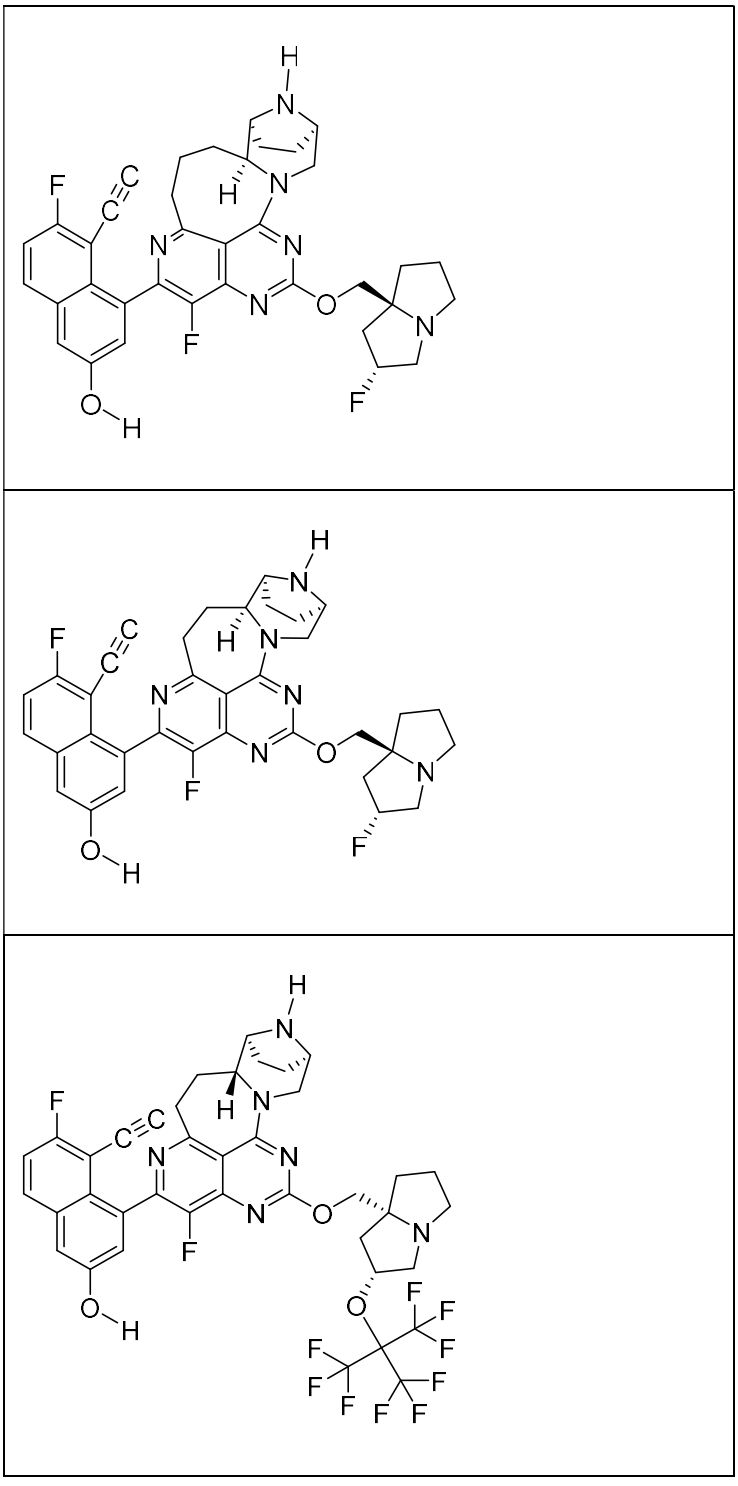


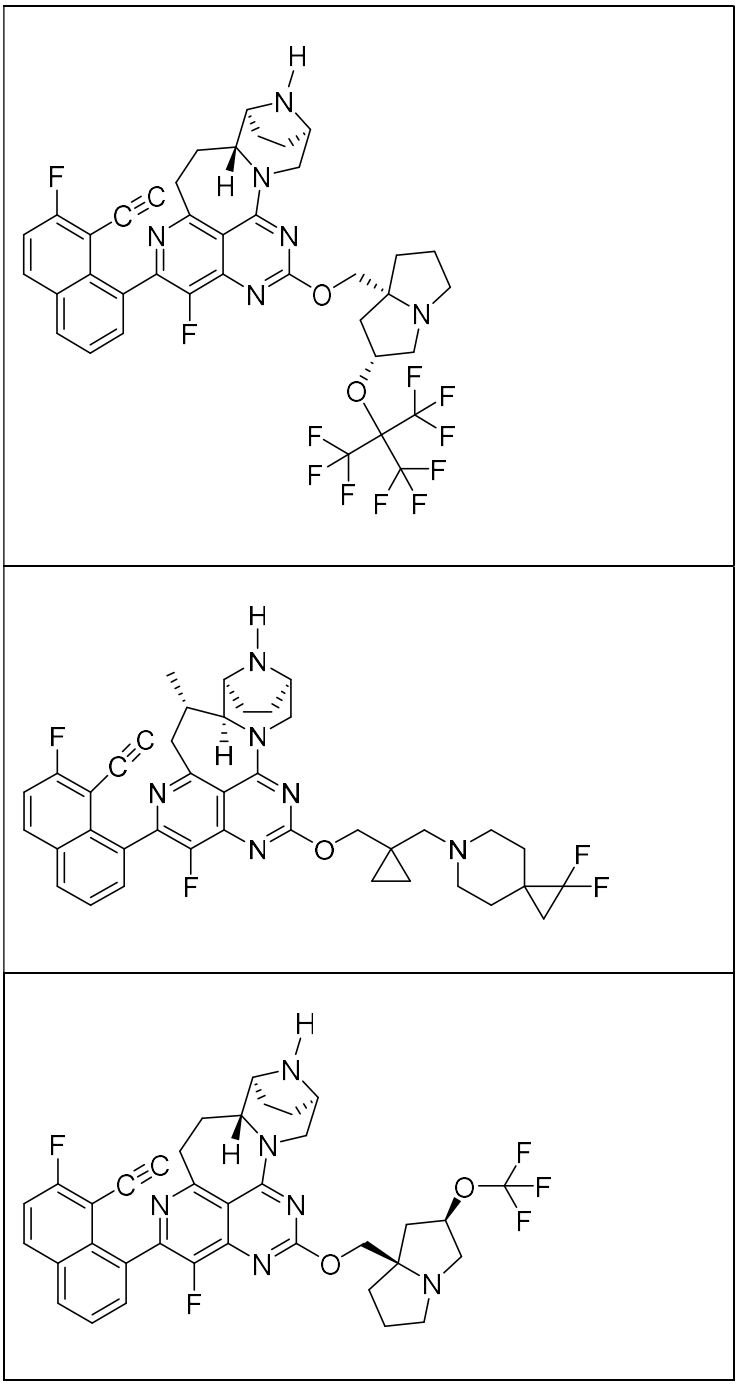


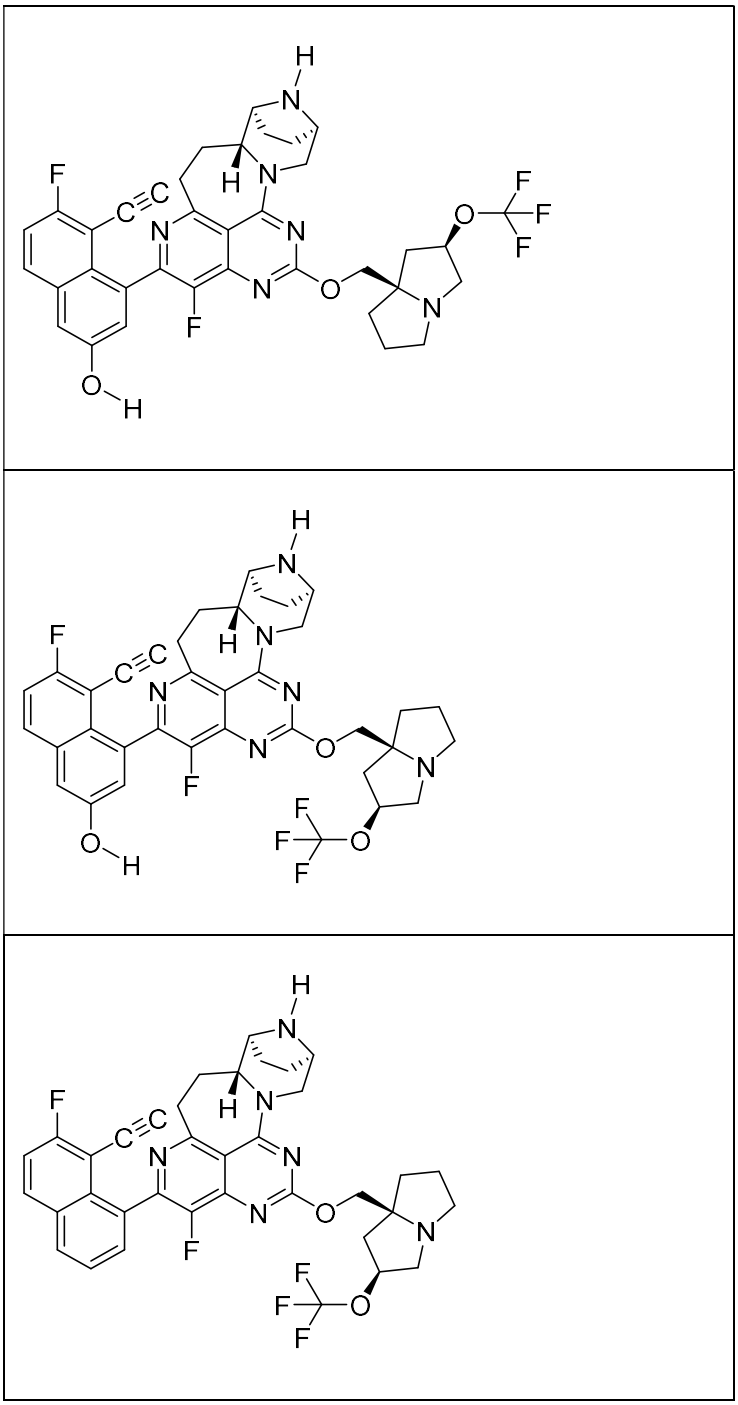


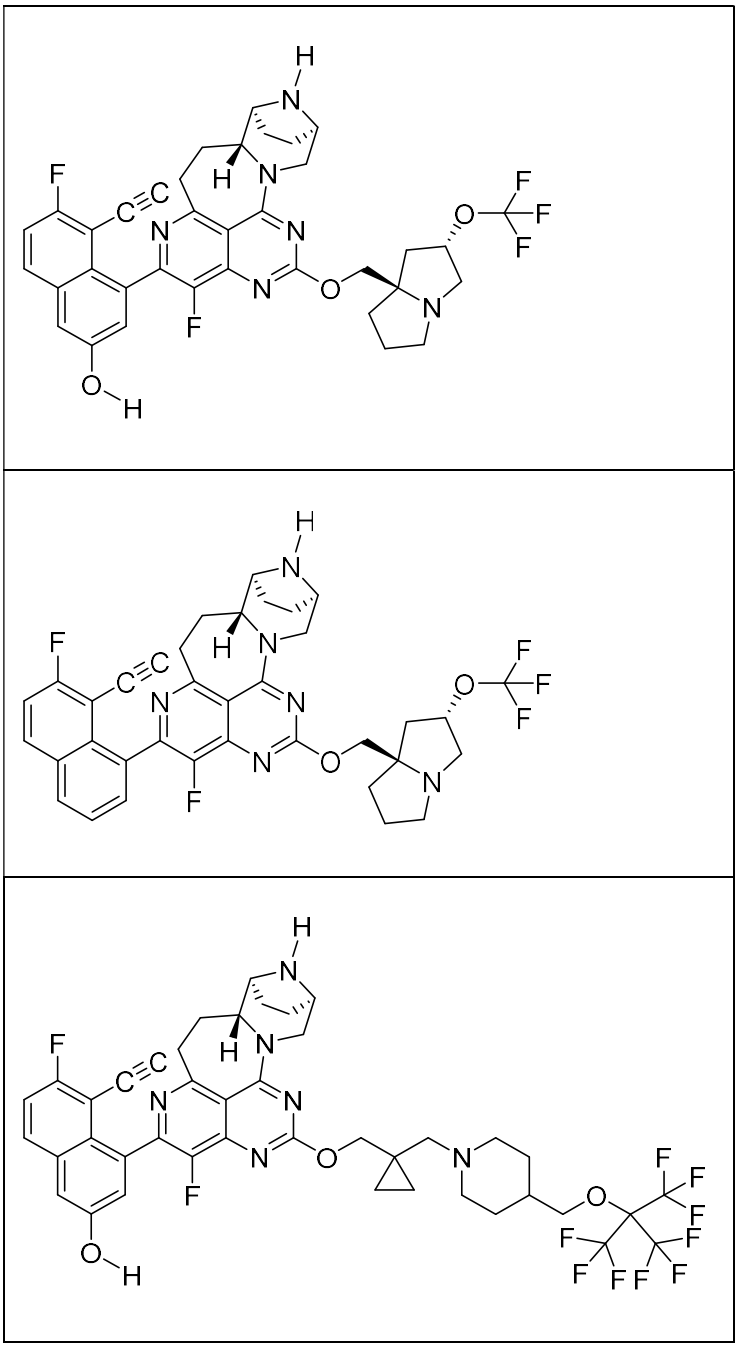


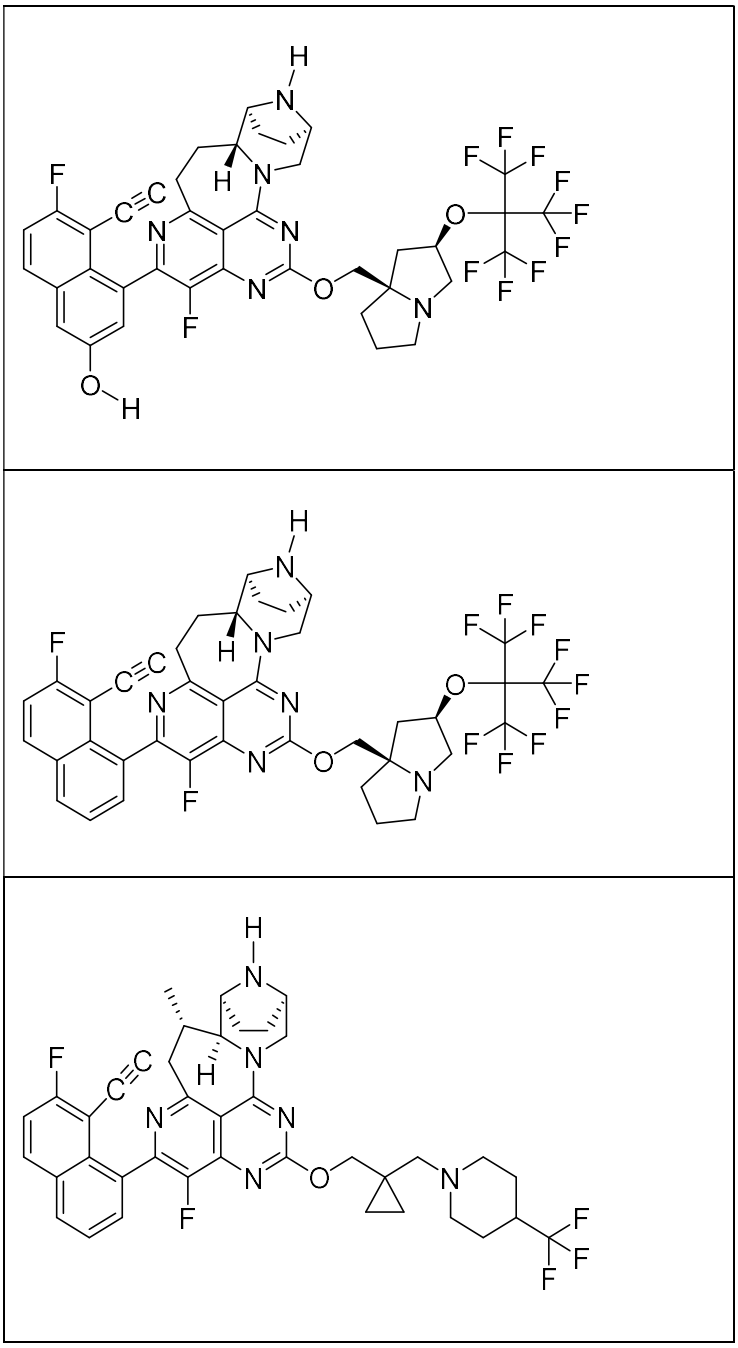


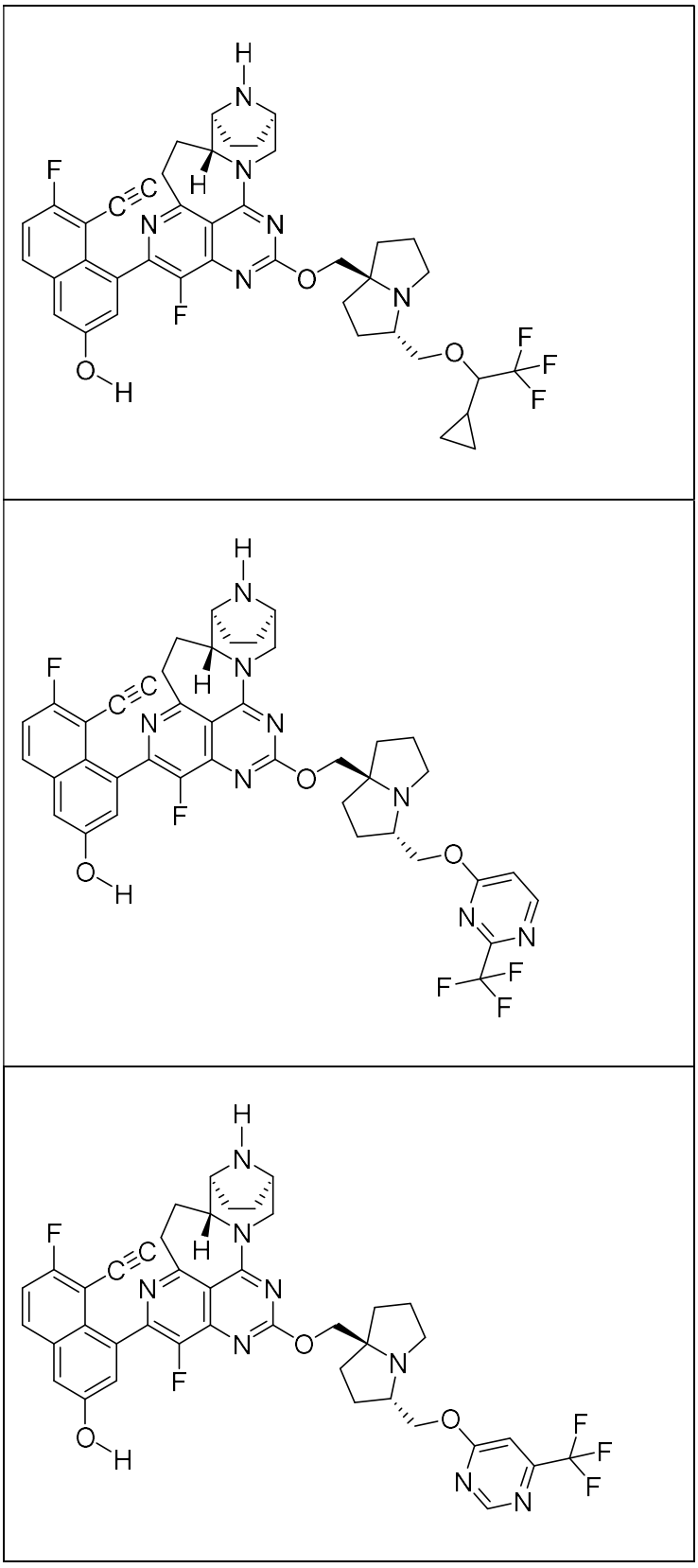


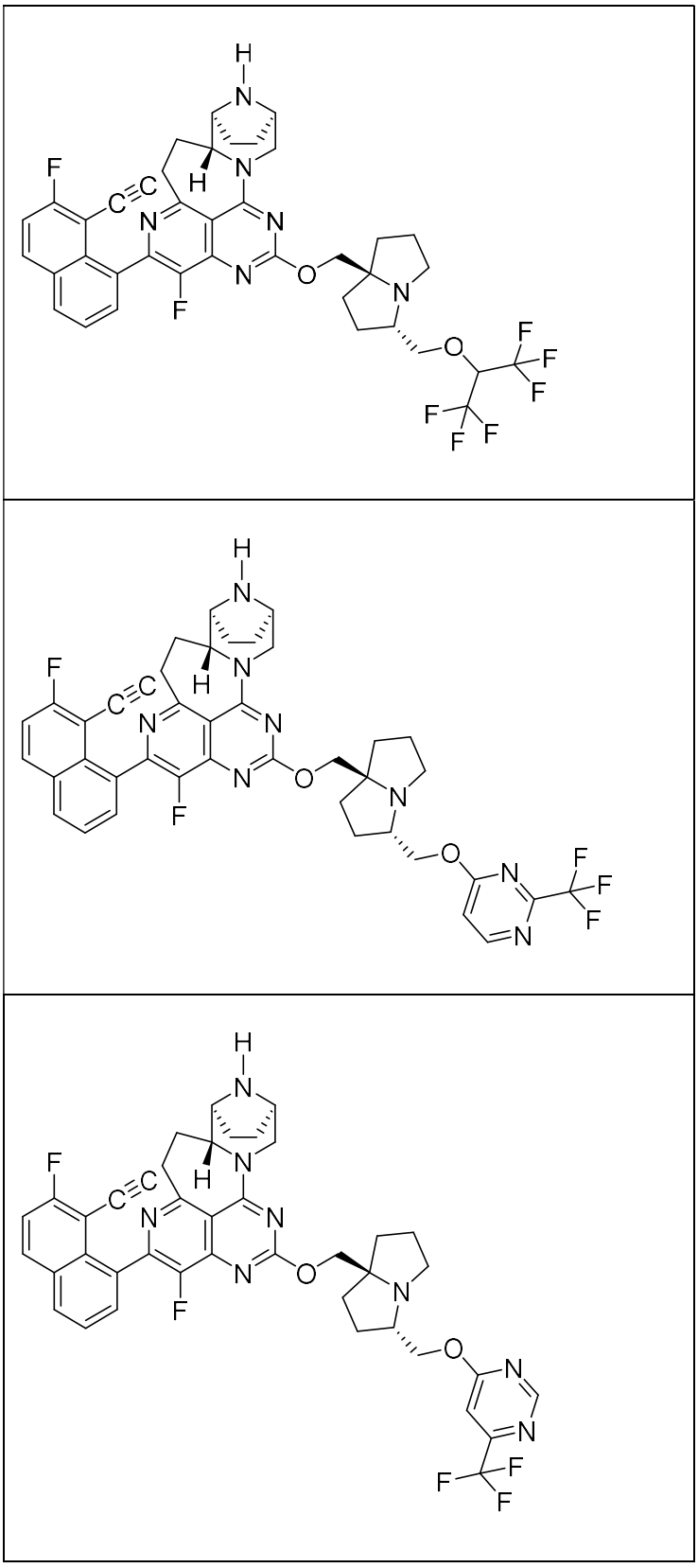


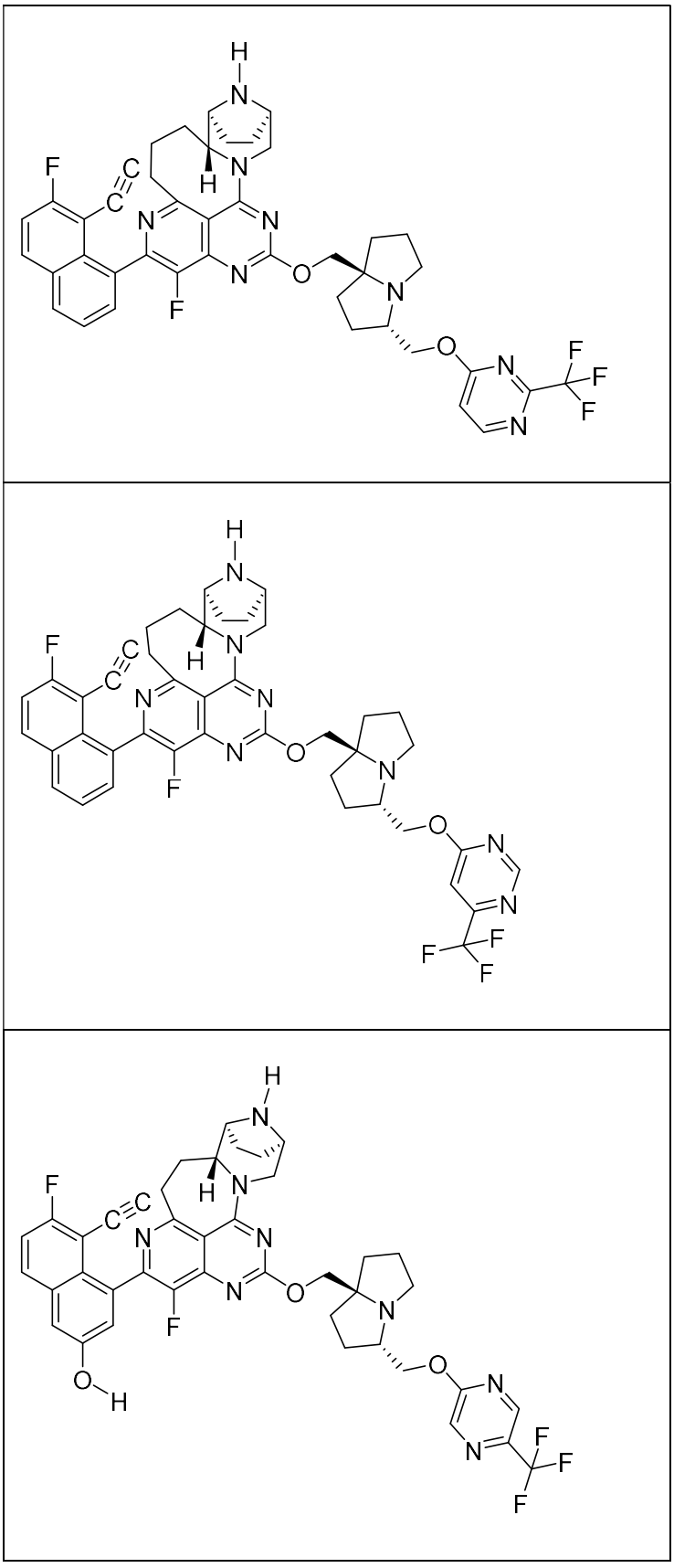


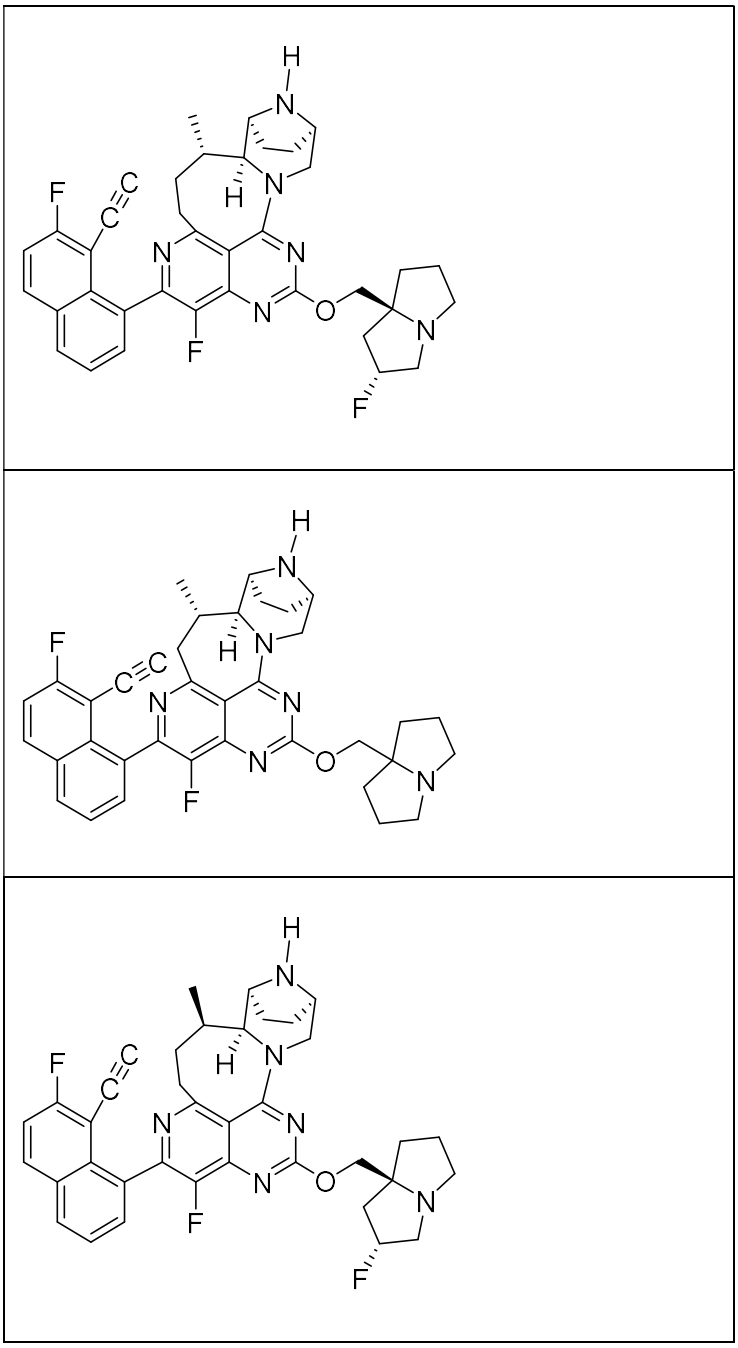


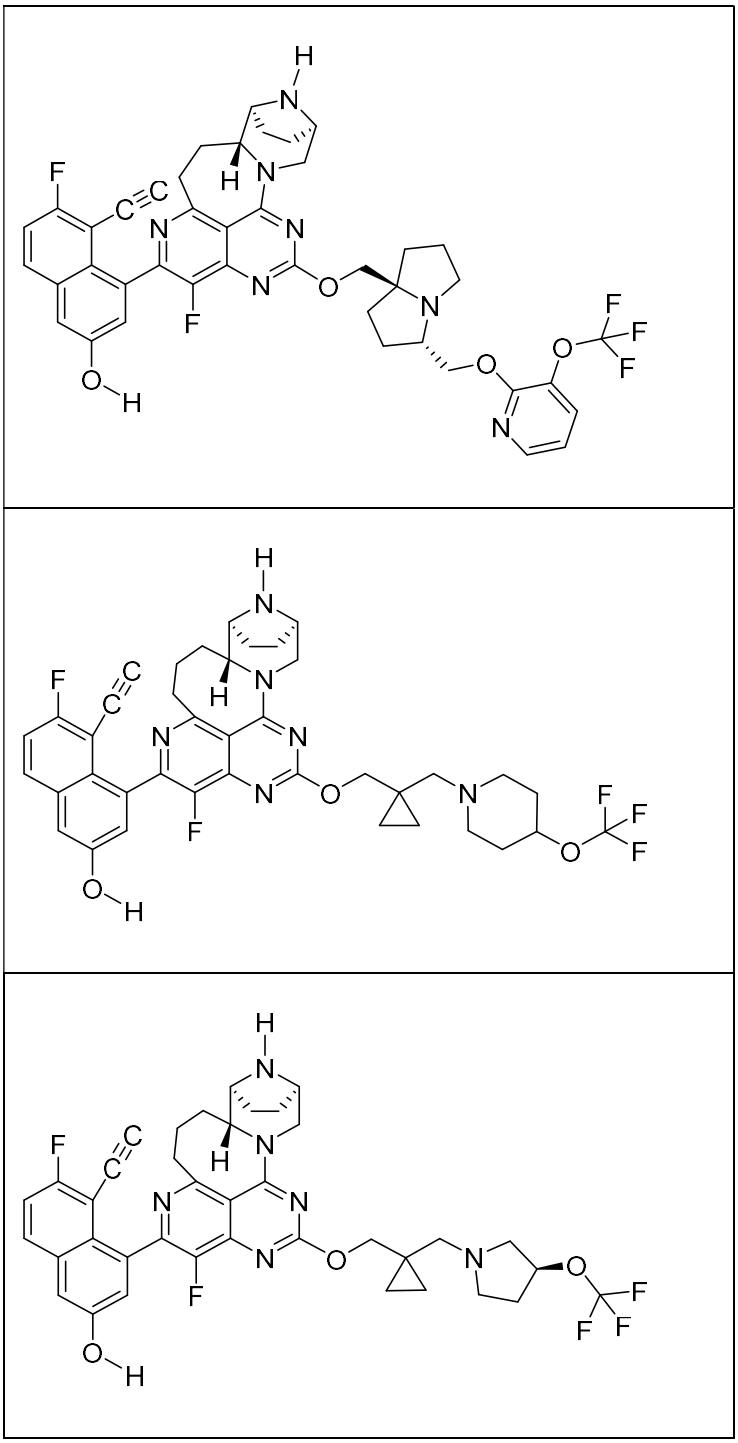


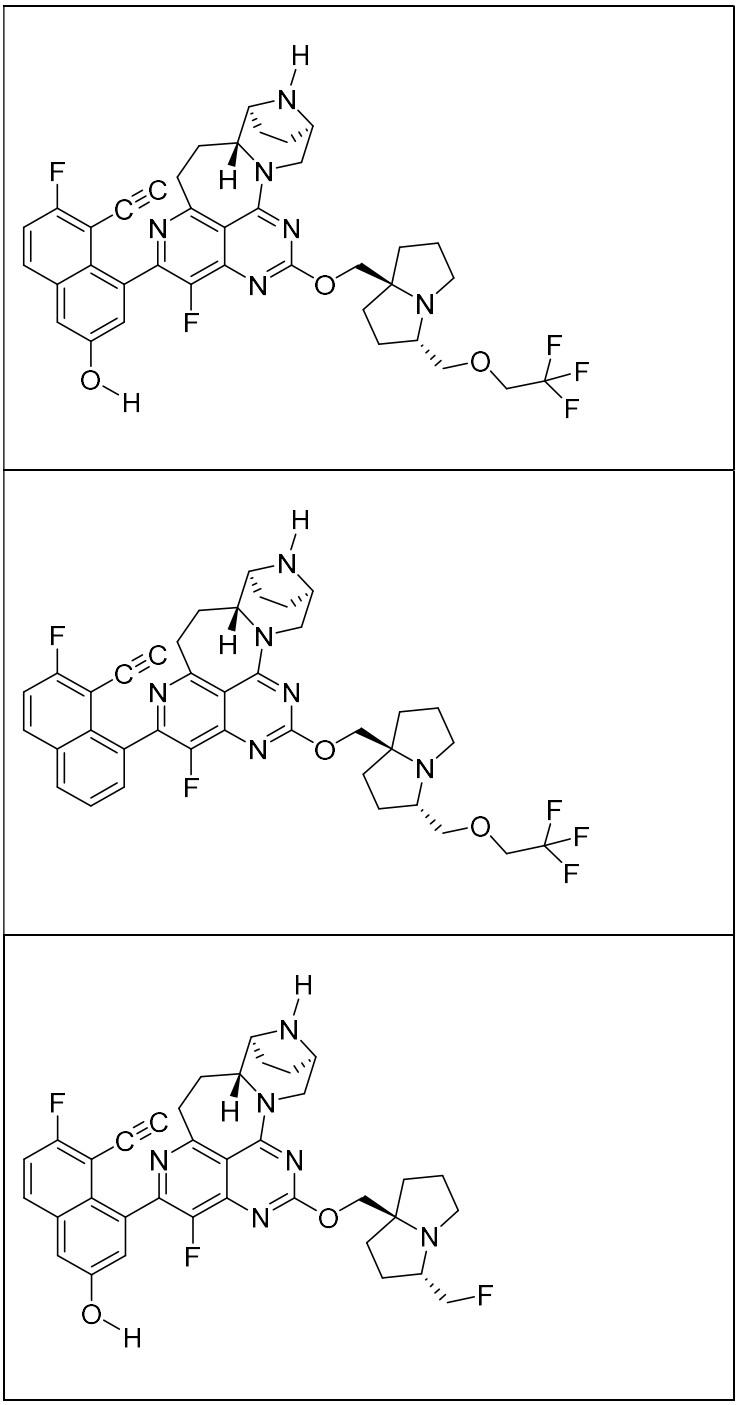


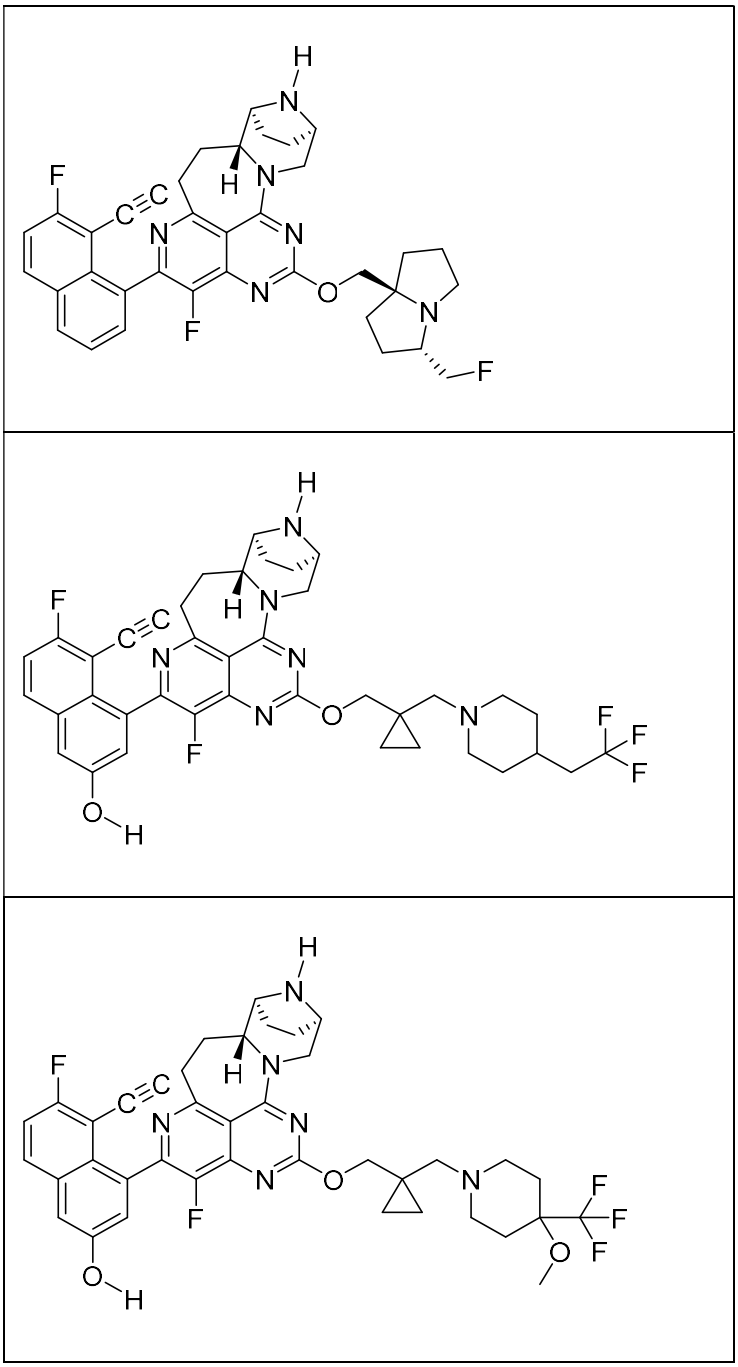


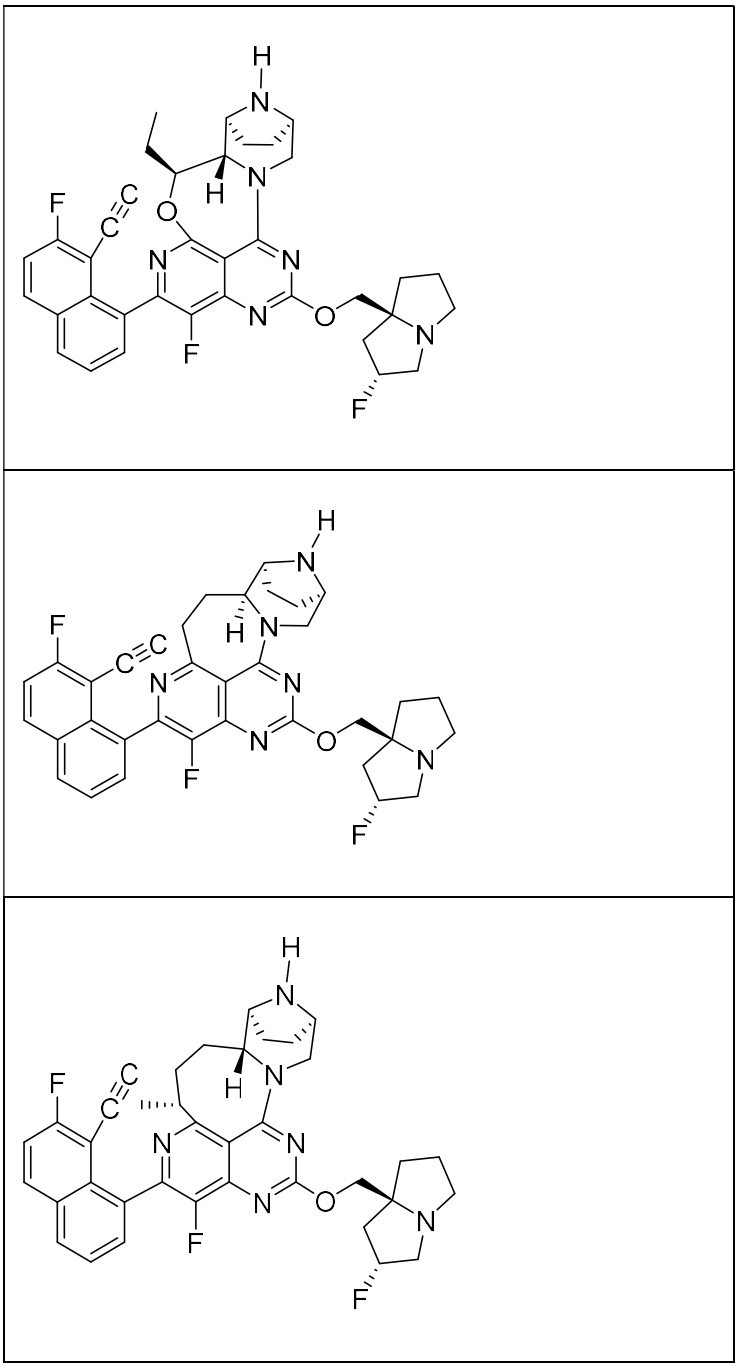


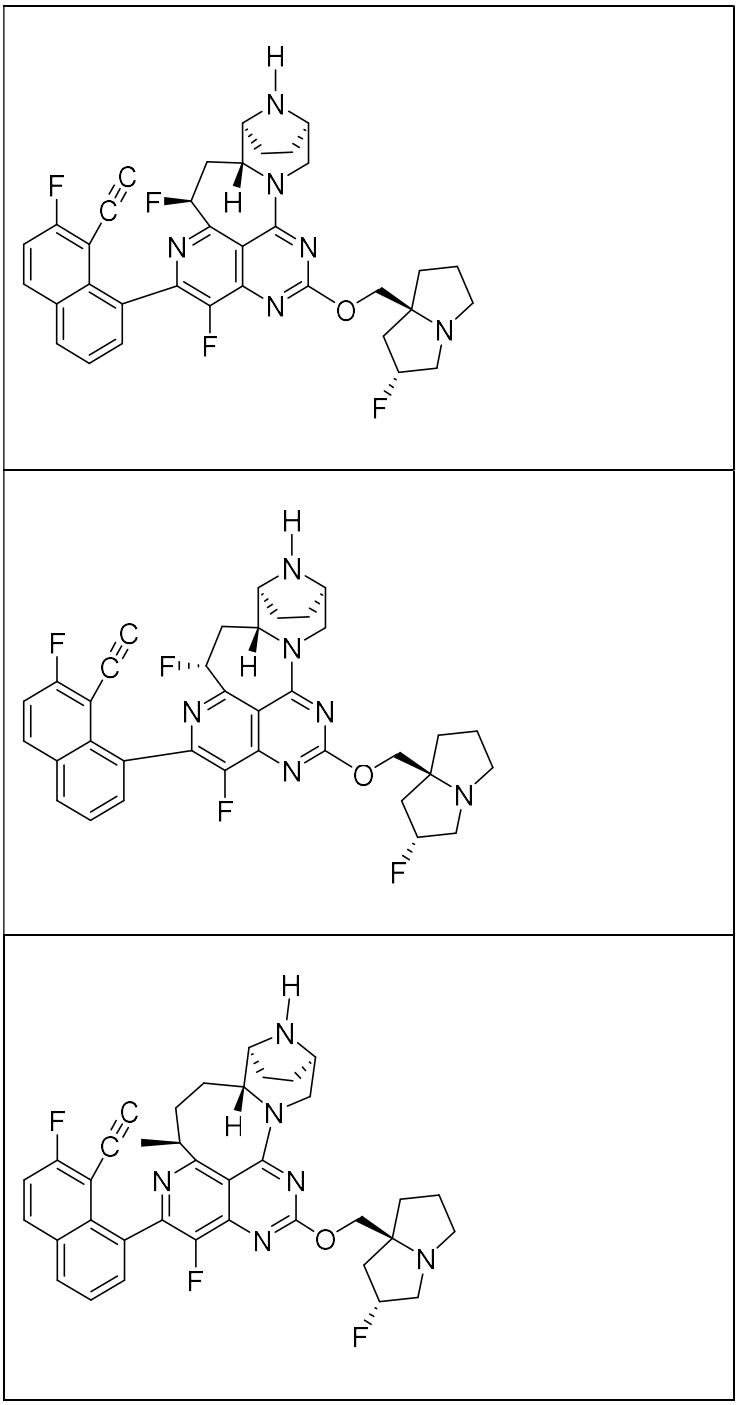


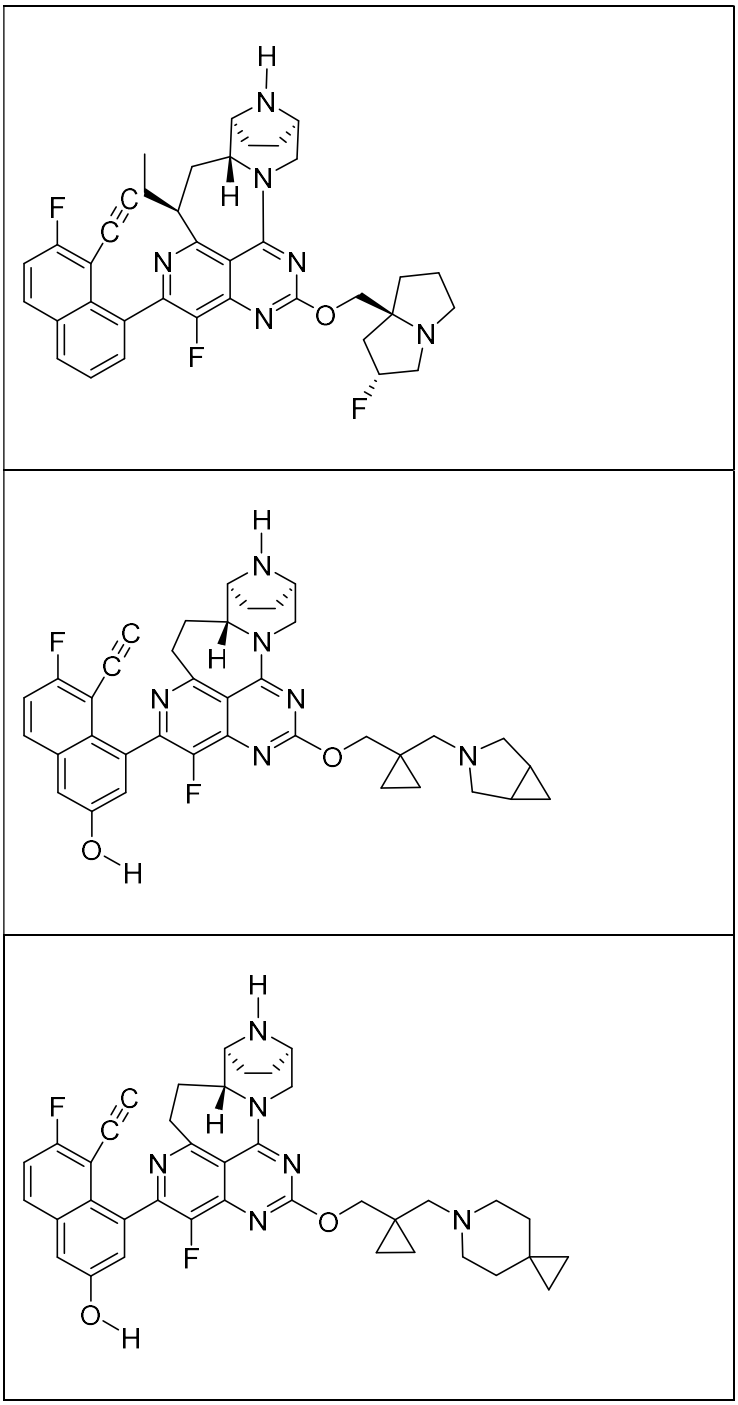


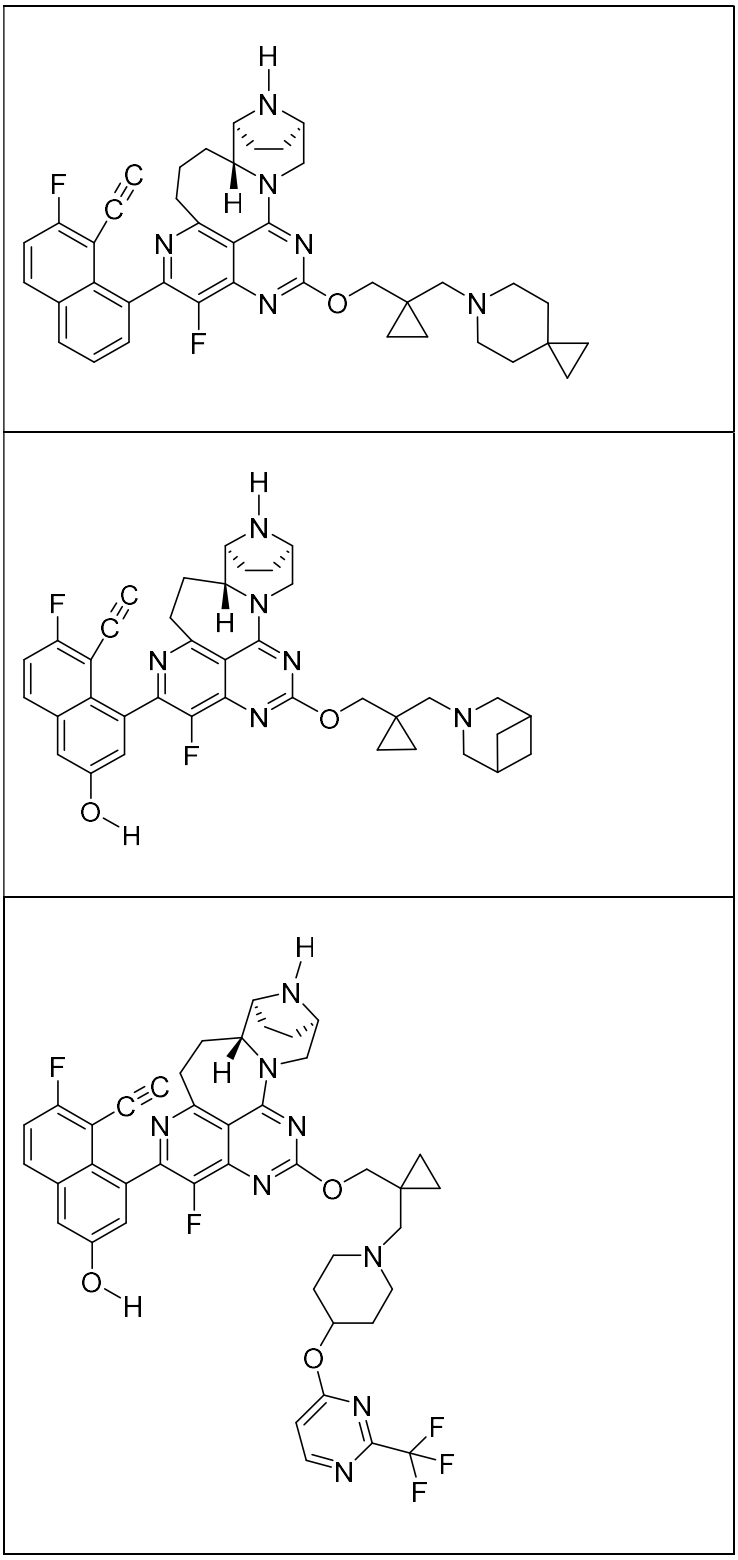


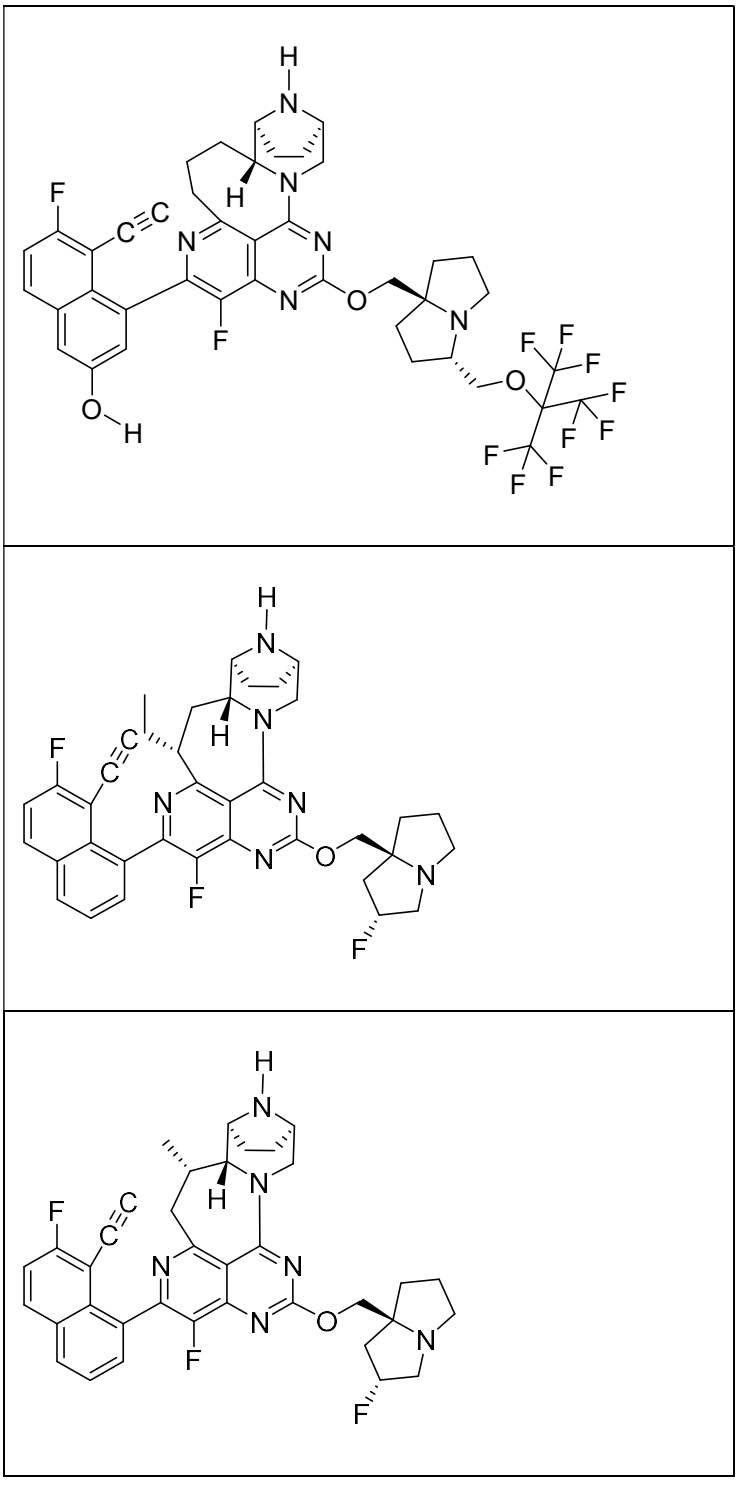


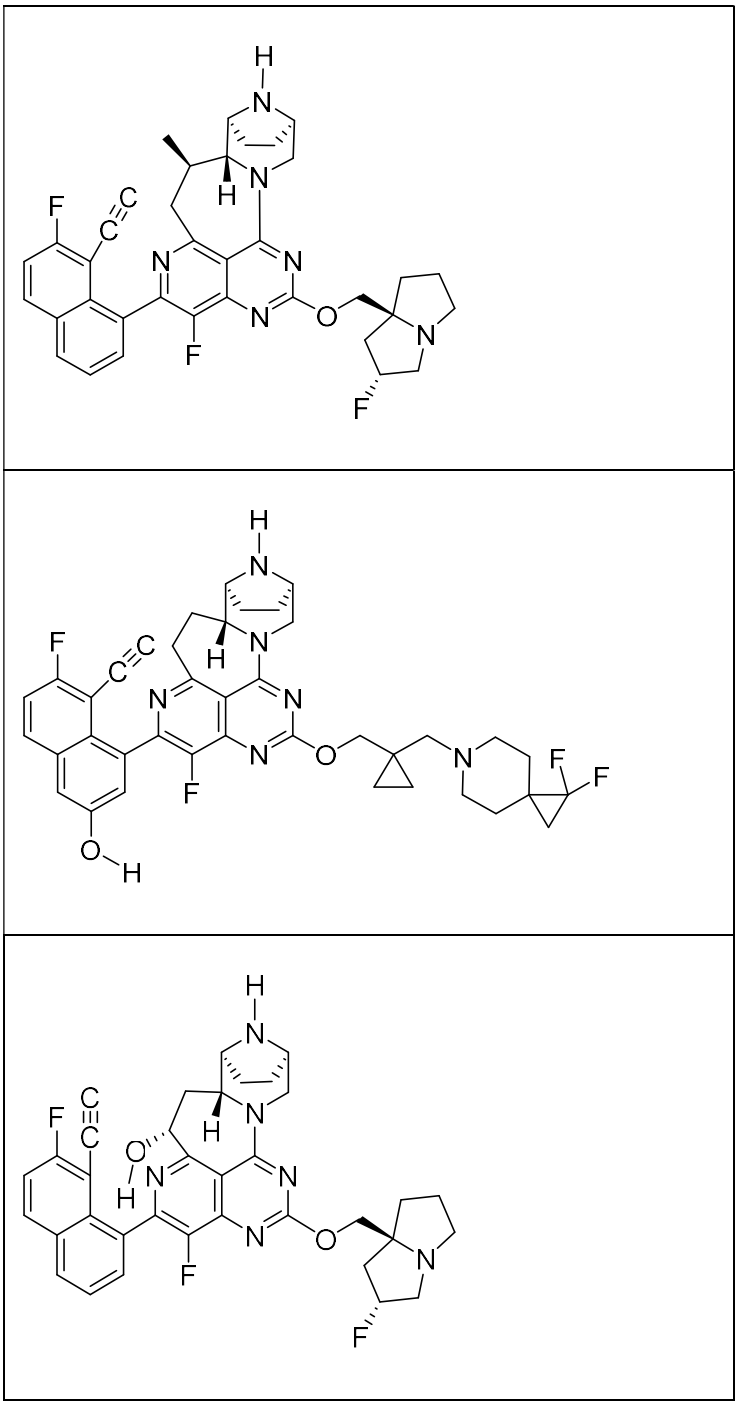


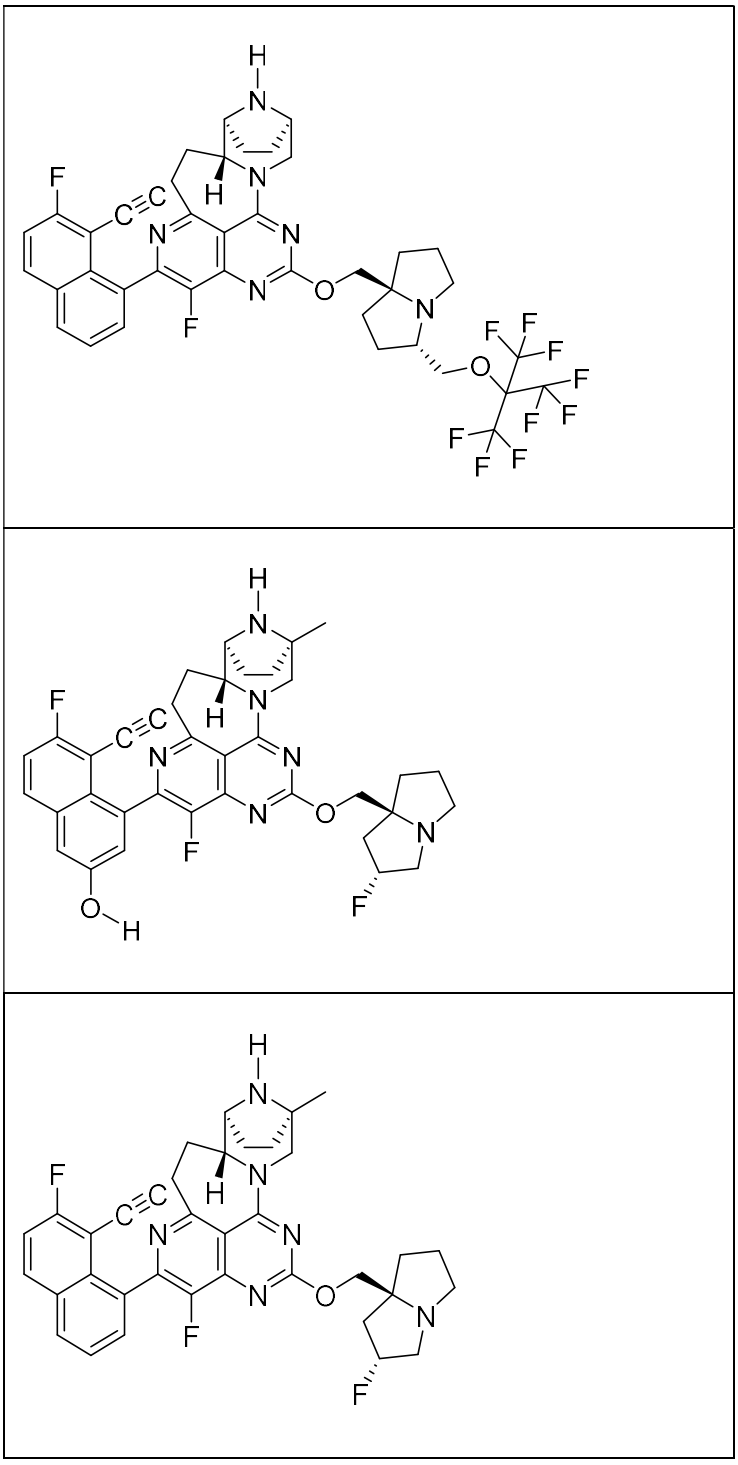


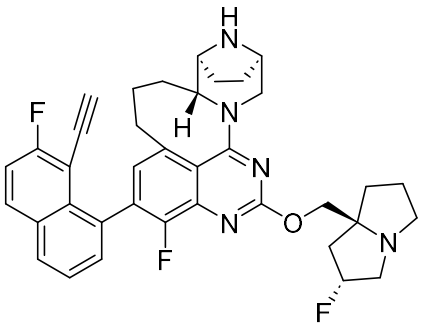


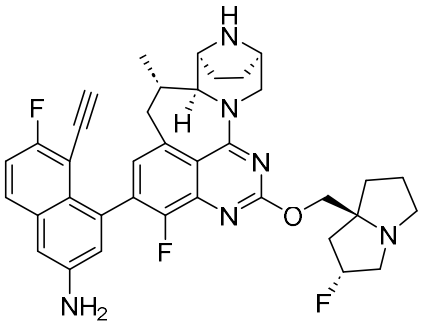


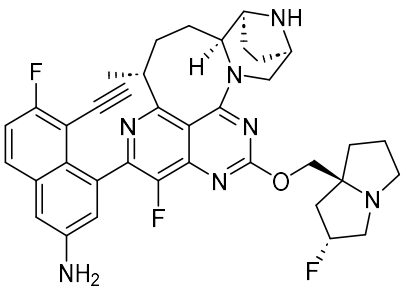


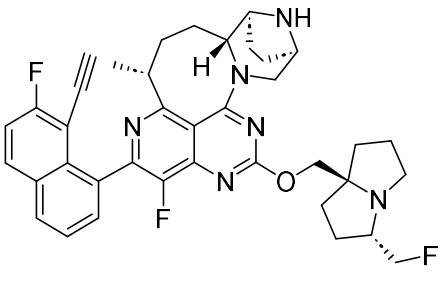


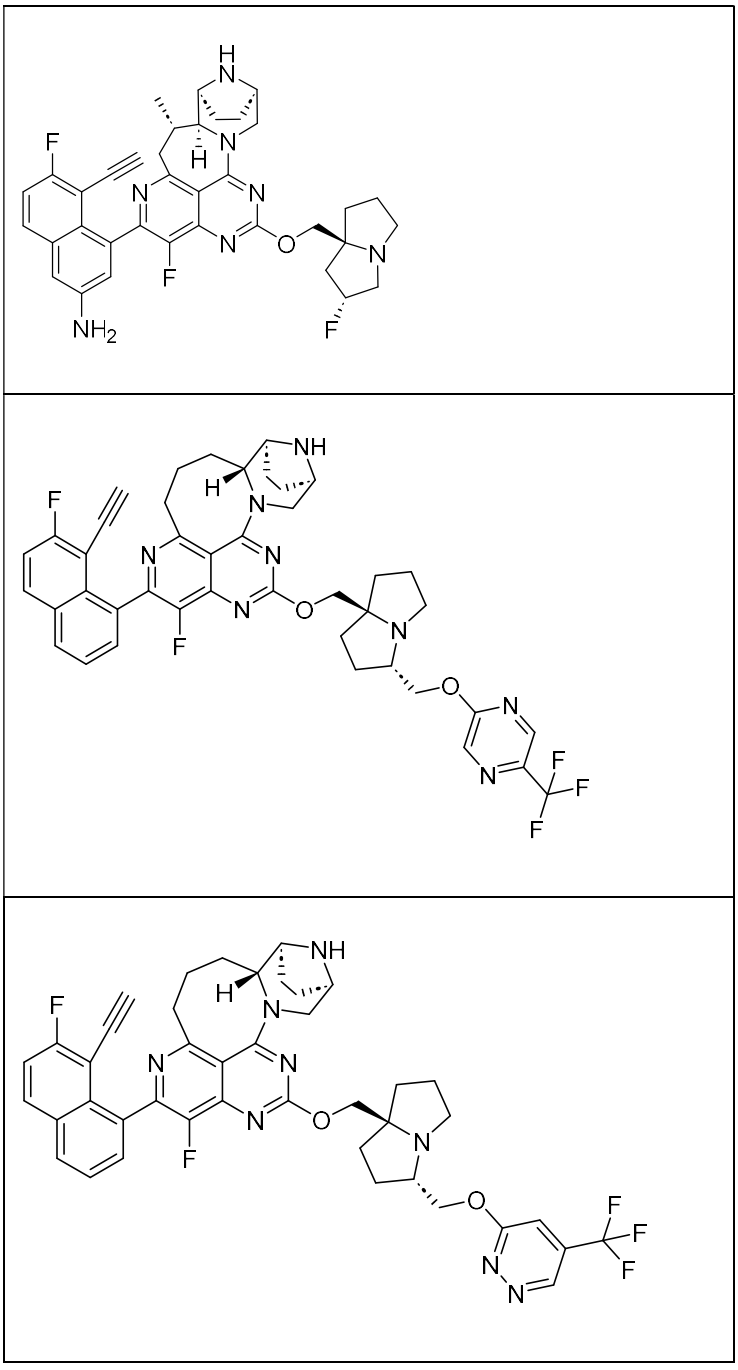


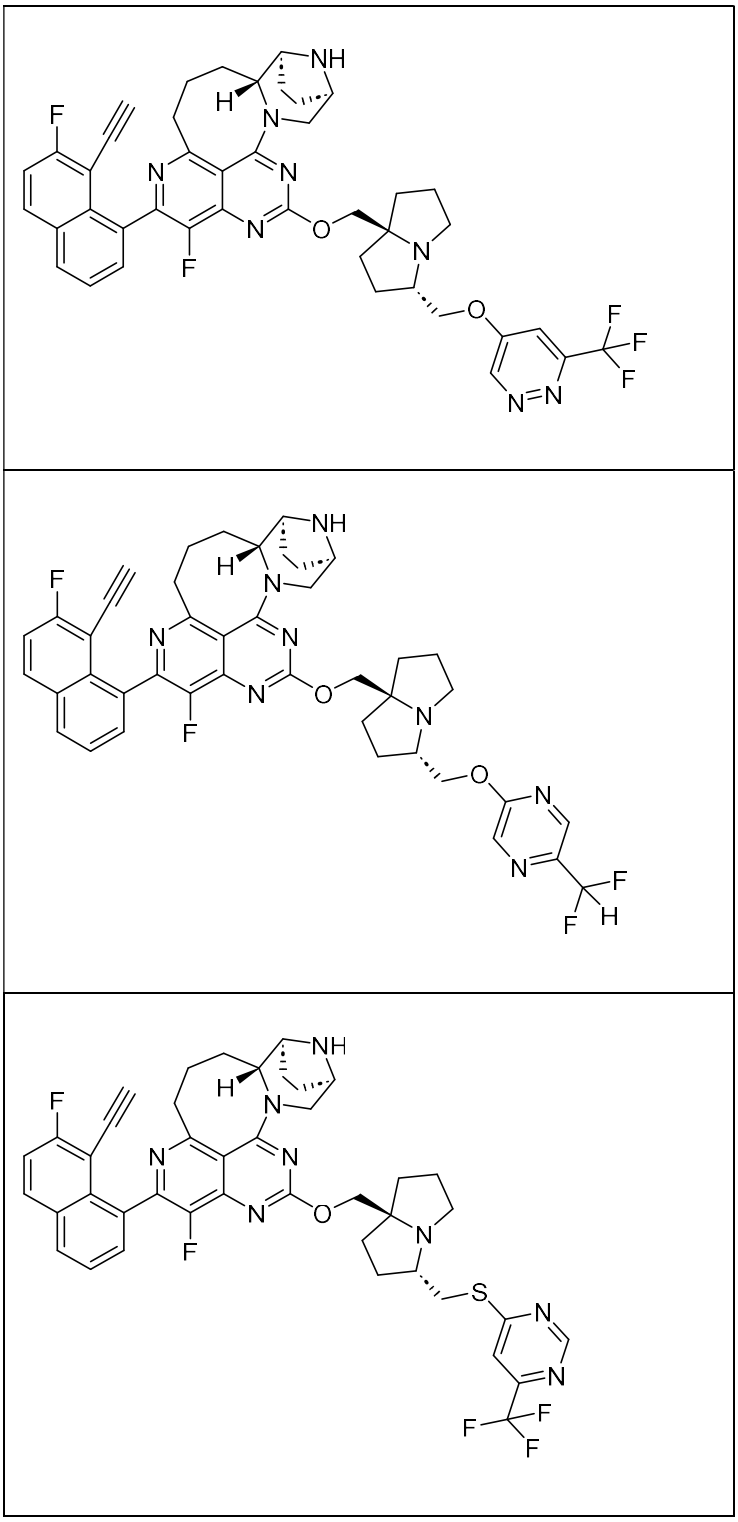


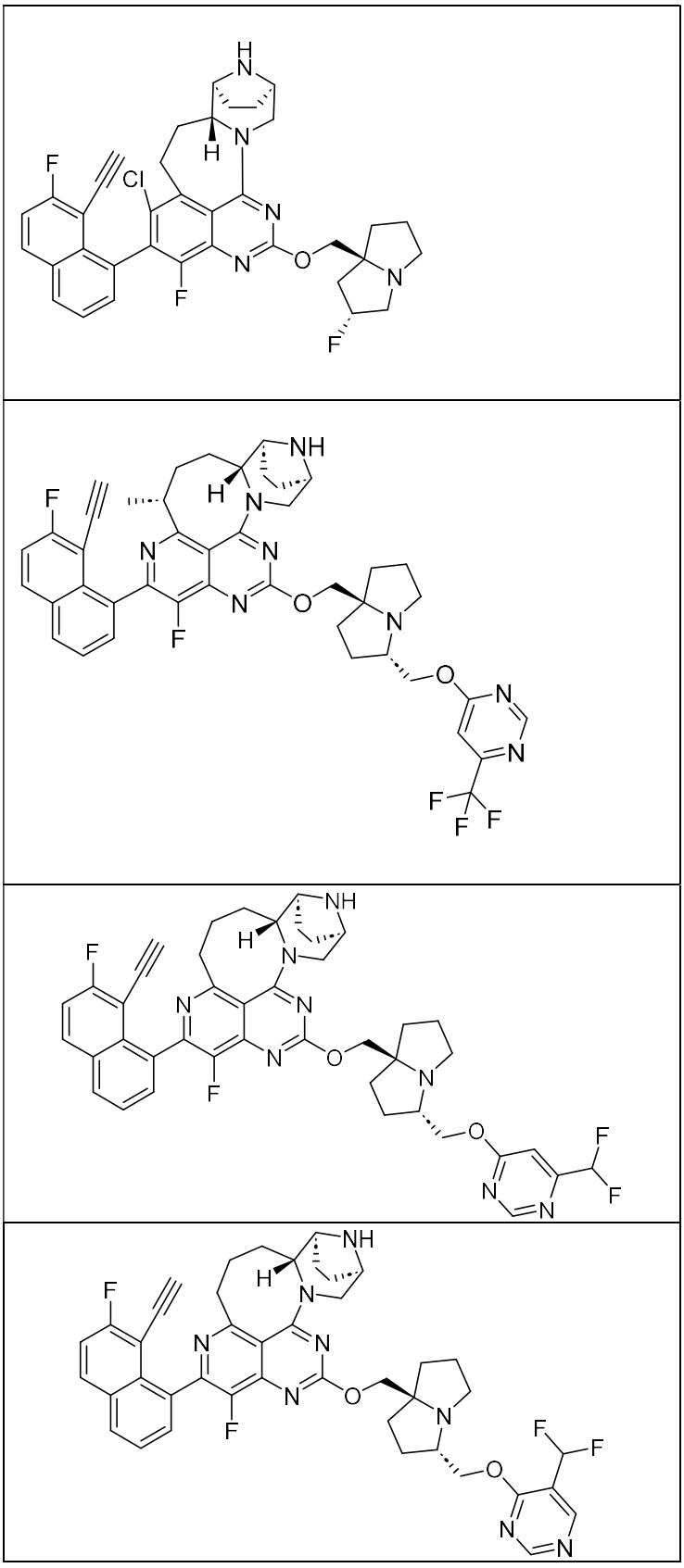


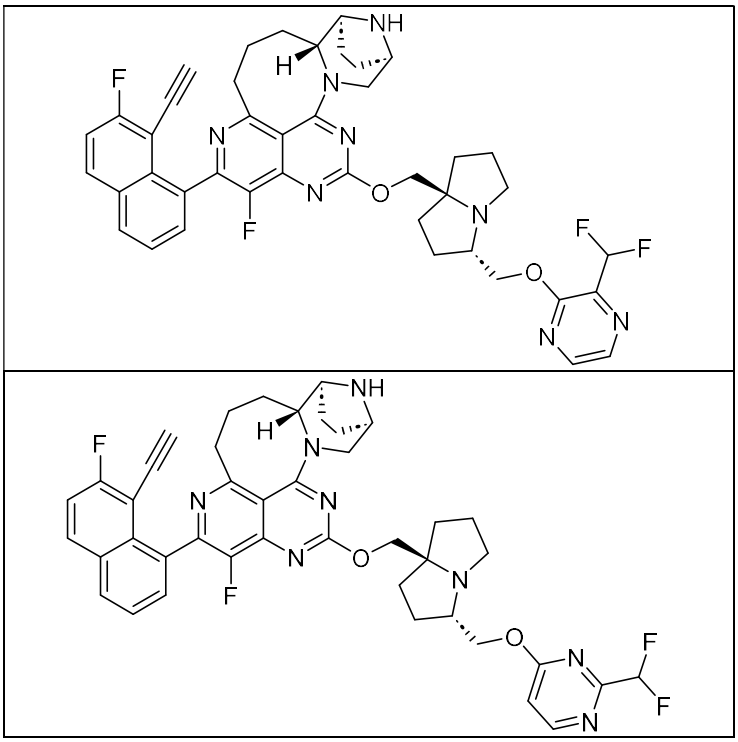












19. A pharmaceutical composition comprising a compound of any one of claims 1 to 18, and a pharmaceutically acceptable excipient.

20. Use of the compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of cancer in a subject.