BIFUNCTIONAL ANDROGEN RECEPTOR COMPOUNDS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/589,861, filed October 12, 2023, and U.S. Provisional Patent Application No. 63/636,293, filed April 19, 2024, which are incorporated herein by reference in their entireties.

FIELD OF THE INVENTION

[0001] Described herein are heterobifunctional small molecules, methods of making, pharmaceutical compositions and medicaments comprising such heterobifunctional small molecules, and methods of using such heterobifunctional small molecules are described herein, in the treatment of diseases and conditions, such as cancer, autoimmune diseases, and inflammatory diseases.

BACKGROUND OF THE INVENTION

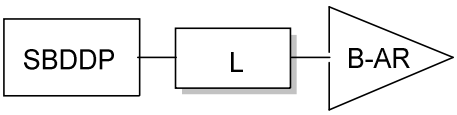
[0002] Cellular homeostasis, a key hallmark of living organisms, arises from interactions between biomolecules, such as protein (e.g., enzyme) and substrate interactions, within and outside the cell. Conventionally, the function of a particular protein in a particular disease state has been investigated and controlled through the use of monofunctional molecules (e.g., an inhibitor), which occupy the active site of the disease protein, thereby forming binary complexes that inhibit or downregulate activity of the disease proteins. Such monofunctional molecules have provided a conceptual pathway toward many FDA-approved drugs as a means for treating the disease state.

[0003] However, many monofunctional molecules lack specificity for the disease proteins in question leading to undesired toxicities or lack of efficacy, or the disease proteins adapts to the monofunctional molecules thereby leading to resistance. An alternative approach with monofunctional molecules is to target the coregulator or coactivator proteins of the disease proteins. However, such coregulator or coactivator proteins are typically present in every cell, healthy or diseased, and inhibiting their activity typically leads to narrower therapeutic indices.

[0004] Described herein are heterobifunctional small molecules that engage the androgen receptor (AR) and a disease-dependent protein, thereby forming ternary complexes only in the disease cells that express both proteins and leading to loss of function of the disease-dependent protein. The heterobifunctional small molecules described herein comprise at least one silent binder to the disease-dependent protein and at least one binder to AR. Such heterobifunctional small molecules offer a new means for treatment of diseases or conditions, with a wider therapeutic index and offer novel therapeutic targets vis a vis expansion of the disease proteins, such as AR.

SUMMARY

[0005] In some examples, disclosed herein is a heterobifunctional conditional inhibitor compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof:



wherein:

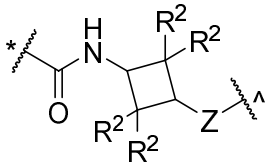
SBDDP is a silent binder of a disease-dependent protein (DDP);

L is an optional linker; wherein L is covalently attached at a position of SBDDP that is solvent exposed when SBDDP binds to the DDP;

B-AR is a binder of the androgen receptor (AR), wherein B-AR comprises:

1) a head group that occupies the ligand-binding domain (LBD) of AR and is covalently attached to a core moiety; and

2) an optional tail moiety covalently attached to the core moiety; wherein the core comprises an optionally substituted cyclobutyl having the structure of Formula (C):



, Formula (C);

the head group is covalently attached to Z at position (^);

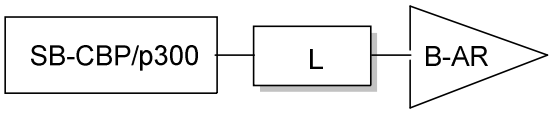
the optional tail moiety comprises a ring D that is covalently attached to the amide (*), wherein ring D is optionally substituted with s R^3;

wherein: Z is -O- or -NR^5-; and R^2 and R^3 is described herein;

wherein L is covalently attached to the core moiety at position (*) if the optional tail moiety is absent, or L is covalently attached to the tail moiety if present;

wherein DDP and AR are both expressed in a cell of interest (COI), and wherein the relative abundance of the AR in the COI is greater than the relative abundance of the DDP in the COI; or the COI is a diseased cell, and the AR is overexpressed, overactive, or both overexpressed and overactive, or amplified in the diseased cell as compared to when the COI is a non-diseased cell.

[0006] In some examples, disclosed herein is a heterobifunctional conditional inhibitor compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof:



wherein:

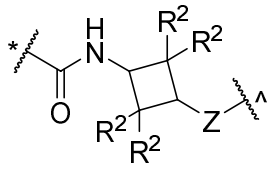
SB-CBP/p300 is a silent binder of human CREB-binding protein (CBP) or human E1A-binding protein p300 (p300) (CBP/p300);

L is an optional linker; wherein L is covalently attached at a position of SB-CBP/p300 that is solvent exposed when SB binds to CBP/p300;

B-AR is a binder of the androgen receptor (AR), wherein the B-AR comprises:

1) a head group that occupies the ligand-binding domain (LBD) of AR and is covalently attached to a core moiety; and

2) an optional tail moiety covalently attached to the core moiety; wherein the core comprises an optionally substituted cyclobutyl having the structure of Formula (C):



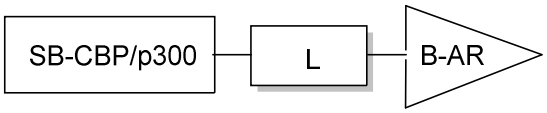
, Formula (C);

wherein: the head group is covalently attached to Z at position (^); the optional tail moiety comprises a ring D that is covalently attached to the amide (*), wherein ring D is optionally substituted with s R^3;

wherein: Z is -O- or -NR^5-; and R^2 and R^3 is described herein;

wherein L is covalently attached to the core moiety at position (*) if the optional tail moiety is absent, or L is covalently attached to the tail moiety if present.

[0006a] In a first aspect of the present disclosure, there is provided a heterobifunctional conditional inhibitor compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof:



wherein:

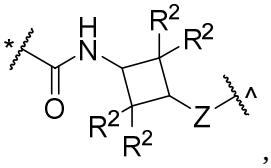
SB-CBP/p300 is a silent binder of human CREB-binding protein (CBP) or human E1A-binding protein p300 (p300) (CBP/p300);

L is an optional linker; wherein L is covalently attached at a position of SB-CBP/p300 that is solvent exposed when SB binds to CBP/p300;

B-AR is a binder of the androgen receptor (AR), wherein the B-AR comprises:

1) a head group that occupies the ligand-binding domain (LBD) of AR and is covalently attached to a core moiety; and

2) an optional tail moiety covalently attached to the core moiety; wherein the core comprises an optionally substituted cyclobutyl having the structure of Formula (C):



, Formula (C);

wherein:

the head group is covalently attached to Z at position (^);

the optional tail moiety comprises a ring D that is covalently attached to the amide (*), wherein ring D is a 5-, 6-, 8-, 9- or 10-membered aryl or a 5-, 6-, 8-, 9- or 10-membered heteroaryl that is optionally substituted with s R^3;

Z is -O- or -NR^5-;

each R^2 is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, -NO_2, -OH, -OR^4, $OC(=O)R^4$, -$S(=O)R^4$, -$S(=O)_2R^5$, -$S(=O)_2N(R^5)_2$, -$N(R^5)_2$, -$NR^5C(=O)NR^5$, -$NR^5C(=O)R^4$, -$C(=O)R^5$, -$C(=O)OR^5$, or -$C(=O)N(R^5)_2$; or

two R^2 on the same carbon atom are taken together with the carbon atom to which they are attached to form a substituted or unsubstituted C_3-C_8cycloalkyl or a substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl;

each R^3 is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, -OH, -OR^4, or -$N(R^5)_2$.

each R^4 is independently substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

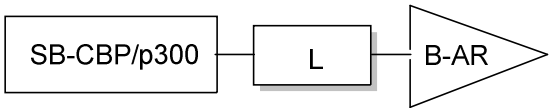
each R^5 is independently hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

or two R^5 on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle; and

each s is 1, 2, or 3;

wherein L is covalently attached to the core moiety at position (*) if the optional tail moiety is absent, or L is covalently attached to the tail moiety if present.

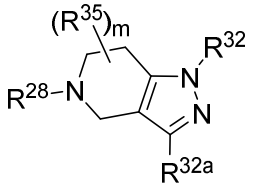
[0007] In some examples, disclosed herein is a heterobifunctional conditional inhibitor compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof:



wherein:

SB-CBP/p300 is a silent binder of the bromodomain of human CREB-binding protein (CBP) or human E1A-binding protein p300 (p300) (CBP/p300), wherein the binder of CBP/p300 comprises:

- an acetyl-lysine mimetic moiety that binds in the acetyl-lysine (KAc) binding site of the bromodomain of human CREB-binding protein (CBP) or human E1A-binding protein p300 (p300) (CBP/p300) and has the structure:



R^{28} is -C(=O)CH_3, -C(=O)CH_2CH_3, -C(=O)NH_2, -C(=O)NH(CH_3); or -C(=O)NH(CH_2CH_3);

R^{32} is a moiety that occupies the BC Loop region of the bromodomain of CBP/p300;

R^{32a} is a moiety that occupies the lipophilic shelf (LPF) region of the bromodomain of CBP/p300;

each R^{35} is independently hydrogen, C_1-C_4alkyl, or C_1-C_4fluoroalkyl;

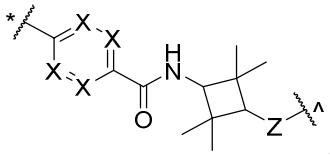
m is 0, 1, 2, 3, or 4;

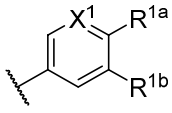
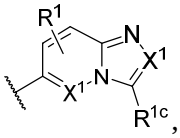
L is an optional linker; wherein L is covalently attached to the R^{32} group, or at the position occupied by R^{32}, or the R^{32a} group;

B-AR is a binder of the androgen receptor (AR), wherein the B-AR comprises:

- a head group that occupies the ligand-binding domain (LBD) of AR and is covalently attached to a core with a tail moiety covalently attached to the core moiety; wherein B-AR has the structure of

Formula (D):


, Formula (D);

wherein head group is , or , and the the head group is covalently attached to Z at position (^), and L is attached at position *;

Z is -O-, -NH- or -N(C_1-C_4alkyl)-; each X^1 is independently -CR^1- or -N-;

R^{1a} is -CN, -NO_2, -C(=O)R^5, -C(=O)OR^5, or -C(=O)$N(R^5)_2$;

R^{1b} is hydrogen, halogen, substituted or unsubstituted C_1-C_4alkyl, C_1-C_4fluoroalkyl, -CN, -OH, or -OR^4;

R^{1c} is hydrogen, halogen, C_1-C_4alkyl, C_1-C_4fluoroalkyl, or -CN;

each R^1 is independently hydrogen, halogen, substituted or unsubstituted C_1-C_4alkyl, C_1-C_4fluoroalkyl, -CN, -OH, or -OR^4;

each X is independently -CR^3- or -N-;

each R^3 is independently hydrogen, halogen, substituted or unsubstituted C_1-C_4alkyl, C_1-C_4fluoroalkyl, -CN, -OH, -OR^4, or -$N(R^5)_2$.

each R^4 is independently substituted or unsubstituted C_1-C_4alkyl, or C_1-C_4fluoroalkyl;

each R^5 is independently hydrogen, substituted or unsubstituted C_1-C_4alkyl, C_1-C_4fluoroalkyl; and

each s is 1, 2, or 3.

[0008] In some examples, disclosed herein is a stable ternary complex comprising:

a. one or more disease-dependent proteins (DDPs);
b. Androgen Receptor (AR); and
c. heterobifunctional conditional inhibitor compound as described herein;

wherein DDP and AR are present in a cell of interest (COI) and the relative abundance of the AR in the COI is greater than the relative abundance of the DDP in the COI.

[0009] In some examples, the DDP is CREB-binding protein (CBP)/p300.

[0010] In some examples, disclosed herein is a stable ternary complex comprising:

d. CBP/p300;
e. Androgen receptor (AR); and
f. heterobifunctional conditional inhibitor compound as described herein;

wherein CBP/p300 and DP are present in a cell of interest (COI) and the relative abundance of the DP in the COI is greater than the relative abundance of CBP/p300 in the COI.

[0011] In another example, described herein is a method of selectively inhibiting the activity of a disease-dependent protein (DDP) in a cell of interest (COI) of a mammal comprising administering a heterobifunctional compound as described herein, or a pharmaceutically acceptable salt or solvate thereof,

wherein the COI expresses the androgen receptor (AR). In some examples, the heterobifunctional compound as described herein, or a pharmaceutically acceptable salt or solvate thereof, inhibits the activity of the DDP in the COI but does not inhibit the activity of the DDP in cells expressing the DDP and not expressing the AR. In some examples, the AR is overexpressed, overactive or both overexpressed and overactive in the COI. In some examples, the DDP is CREB-binding protein (CBP)/p300.

[0012] In another example, described herein is a method of treating cancer in a mammal comprising administering to the mammal a therapeutically effective amount of a compound as described herein, or a pharmaceutically acceptable salt or solvate thereof. In some examples, the cancer is a hormone dependent cancer. In some examples, the cancer is prostate cancer.

[0012a] In another aspect of the present disclosure, there is provided a use of a compound as disclosed herein, or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating prostate cancer in a mammal.

[0013] In another example, described herein is a method of treating an androgen receptor dependent or androgen receptor mediated disease or condition in mammal comprising administering to the mammal a therapeutically effective amount of a compound as described herein, or a pharmaceutically acceptable salt or solvate thereof. In some examples, the androgen receptor dependent or androgen receptor mediated disease or condition is selected from benign prostate hyperplasia, hirsutism, adenomas and neoplasms of the prostate, benign or malignant tumor cells containing the androgen receptor, prostate cancer, breast cancer, endometrial cancer, and uterine cancer.

[0013a] In a further aspect of the present disclosure, there is provided a use of a compound as disclosed herein, or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating an androgen receptor dependent or androgen receptor mediated disease or condition in a mammal.

[0013b] In another aspect of the present disclosure, there is provided a compound as disclosed herein, or a pharmaceutically acceptable salt of solvate thereof, for use in therapy.

[0014] Also described herein is a pharmaceutical composition comprising a heterobifunctional compound described herein, or a pharmaceutically acceptable salt, or solvate thereof, and at least one pharmaceutically acceptable excipient. In some examples, the pharmaceutical composition is formulated for administration to a mammal by oral administration, intravenous administration, or subcutaneous administration. In some examples, the pharmaceutical composition is formulated for administration to a mammal by oral administration. In some examples, the pharmaceutical composition is in the form of a tablet, a pill, a capsule, a liquid, or a suspension.

[0014a] In yet another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound as disclosed herein, or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient.

[0015] In one example, the heterobifunctional compounds described herein, or a pharmaceutically acceptable salt, or solvate thereof, are used in the treatment of diseases or conditions, such as cancer, autoimmune diseases, and inflammatory diseases. In some examples, the disease or condition is cancer. In some examples, the cancer comprises altered AR expression levels. In some examples, the cancer comprises altered androgen receptor expression levels. In some examples, altered DP expression levels comprises overexpressed AR, overactive AR, amplified AR, or combinations thereof.

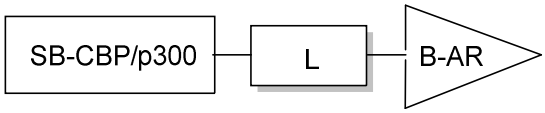
[0016] In any of the examples disclosed herein, the mammal is a human. In some examples, compounds disclosed herein are orally administered to a human.

[0017] Other objects, features and advantages of the compounds, methods and compositions described herein will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating specific examples, are given by way of illustration only, since various changes and modifications within the spirit and scope of the instant disclosure will become apparent to those skilled in the art from this detailed description.

CLAIMS

WHAT IS CLAIMED IS:

1. A heterobifunctional conditional inhibitor compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof:



wherein:

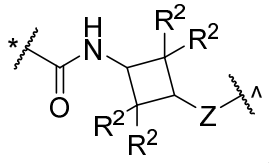
SB-CBP/p300 is a silent binder of human CREB-binding protein (CBP) or human E1A-binding protein p300 (p300) (CBP/p300);

L is an optional linker; wherein L is covalently attached at a position of SB-CBP/p300 that is solvent exposed when SB binds to CBP/p300;

B-AR is a binder of the androgen receptor (AR), wherein the B-AR comprises:

1) a head group that occupies the ligand-binding domain (LBD) of AR and is covalently attached to a core moiety; and

2) an optional tail moiety covalently attached to the core moiety; wherein the core comprises an optionally substituted cyclobutyl having the structure of Formula (C):



, Formula (C);

wherein:

the head group is covalently attached to Z at position (^);

the optional tail moiety comprises a ring D that is covalently attached to the amide (*), wherein ring D is a 5-, 6-, 8-, 9- or 10-membered aryl or a 5-, 6-, 8-, 9- or 10-membered heteroaryl that is optionally substituted with s R^3;

Z is -O- or -NR^5-;

each R^2 is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, -NO_2, -OH, -OR^4, $OC(=O)R^4$, -$S(=O)R^4$, -$S(=O)_2R^5$, -$S(=O)_2N(R^5)_2$, -$N(R^5)_2$, -$NR^5C(=O)NR^5$, -$NR^5C(=O)R^4$, -$C(=O)R^5$, -$C(=O)OR^5$, or -$C(=O)N(R^5)_2$; or

two R^2 on the same carbon atom are taken together with the carbon atom to which they are attached to form a substituted or unsubstituted C_3-C_8cycloalkyl or a substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl;

each R^3 is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, -OH, -OR^4, or -

$N(R^5)_2$.

each R^4 is independently substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

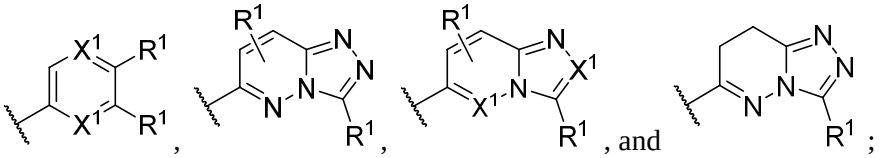
each R^5 is independently hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

or two R^5 on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle; and

each s is 1, 2, or 3;

wherein L is covalently attached to the core moiety at position (*) if the optional tail moiety is absent, or L is covalently attached to the tail moiety if present.

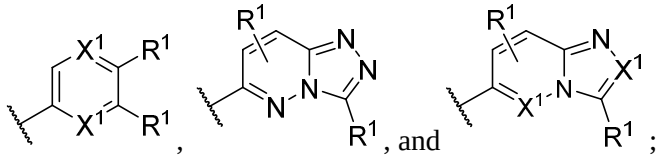
2. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein B-AR comprises a head group and an optional core, wherein the head group is selected from:



each X^1 is independently -CR^1- or -N-;

each R^1 is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted 3- to 8-membered heterocycloalkyl, -CN, -NO_2, -OH, -OR^4, OC(=O)R^4, -OC(=O)N$(R^5)_2$, -OC(=O)OR^5, -OC(=O)NR^5, -SH, -SR^4, -S(=O)R^4, -$S(=O)_2R^5$, -$S(=O)_2OR^4$, -$S(=O)_2N(R^5)_2$, -$N(R^5)_2$, -$NR^5C(=O)NR^5$, -$NR^5C(=O)R^4$, -$NR^5C(=O)OR^5$, -$NR^5S(=O)_2R^5$, -$C(=O)R^5$, -$C(=O)OR^5$, or -$C(=O)N(R^5)_2$.

3. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein B-AR comprises a head group and an optional core, wherein the head group is selected from:

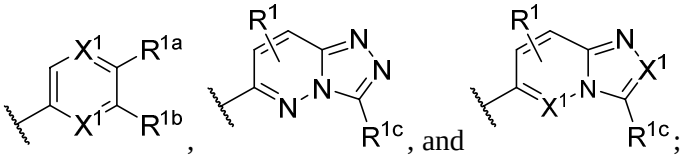


one X^1 is -CR^1- and the other X^1 is -CR^1- or -N-;

each R^1 is independently hydrogen, F, Cl, Br, I, -CH_3, -CD_3, -CH_2CH_3, -CH_2F, -CHF_2, -CF_3, -CH_2CH_2F, -CH_2CHF_2, - CH_2CF_3, -OH, -OCF_3, -OCH_3, -OCD_3, -OCH_2CH_3, -CN, -$C(=O)NH_2$ - C(=O)NH(CH_3)or -C(=O)NH(CD_3).

4. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein B-AR

comprises a head group and an optional core, wherein the head group is selected from:



one X^1 is $-CR^1-$ and the other X^1 is $-CR^1-$ or -N-;

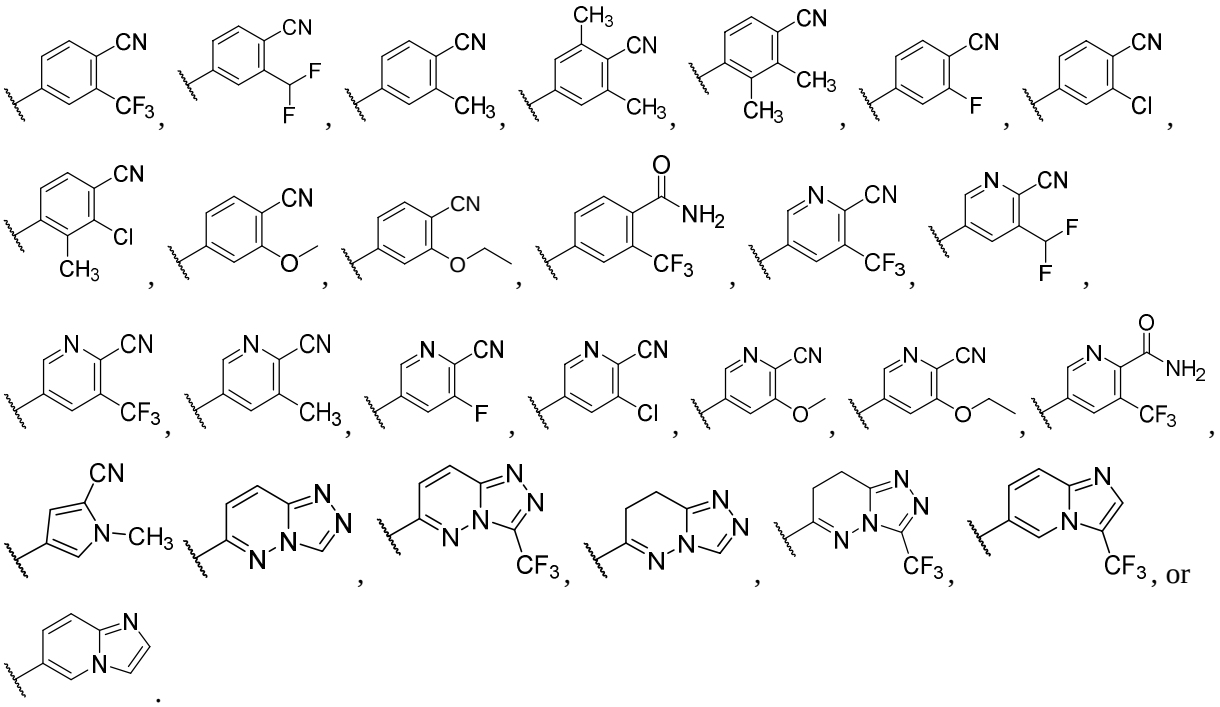
R^{1a} is -CN, $-NO_2$, $-C(=O)NH_2$ or $-C(=O)NH(CH_3)$;

R^{1b} is hydrogen, F, Cl, Br, I, $-CH_3$, $-CH_2CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, -OH, $-OCF_3$, $-OCH_3$, $-OCH_2CH_3$, or -CN;

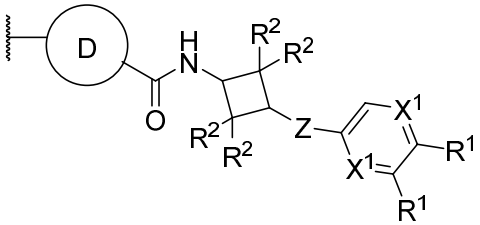
each R^{1c} is hydrogen, F, Cl, Br, $-CH_3$, $-CH_2F$, $-CHF_2$, or $-CF_3$;

each R^1 is independently hydrogen, F, Cl, Br, I, $-CH_3$, $-CH_2CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2CH_2F$, $-CH_2CHF_2$, $-CH_2CF_3$, -OH, $-OCF_3$, $-OCH_3$, or $-OCH_2CH_3$.

5. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein B-AR comprises a head group and an optional core, wherein the head group is selected from:



6. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein B-AR has the structure of Formula (IIa), or a pharmaceutically acceptable salt or solvate thereof:



Formula (IIa)

wherein:

each X^1 is independently $-CR^1-$ or -N-;

Z is -O- or -NR^5-;

each R^1 is independently hydrogen, F, Cl, Br, I, -CH_3, -CH_2CH_3, -CH_2F, -CHF_2, -CF_3, -CH_2CH_2F, -CH_2CHF_2, - CH_2CF_3, -OH, -OCF_3, -OCH_3, -OCH_2CH_3, -CN, -C(=O)NH_2 or -C(=O)NH(CH_3);

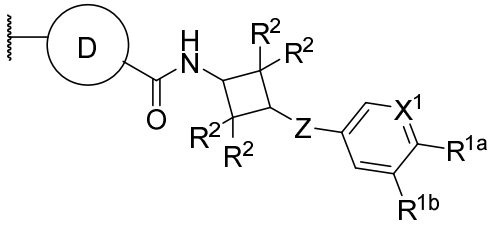
each R^2 is C_1-C_6alkyl;

ring D that is a 5-, 6-, 8-, 9- or 10-membered aryl or a 5-, 6-, 8-, 9- or 10-membered heteroaryl that is optionally substituted with s R^3;

each R^3 is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, -OH, -OR^4, or -$N(R^5)_2$;

s is 1, 2, or 3.

7. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein B-AR has the structure of Formula (IIIa), or a pharmaceutically acceptable salt or solvate thereof:



Formula (IIIa)

wherein:

X^1 is -CR^1- or -N-;

Z is -O- or -NR^5-;

R^{1a} is -CN, -NO_2, -C(=O)R^5, -C(=O)OR^5, or -C(=O)$N(R^5)_2$;

R^{1b} is hydrogen, halogen, C_1-C_4alkyl, C_1-C_4fluoroalkyl, -CN, -OH, or -OR^4;

each R^1 is independently hydrogen, halogen, C_1-C_4alkyl, C_1-C_4fluoroalkyl, -CN, -OH, or -OR^4;

each R^2 is -CH_3;

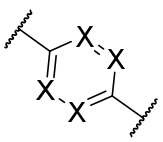
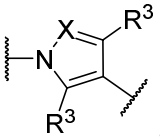
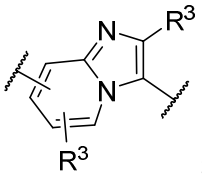
ring D that is a 5-, 6-, 8-, 9- or 10-membered aryl or a 5-, 6-, 8-, 9- or 10-membered heteroaryl that is optionally substituted with s R^3;

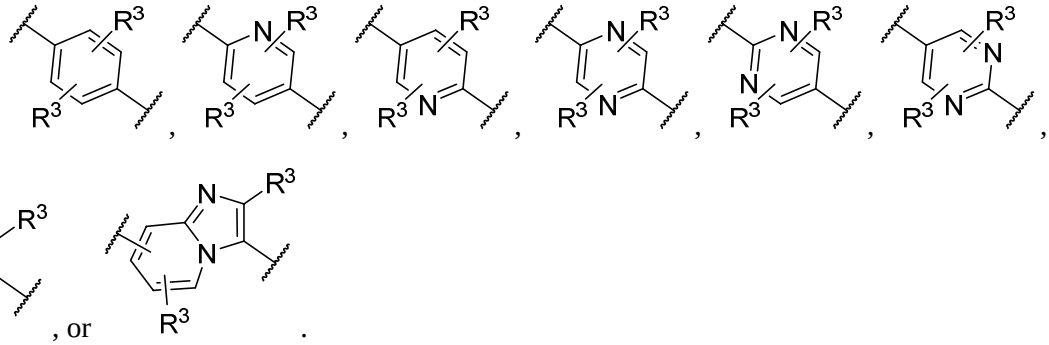
each R^3 is independently hydrogen, halogen, substituted or unsubstituted C_1-C_4alkyl, C_1-C_4fluoroalkyl, -CN, -OH, -OR^4, or -$N(R^5)_2$;

s is 1, 2, or 3;

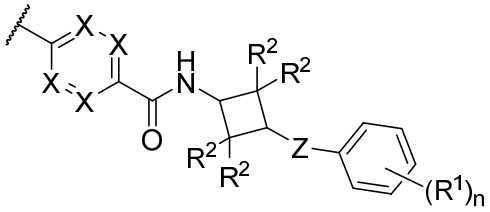
each R^4 is independently C_1-C_4alkyl, or C_1-C_4fluoroalkyl;

each R^5 is independently hydrogen, C_1-C_4alkyl, or C_1-C_4fluoroalkyl.

8. The compound of claim 6 or claim 7, or a pharmaceutically acceptable salt or solvate thereof, wherein ring D is , , or ; and each X is independently -CR^3- or -N-.

9. The compound of claim 6 or claim 7, or a pharmaceutically acceptable salt or solvate thereof, wherein ring D is , or .

10. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein B-AR has the structure of Formula (IVa), or a pharmaceutically acceptable salt or solvate thereof:



Formula (IVa)

wherein:

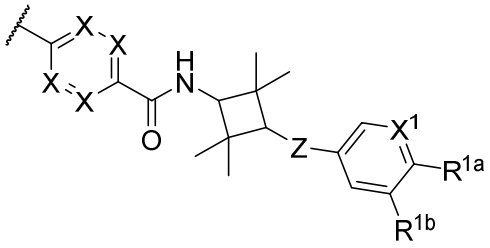
each X is independently -CR^3- or -N-;

Z is -O- or -NR^5-;

n is 2 and one R^1 is halogen, -CH_3, -OCH_3, or -CF_3, and the other R^1 is -CN;

each R^2 is -CH_3.

11. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein B-AR has the structure of Formula (Va), or a pharmaceutically acceptable salt or solvate thereof:



Formula (Va)

wherein:

each X is independently -CR^3- or -N-;

Z is -O- or -NR^5-;

X^1 is -CR^1- or -N-;

R^{1a} is -CN;

R^{1b} is hydrogen, F, Cl, Br, I, -CH_3, -CH_2CH_3, -CH_2F, -CHF_2, -CF_3, -OH, -OCF_3, -OCH_3, or -CN;

R^1 is hydrogen, F, Cl, Br, I, -CH_3, -CH_2CH_3, -CH_2F, -CHF_2, -CF_3, -CH_2CF_3, -OH, -OCF_3, -OCH_3, -OCH_2CH_3, or -OCH_2CF_3;

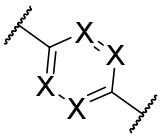
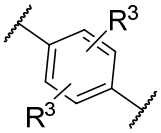
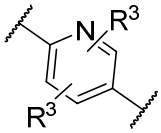
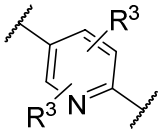
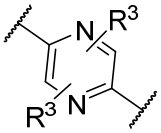
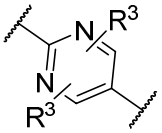
each R^3 is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted

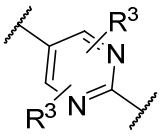
or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, -OH, -OR^4, or -$N(R^5)_2$;

each R^4 is independently substituted or unsubstituted C_1-C_6alkyl, or C_1-C_6fluoroalkyl;

each R^5 is independently hydrogen, substituted or unsubstituted C_1-C_6alkyl, C_1-C_6fluoroalkyl.

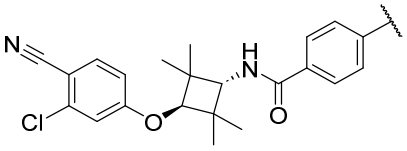
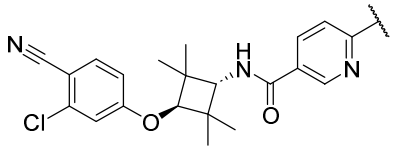
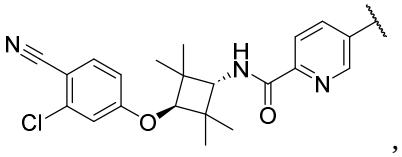
12. The compound of claim 10 or claim 11, or a pharmaceutically acceptable salt or solvate thereof,

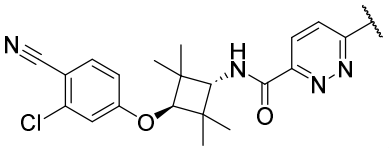
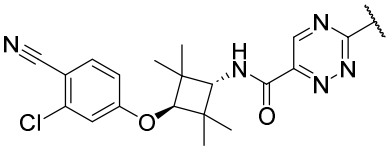
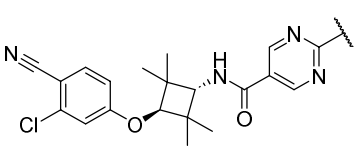
wherein  is , , , , ,

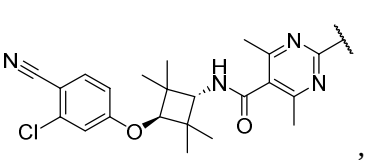
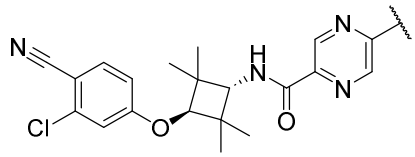
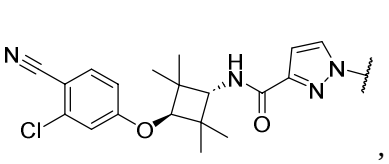
or , and

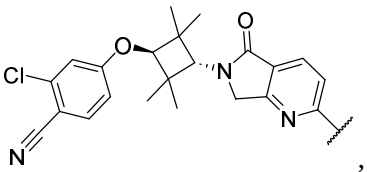
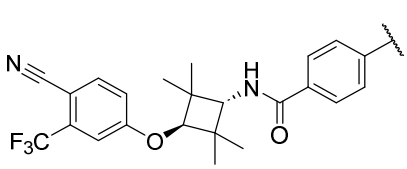
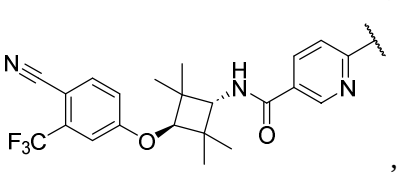
each R^3 is independently hydrogen, F, Cl, Br, I, -CH_3, -CH_2CH_3, -CH_2F, -CHF_2, -CF_3, -CH_2CH_2F, -CH_2CHF_2, - CH_2CF_3, -OH, -OCF_3, -OCH_3, -OCH_2CH_3, -CN, -C(=O)NH_2, or -C(=O)$NH(CH_3)$.

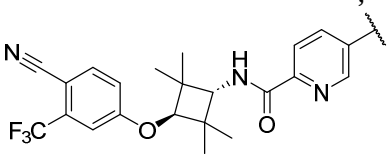
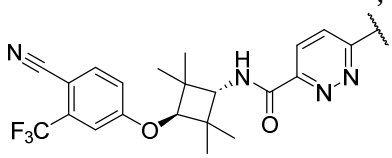
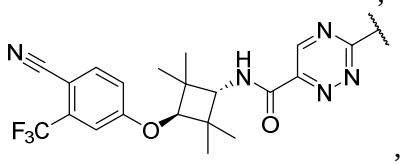
13. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein B-AR has one of the following structures:

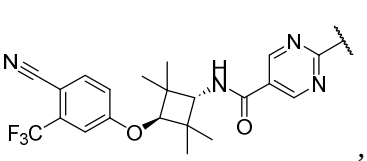
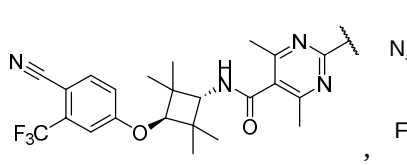
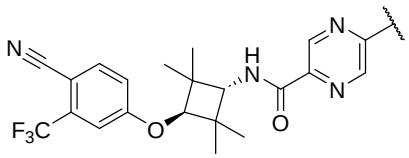
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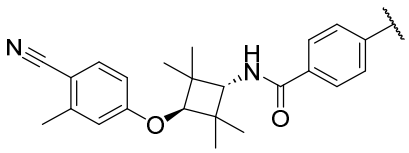
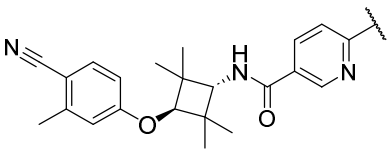
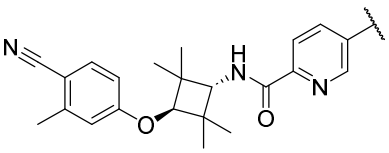
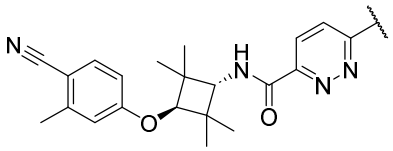
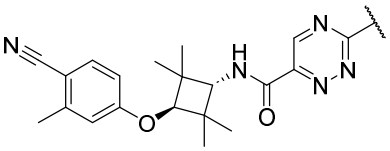
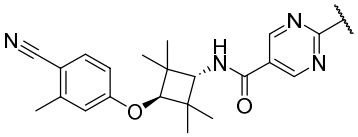
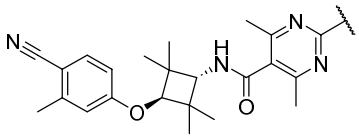
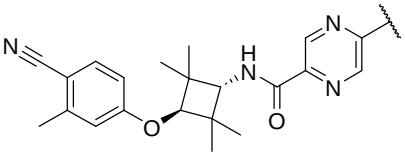
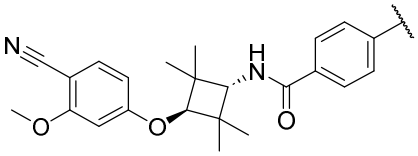
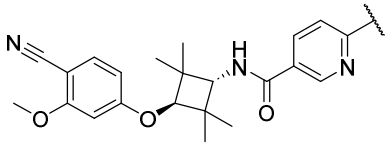
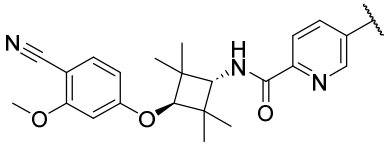
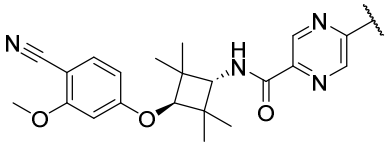
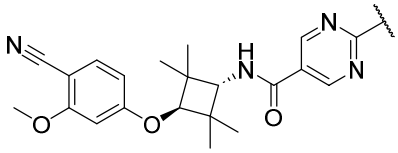
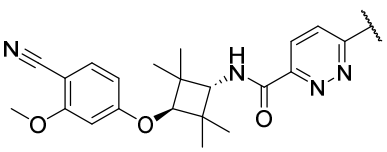
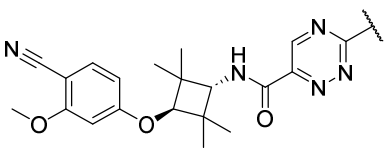
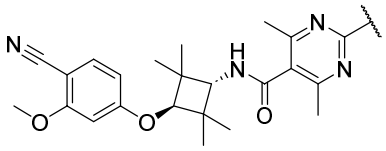
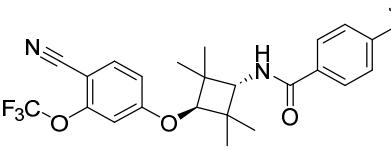
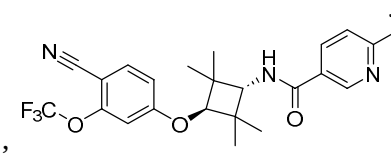
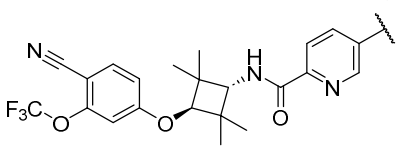
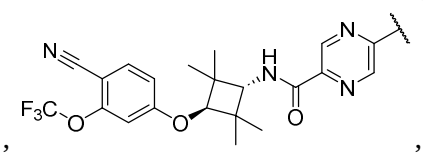
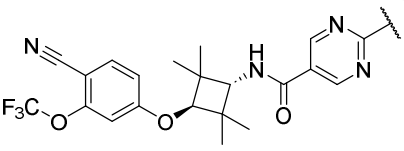
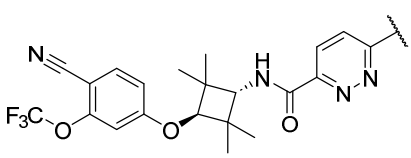
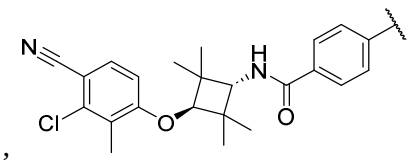
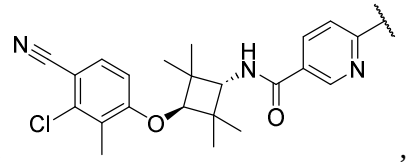
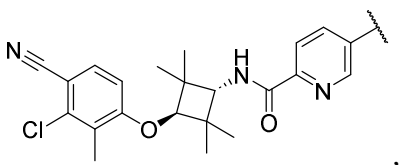
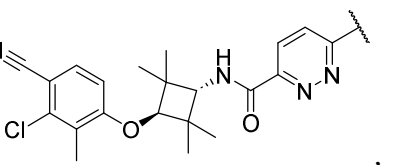
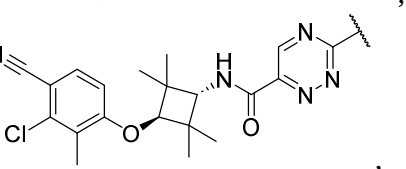
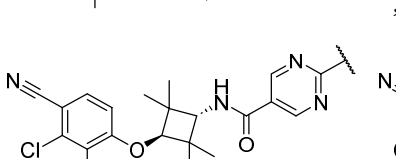
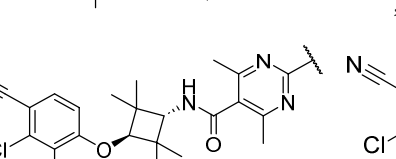
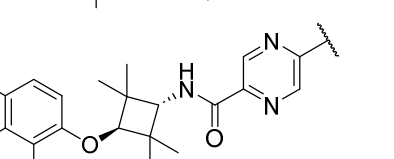
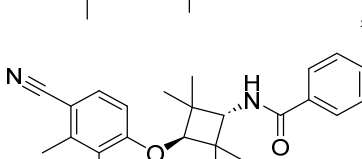
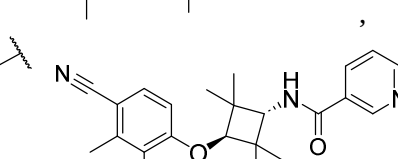
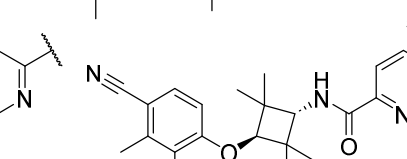
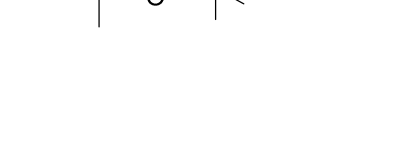
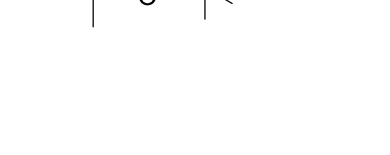
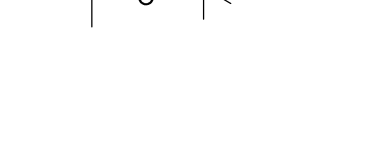
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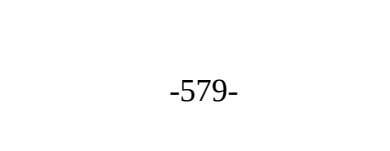
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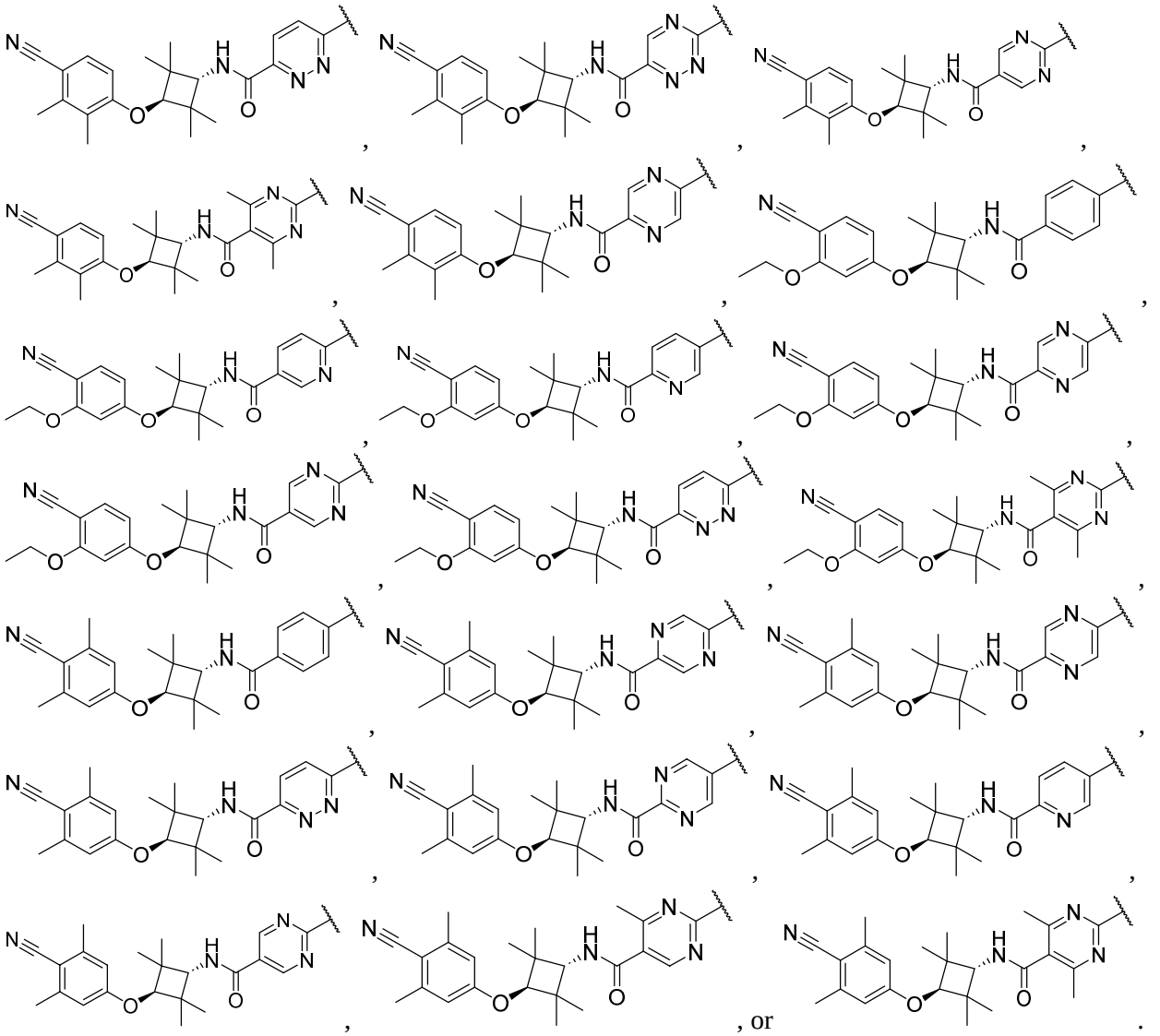
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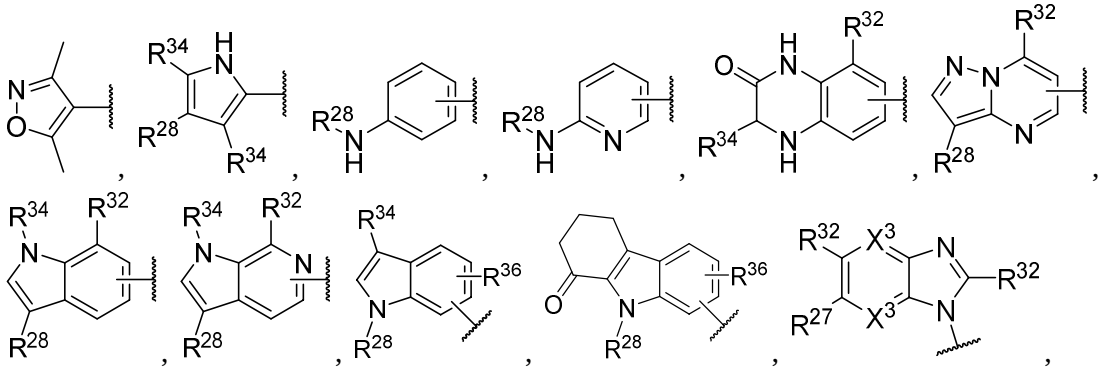
14. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt or solvate thereof, wherein SB-CBP/p300 comprises an acetyl-lysine mimetic moiety that binds in the acetyl-lysine (KAc) binding site of the bromodomain of CBP/p300, and further comprises:

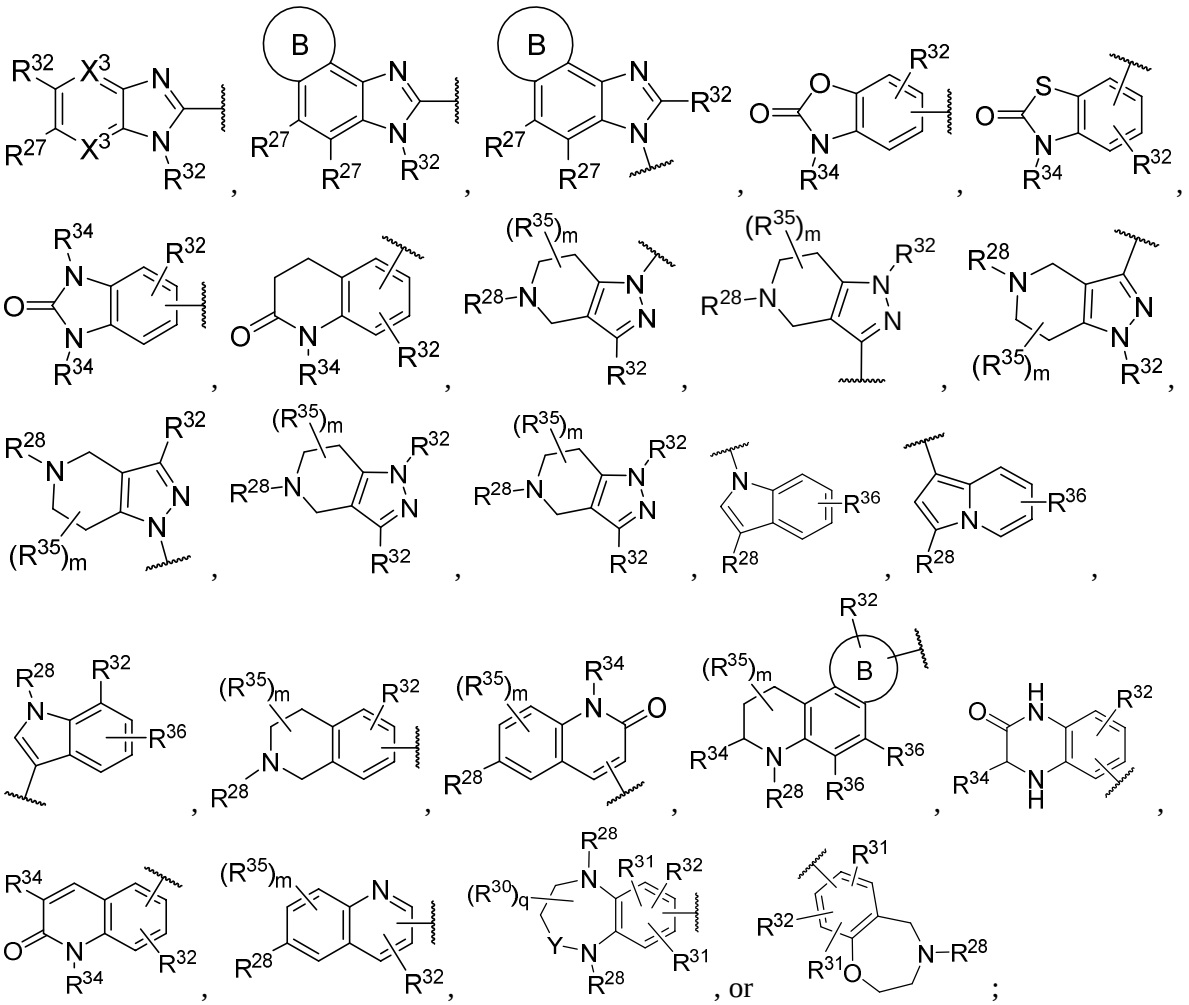
    1) a moiety that occupies the lipophilic shelf (LPF) region of the bromodomain of CBP/p300; or

    2) a moiety that occupies the BC Loop region of the bromodomain of CBP/p300; or

    3) both 1) and 2).

15. The compound of claim 14, or a pharmaceutically acceptable salt or solvate thereof, wherein the moiety comprising an acetyl-lysine mimetic comprises a moiety selected from:





each R^{32} is independently an optional moiety that occupies the lipophilic shelf (LPF) region of the bromodomain of CBP/p300;

or each R^{32} is independently an optional moiety that occupies the BC Loop region of the bromodomain of CBP/p300;

—≈ is the point of attachment to L that covalently connects SB-CBP/p300 to B-AR;

or R^{32} comprises —≈ and L that covalently connects SB-CBP/p300 to B-AR is attached to R^{32};

each R^{28} is independently hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, -C(=O)R^b, or -C(=O)N(R^b)$_2$;

each R^{34} is independently hydrogen or substituted or unsubstituted C_1-C_6alkyl;

each R^{35} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, or substituted or unsubstituted 3- to 8-membered heterocycloalkyl, -CN, -OH, -OR^a, or -N(R^b)$_2$;

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

each R^{27} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted 3- to 8-membered heterocycloalkyl,

substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, -NO_2, -OH, -OR^a, $OC(=O)R^a$, -$OC(=O)N(R^b)_2$, -$OC(=O)OR^a$, -$OC(=O)N(R^b)_2$, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2N(R^b)_2$, -$N(R^b)_2$, -$NR^bC(=O)N(R^b)_2$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^a$, -$NR^bS(=O)_2R^a$, -$C(=O)R^b$, -$C(=O)OR^b$, or -$C(=O)N(R^b)_2$;

Y is -$C(R^{30})_2$- or C(=O);

each X^3 is independently CR^{27} or N;

each R^{30} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, -NO_2, -OH, -OR^a, $OC(=O)R^a$, -$OC(=O)N(R^b)_2$, -$OC(=O)OR^a$, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2N(R^b)_2$, -$N(R^b)_2$, -$NR^bC(=O)N(R^b)_2$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^a$, -$NR^bS(=O)_2R^a$, -$C(=O)R^b$, -$C(=O)OR^b$, or -$C(=O)N(R^b)_2$;

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

each R^{31} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, -CN, -NO_2, -OH, -OR^a, $OC(=O)R^a$, -$OC(=O)N(R^b)_2$, -$OC(=O)OR^a$, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2N(R^b)_2$, -$N(R^b)_2$, -$NR^bC(=O)NR^b$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^a$, -$NR^bS(=O)_2R^a$, -$C(=O)R^b$, -$C(=O)OR^b$, or -$C(=O)N(R^b)_2$;

each R^{36} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, -OH, -OR^a, or -$N(R^b)_2$;

Ring B is a fused substituted or unsubstituted 5 or 6 membered heterocycloalkyl;

each R^a is independently substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

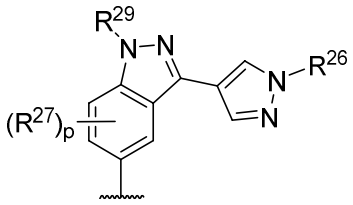
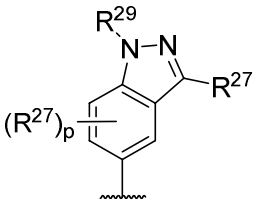
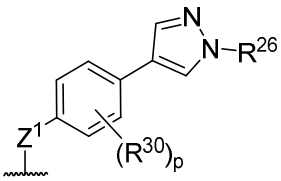
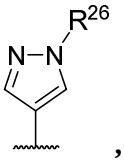
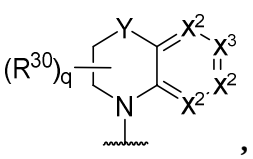
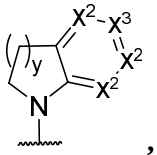
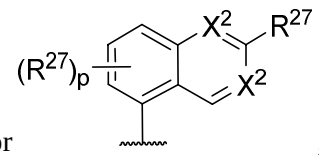
each R^b is independently hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

or two R^b on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle.

16. The compound of claim 15, or a pharmaceutically acceptable salt or solvate thereof, wherein the moiety that occupies the lipophilic shelf (LPF) region of the bromodomain of CBP/p300 is R^{32}, wherein:

R^{32} is hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_2-C_6alkenyl, substituted or unsubstituted C_2-C_6alkynyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_{12}cycloalkyl, substituted or unsubstituted 3- to 12-membered heterocycloalkyl,

substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

or R^{32} is , , , , , , or ;

y is 1 or 2;

Z^1 is $-NR^c-$, -O-, or -S-;

R^c is hydrogen or substituted or unsubstituted C_1-C_6alkyl;

R^{26} is hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, or substituted or unsubstituted 3- to 8-membered heterocycloalkyl;

each X^2 is independently $-CR^{30}-$ or -N-;

each X^3 is independently $-CR^{27}-$ or -N-;

each R^{27} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, $-NO_2$, -OH, $-OR^a$, $OC(=O)R^a$, $-OC(=O)N(R^b)_2$, $-OC(=O)OR^a$, $-OC(=O)N(R^b)_2$, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2N(R^b)_2$, $-N(R^b)_2$, $-NR^bC(=O)N(R^b)_2$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^a$, $-NR^bS(=O)_2R^a$, $-C(=O)R^b$, $-C(=O)OR^b$, or $-C(=O)N(R^b)_2$;

p is 0, 1, 2, or 3;

R^{28} is hydrogen or substituted or unsubstituted C_1-C_6alkyl;

R^{29} is hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, or substituted or unsubstituted 3- to 8-membered heterocycloalkyl;

Y is $-C(R^{30})_2-$ or $N(R^{28})-$;

each R^{30} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, $-NO_2$, -OH, $-OR^a$, $OC(=O)R^a$, $-OC(=O)N(R^b)_2$, $-OC(=O)OR^a$, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2N(R^b)_2$, $-N(R^b)_2$, $-NR^bC(=O)N(R^b)_2$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^a$, $-NR^bS(=O)_2R^a$, $-C(=O)R^b$, $-C(=O)OR^b$, or $-C(=O)N(R^b)_2$;

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

or R^{32} is -L-C;

L is substituted or unsubstituted C_1-C_6alkyl or substituted or unsubstituted C_1-C_6heteroalkyl;

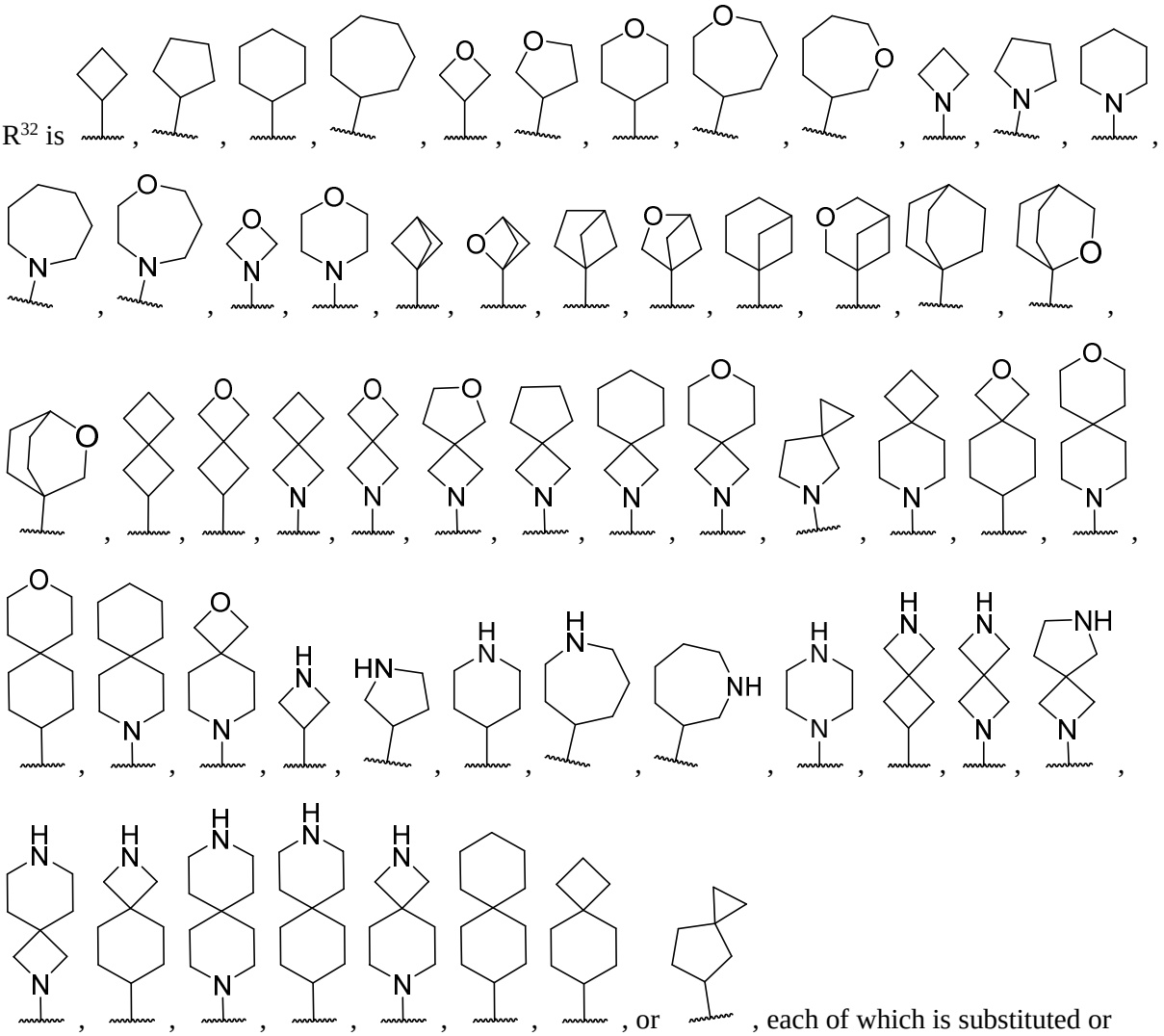
C is substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

each R^a is independently substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

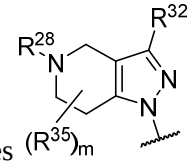
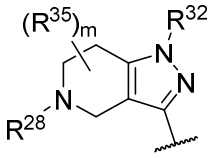
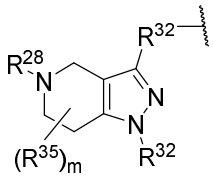
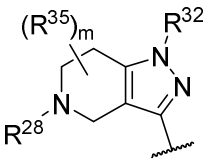
each R^b is independently hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

or two R^b on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle.

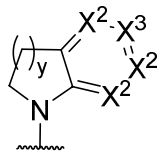
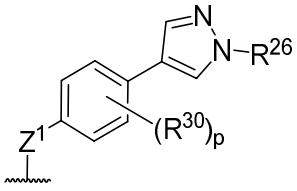
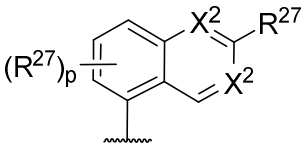
17. The compound of claim 15 or claim 16, or a pharmaceutically acceptable salt or solvate thereof, wherein the moiety that occupies the BC Loop region of the bromodomain of CBP/p300 is R^{32}, wherein:

R^{32} is , each of which is substituted or

unsubstituted.

18. The compound of claim 14, or a pharmaceutically acceptable salt or solvate thereof, wherein the moiety comprising an acetyl-lysine mimetic comprises  ,   or  .

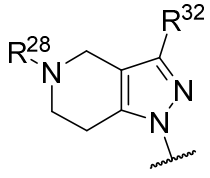
19. The compound of claim 18, or a pharmaceutically acceptable salt or solvate thereof, wherein:

R^{32} is  ,  , or  ;

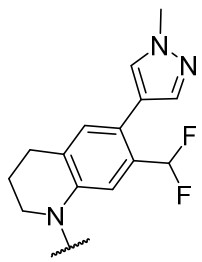
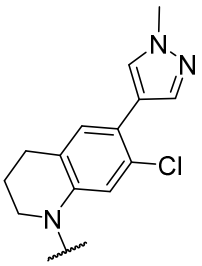
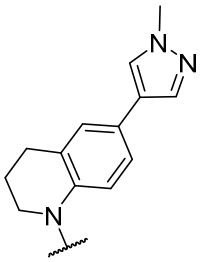
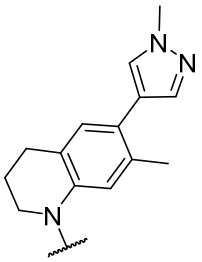
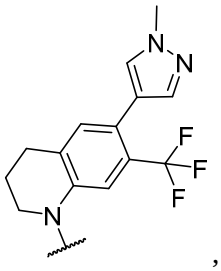
R^{27} is hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, -OH, or -OR^a; and

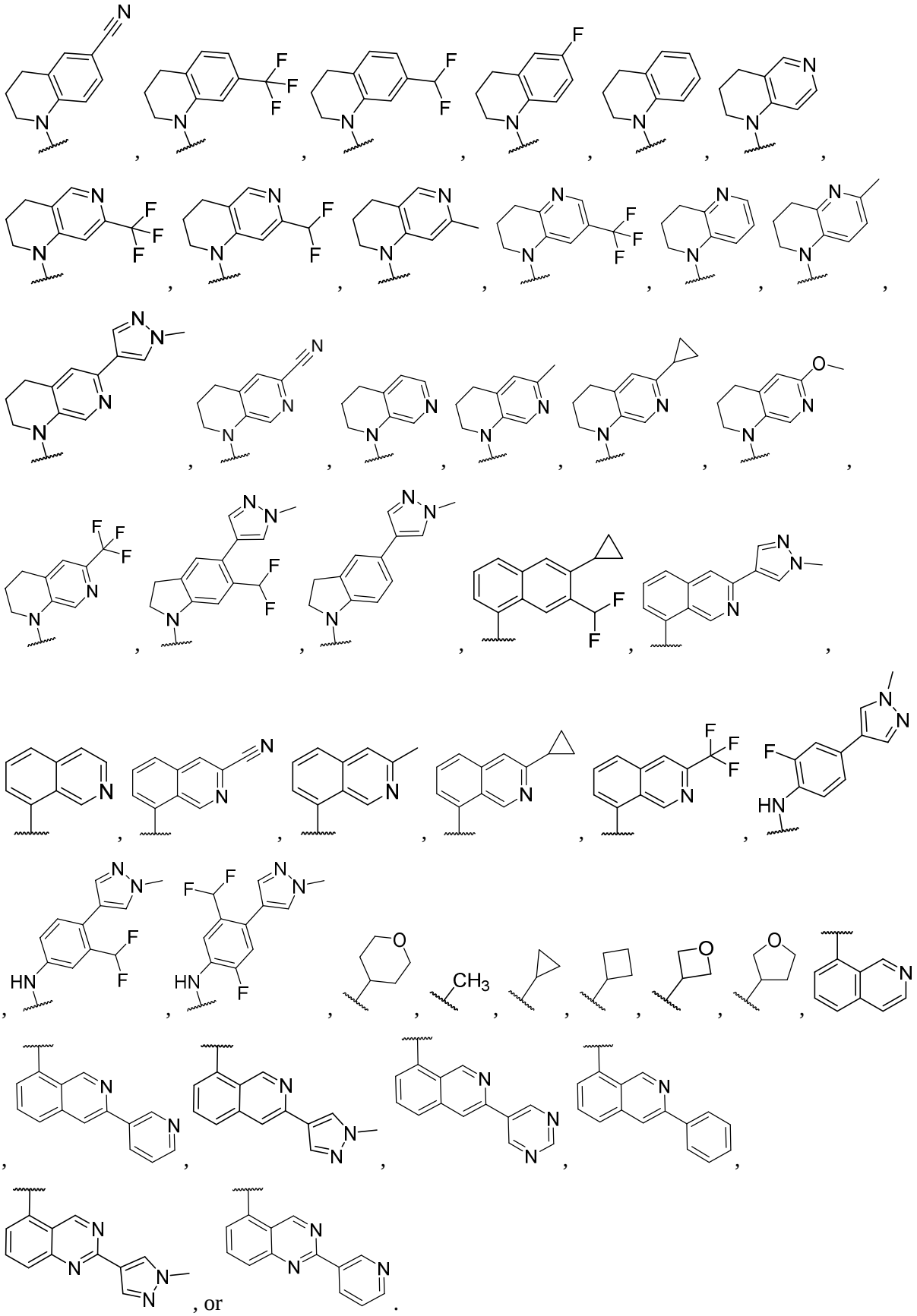
each R^{27} is independently hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, -OH, or -OR^a; and

each R^a is independently substituted or unsubstituted C_1-C_6alkyl.

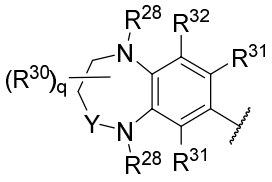
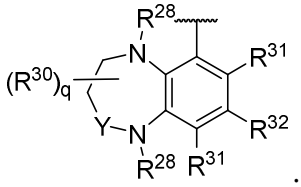
20. The compound of claim 18, or a pharmaceutically acceptable salt or solvate thereof, wherein the moiety comprising an acetyl-lysine mimetic comprises  .

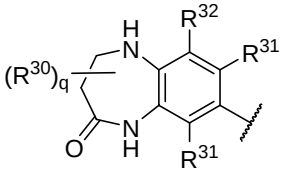
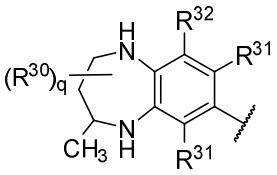
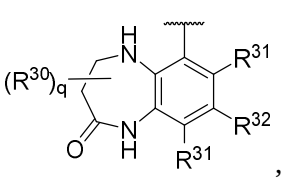
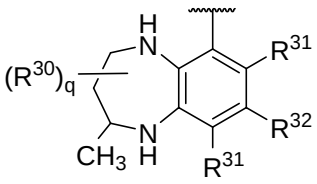
21. The compound of claim 20, or a pharmaceutically acceptable salt or solvate thereof, wherein:

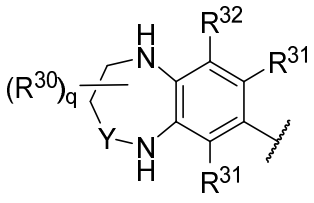
R^{32} is  ,  ,  ,  ,  ,



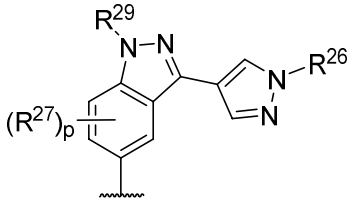
22. The compound of claim 14, or a pharmaceutically acceptable salt or solvate thereof, wherein the

moiety comprising an acetyl-lysine mimetic comprises  or .

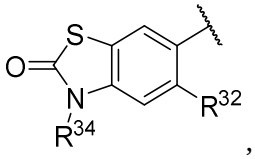
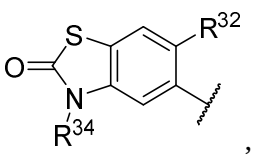
23. The compound of claim 22, or a pharmaceutically acceptable salt or solvate thereof, wherein the moiety comprising an acetyl-lysine mimetic comprises , , , or .

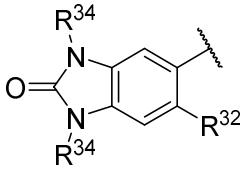
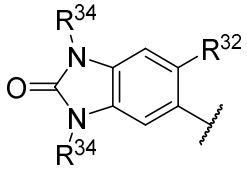
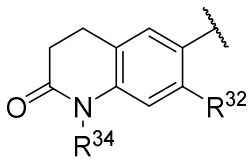
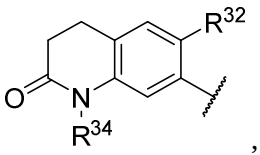
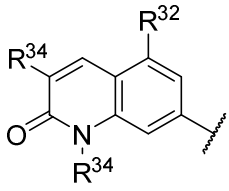
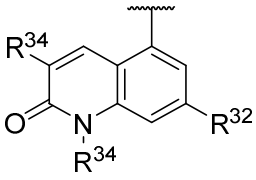
24. The compound of claim 22, or a pharmaceutically acceptable salt or solvate thereof, wherein the moiety comprising an acetyl-lysine mimetic comprises ;

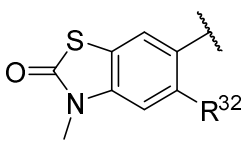
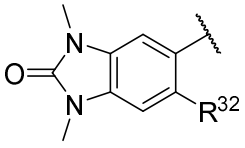
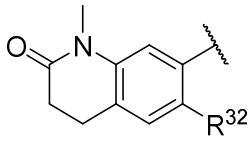
wherein:

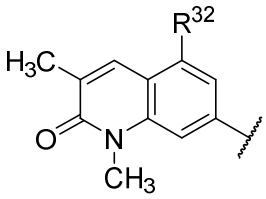
R^{32} is ; and

each R^{27} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, -NO_2, -OH, -OR^a, $OC(=O)R^a$, -$OC(=O)N(R^b)_2$, -$OC(=O)OR^a$, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2N(R^b)_2$, -$N(R^b)_2$, -$NR^bC(=O)N(R^b)_2$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^a$, -$NR^bS(=O)_2R^a$, -$C(=O)R^b$, -$C(=O)OR^b$, or -$C(=O)N(R^b)_2$.

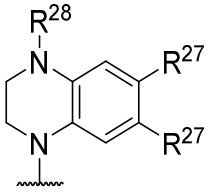
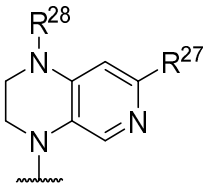
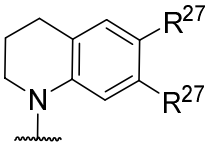
25. The compound of claim 14, or a pharmaceutically acceptable salt or solvate thereof, wherein the moiety comprising an acetyl-lysine mimetic comprises , ,

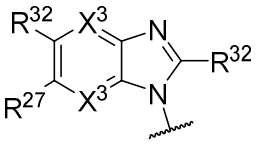
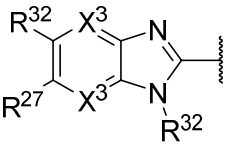
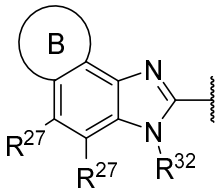
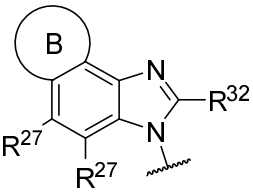







26. The compound of claim 25, or a pharmaceutically acceptable salt or solvate thereof, wherein the moiety comprising an acetyl-lysine mimetic comprises , , or .

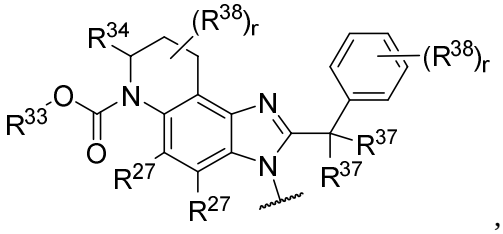
27. The compound of claim 25, or a pharmaceutically acceptable salt or solvate thereof, wherein the moiety comprising an acetyl-lysine mimetic comprises: .

28. The compound of claim 27, or a pharmaceutically acceptable salt or solvate thereof, wherein:

R^{32} is , , or .

29. The compound of claim 14, or a pharmaceutically acceptable salt or solvate thereof, wherein the moiety comprising an acetyl-lysine mimetic comprises , , , or .

30. The compound of claim 29, or a pharmaceutically acceptable salt or solvate thereof, wherein the

moiety comprising an acetyl-lysine mimetic comprises ,

wherein:

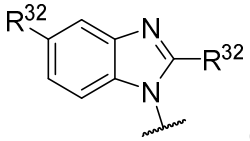
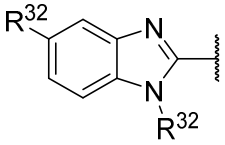
each R^{27} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, -OH, -OR^a, or -$N(R^b)_2$;

R^{33} is hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, or substituted or unsubstituted C_1-C_6heteroalkyl;

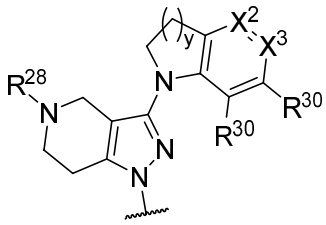
R^{34} is hydrogen or substituted or unsubstituted C_1-C_6alkyl;

each R^{38} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted 3- to 8-membered heterocycloalkyl, -CN, -NO_2, -OH, -OR^a, -$OC(=O)R^a$, -$OC(=O)N(R^b)_2$, -$OC(=O)OR^a$, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2N(R^b)_2$, -$N(R^b)_2$, -$NR^bC(=O)N(R^b)_2$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^a$, -$NR^bS(=O)_2R^a$, -$C(=O)R^b$, -$C(=O)OR^b$, or -$C(=O)N(R^b)_2$; and

r is 0, 1, 2, 3, or 4.

31. The compound of claim 29, or a pharmaceutically acceptable salt or solvate thereof, wherein the moiety comprising an acetyl-lysine mimetic comprises  or .

32. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein SB-CBP/p300 has the structure of Formula (IIIb):



Formula (IIIb)

wherein:

X^2 is -CR^{30}- or -N-;

X^3 is -CR^{27}- or -N-;

each R^{27} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted

or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, -NO_2, -OH, -OR^a, $OC(=O)R^a$, -$OC(=O)N(R^b)_2$, -$OC(=O)OR^a$, -$OC(=O)N(R^b)_2$, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2N(R^b)_2$, -$N(R^b)_2$, -$NR^bC(=O)N(R^b)_2$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^a$, -$NR^bS(=O)_2R^a$, -$C(=O)R^b$, -$C(=O)OR^b$, or -$C(=O)N(R^b)_2$;

R^{28} is hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, -$C(=O)R^b$, or -$C(=O)N(R^b)_2$;

each R^{30} is independently hydrogen, halogen, C_1-C_4alkyl, C_1-C_4fluoroalkyl, -CN, -OH, or -OR^a;

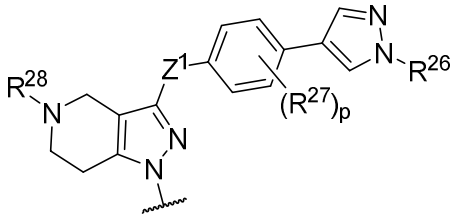
y is 1 or 2;

each R^a is independently substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

each R^b is independently hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

or two R^b on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle.

33. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein SB-CBP/p300 has the structure of Formula (IIIc):



Formula (IIIc)

wherein:

R^{26} is hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, or substituted or unsubstituted 3- to 8-membered heterocycloalkyl;

each R^{27} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, -NO_2, -OH, -OR^a, $OC(=O)R^a$, -$OC(=O)N(R^b)_2$, -$OC(=O)OR^a$, -$OC(=O)N(R^b)_2$, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2N(R^b)_2$, -$N(R^b)_2$, -$NR^bC(=O)N(R^b)_2$, -$NR^bC(=O)R^a$,

$-NR^bC(=O)OR^a$, $-NR^bS(=O)_2R^a$, $-C(=O)R^b$, $-C(=O)OR^b$, or $-C(=O)N(R^b)_2$;

p is 0, 1, 2, or 3;

R^{28} is hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, $-C(=O)R^a$, or $-C(=O)N(R^b)_2$;

Z^1 is $-NR^c$-, -O-, or -S-;

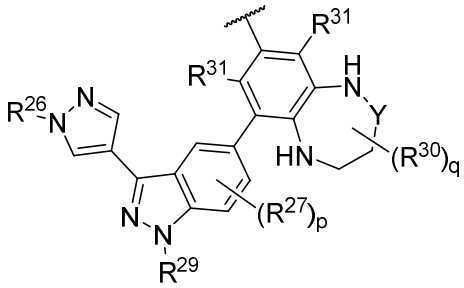
R^c is hydrogen or substituted or unsubstituted C_1-C_6alkyl;

each R^a is independently substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

each R^b is independently hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

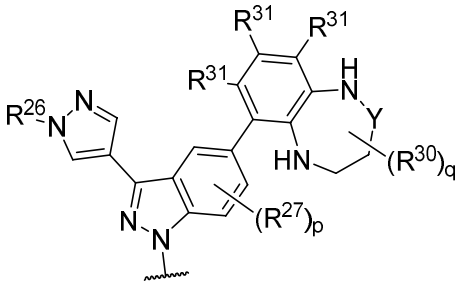
or two R^b on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle.

34. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein SB-CBP/p300 has the structure of Formula (IIId-1) or (IIId-2):



Formula (IIId-1)

or



Formula (IIId-2)

wherein:

R^{26} is hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, or substituted or unsubstituted 3- to 8-membered heterocycloalkyl;

each R^{27} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, $-NO_2$, -OH, $-OR^a$, $OC(=O)R^a$, $-OC(=O)N(R^b)_2$, $-OC(=O)OR^a$, $-OC(=O)N(R^b)_2$, $-SR^b$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-S(=O)_2OR^b$, $-S(=O)_2N(R^b)_2$, $-N(R^b)_2$, $-NR^bC(=O)N(R^b)_2$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^a$, $-NR^bS(=O)_2R^a$, $-C(=O)R^b$, $-C(=O)OR^b$, or $-C(=O)N(R^b)_2$;

p is 0, 1, 2, or 3;

R^{29} is hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, or substituted or unsubstituted 3- to 8-membered heterocycloalkyl;

each R^{30} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, -CN, -NO_2, -OH, -OR^a, $OC(=O)R^a$, -$OC(=O)N(R^b)_2$, -$OC(=O)OR^a$, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2N(R^b)_2$, -$N(R^b)_2$, -$NR^bC(=O)N(R^b)_2$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^a$, -$NR^bS(=O)_2R^a$, -$C(=O)R^b$, -$C(=O)OR^b$, or -$C(=O)N(R^b)_2$;

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

each R^{31} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, -CN, -NO_2, -OH, -OR^a, $OC(=O)R^a$, -$OC(=O)N(R^b)_2$, -$OC(=O)OR^a$, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2N(R^b)_2$, -$N(R^b)_2$, -$NR^bC(=O)NR^b$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^a$, -$NR^bS(=O)_2R^a$, -$C(=O)R^b$, -$C(=O)OR^b$, or -$C(=O)N(R^b)_2$;

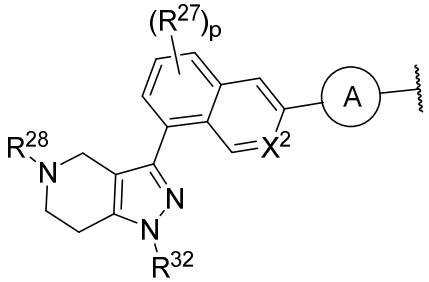
Y is -$C(R^{30})_2$- or C(=O);

each R^a is independently substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

each R^b is independently hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

or two R^b on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle.

35. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein SB-CBP/p300 has the structure of Formula (IIIe):



Formula (IIIe)

wherein:

X^2 is -CR^{27}- or -N-;

each R^{27} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, -NO_2, -OH, -OR^a, $OC(=O)R^a$, -$OC(=O)N(R^b)_2$, -$OC(=O)OR^a$, -$OC(=O)N(R^b)_2$, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2N(R^b)_2$, -$N(R^b)_2$, -$NR^bC(=O)N(R^b)_2$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^a$, -$NR^bS(=O)_2R^a$, -$C(=O)R^b$, -$C(=O)OR^b$, or -$C(=O)N(R^b)_2$;

p is 0, 1, 2, or 3;

R^{28} is hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, -$C(=O)R^b$, or -$C(=O)N(R^b)_2$;

R^{32} is hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, or substituted or unsubstituted 3- to 8-membered heterocycloalkyl;

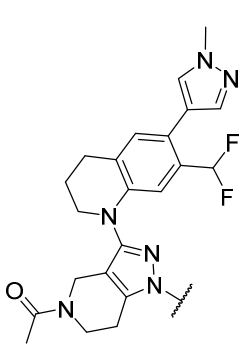
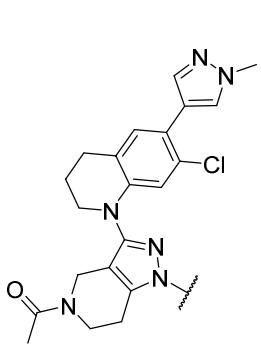
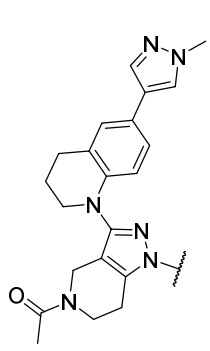
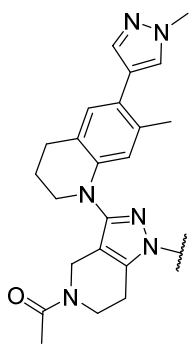
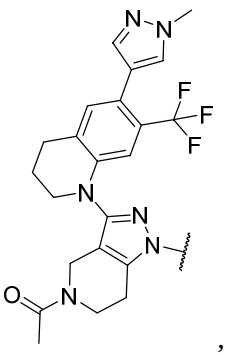
Ring A is absent or substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

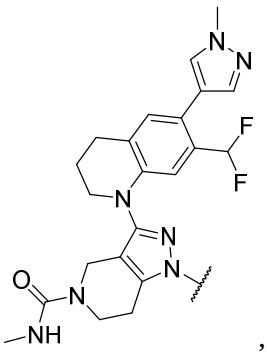
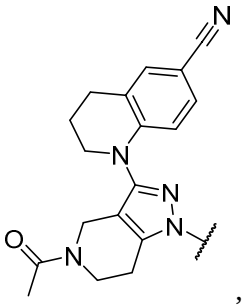
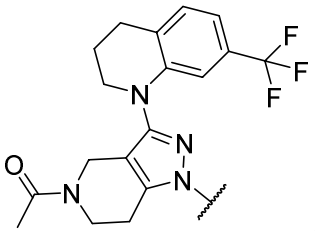
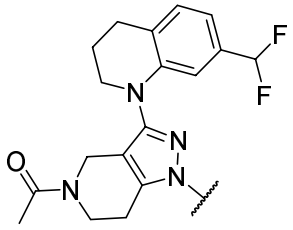
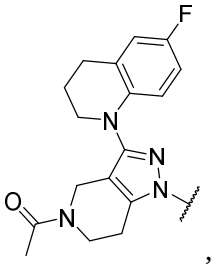
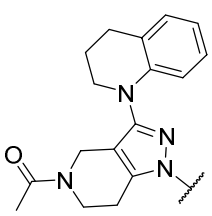
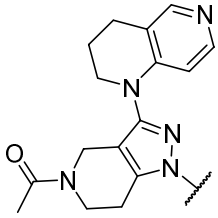
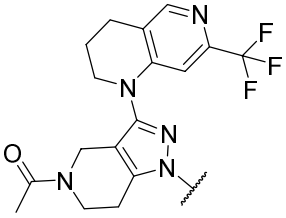
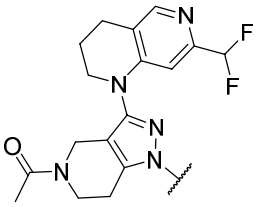
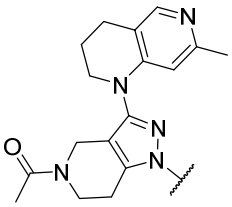
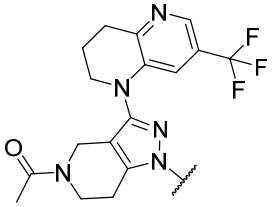
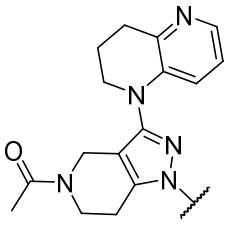
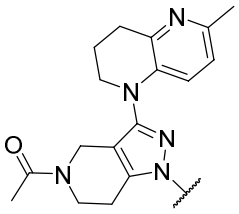
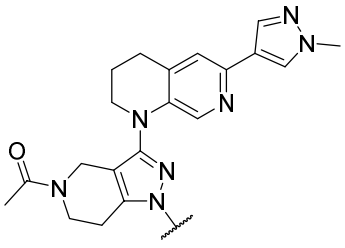
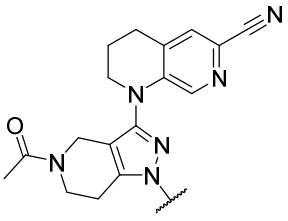
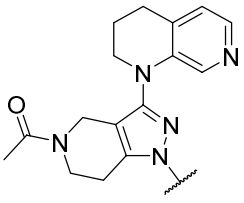
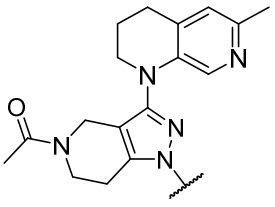
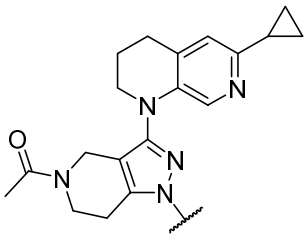
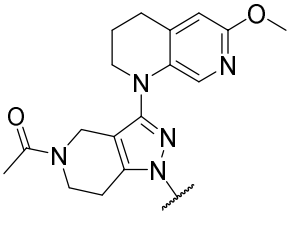
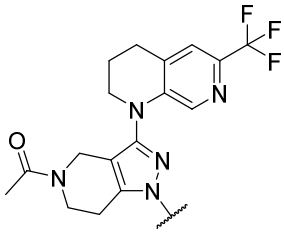
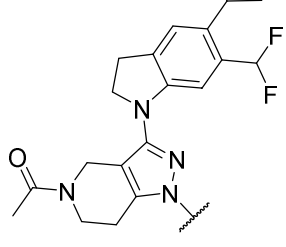
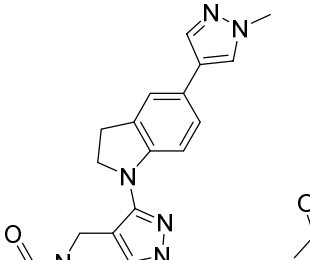
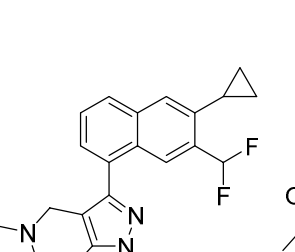
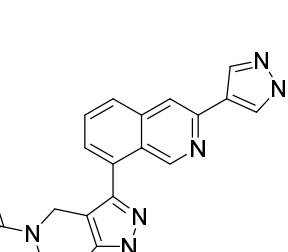
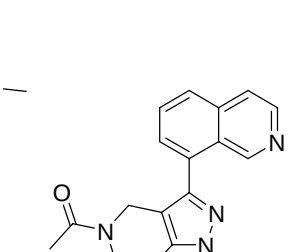
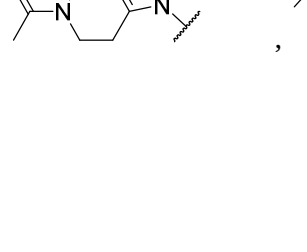
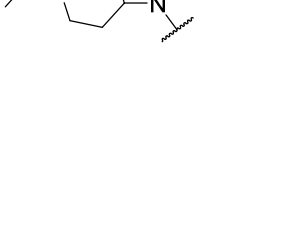
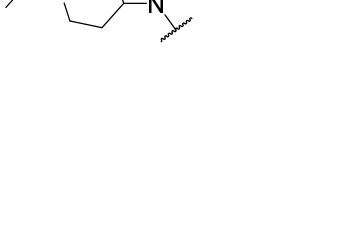
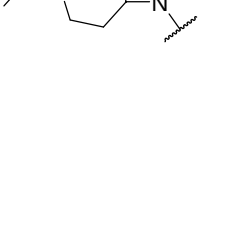
each R^a is independently substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

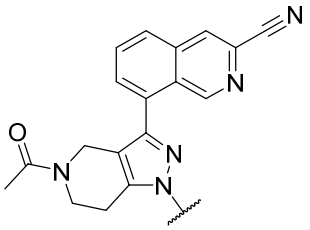
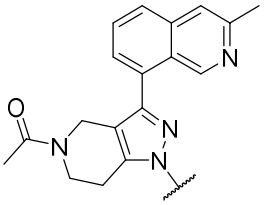
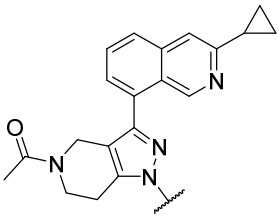
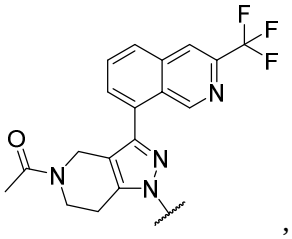
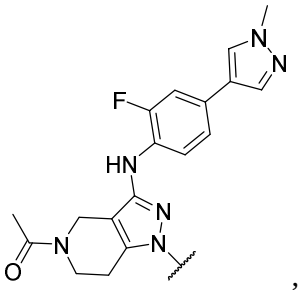
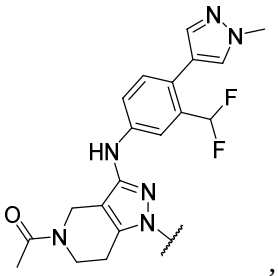
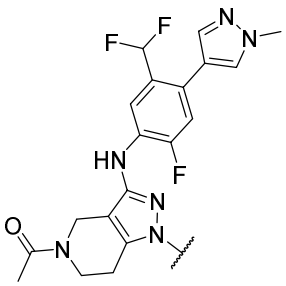
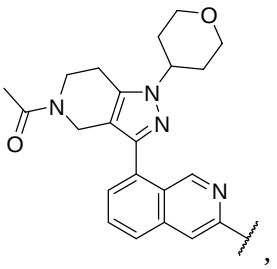
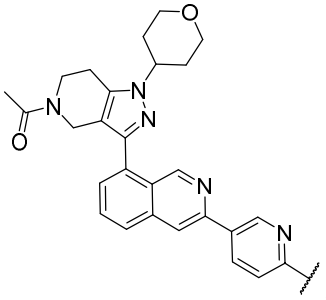
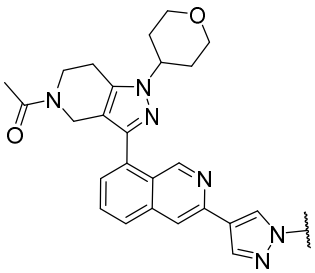
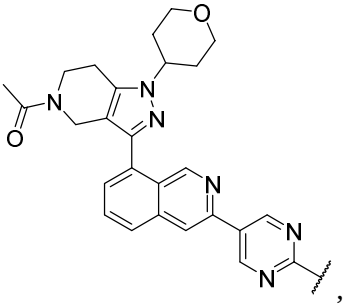
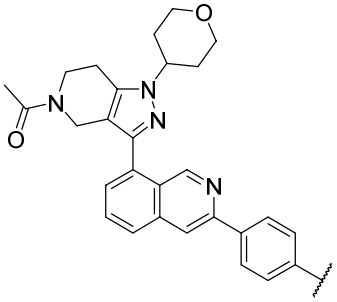
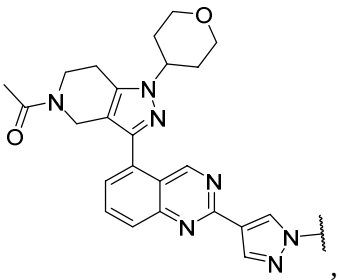
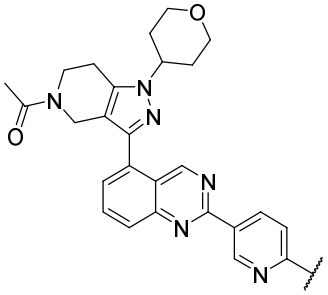
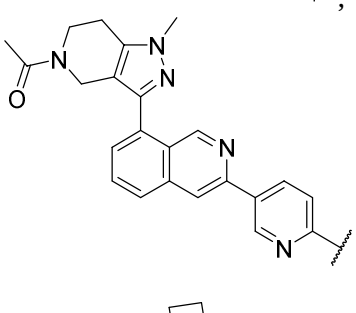
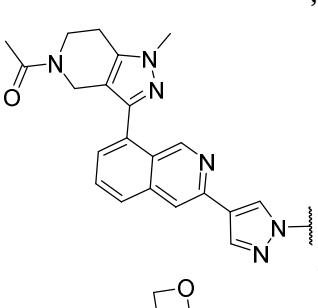
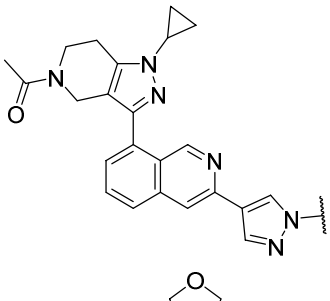
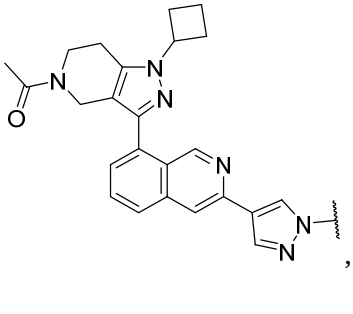
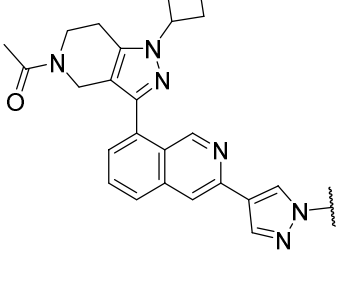
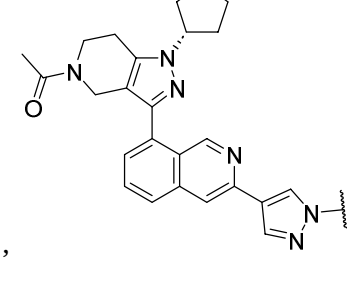
each R^b is independently hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

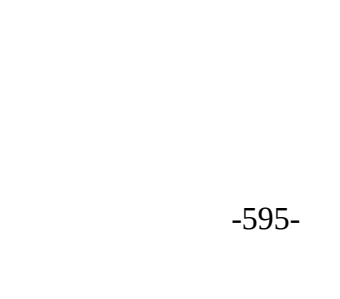
or two R^b on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle.

36. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein SB-CBP/p300 has one of the following structures:

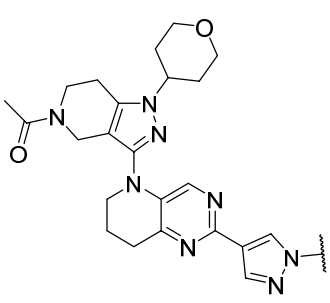
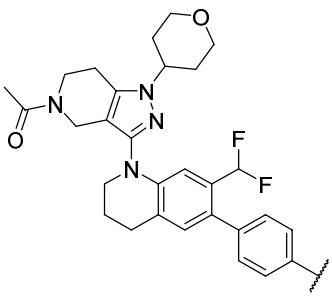
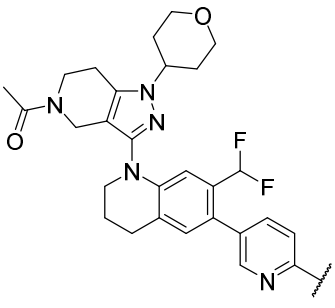
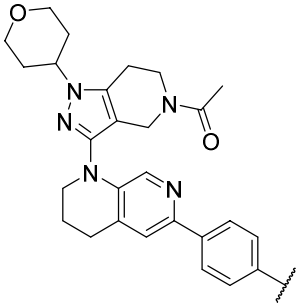
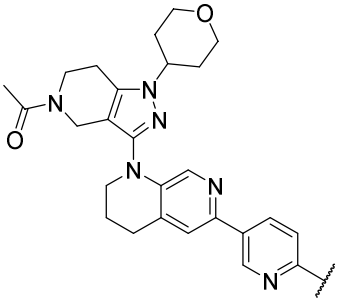
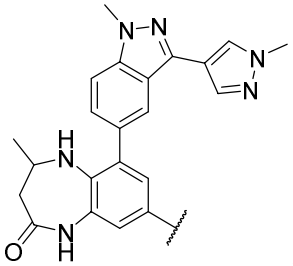
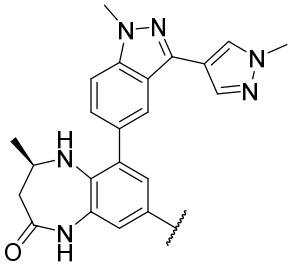
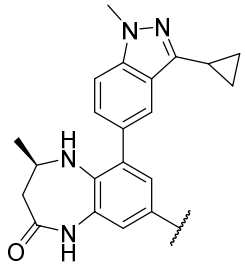
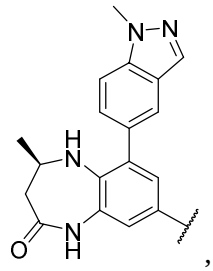
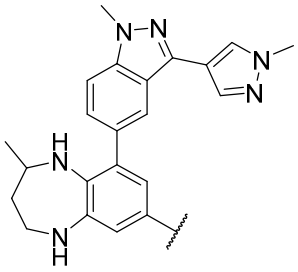
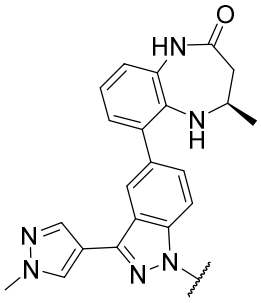
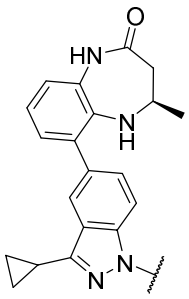
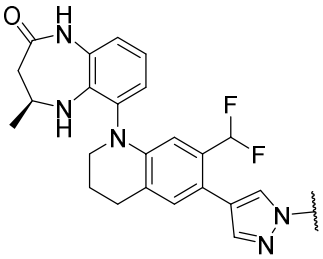
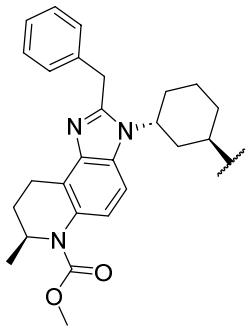
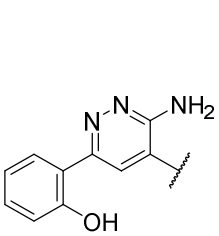
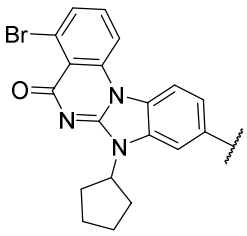
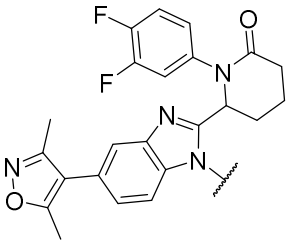
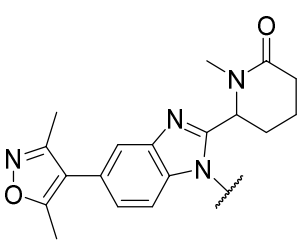
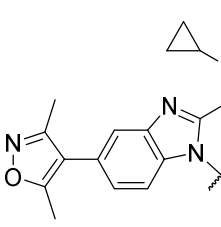
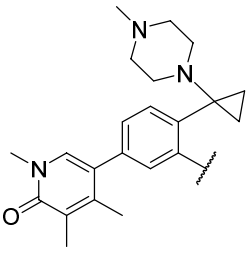
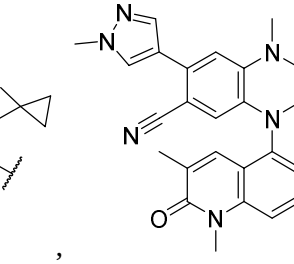
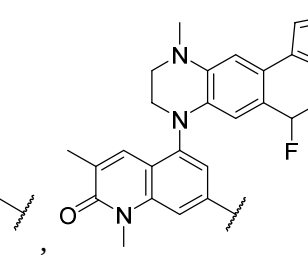

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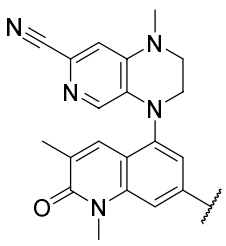
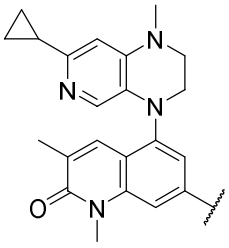
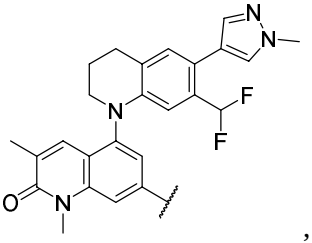
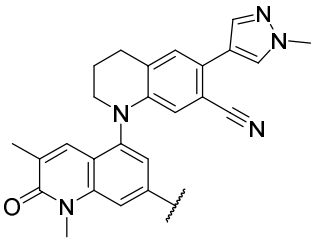
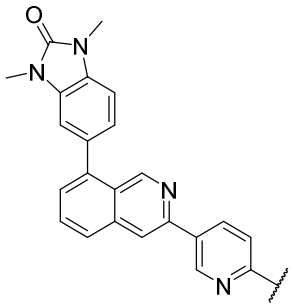
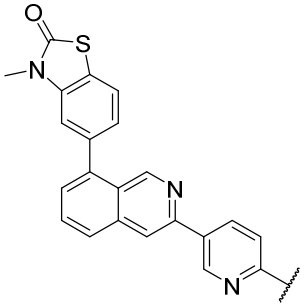
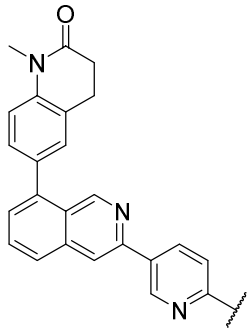
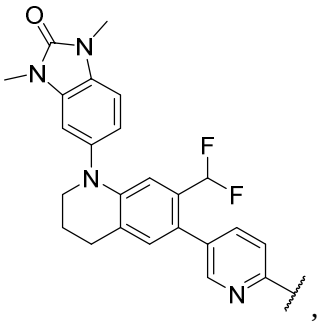
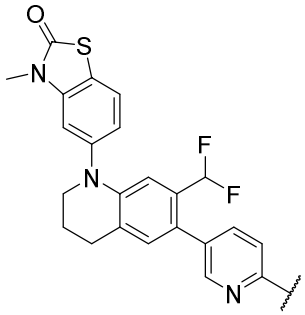
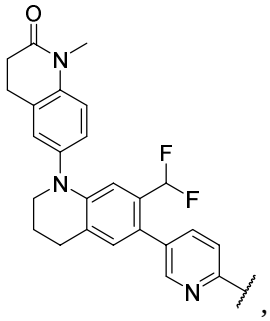
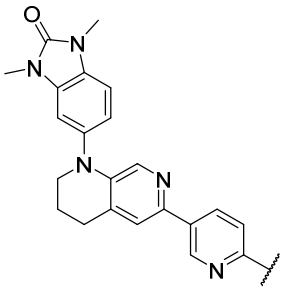
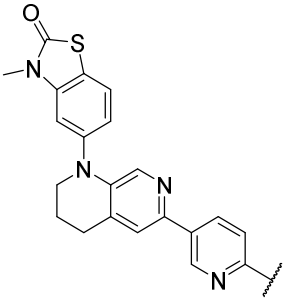
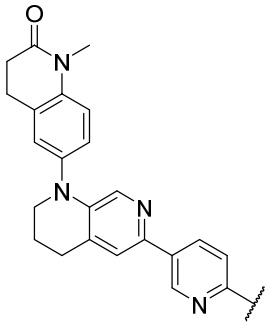

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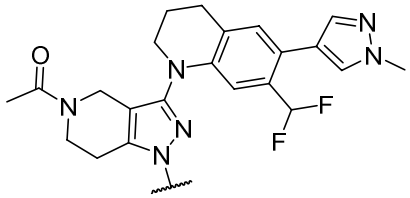
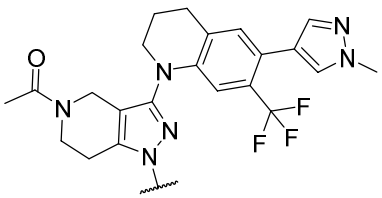
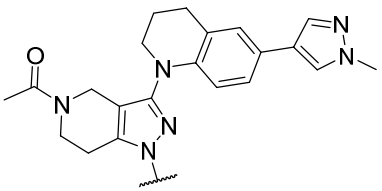
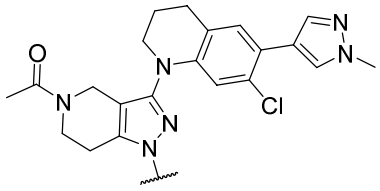
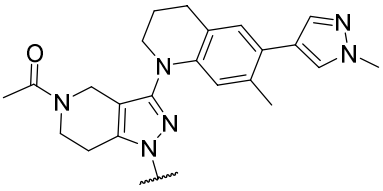
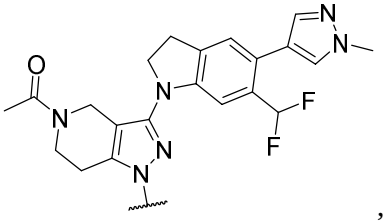
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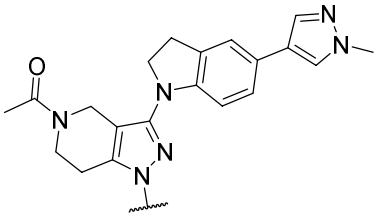
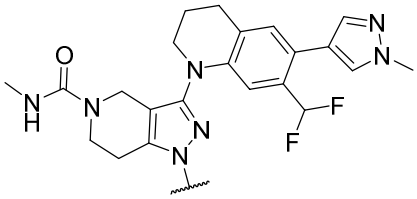
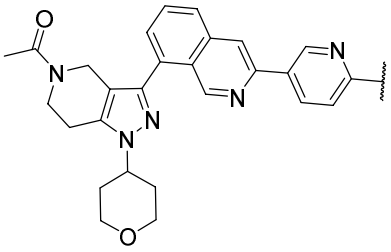
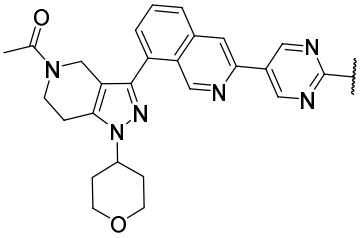
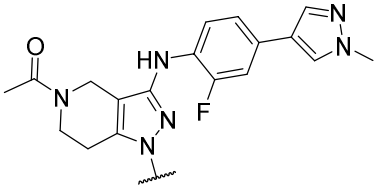
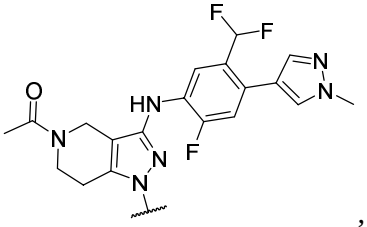
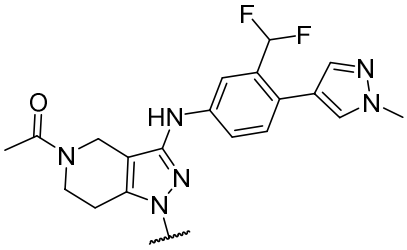
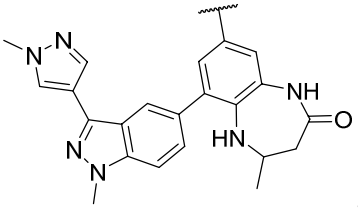
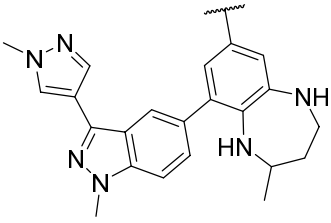
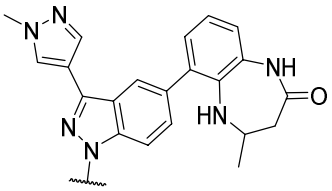
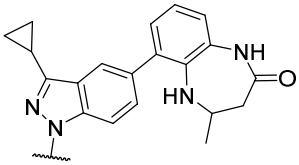
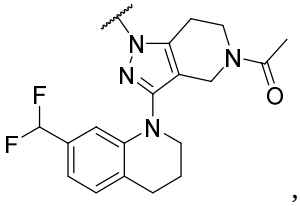
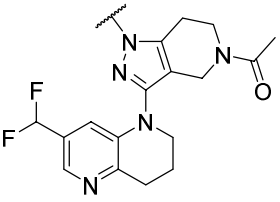
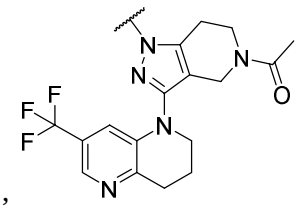
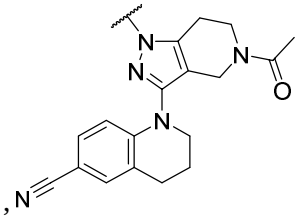
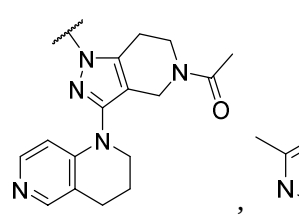
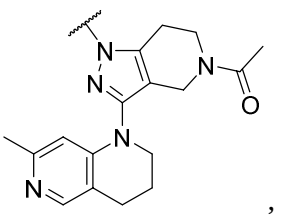
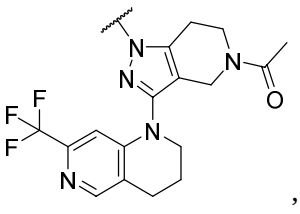
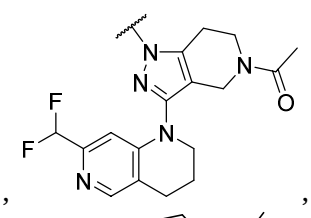
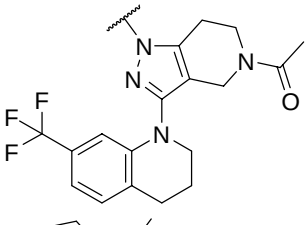
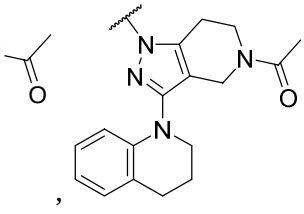
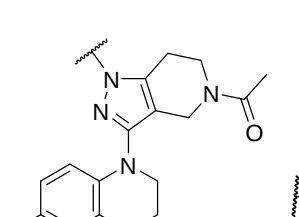
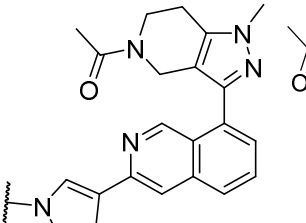
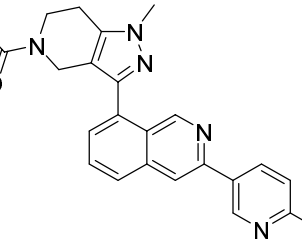
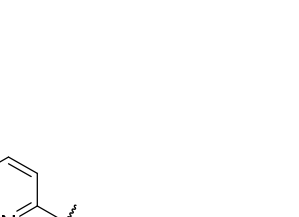
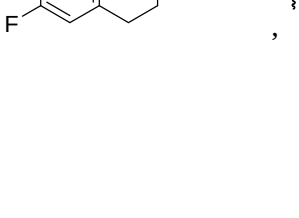
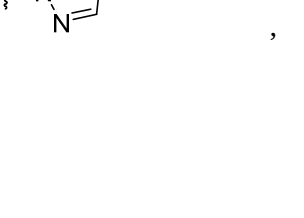
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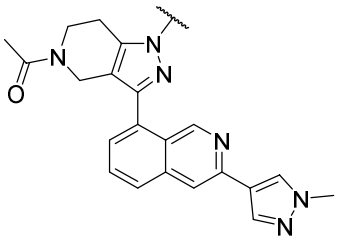
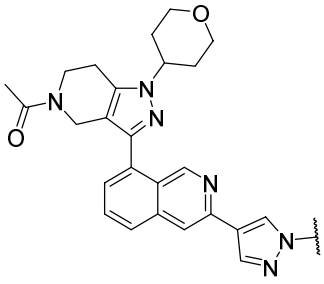
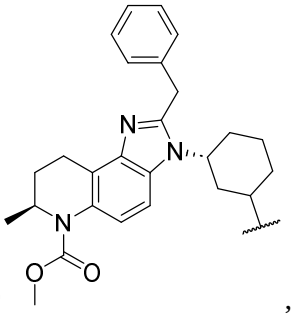

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37. The compound of claim 1, wherein SB-CBP/p300 has one of the following structures:

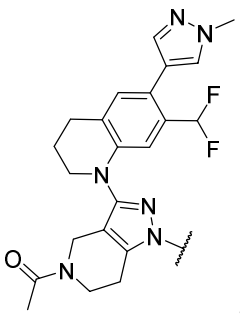
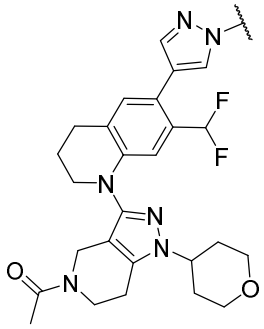
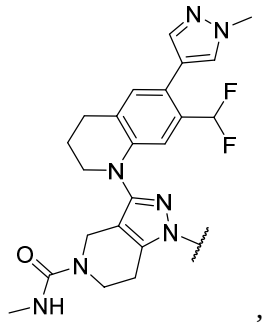
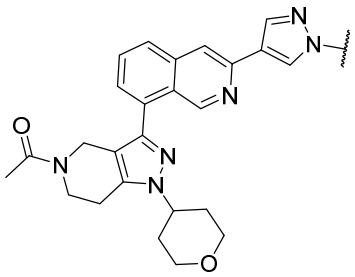
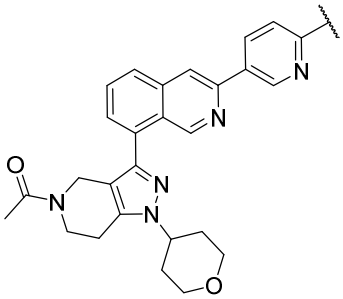

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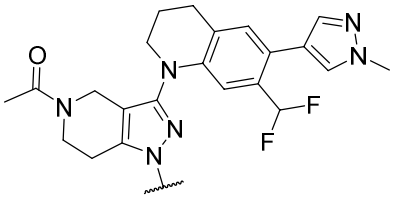
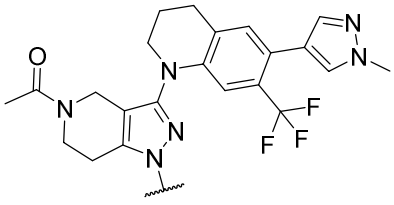
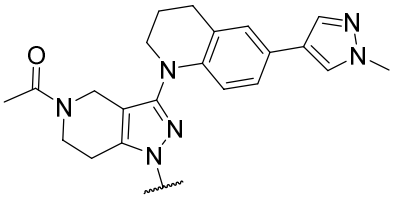
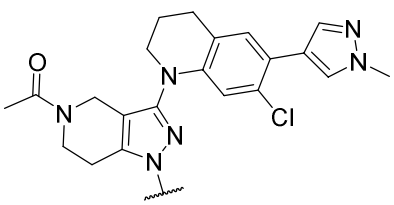
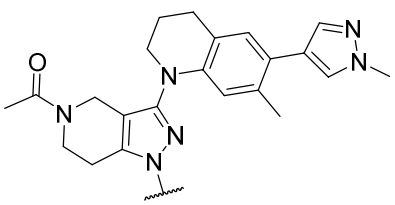
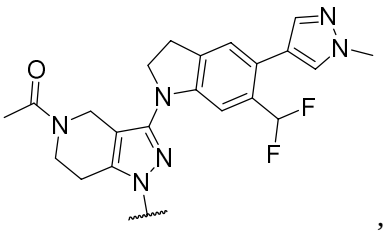
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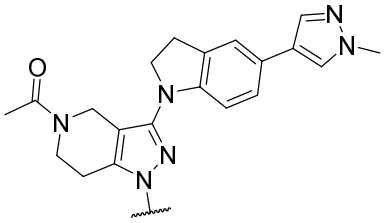
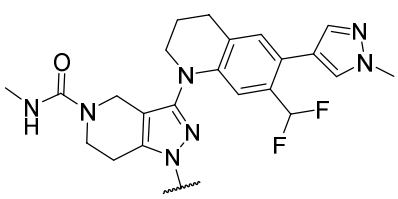
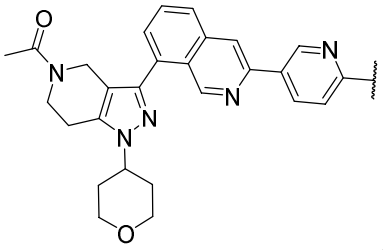
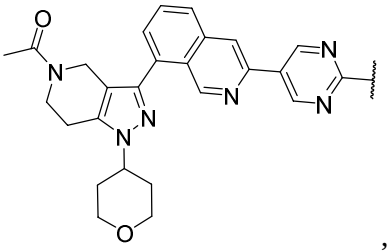
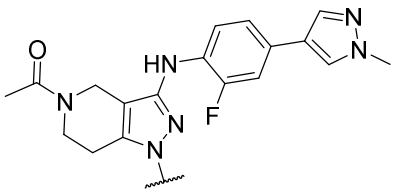
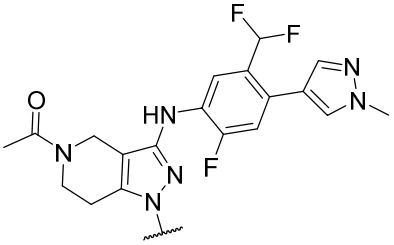
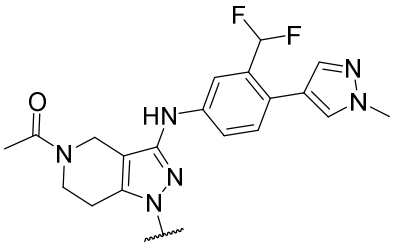
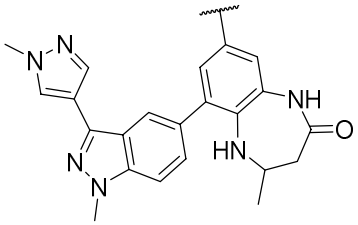
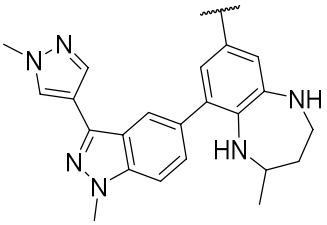
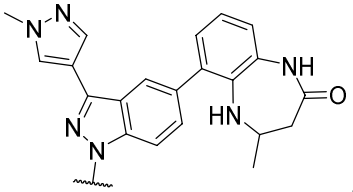
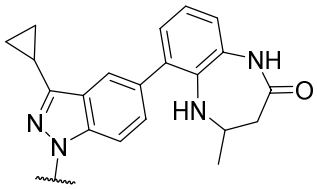
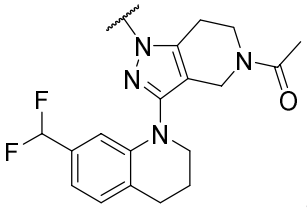
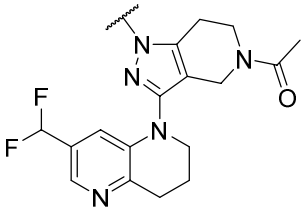
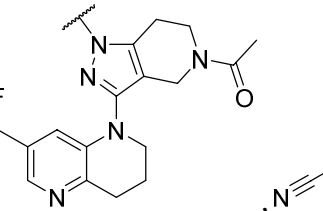

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or a pharmaceutically acceptable salt or solvate thereof.

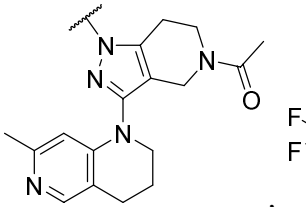
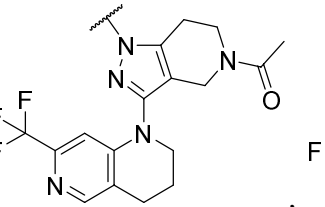
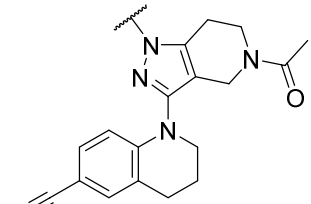
38. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein SB-CBP/p300 has one of the following structures:


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39. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein SB-CBP/p300 has one of the following structures:

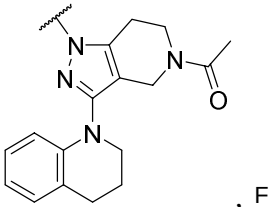
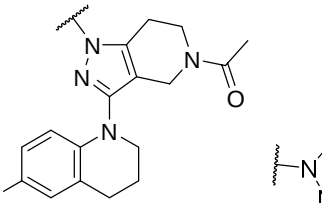
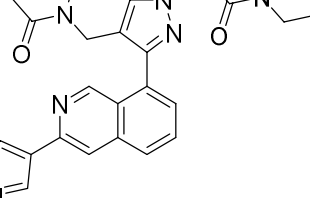
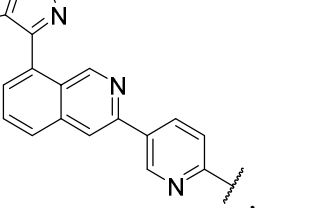

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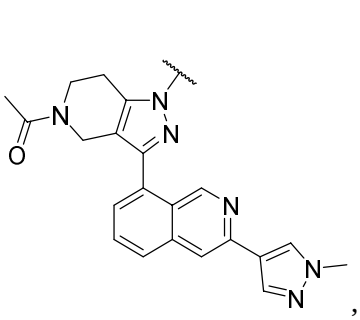
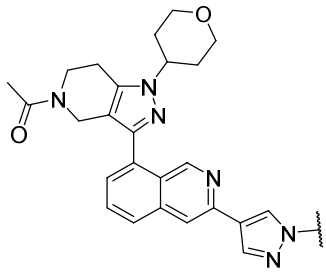
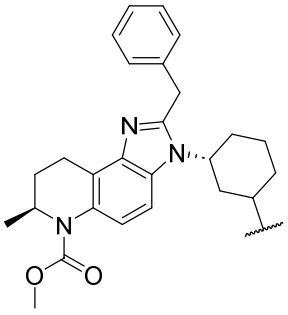
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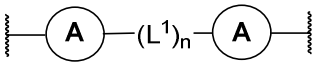
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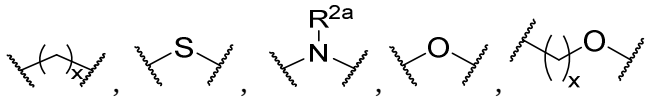
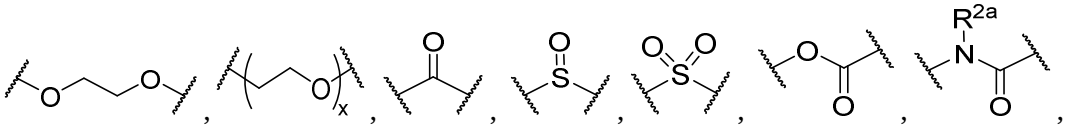
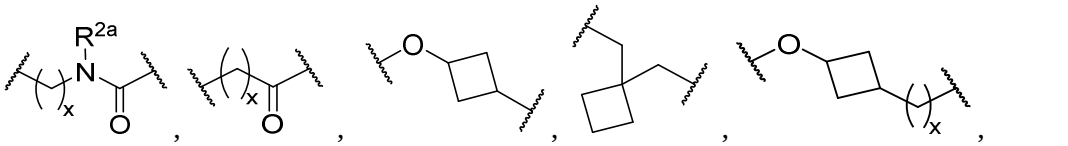
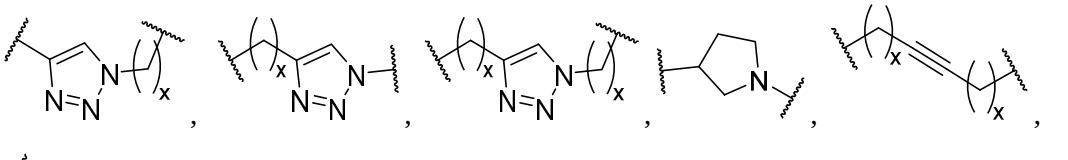
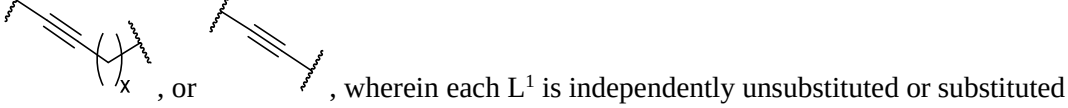
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, or 
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40. The compound of any one of claims 1-39, or a pharmaceutically acceptable salt or solvate thereof,

wherein L is absent or 
, wherein:

each A is independently absent, substituted or unsubstituted monocyclic C_3-C_{10}cycloalkyl, substituted or unsubstituted bridged bicyclic C_3-C_{10}cycloalkyl, substituted or unsubstituted fused bicyclic C_3-C_{10}cycloalkyl, substituted or unsubstituted spiro bicyclic C_3-C_{10}cycloalkyl, substituted or unsubstituted monocyclic 3- to 10-membered heterocycloalkyl, substituted or unsubstituted bridged bicyclic 3- to 10-membered heterocycloalkyl, substituted or unsubstituted fused bicyclic 3- to 10-membered heterocycloalkyl, substituted or unsubstituted spiro bicyclic 3- to 10-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl, wherein each A is independently unsubstituted or substituted with x R^{2b};

each L^1 is independently absent, 
, 
, 
, 
, 
, or
, wherein each L^1 is independently unsubstituted or substituted with x R^{2b};

n is 1, 2, 3, 4, 5, or 6;

each x is independently 1, 2, 3, 4, 5, 6, 7, or 8;

each R^{2a} is independently hydrogen or substituted or unsubstituted C_1-C_6alkyl; and

each R^{2b} is independently hydrogen, halogen, substituted or unsubstituted C_1-C_6alkyl, substituted

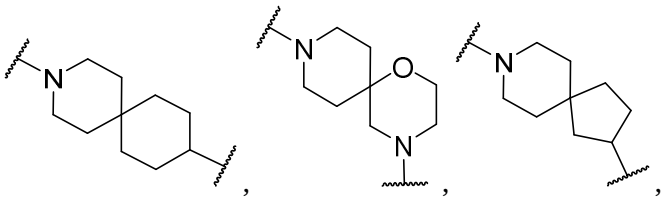
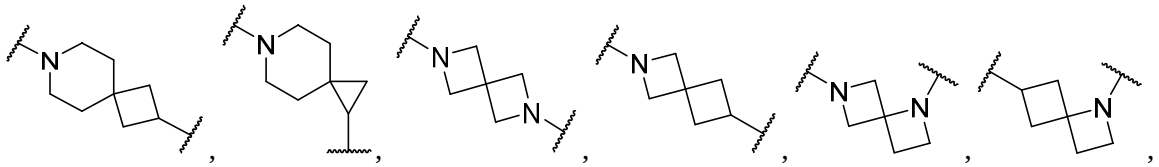
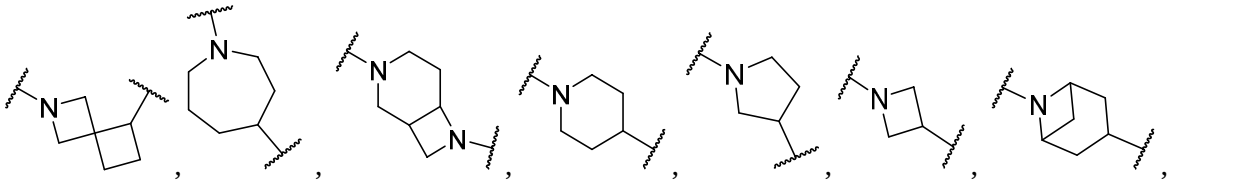
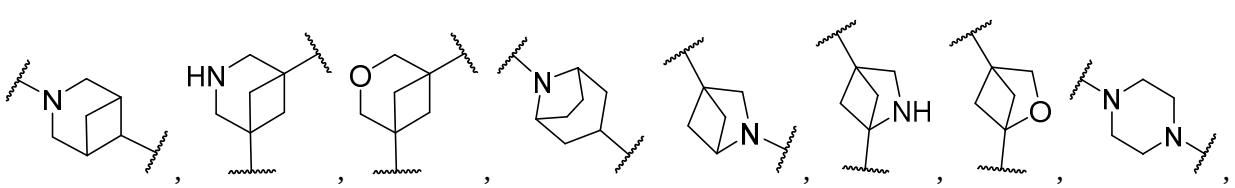
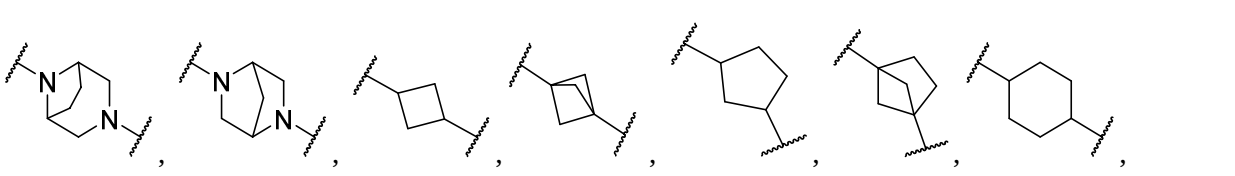
or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, -CN, -NO_2, -OH, -OR^a, -$OC(=O)R^a$, -$OC(=O)N(R^b)_2$, -$OC(=O)OR^a$, -SR^b, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2OR^b$, -$S(=O)_2N(R^b)_2$, -$N(R^b)_2$, -$NR^bC(=O)N(R^b)_2$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^a$, -$NR^bS(=O)_2R^a$, -$C(=O)R^b$, -$C(=O)OR^b$, or -$C(=O)N(R^b)$;

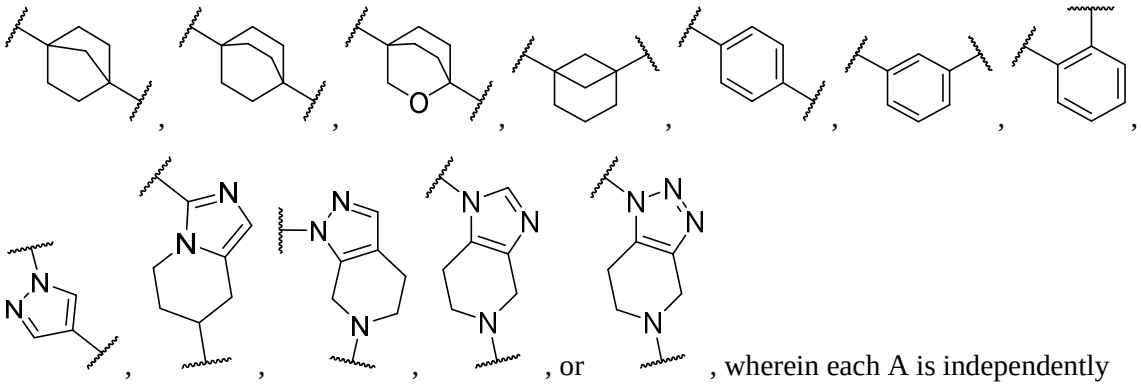
each R^a is independently substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

each R^b is independently hydrogen, substituted or unsubstituted C_1-C_6alkyl, substituted or unsubstituted C_1-C_6fluoroalkyl, substituted or unsubstituted C_1-C_6heteroalkyl, substituted or unsubstituted C_3-C_8cycloalkyl, substituted or unsubstituted monocyclic 3- to 8-membered heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted monocyclic heteroaryl;

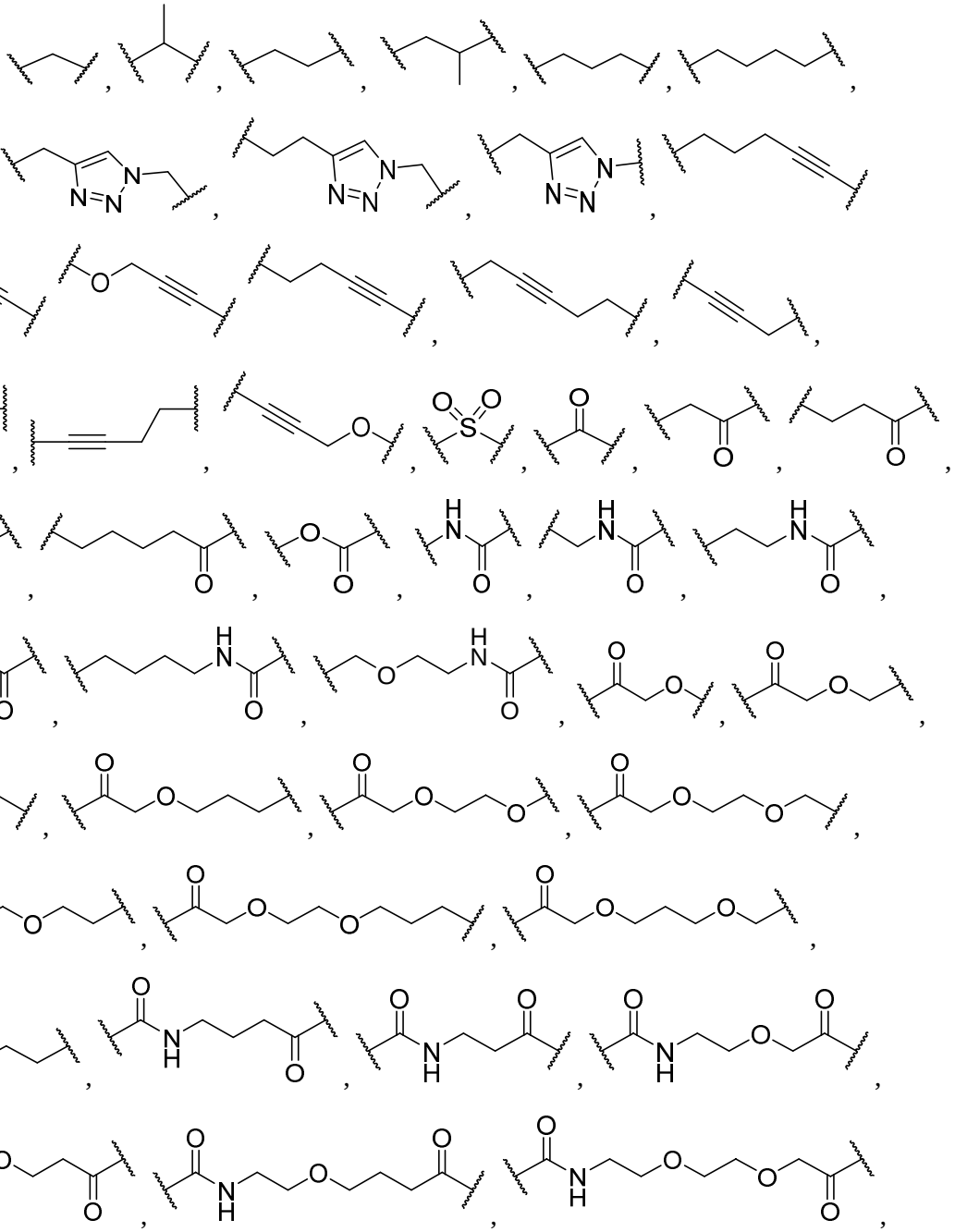
or two R^b on the same N atom are taken together with the N atom to which they are attached to form a substituted or unsubstituted N-containing heterocycle.

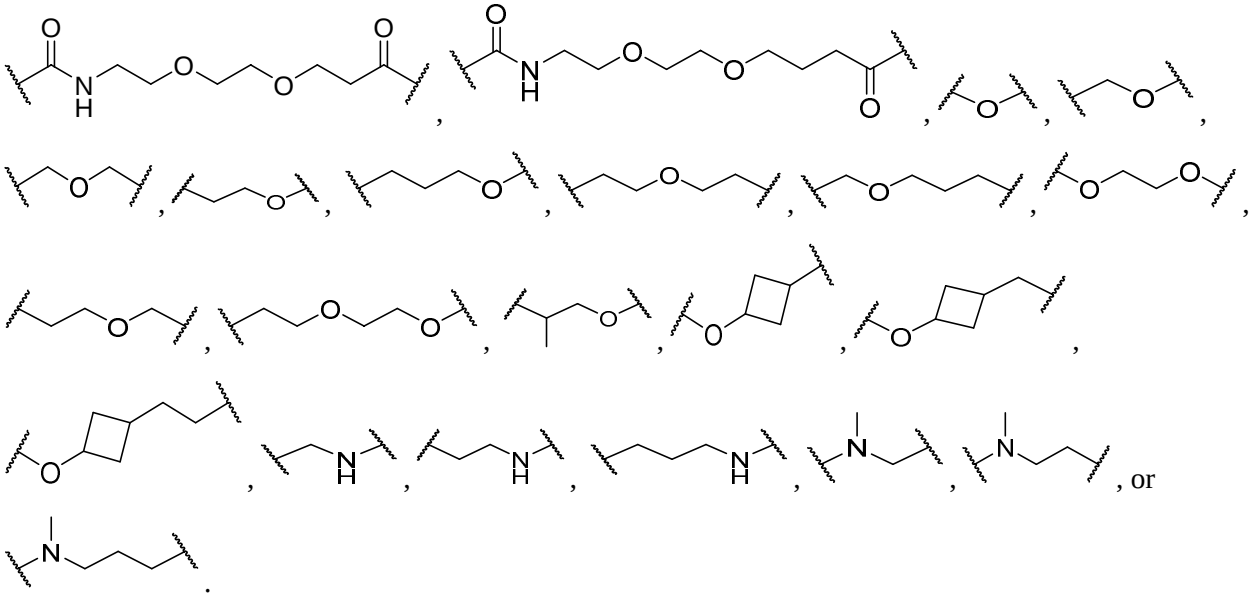
41. The compound of claim 40, or a pharmaceutically acceptable salt or solvate thereof, wherein:

each A is independently absent, , , , , 

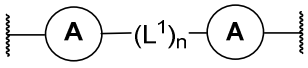


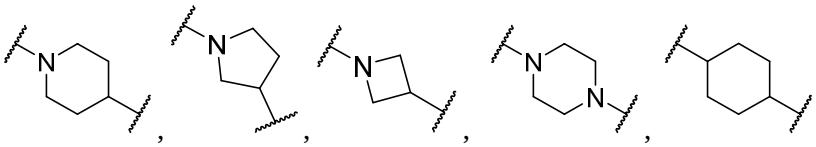
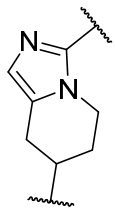
unsubstituted or substituted with x R^{2b};

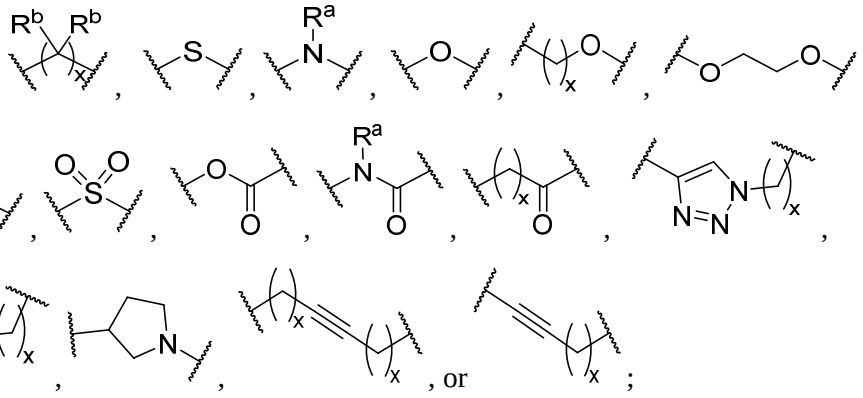
$(L^1)_n$ is absent, 



42. The compound of any one of claims 1-39, or a pharmaceutically acceptable salt or solvate thereof,

wherein L is absent or  wherein:

each A is independently absent, , or ;

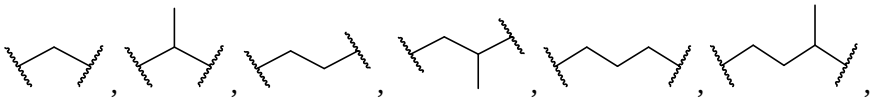
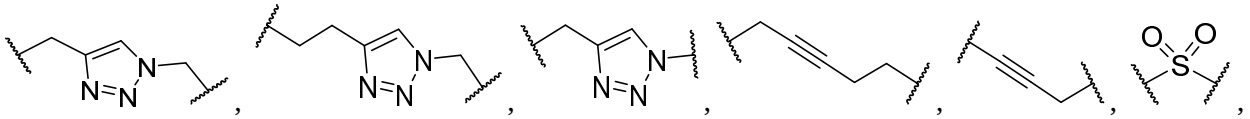
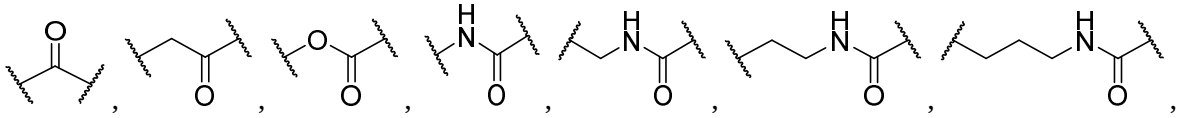
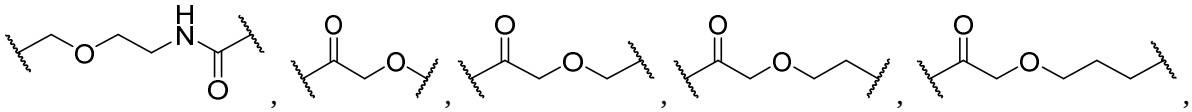
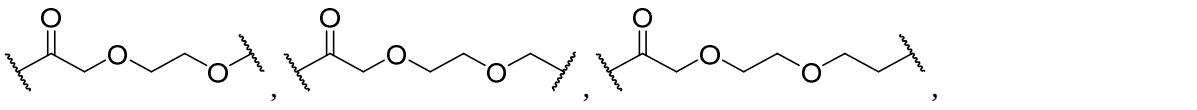
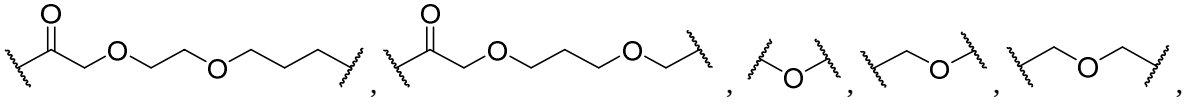
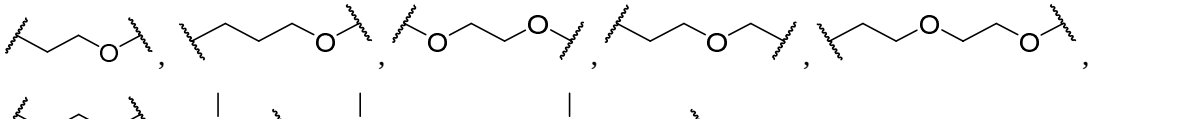
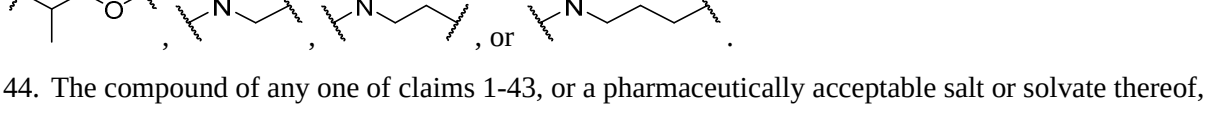
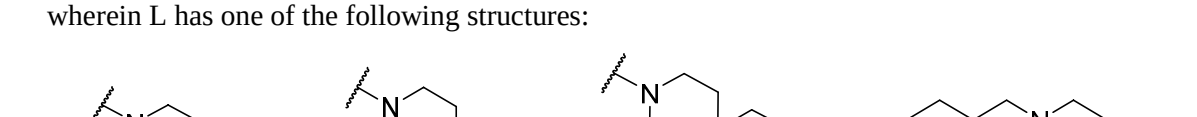
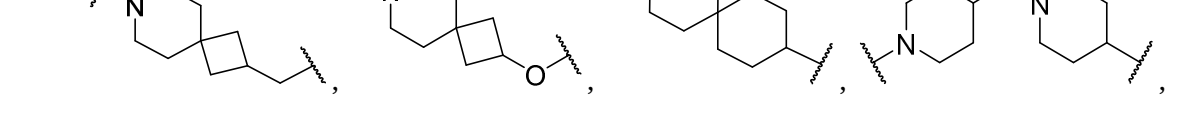
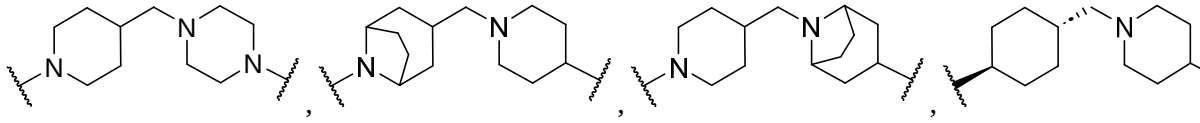
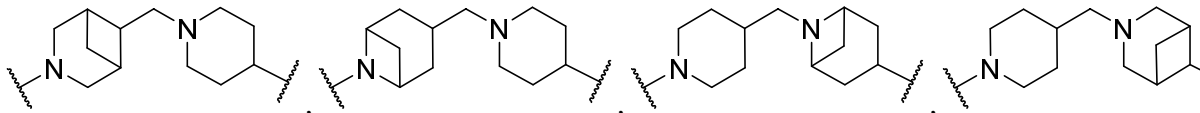
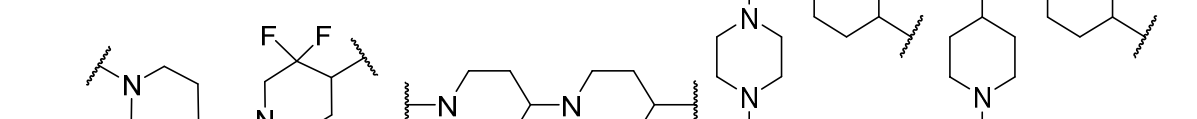
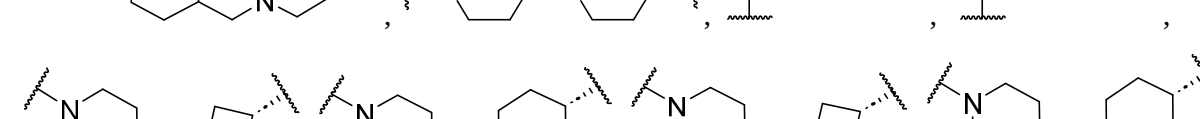
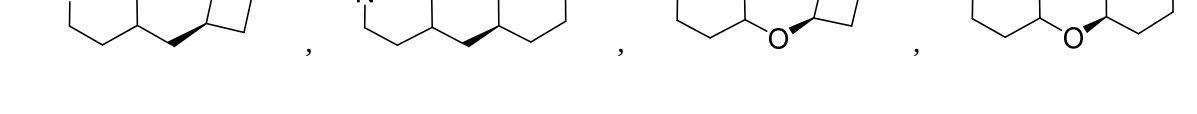
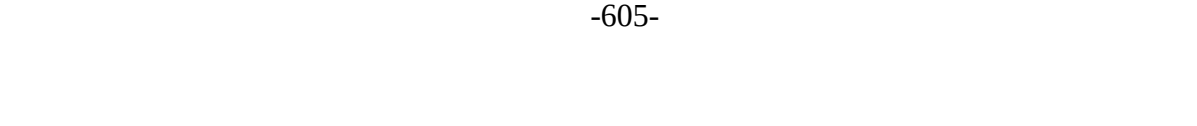
each L^1 is independently absent, ;

n is 1, 2, or 3; each x is independently 1, 2, 3, 4, 5, or 6;

each R^a is independently hydrogen or substituted or unsubstituted C_1-C_6alkyl; and

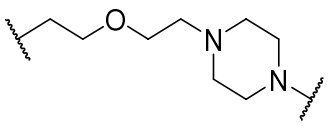
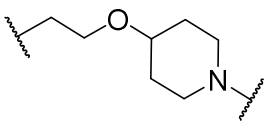
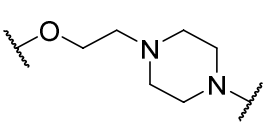
each R^b is independently hydrogen, halogen, or substituted or unsubstituted C_1-C_6alkyl.

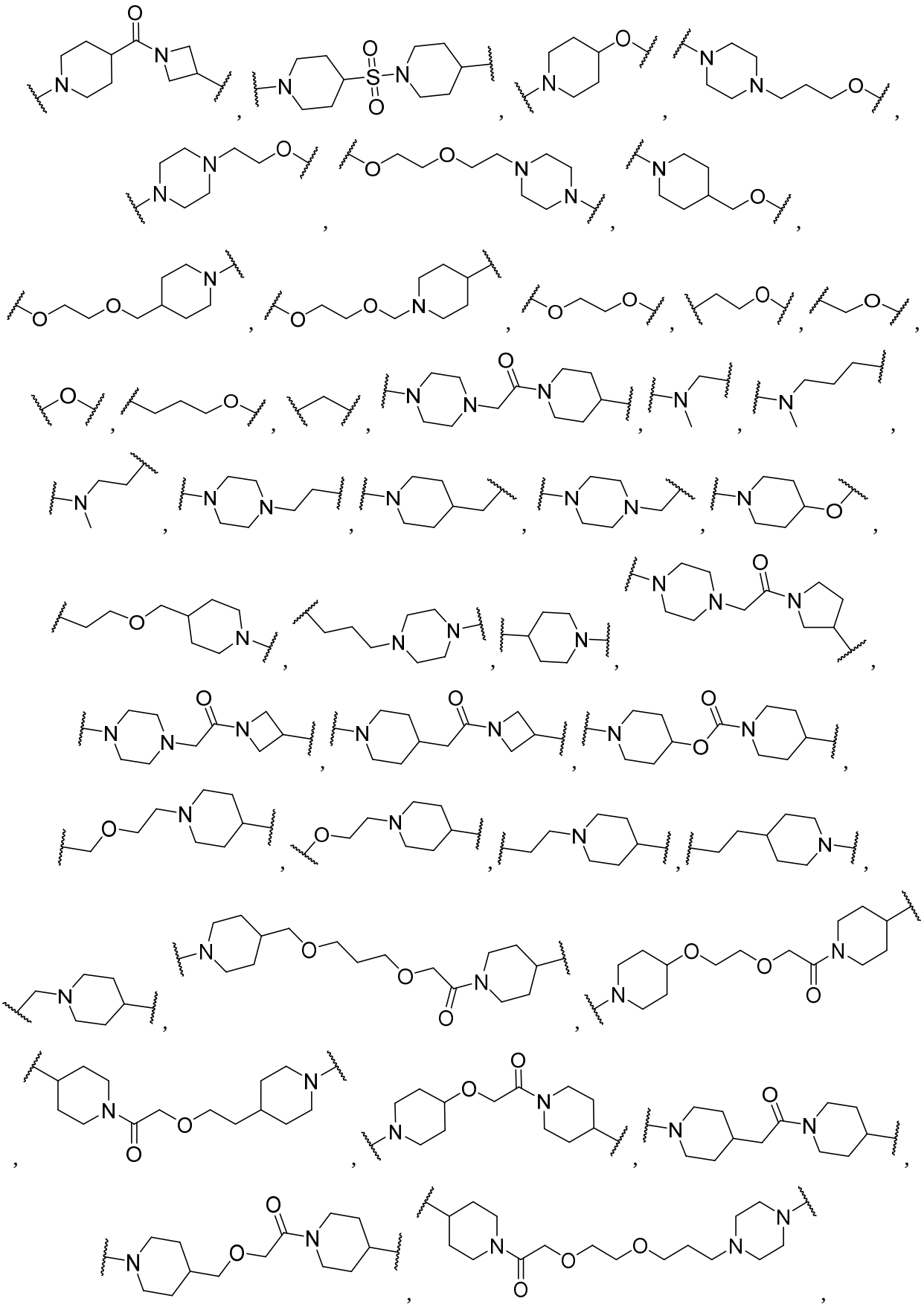
43. The compound of any one of claims 40-42, or a pharmaceutically acceptable salt or solvate thereof, wherein:

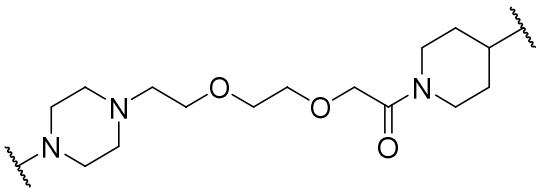
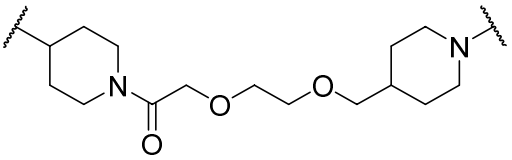
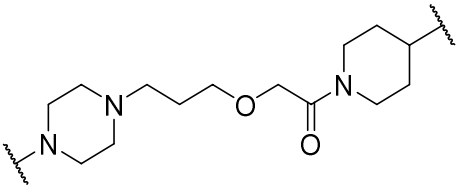
$(L^1)_n$ is absent, , , , , , , , , , , , , , , , , , or .

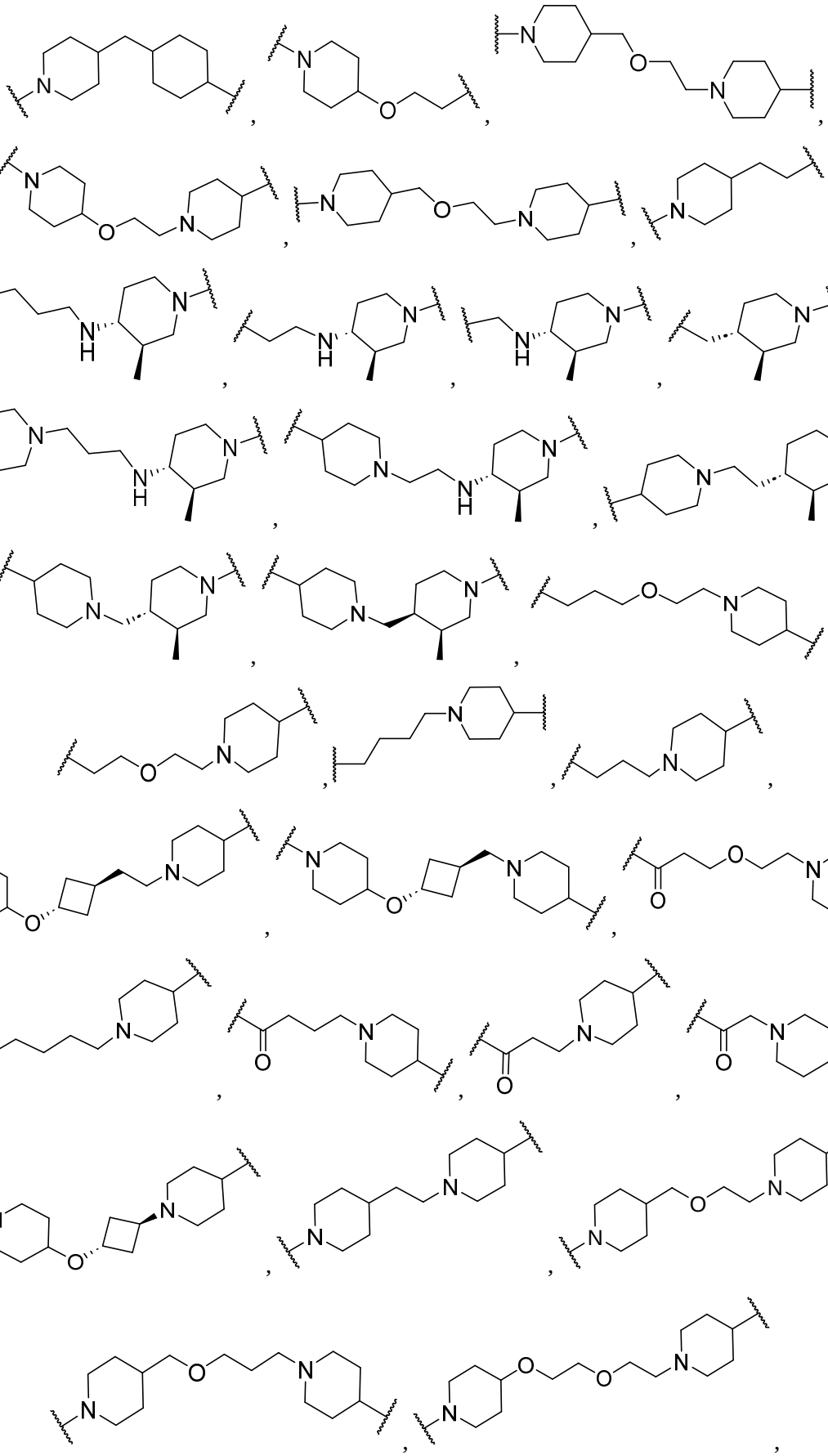
44. The compound of any one of claims 1-43, or a pharmaceutically acceptable salt or solvate thereof, wherein L has one of the following structures:

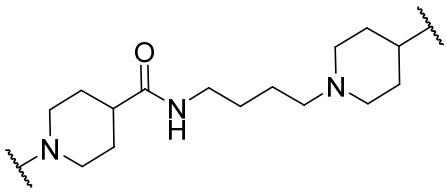
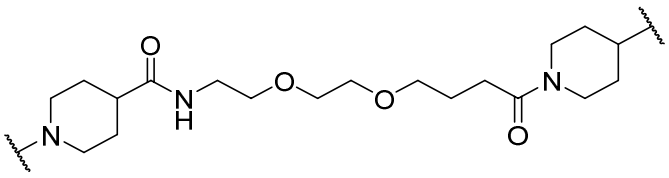
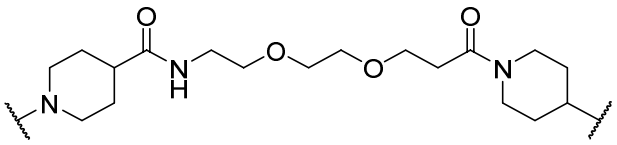
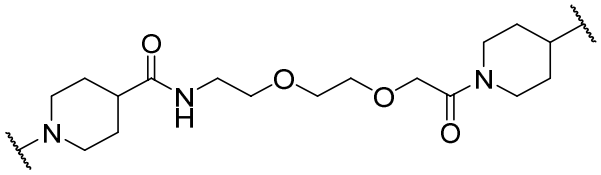
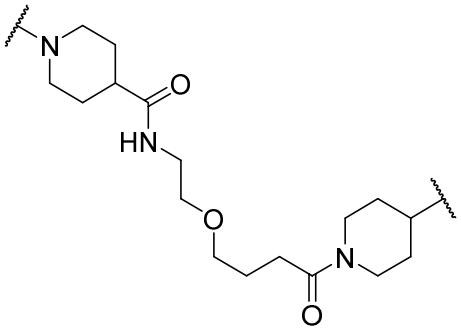
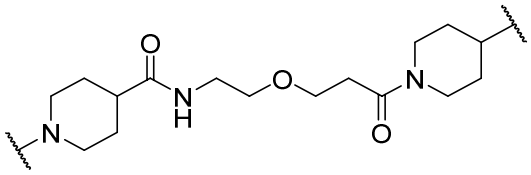
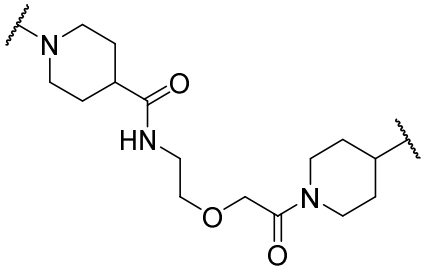
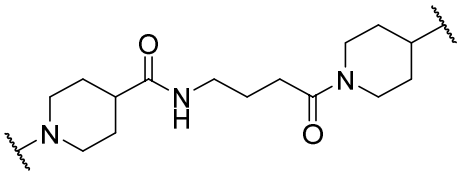
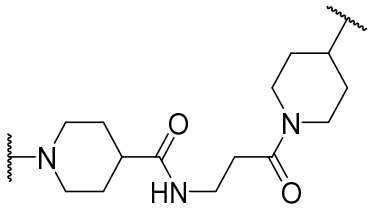
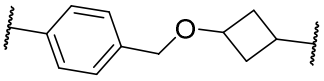
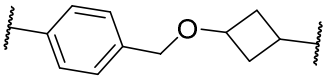
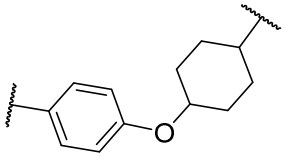
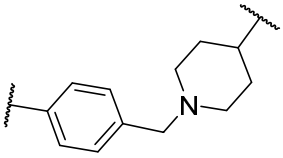
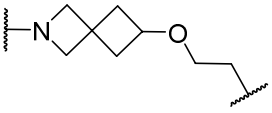
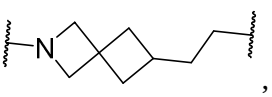
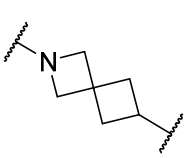
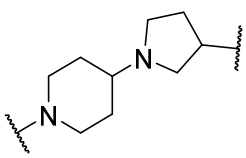
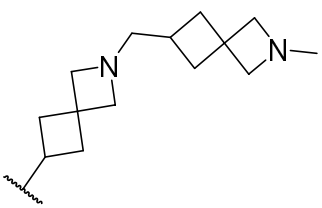
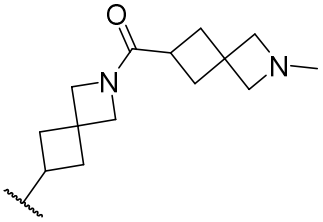
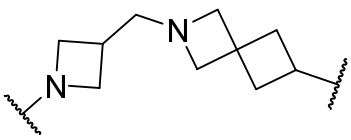
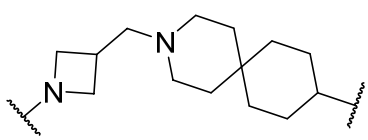
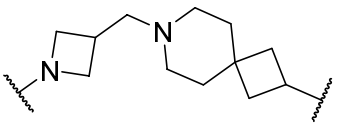
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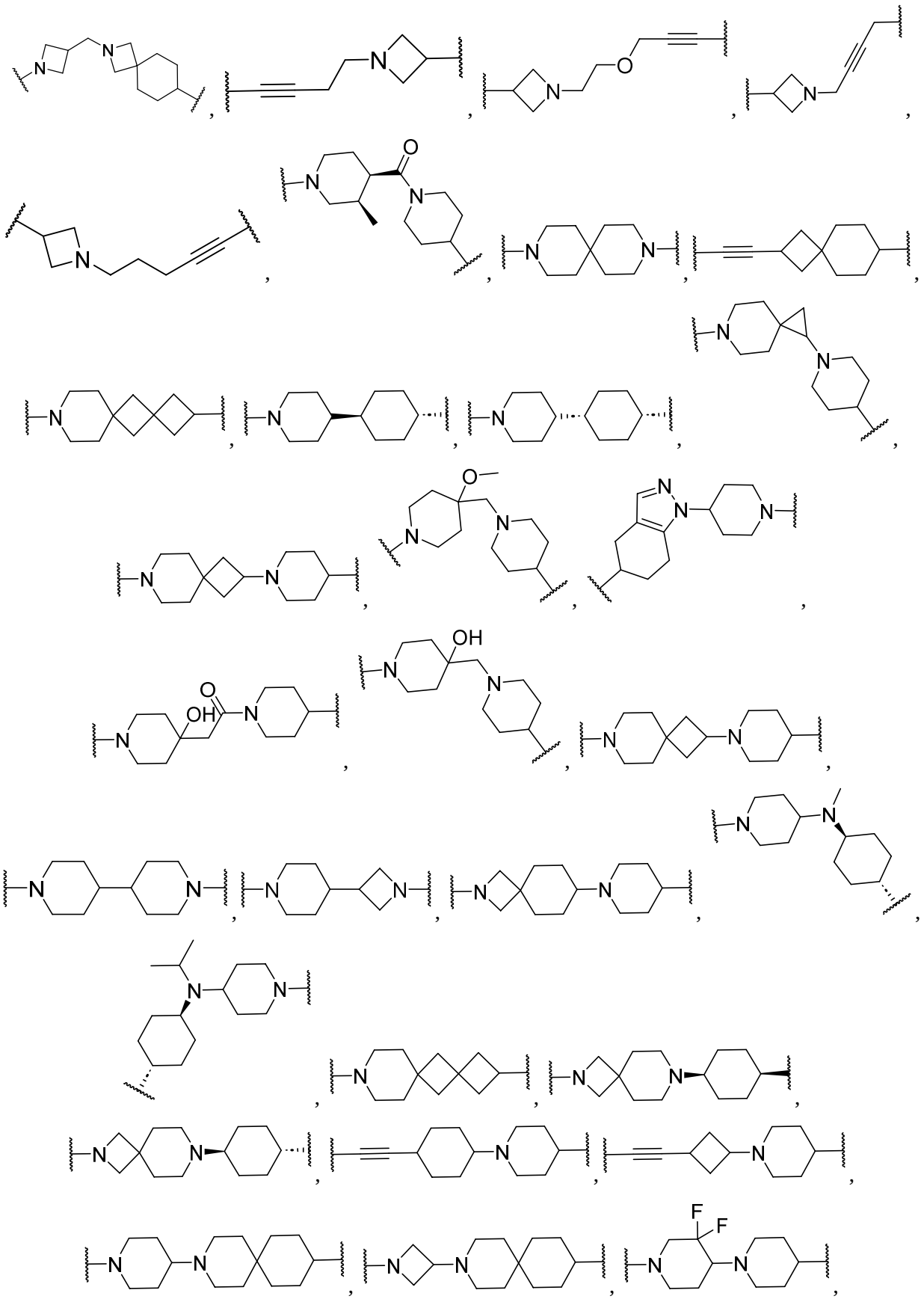

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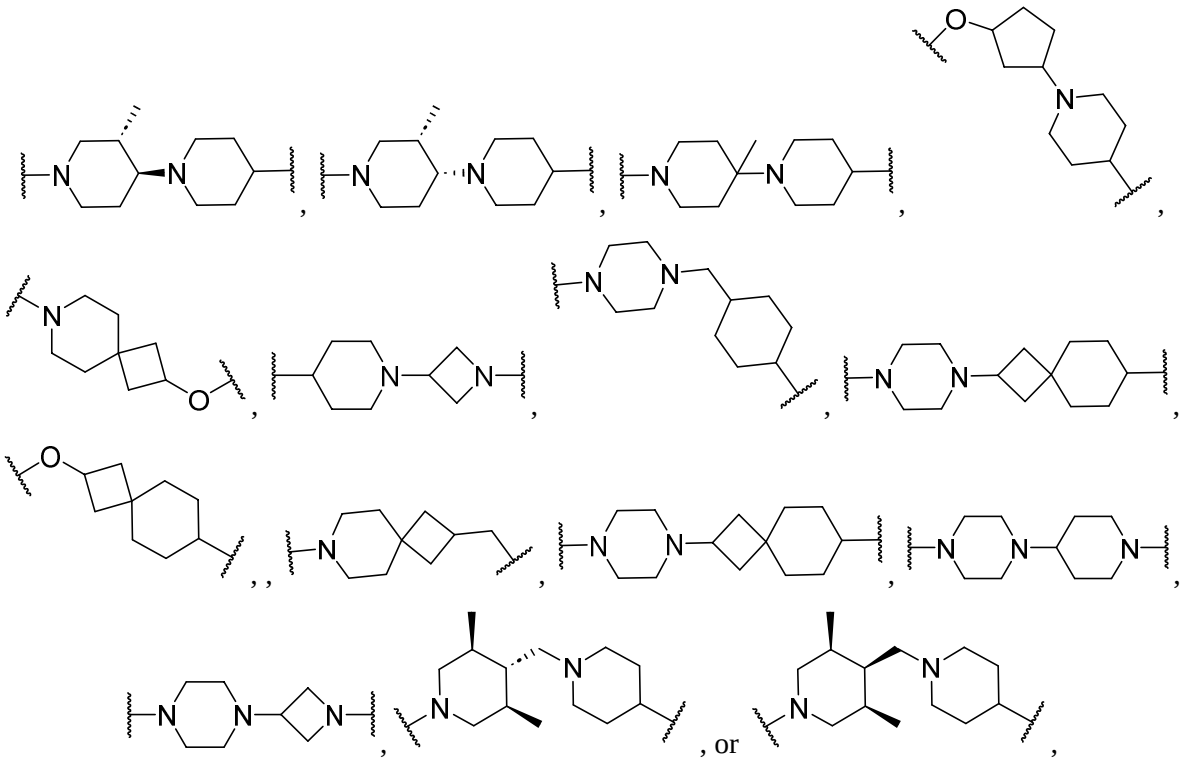



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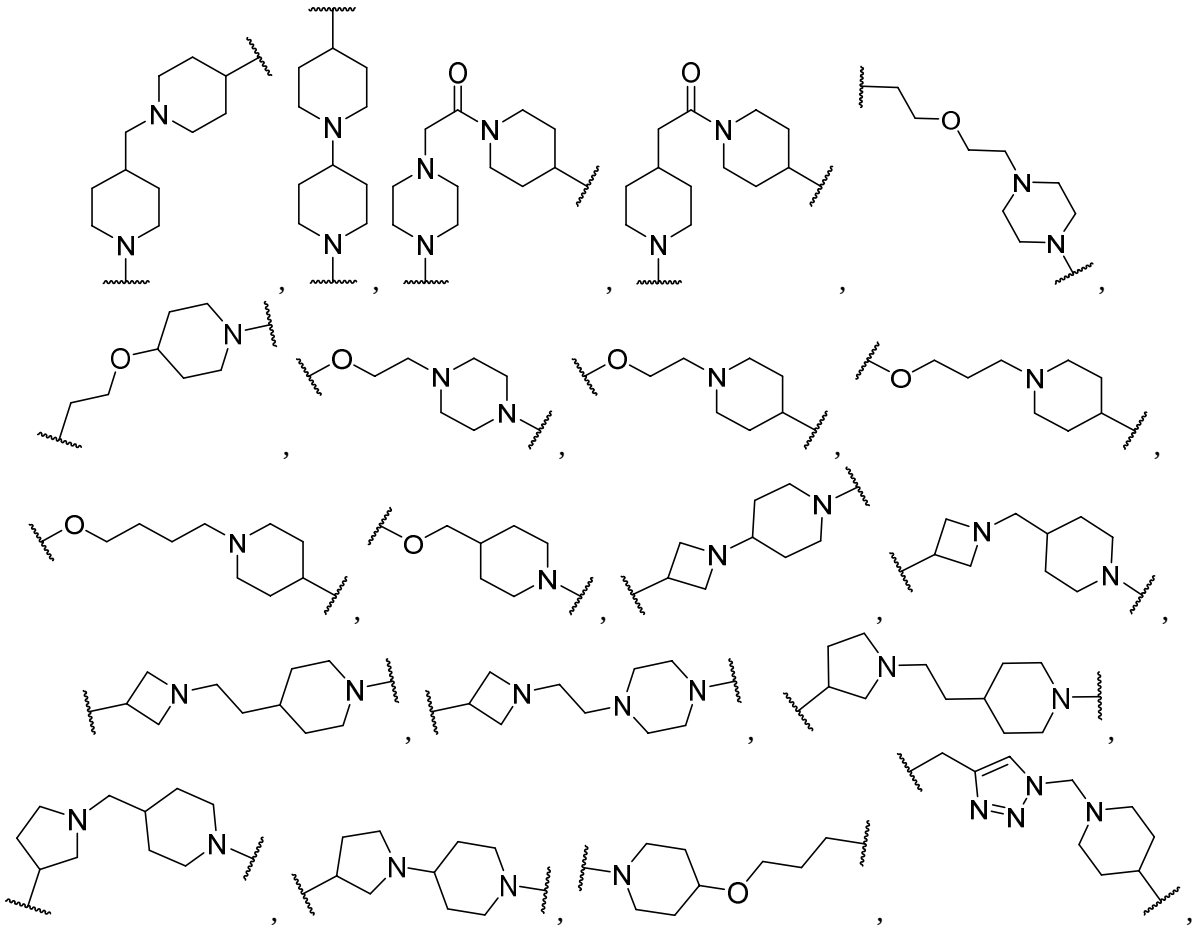

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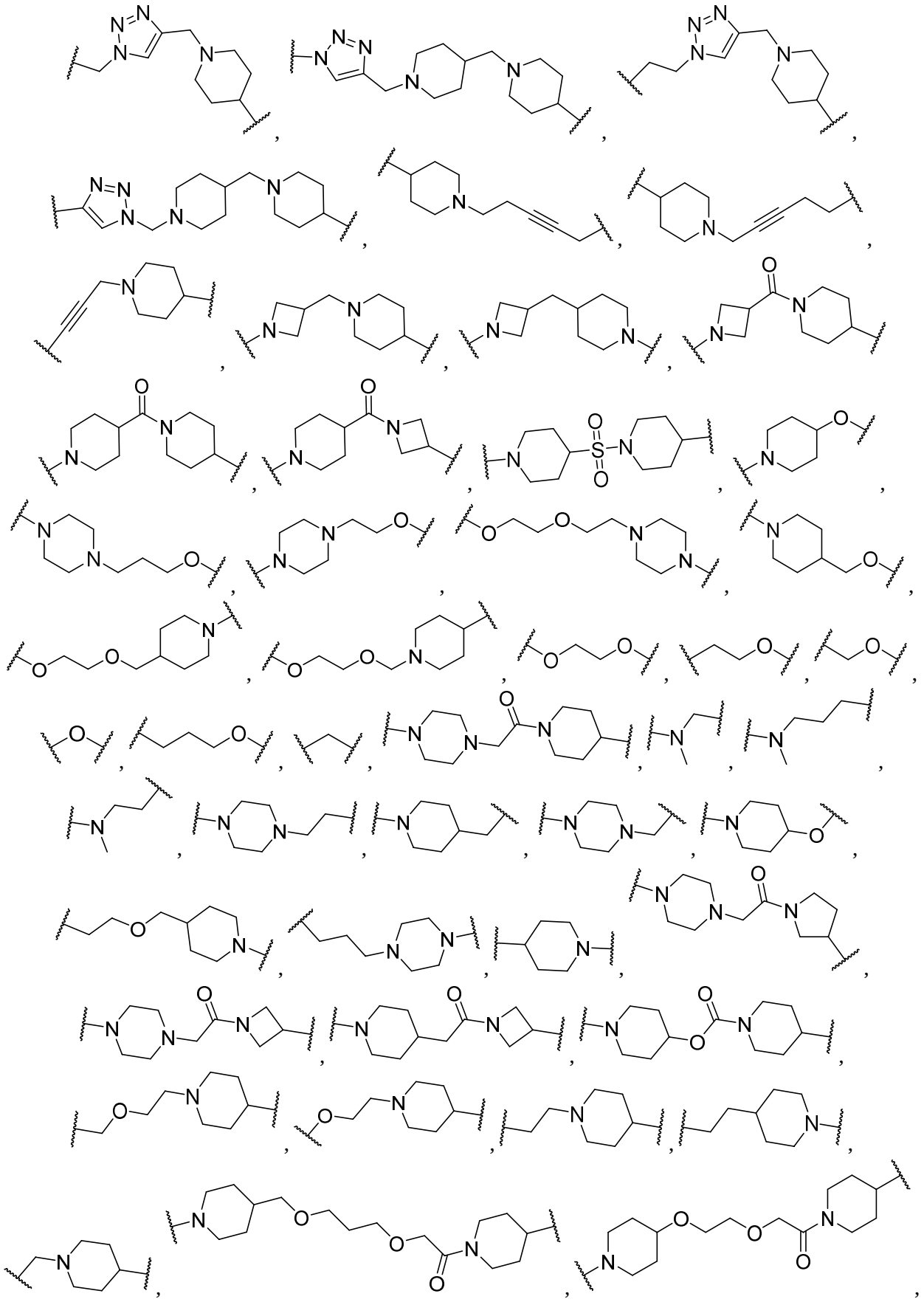


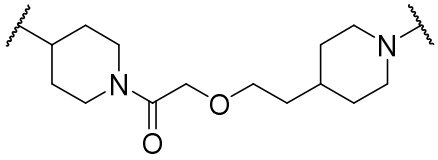
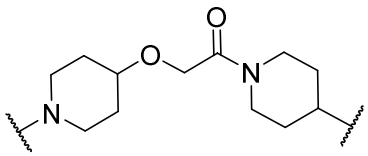
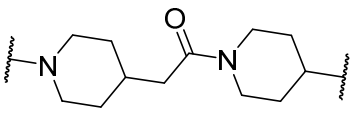
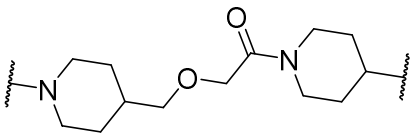
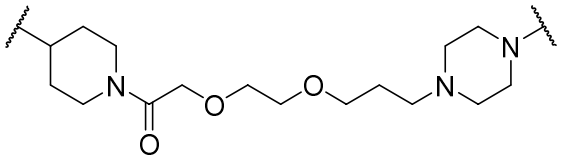
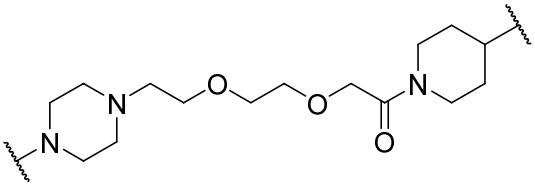
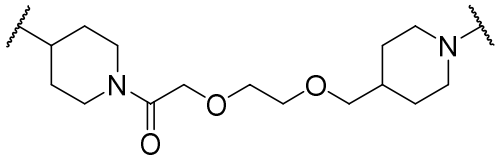
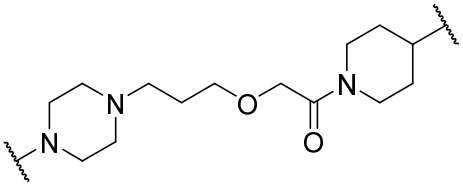
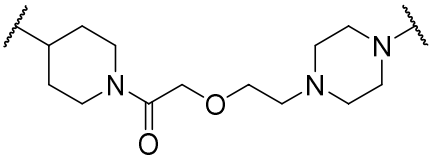
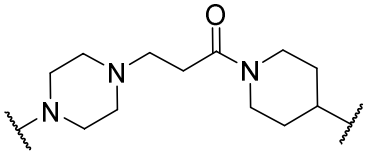
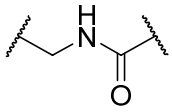
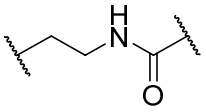
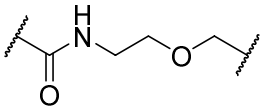
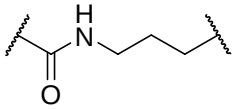
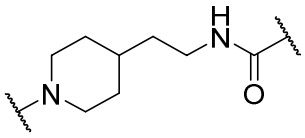
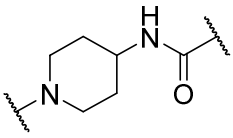
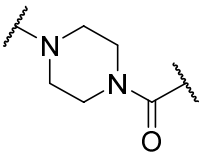
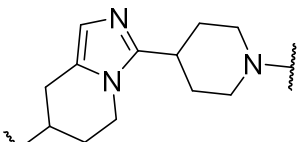


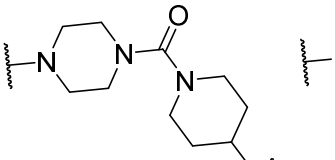
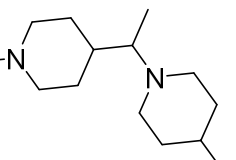
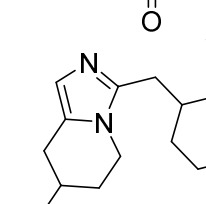
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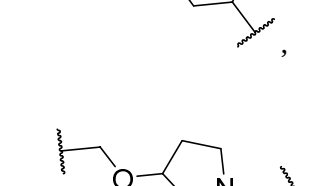
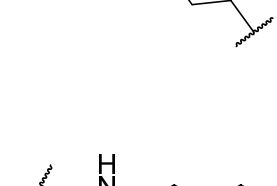
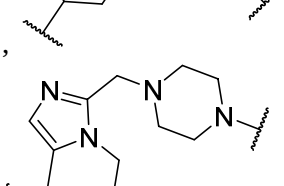
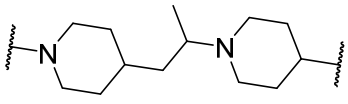
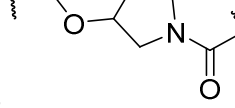
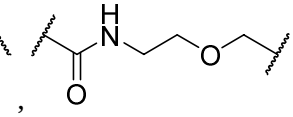
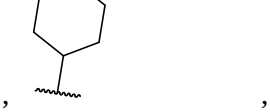
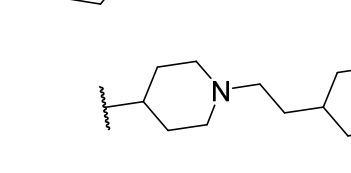
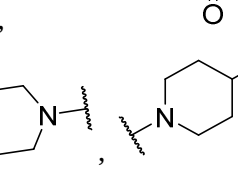
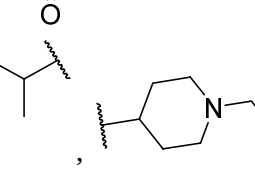
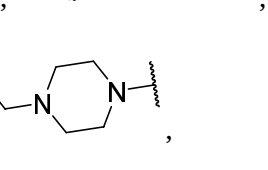
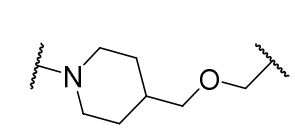
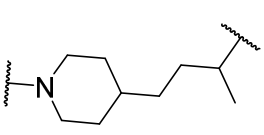
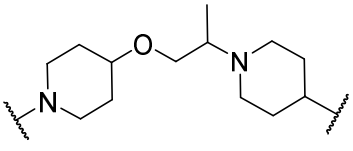
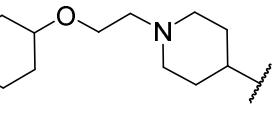
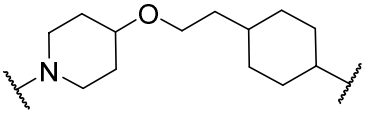
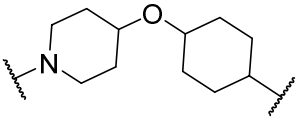
45. The compound of any one of claims 1-43, or a pharmaceutically acceptable salt or solvate thereof, wherein L has one of the following structures:

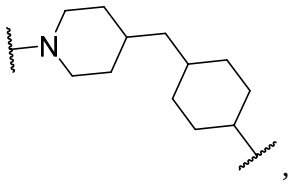





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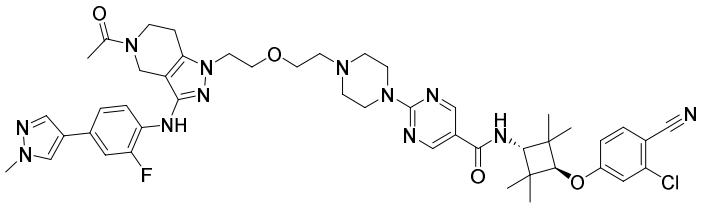
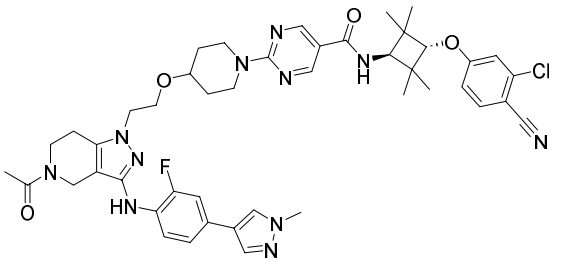
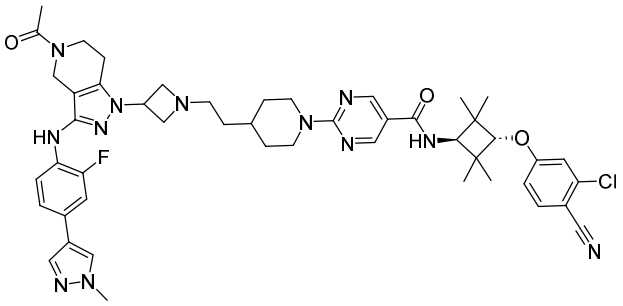
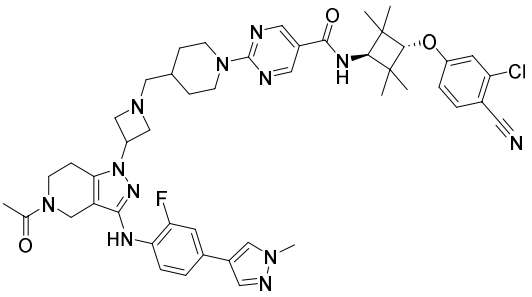
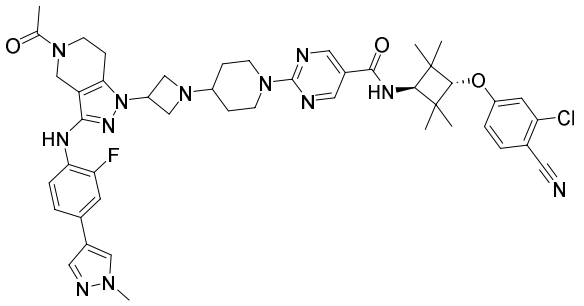
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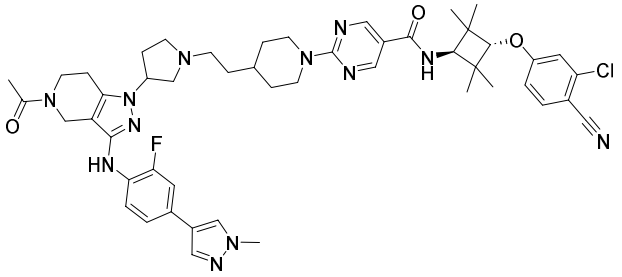
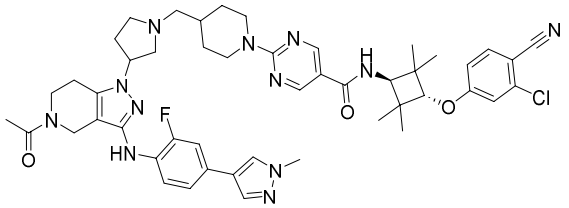
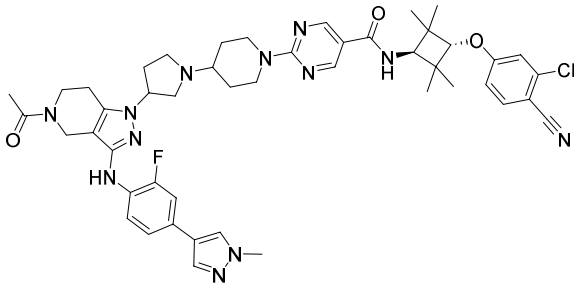
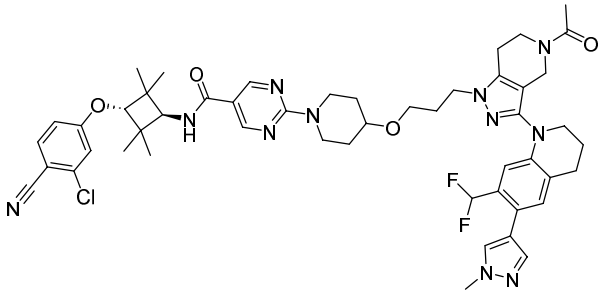
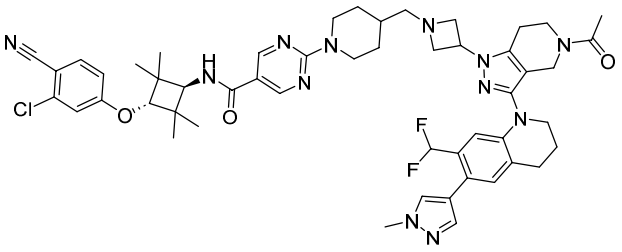
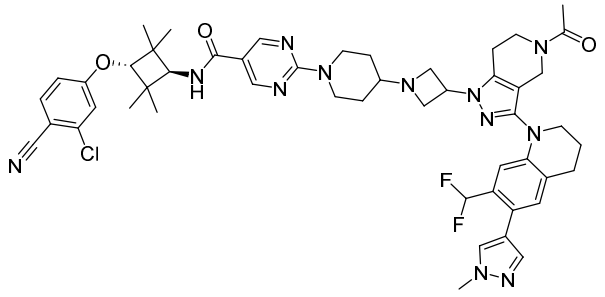
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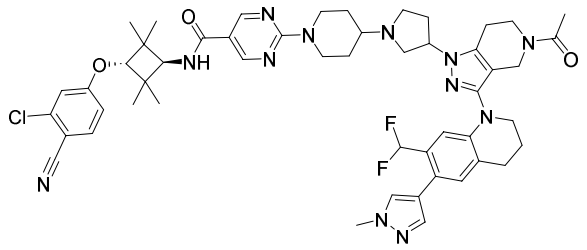
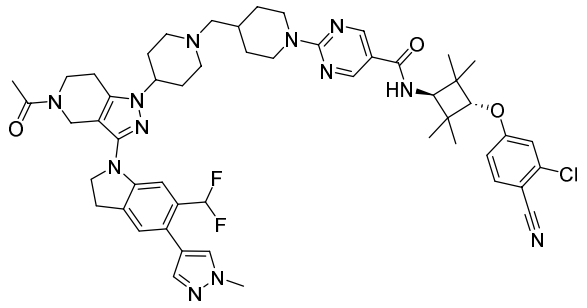
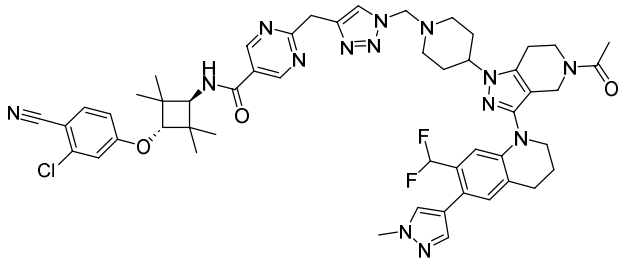
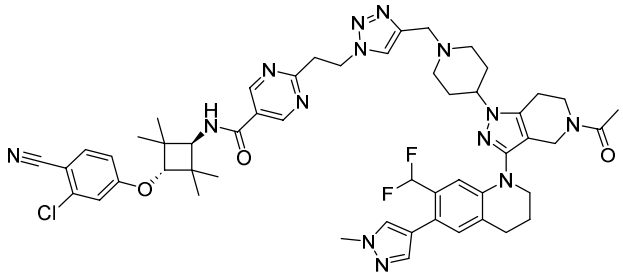
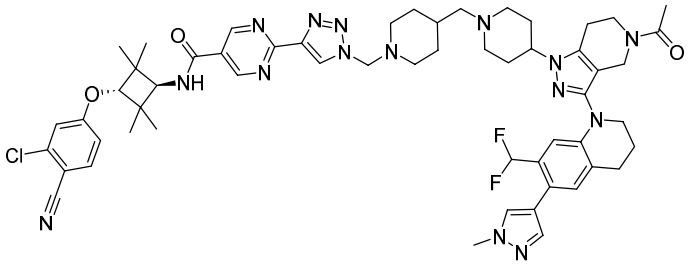
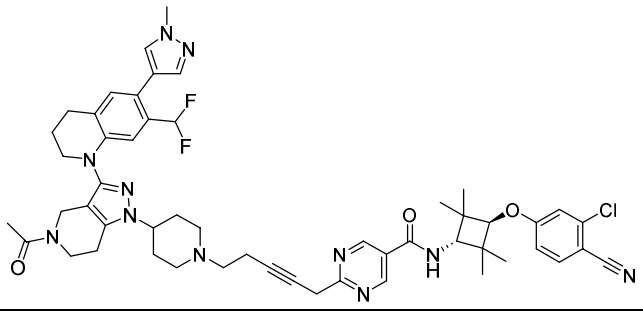


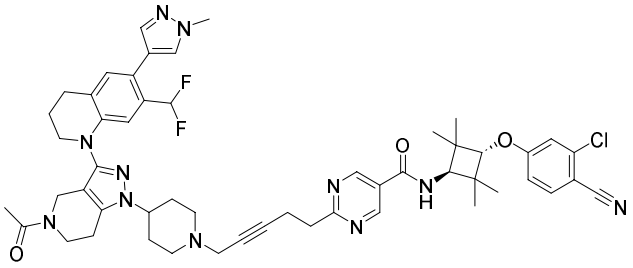
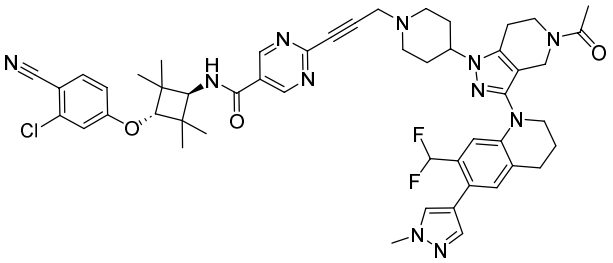
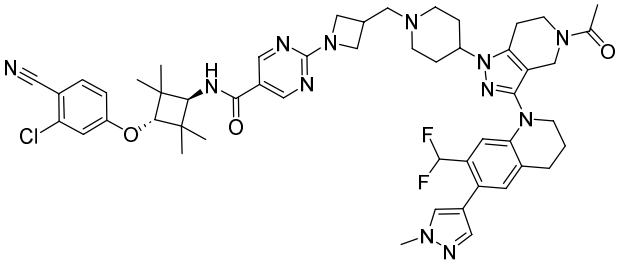
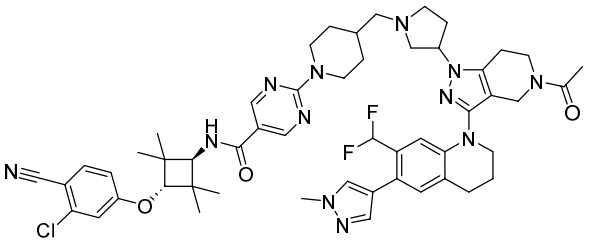
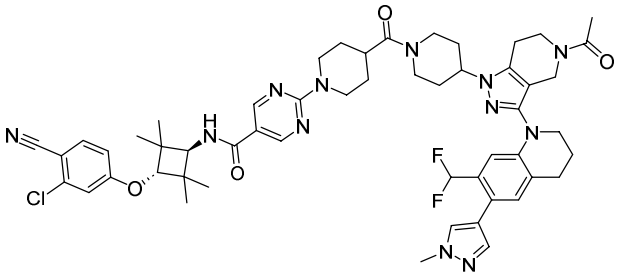
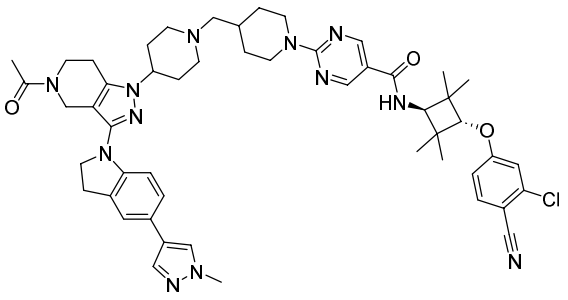
or a pharmaceutically acceptable salt or solvate thereof.

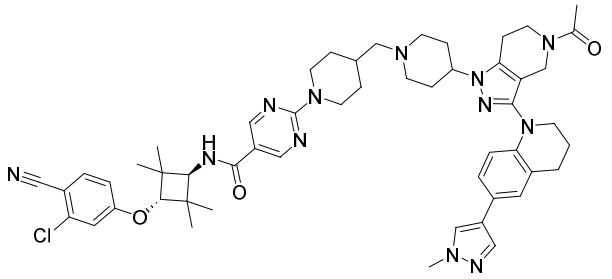
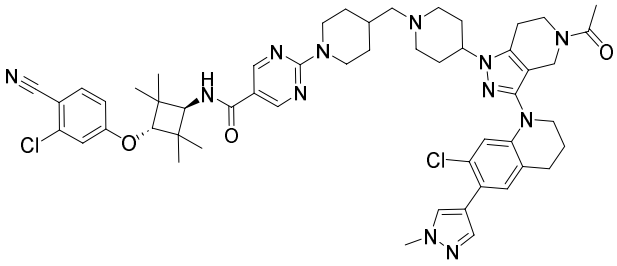
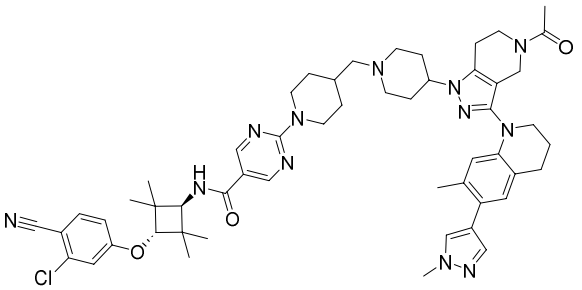
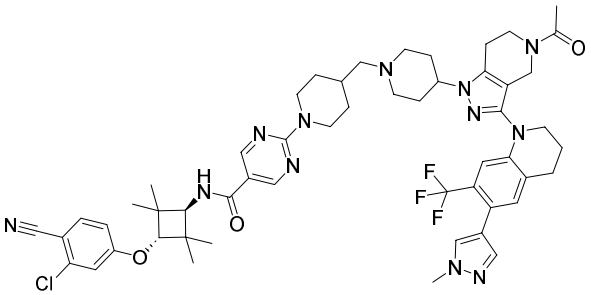
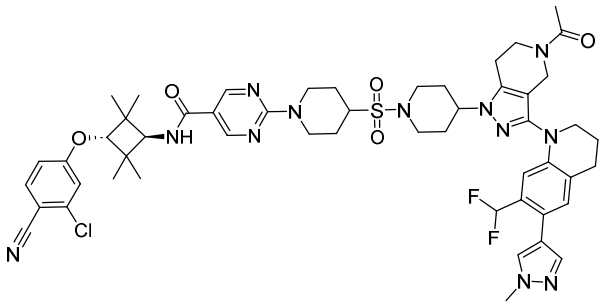
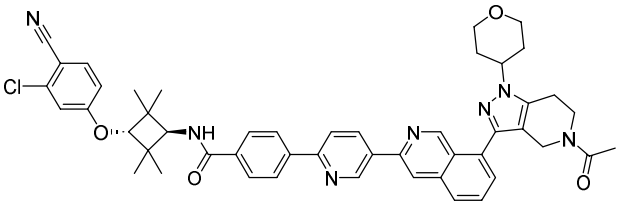
46. The compound of claim 1, selected from any one of the following compounds, or a pharmaceutically acceptable salt or solvate thereof:

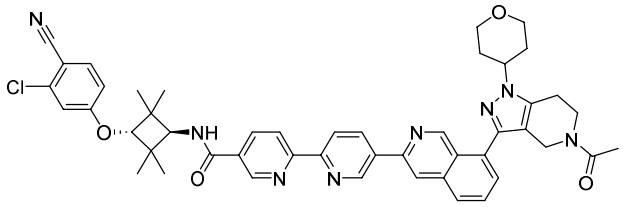
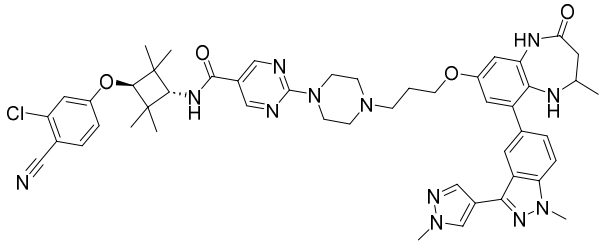
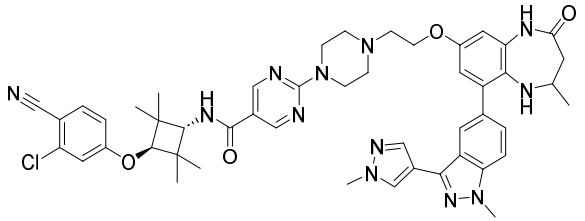
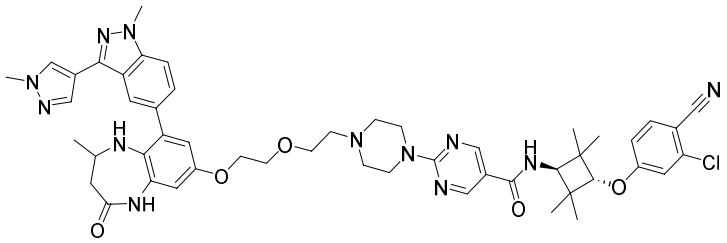
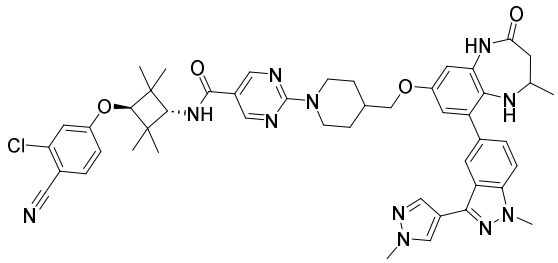
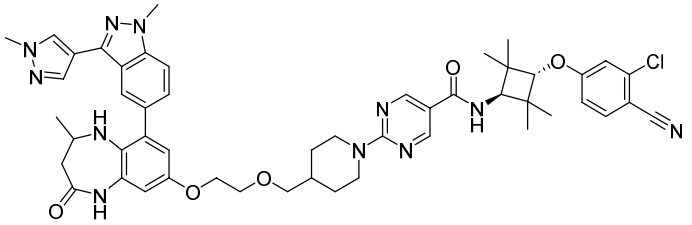
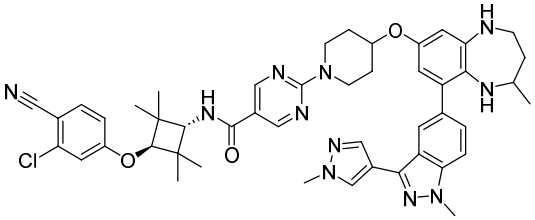
Compound	Structure
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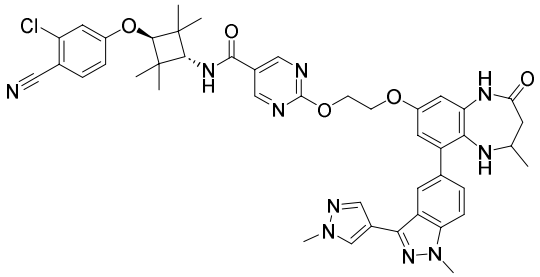
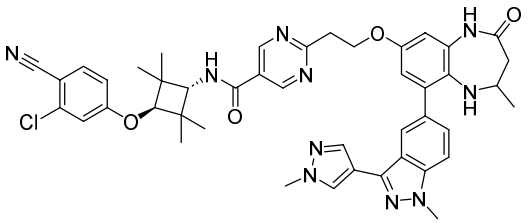
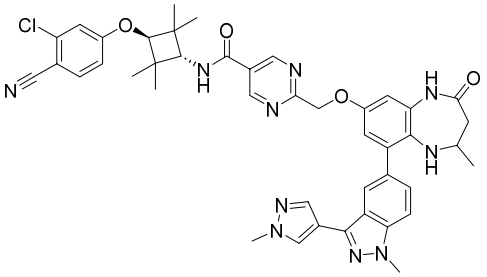
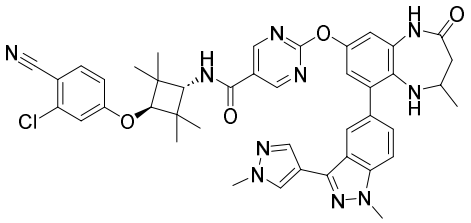
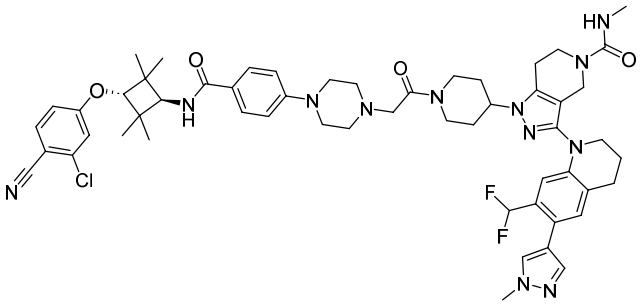
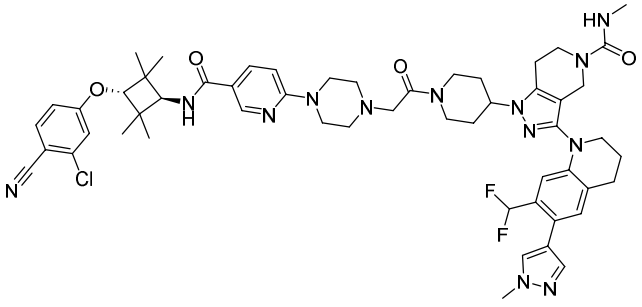
Compound	Structure
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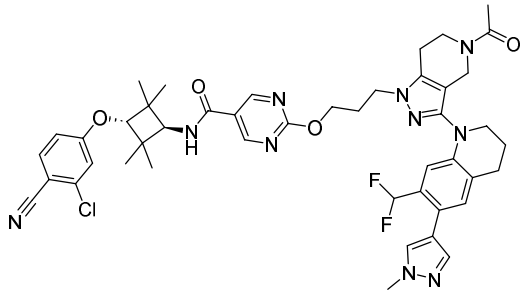
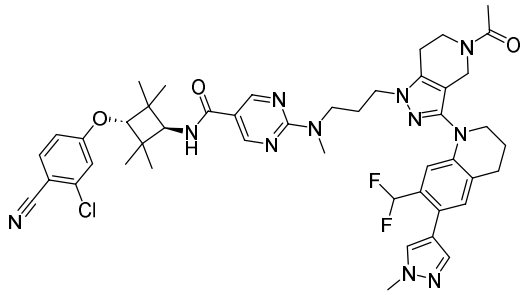
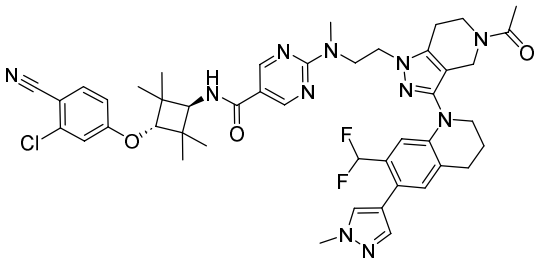
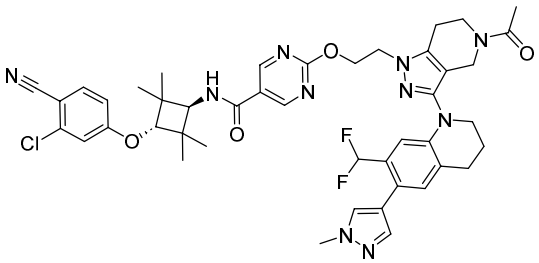
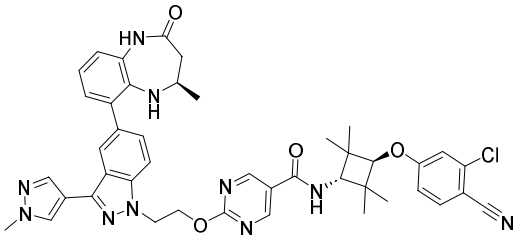
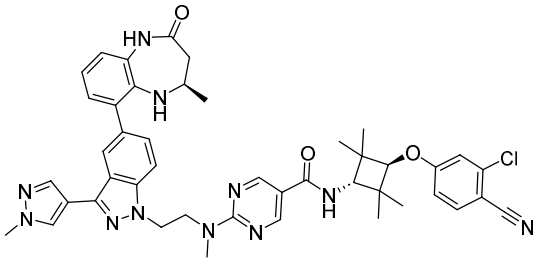
Compound	Structure
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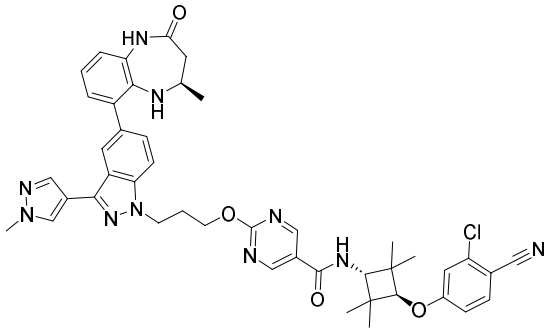
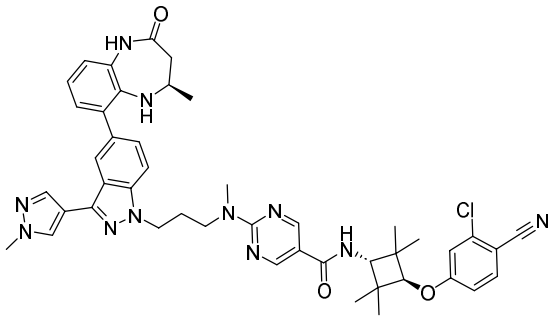
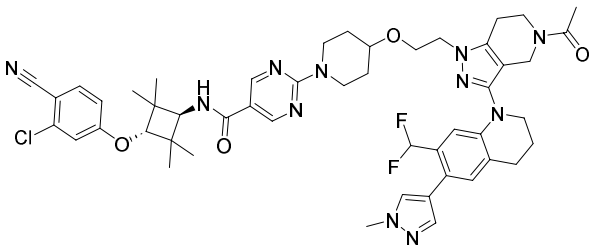
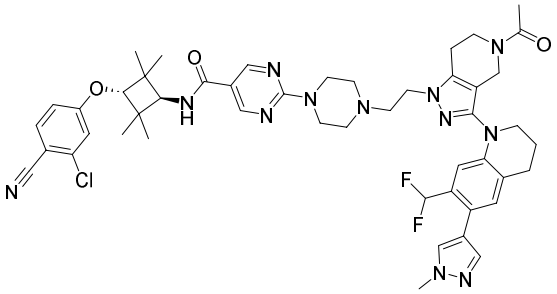
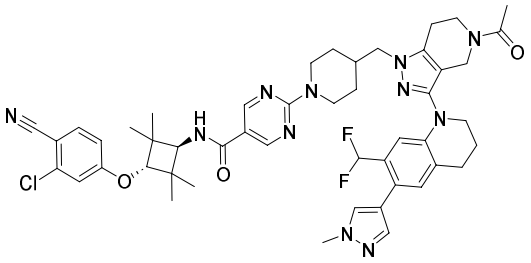
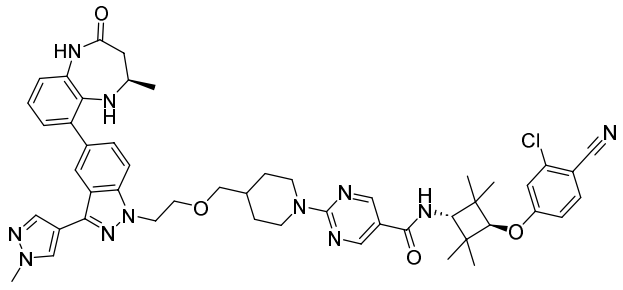
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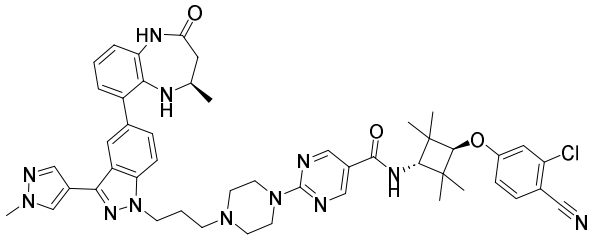
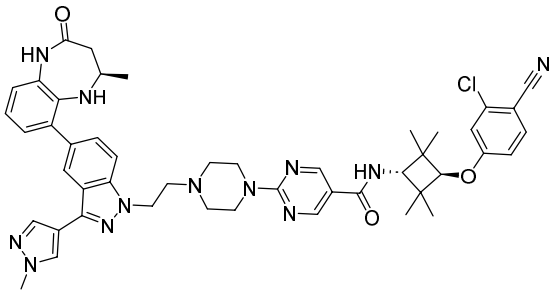
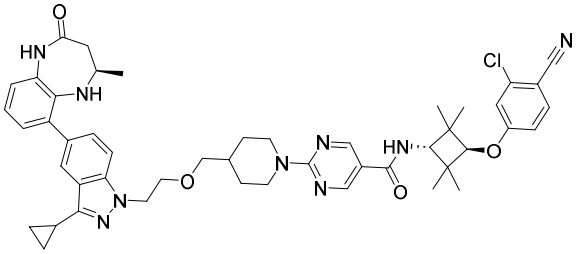
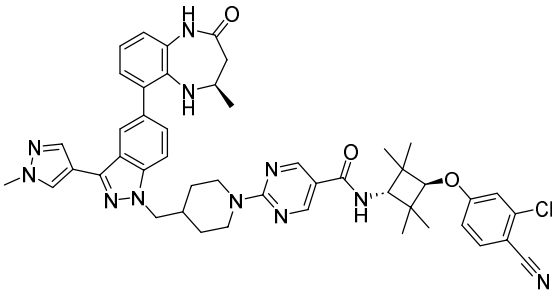
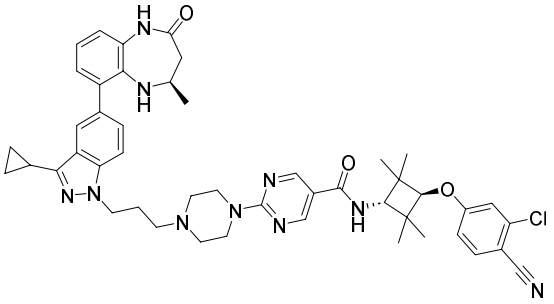
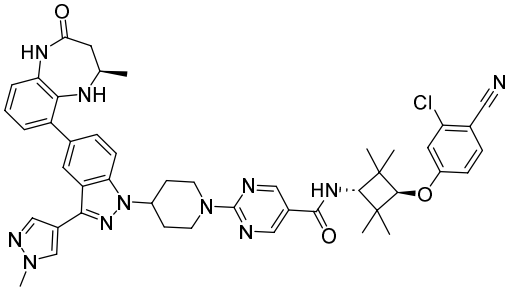
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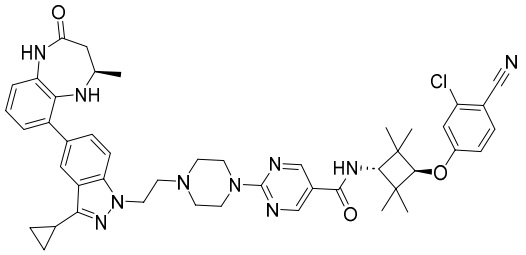
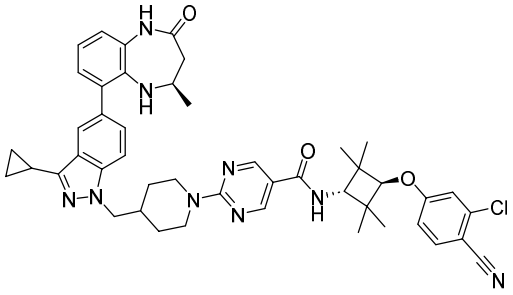
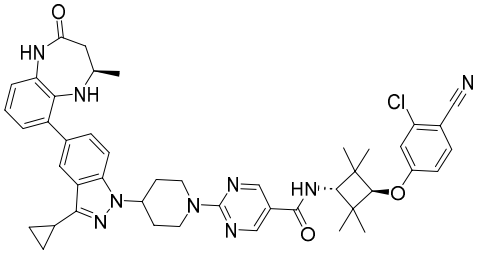
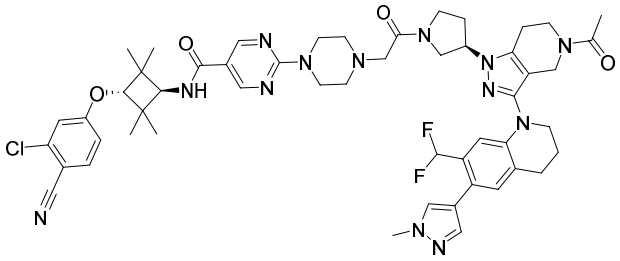
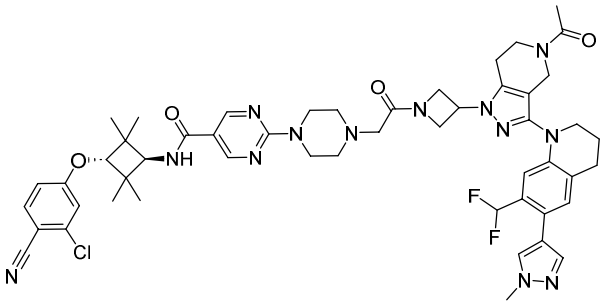
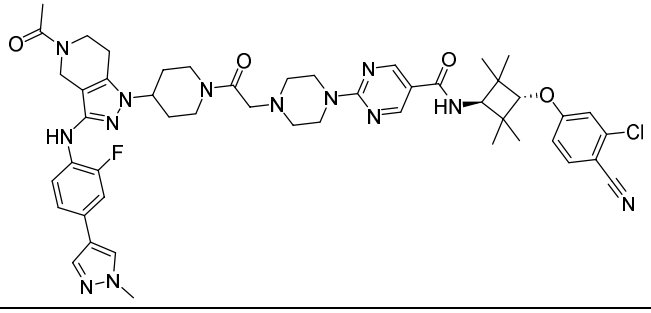
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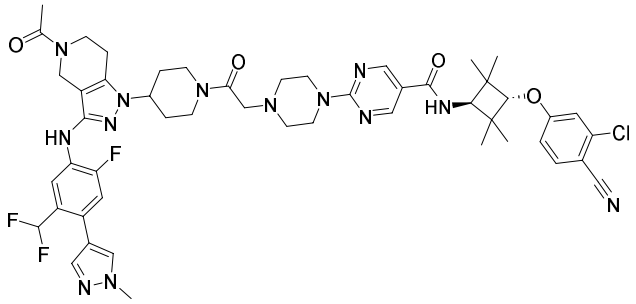
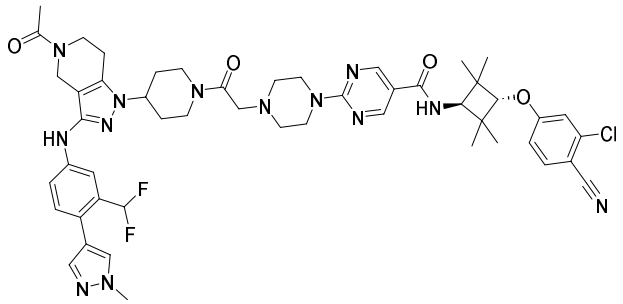
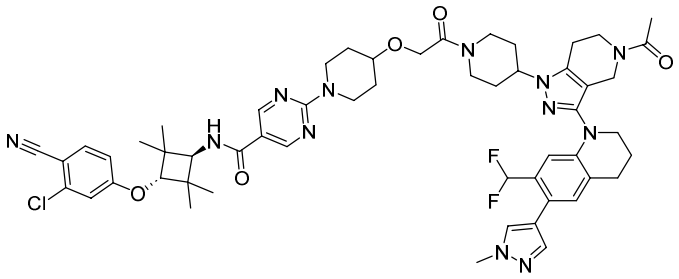
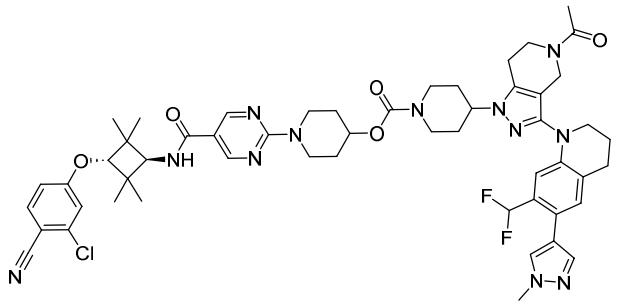
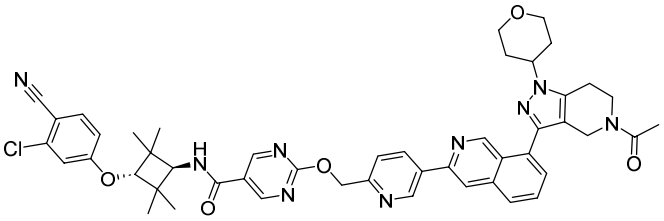
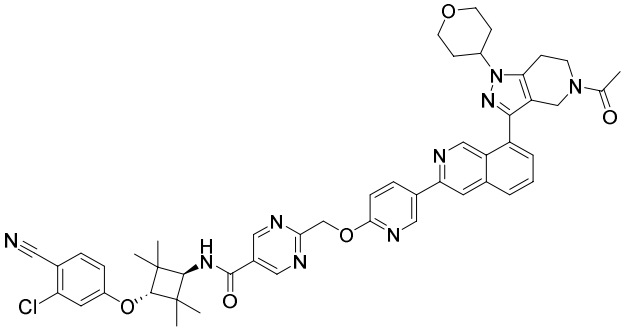
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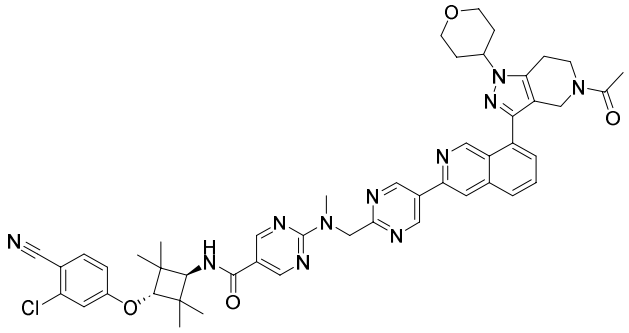
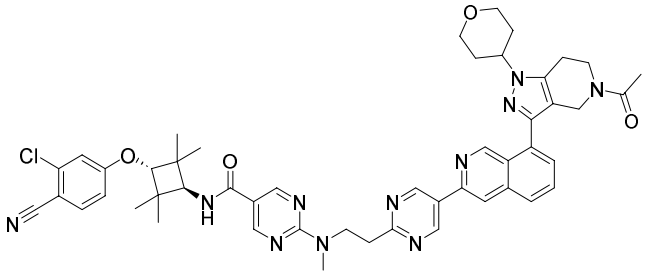
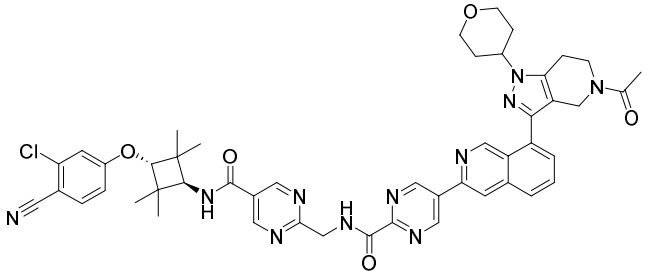
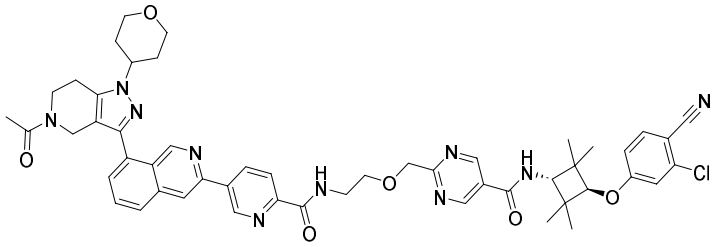
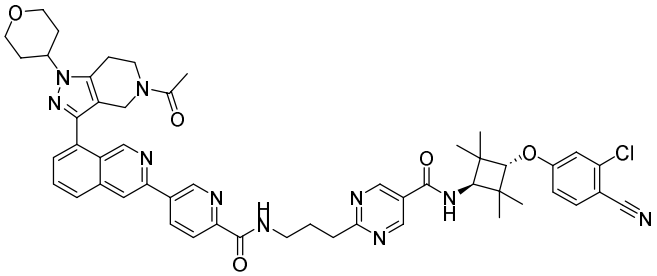
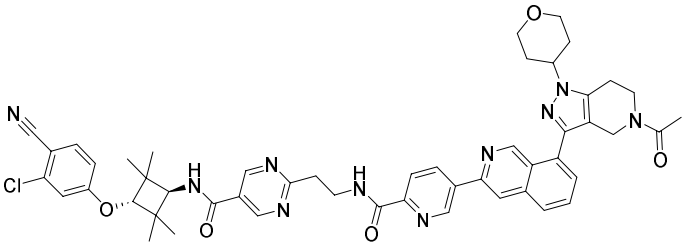
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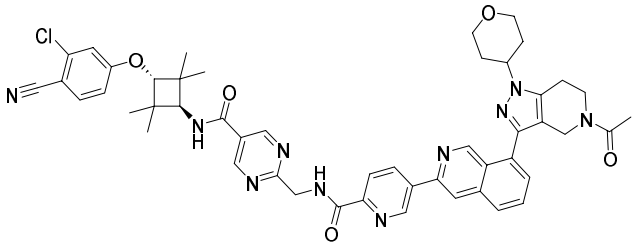
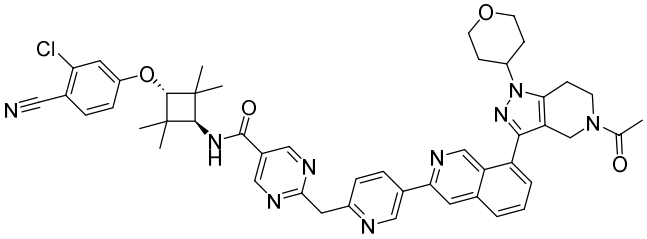
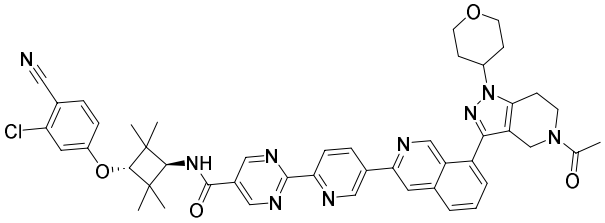
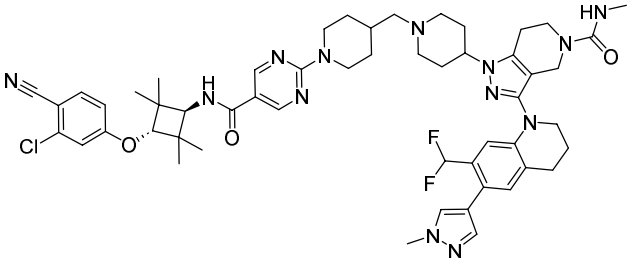
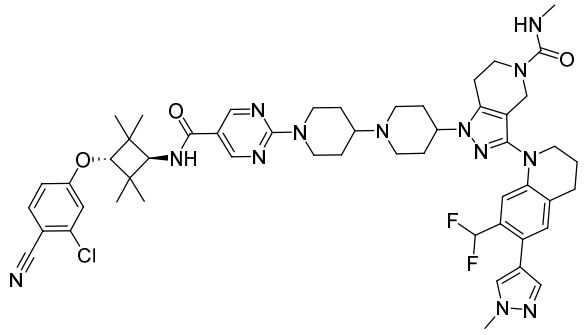
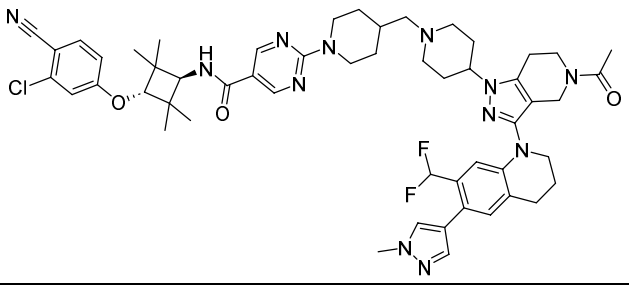
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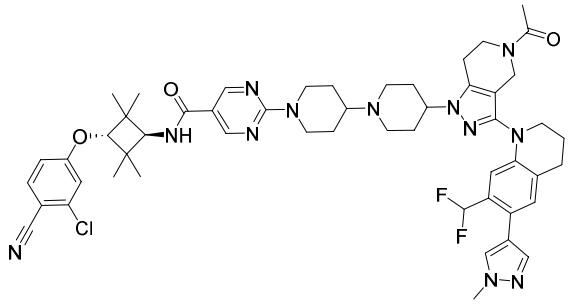
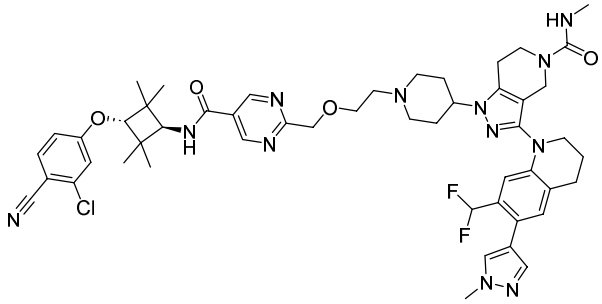
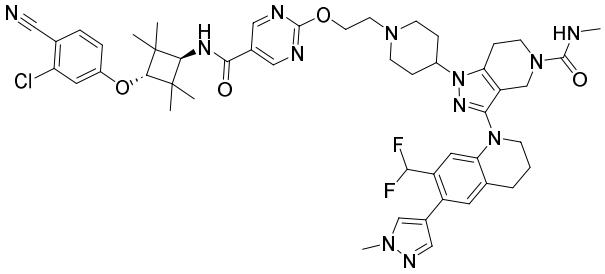
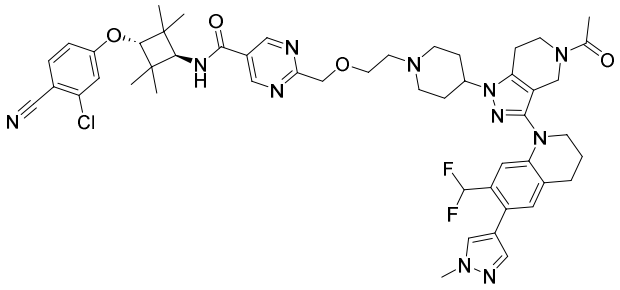
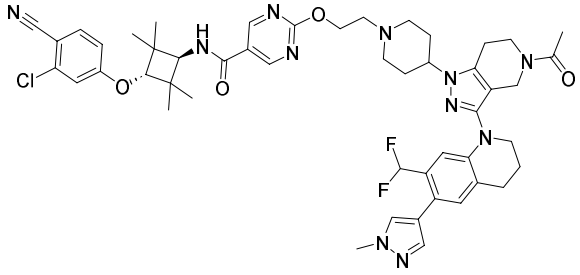
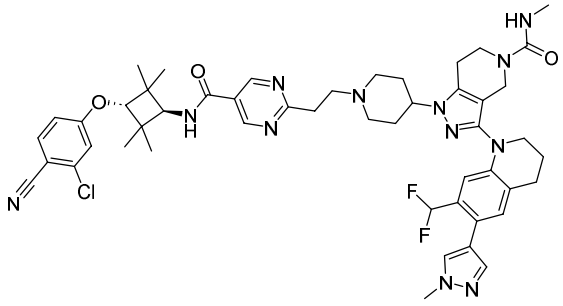
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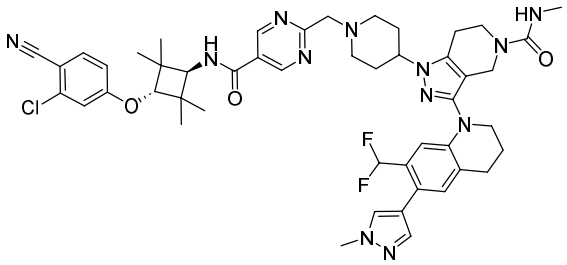
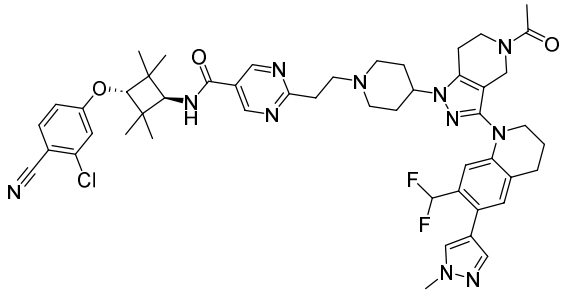
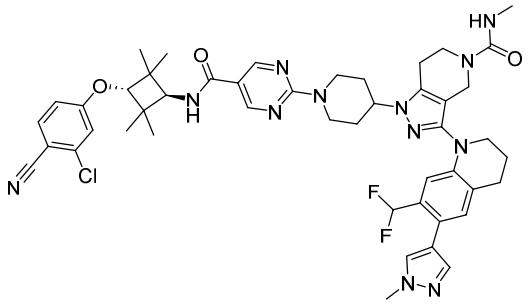
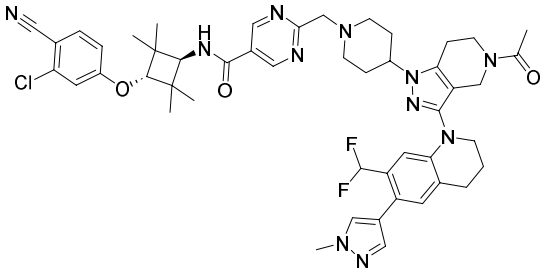
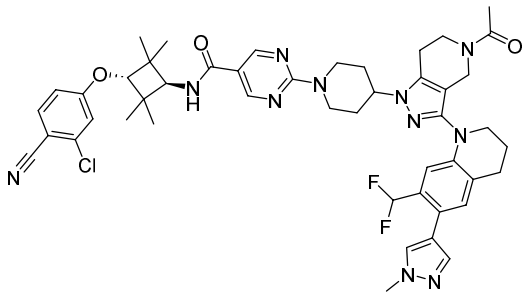
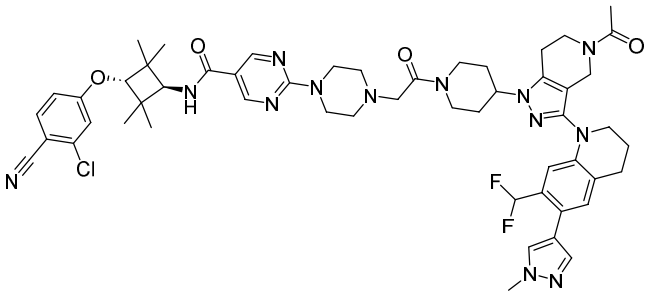
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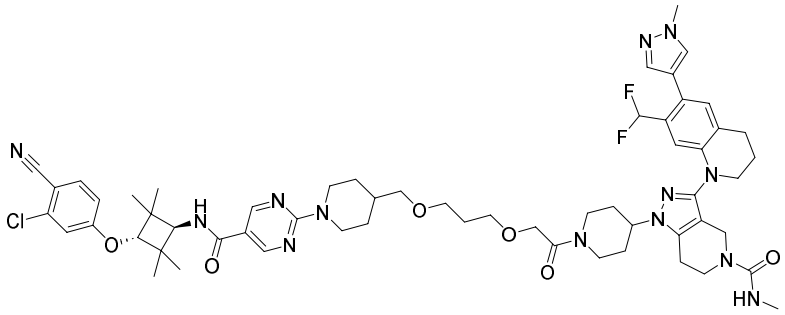
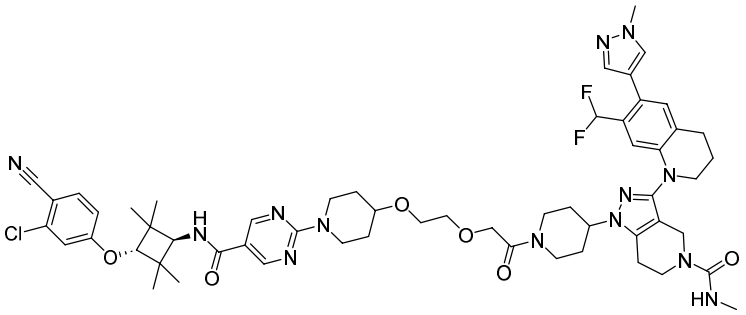
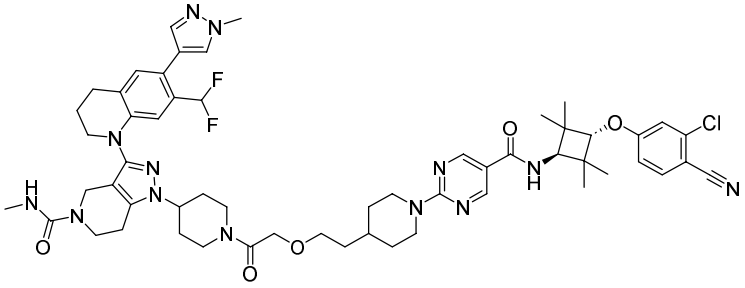
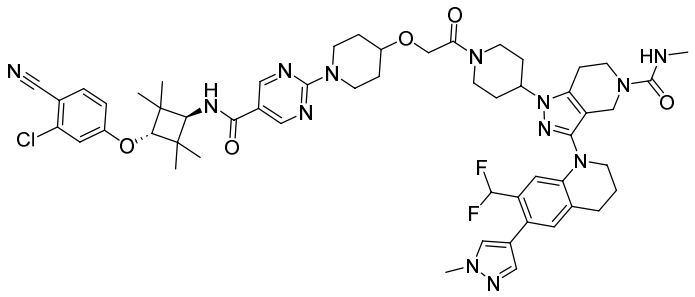
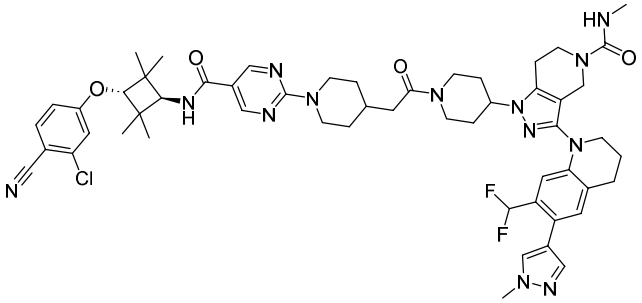
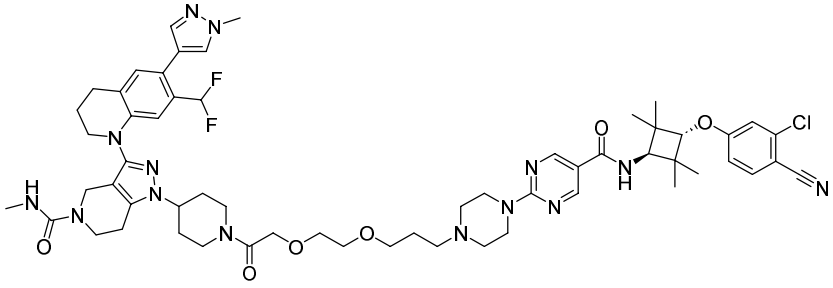
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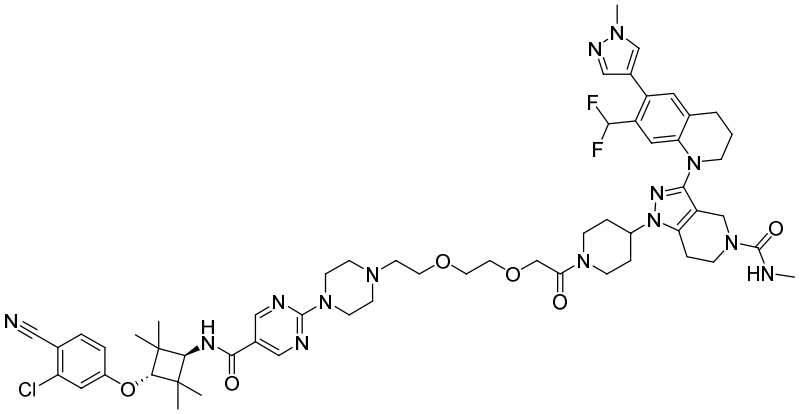
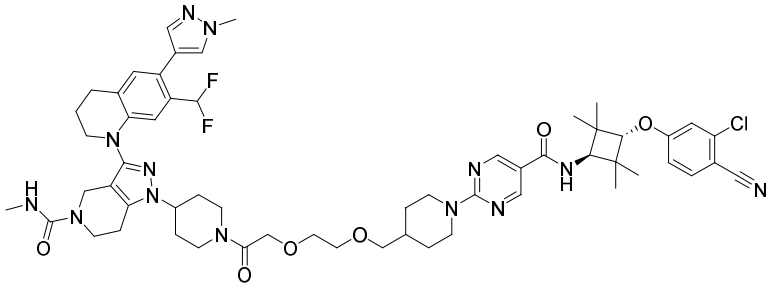
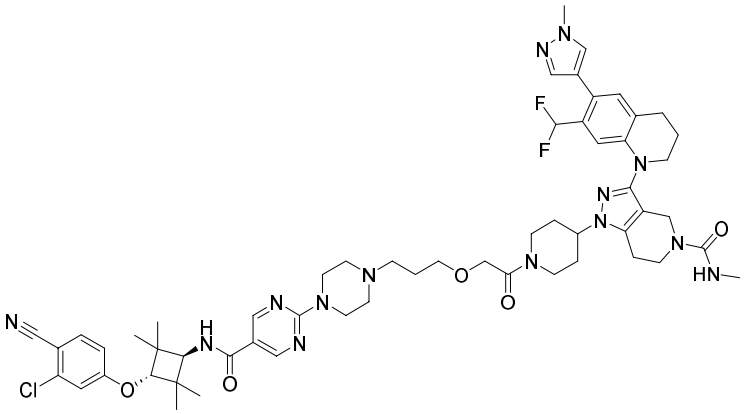
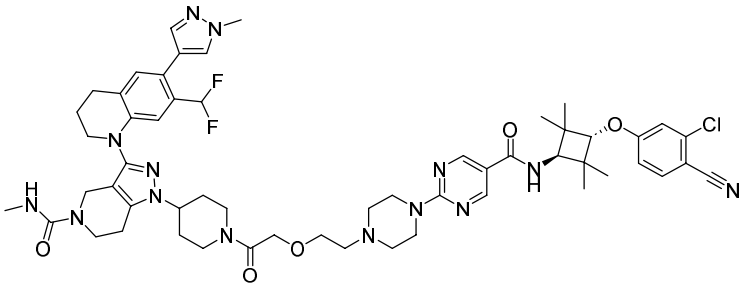
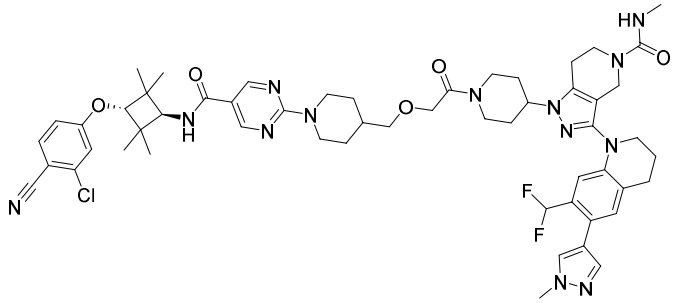
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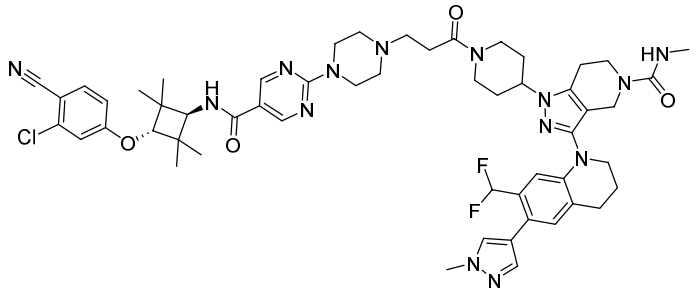
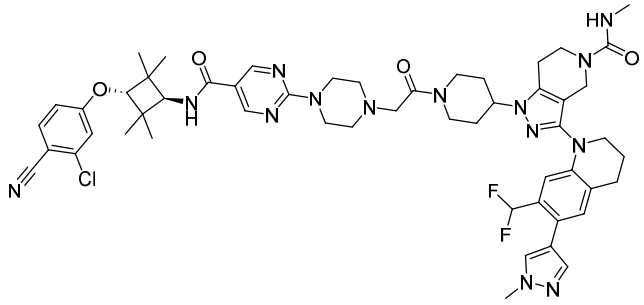
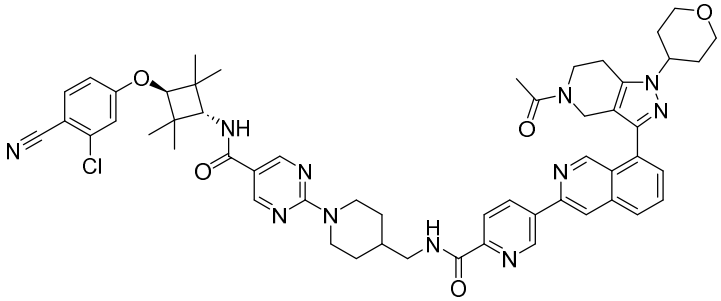
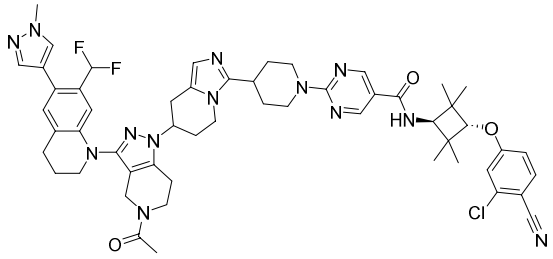
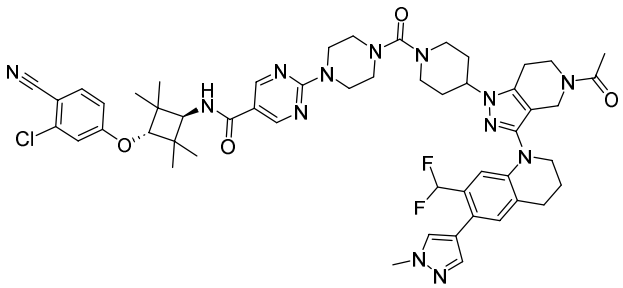
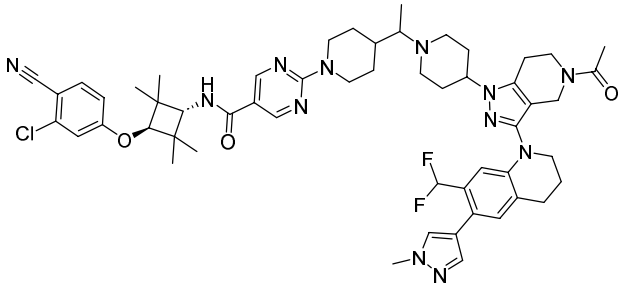
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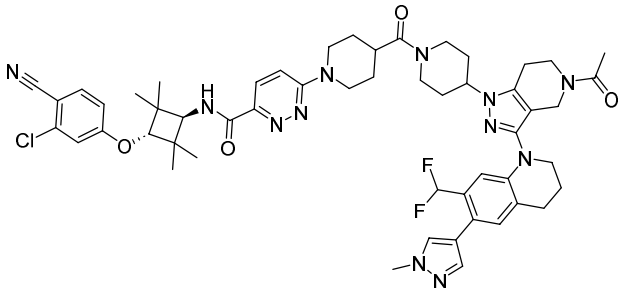
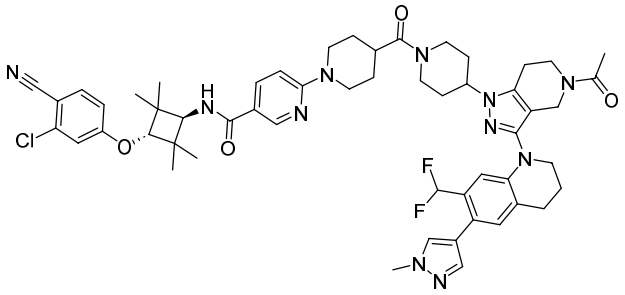
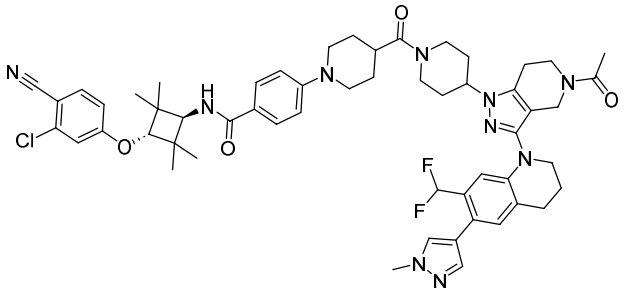
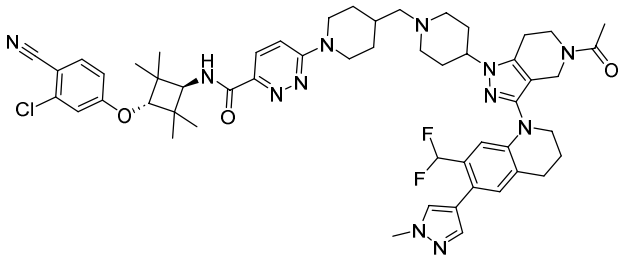
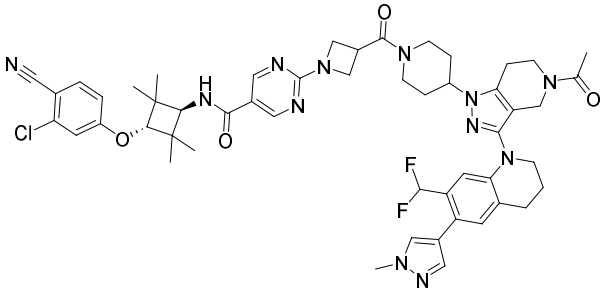
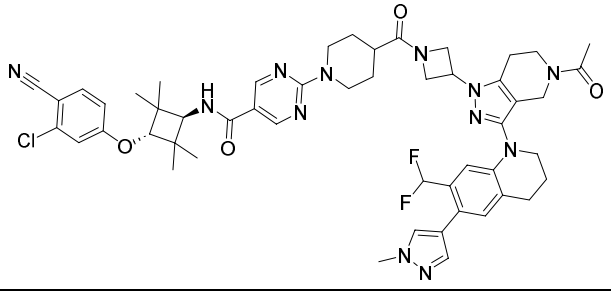
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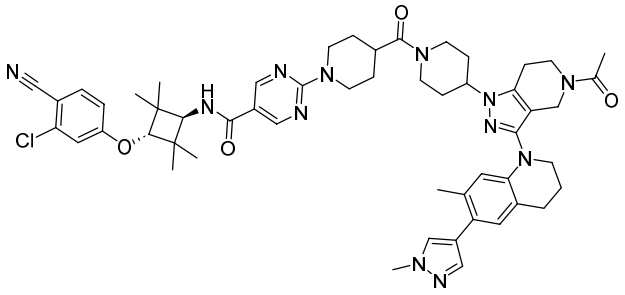
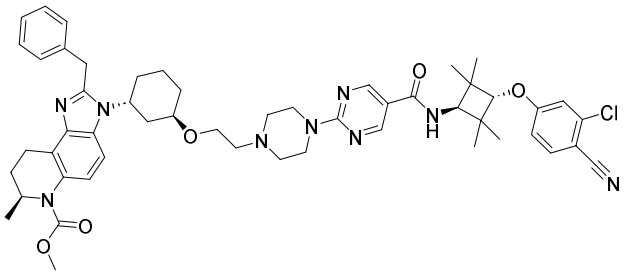
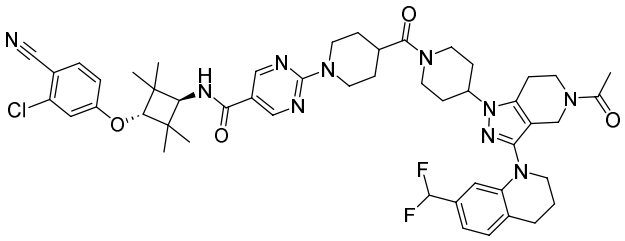
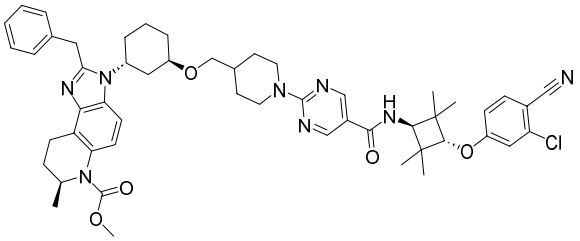
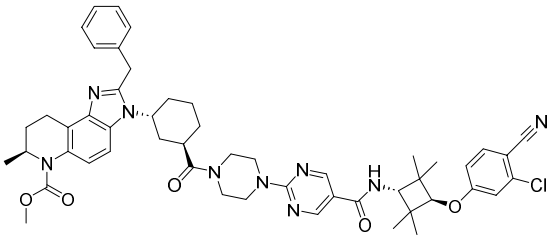
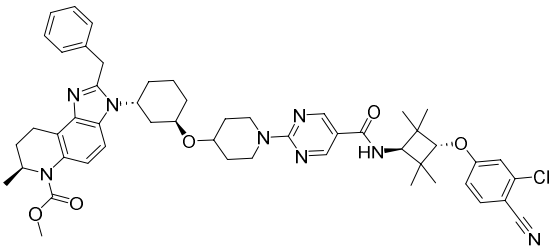
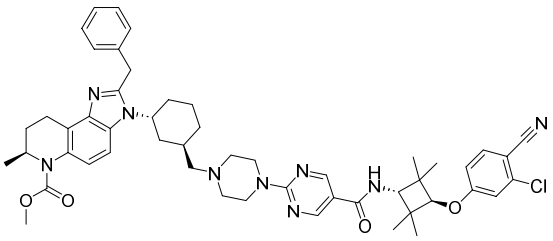
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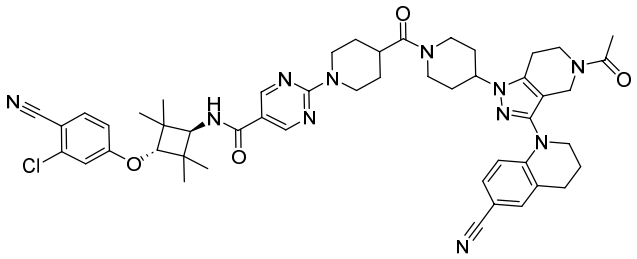
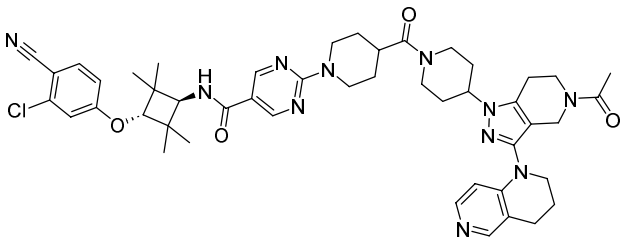
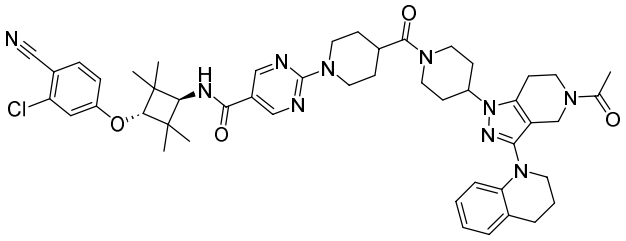
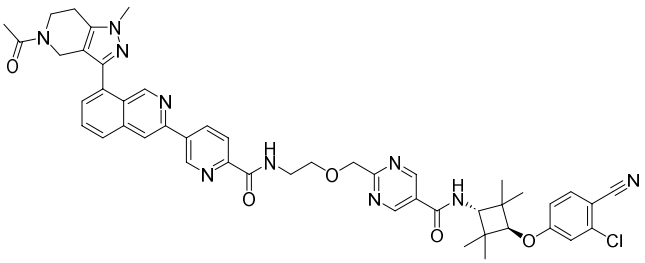
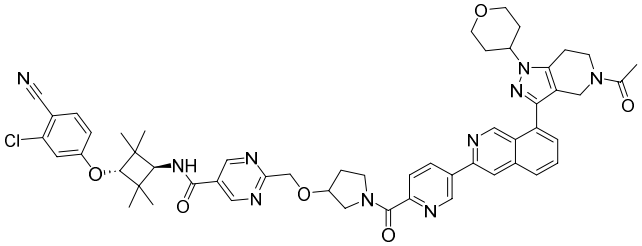
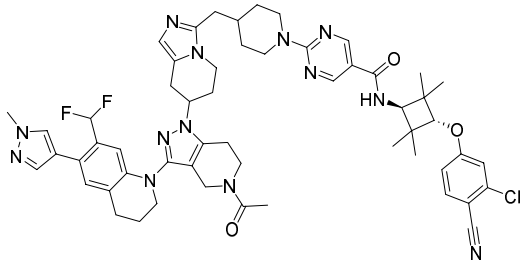
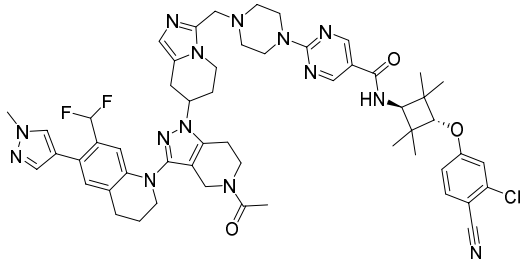
Compound	Structure
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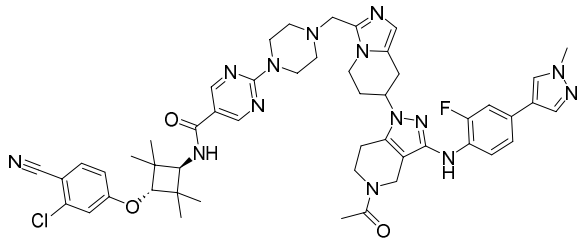
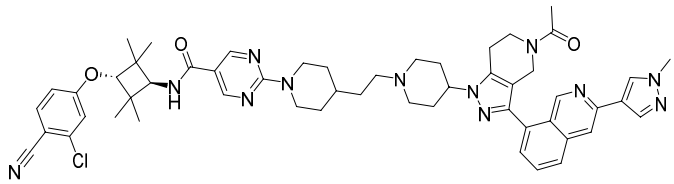
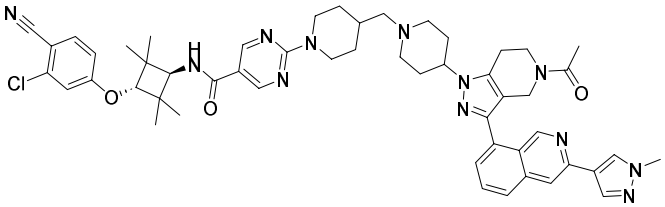
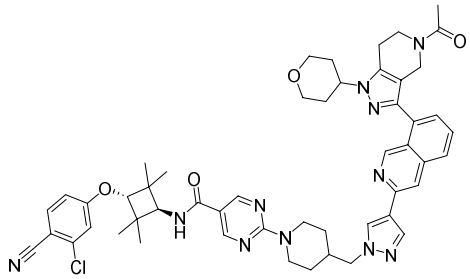
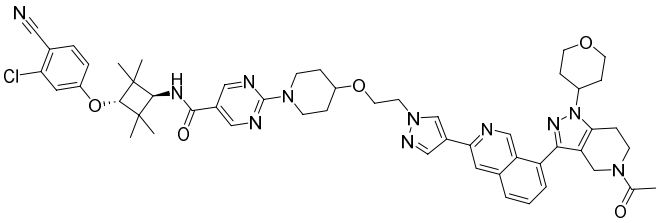
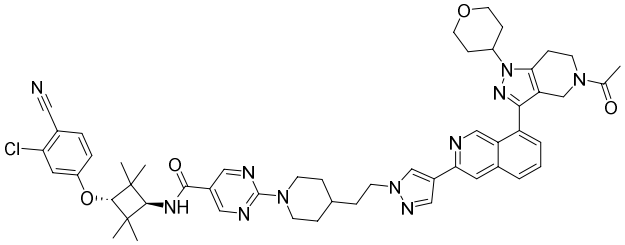
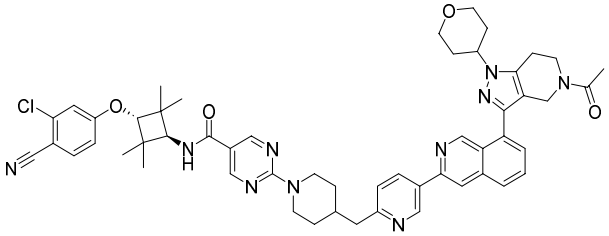
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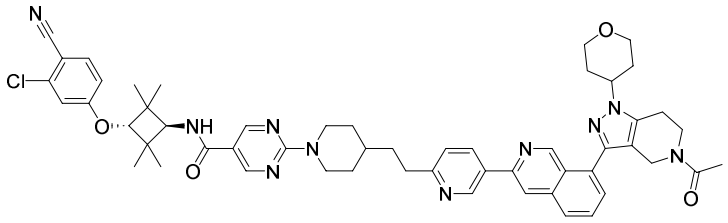
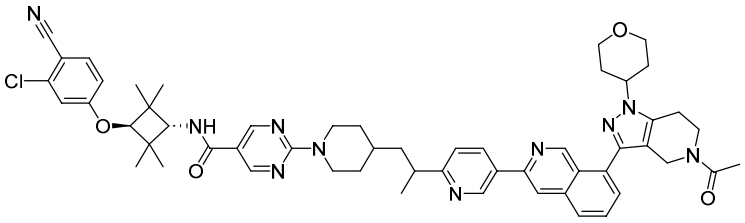
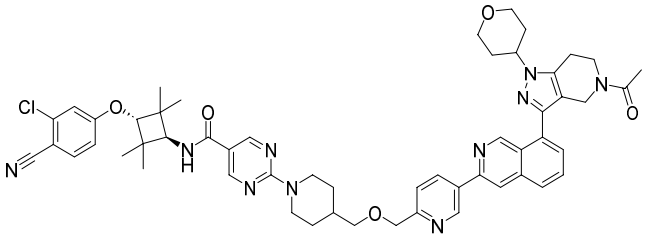
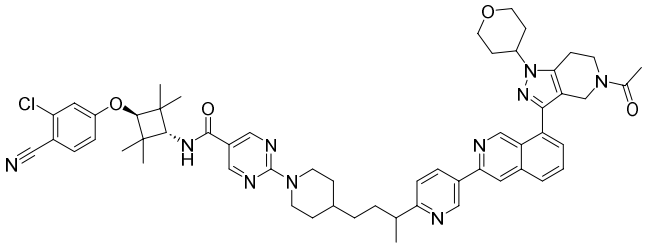
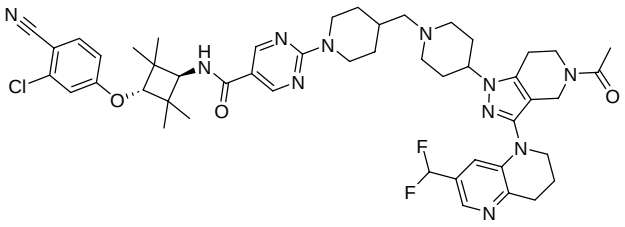
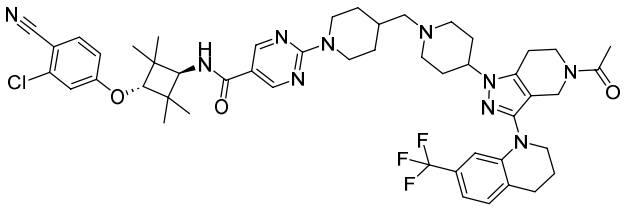
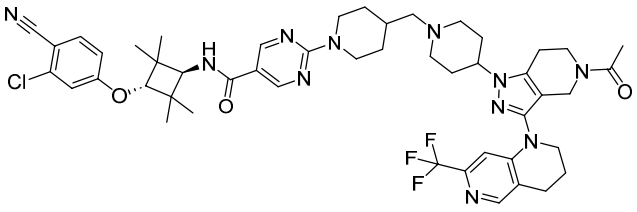
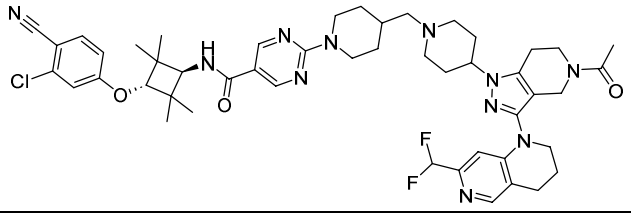
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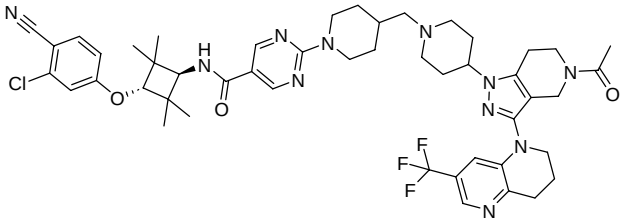
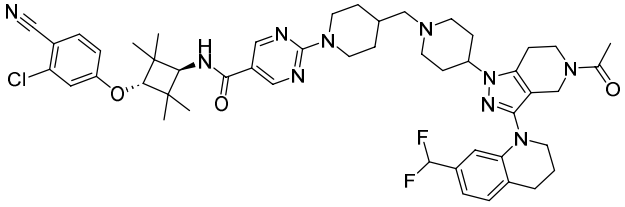
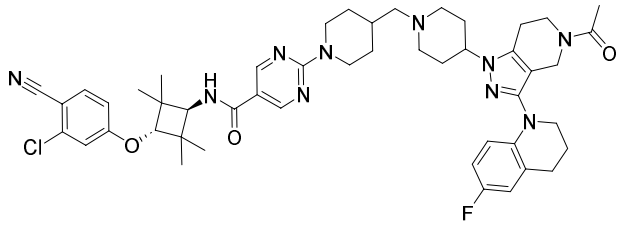
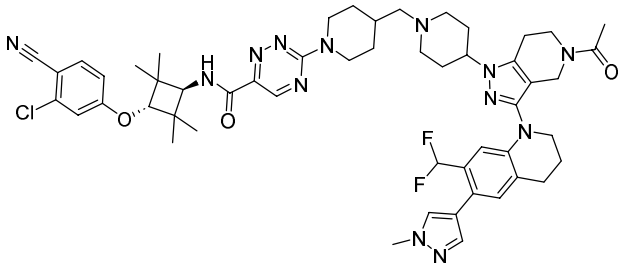
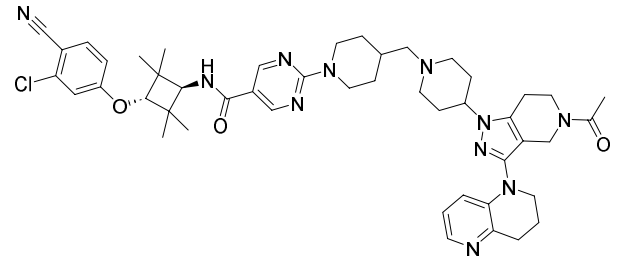
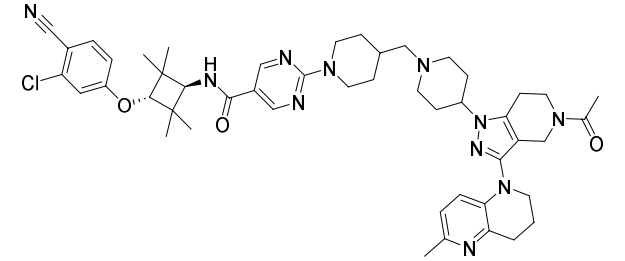
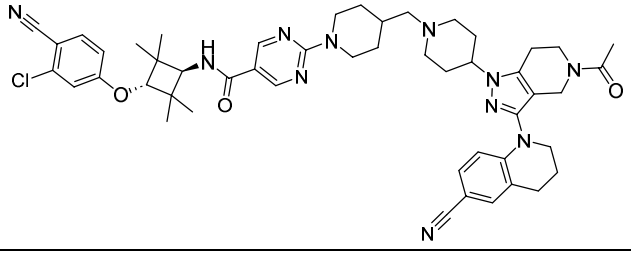
Compound	Structure
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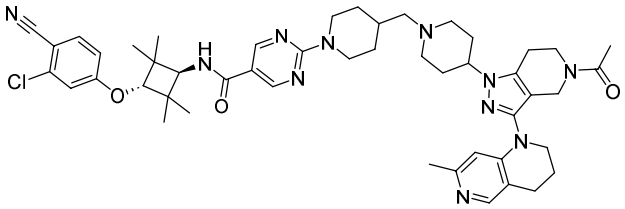
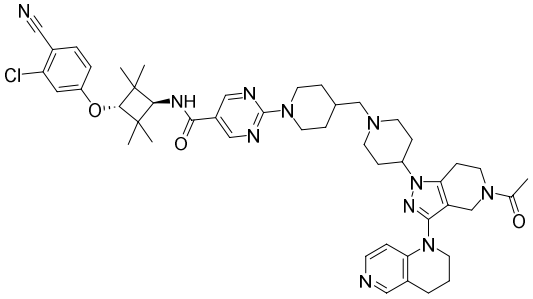
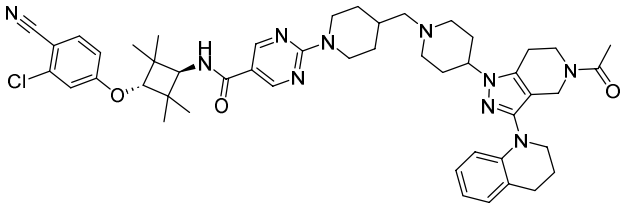
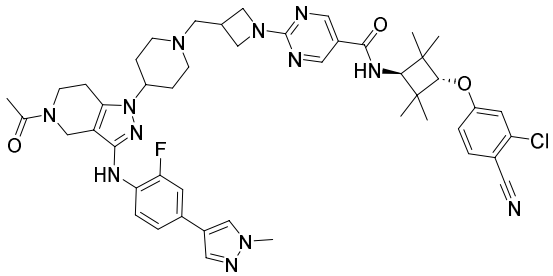
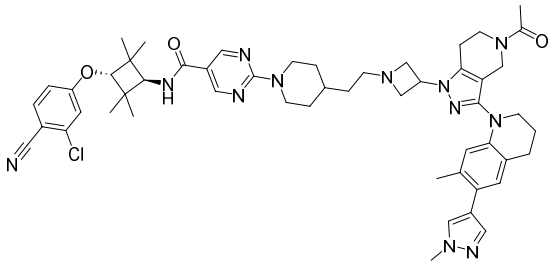
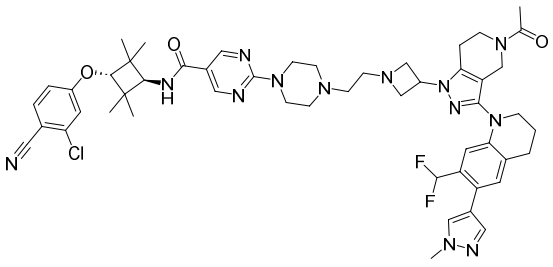
Compound	Structure
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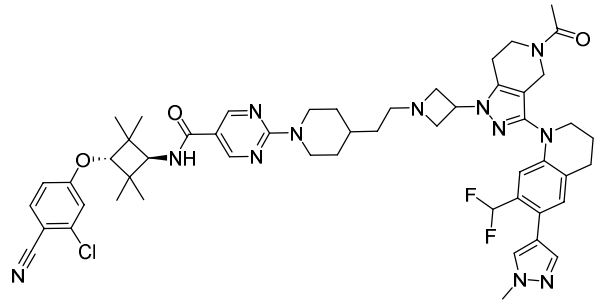
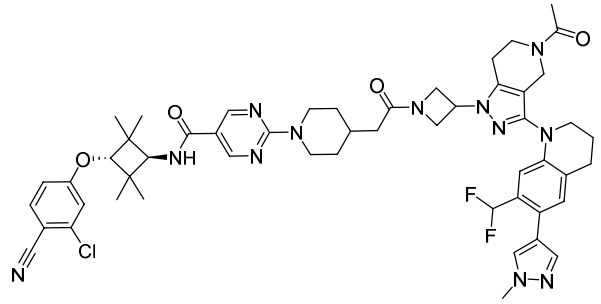
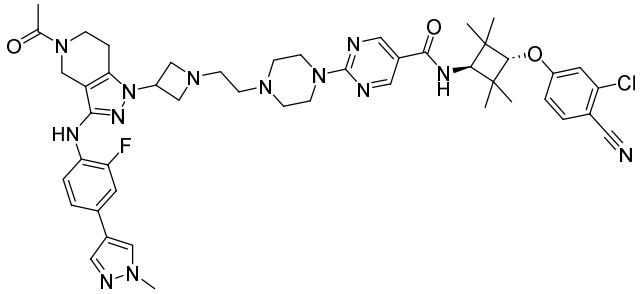
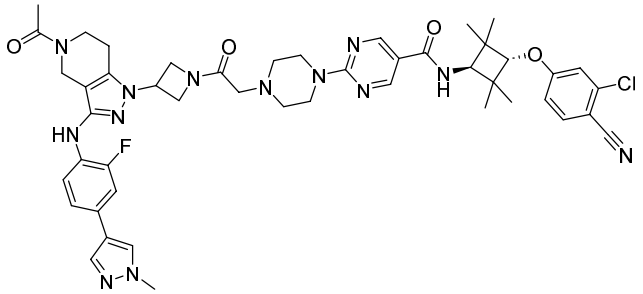
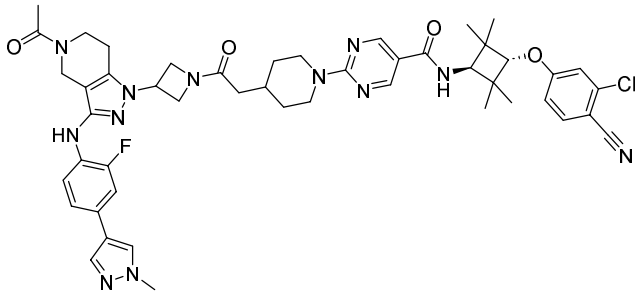
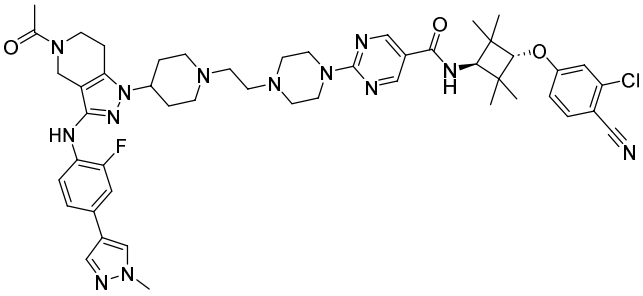
Compound	Structure
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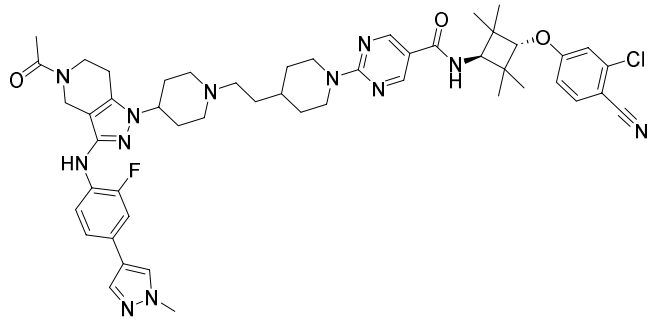
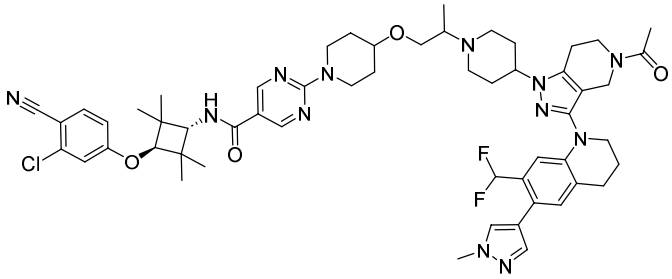
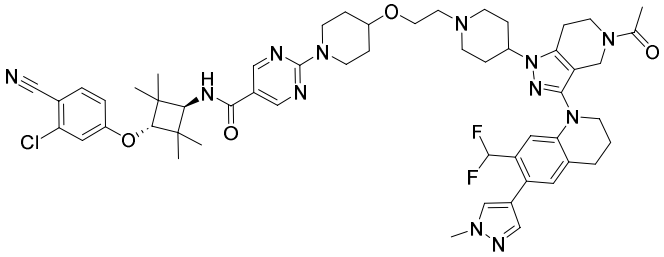
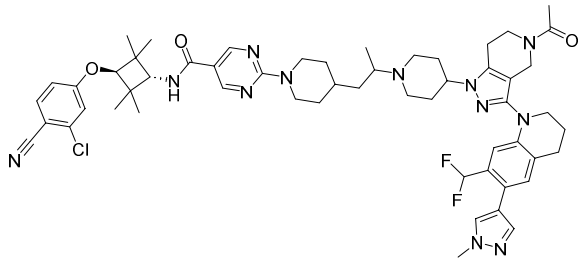
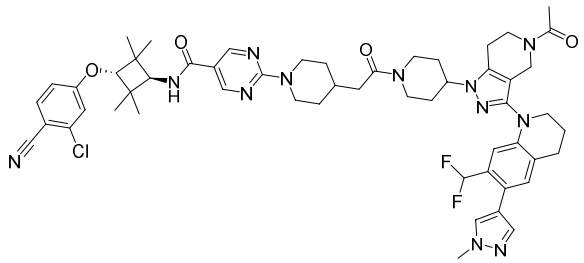
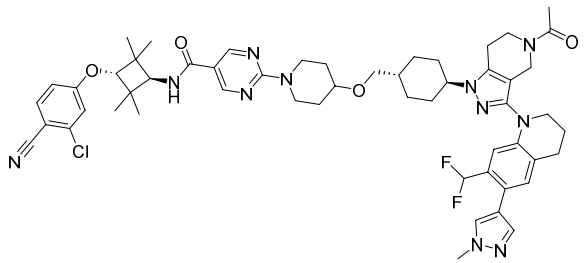
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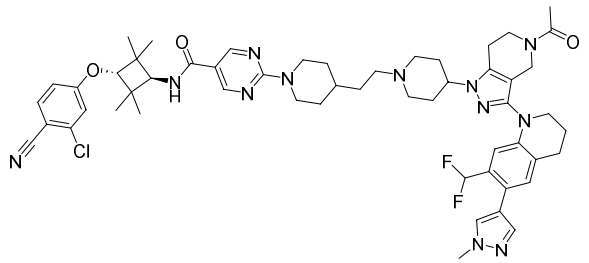
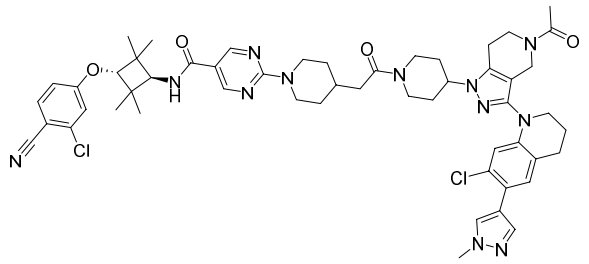
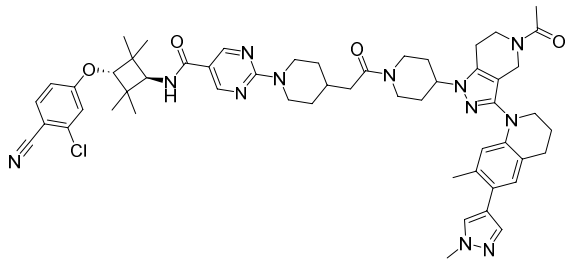
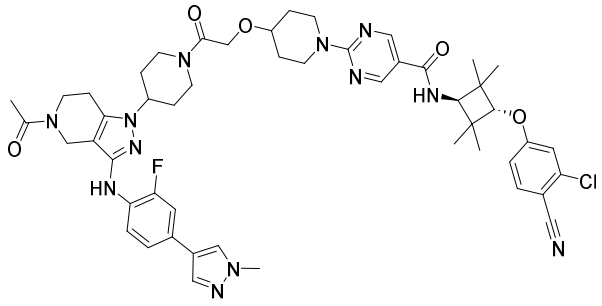
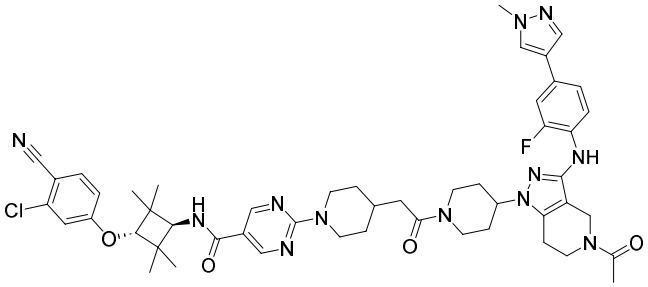
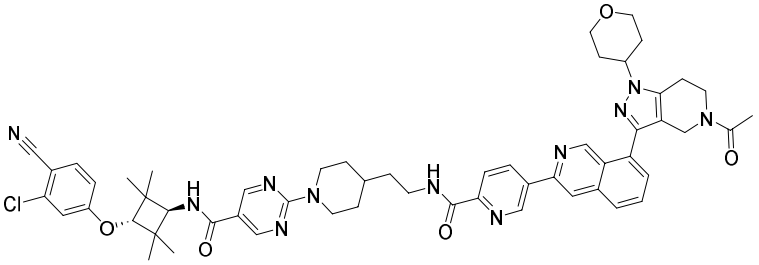
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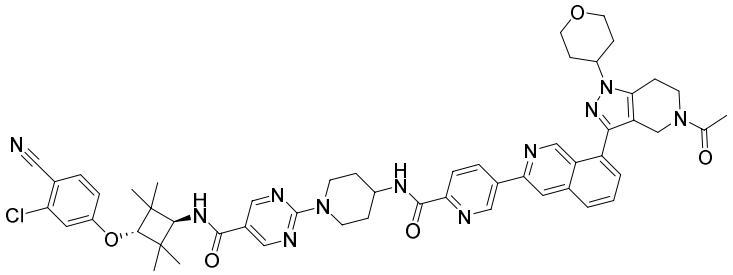
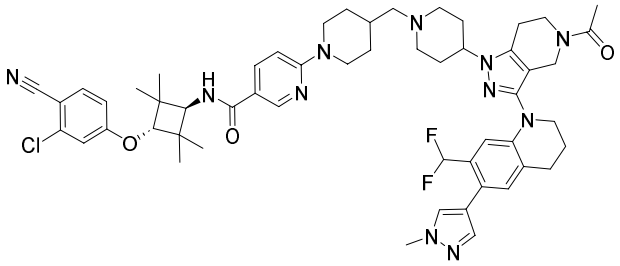
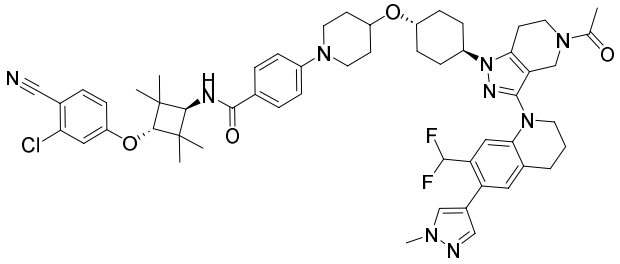
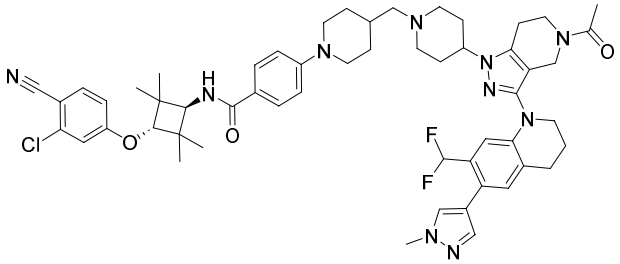
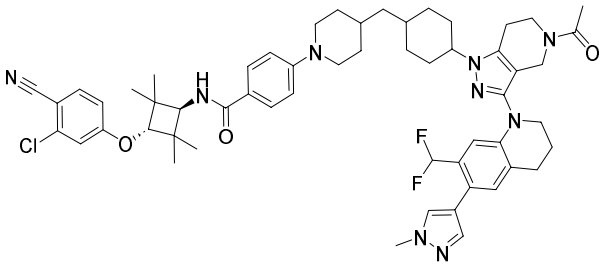
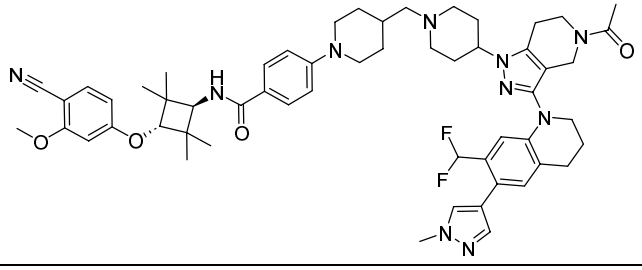
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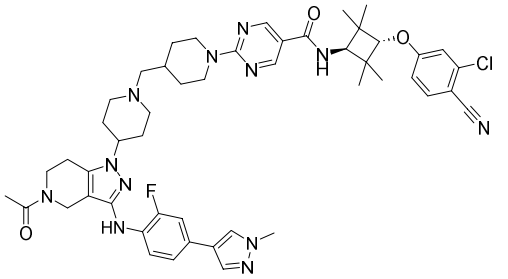
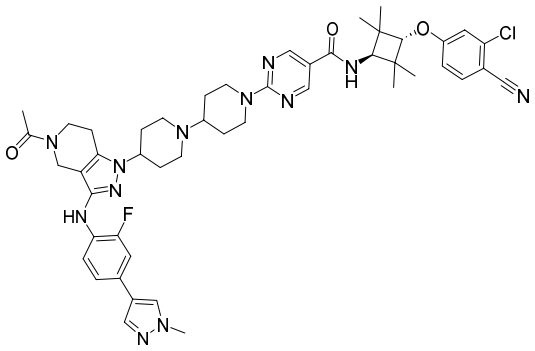
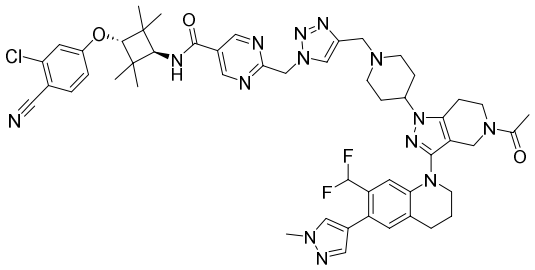
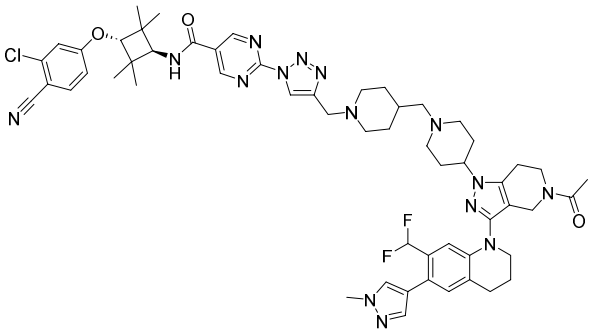
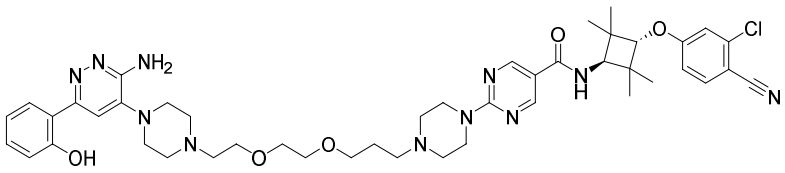
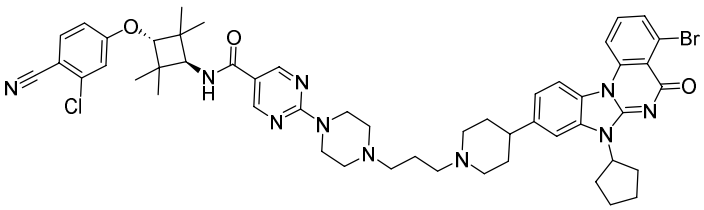
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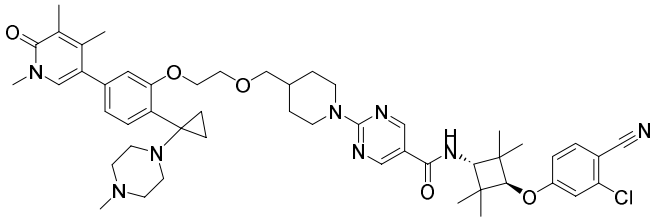
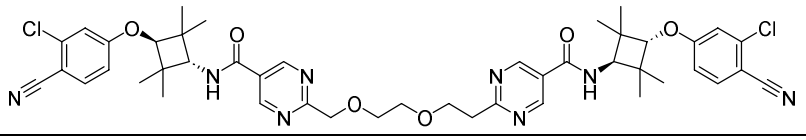
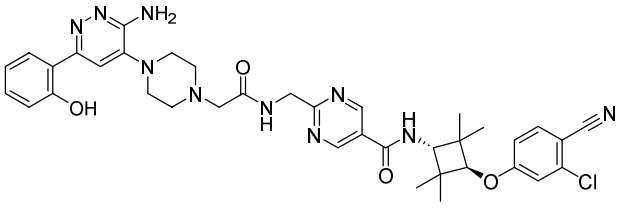
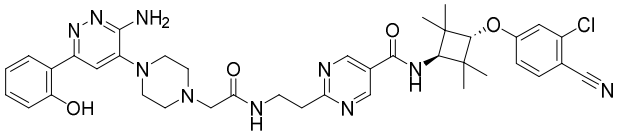
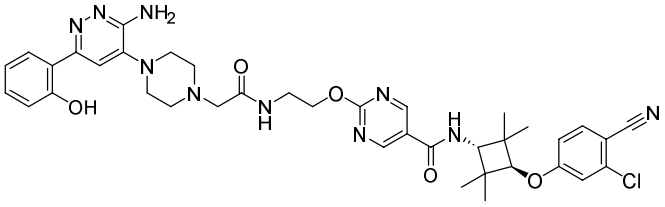
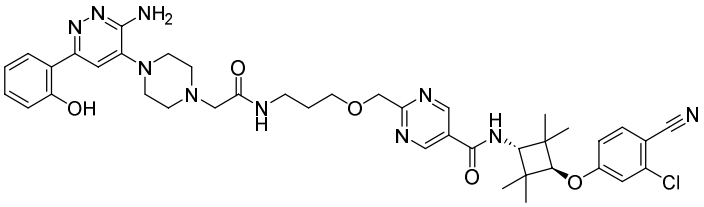
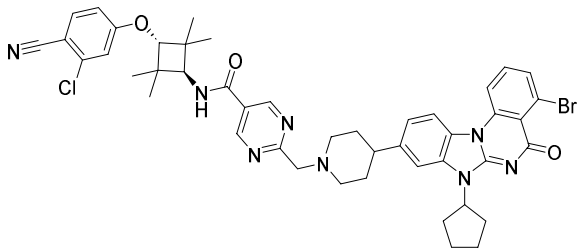
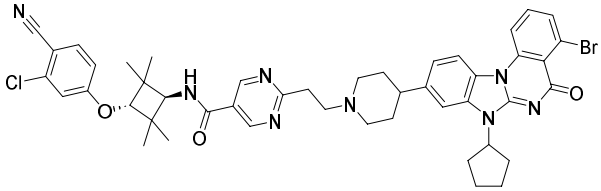
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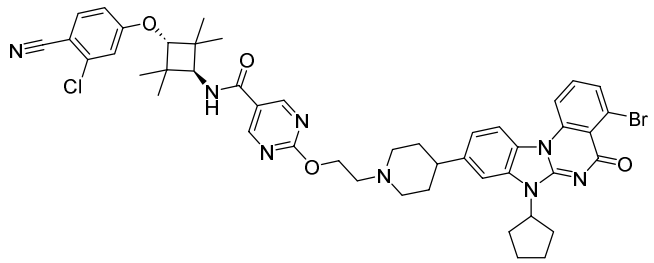
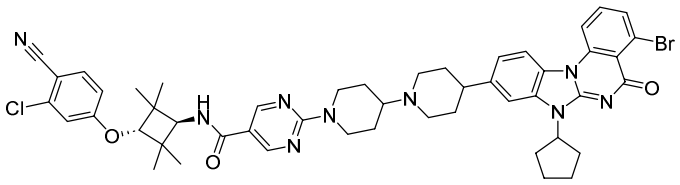
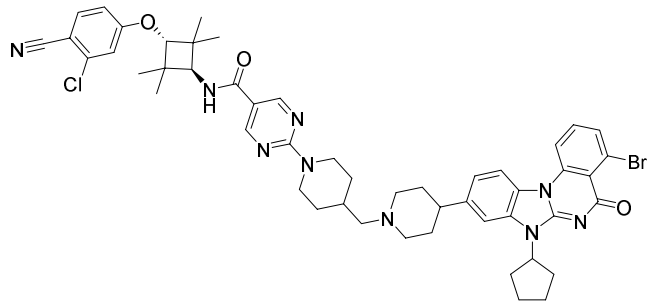
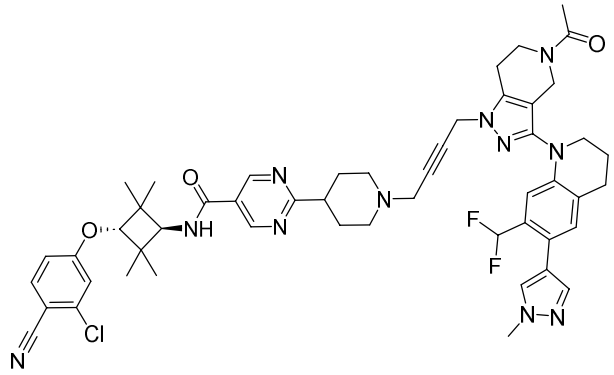
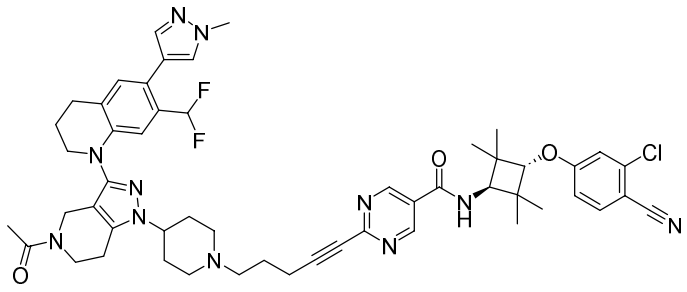
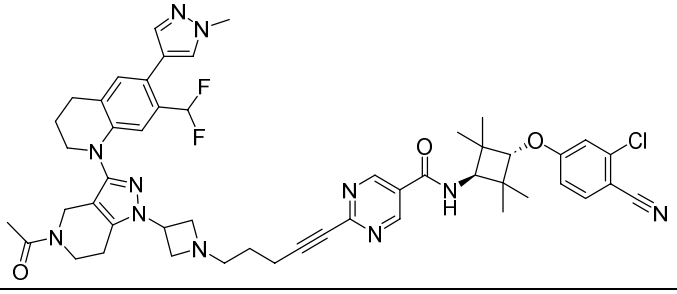
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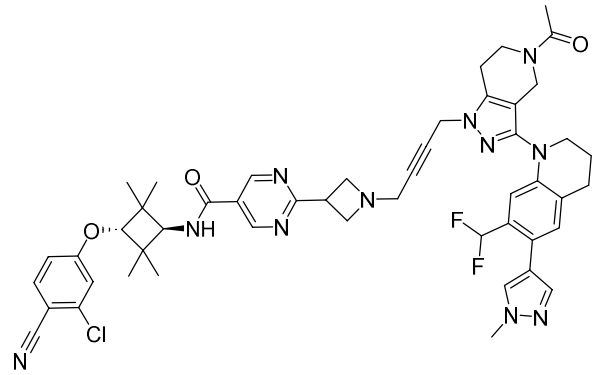
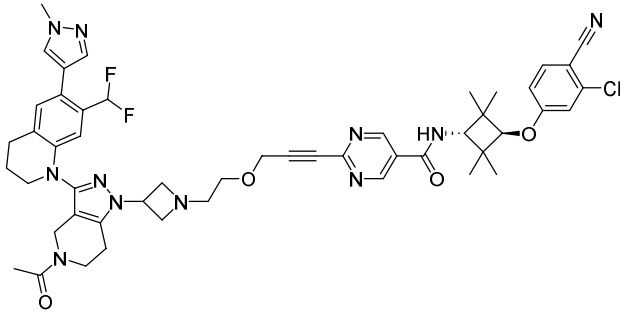
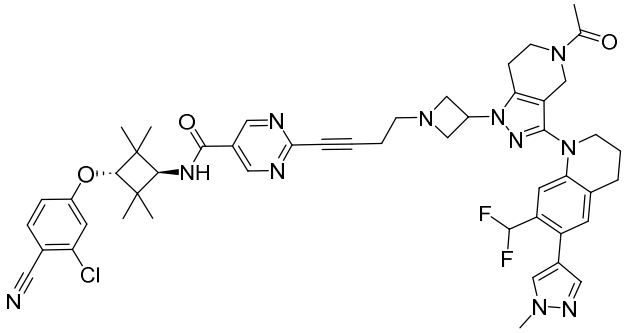
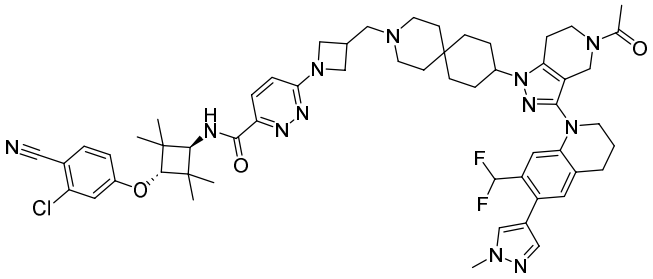
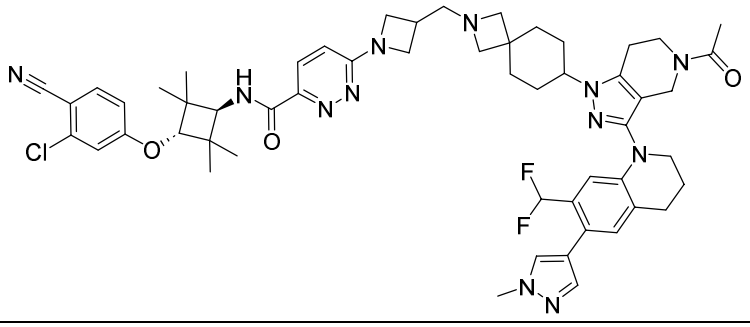
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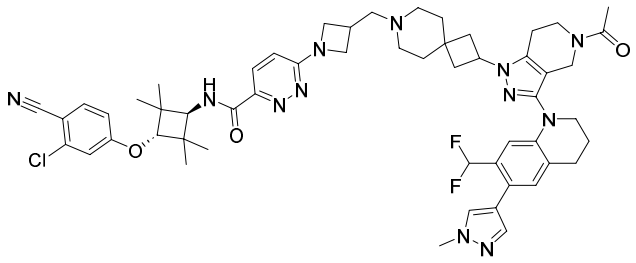
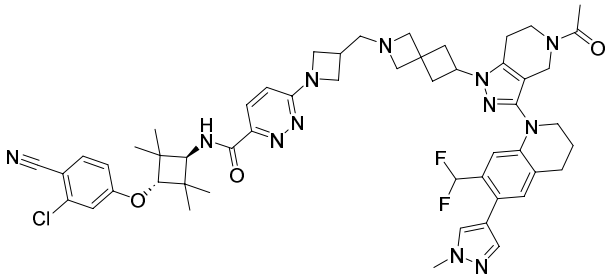
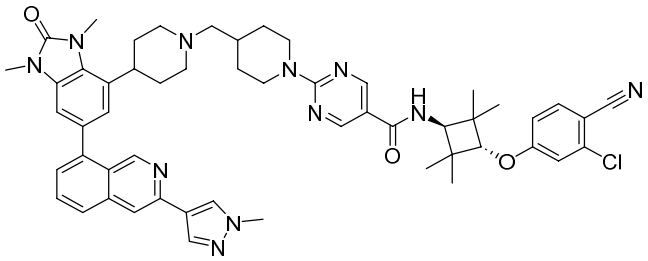
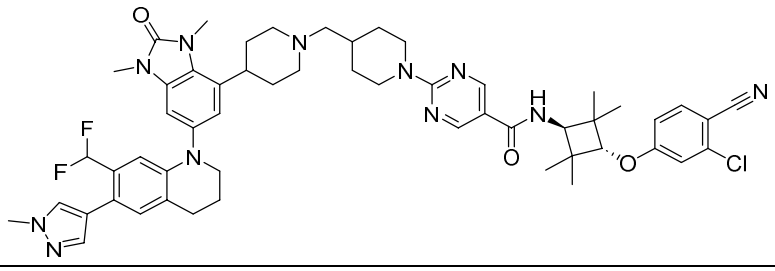
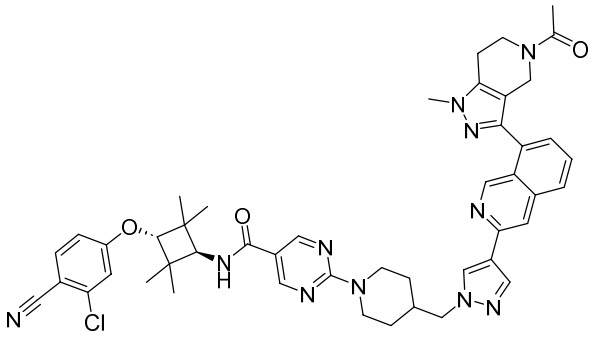
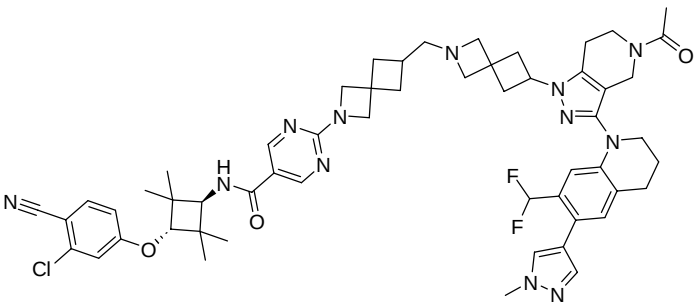
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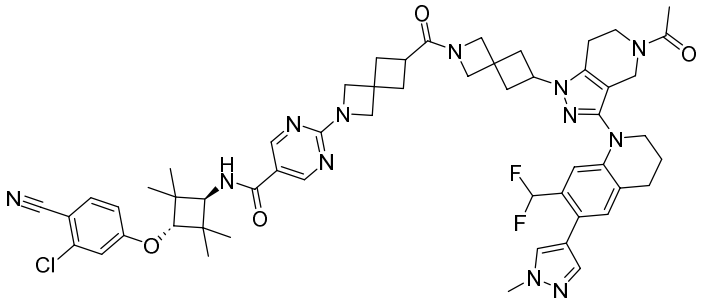
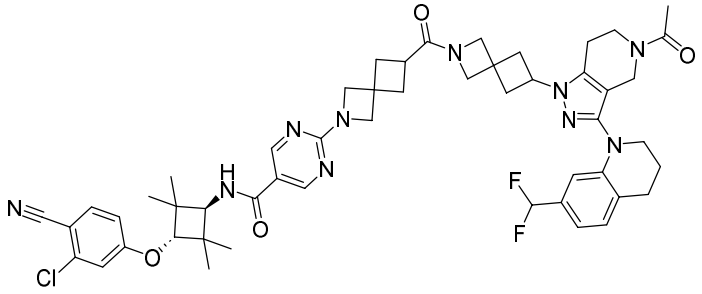
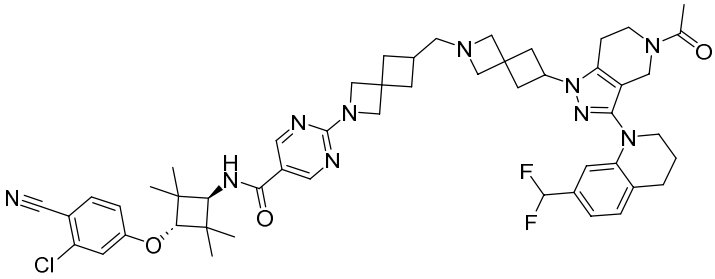
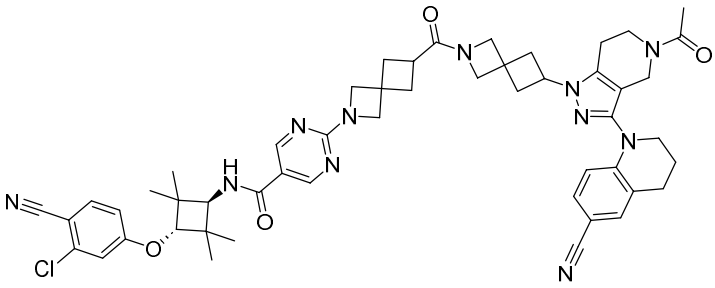
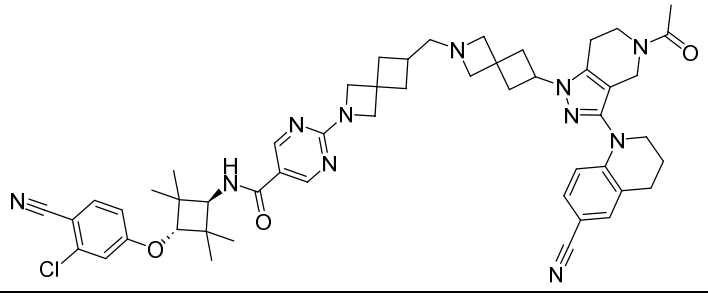
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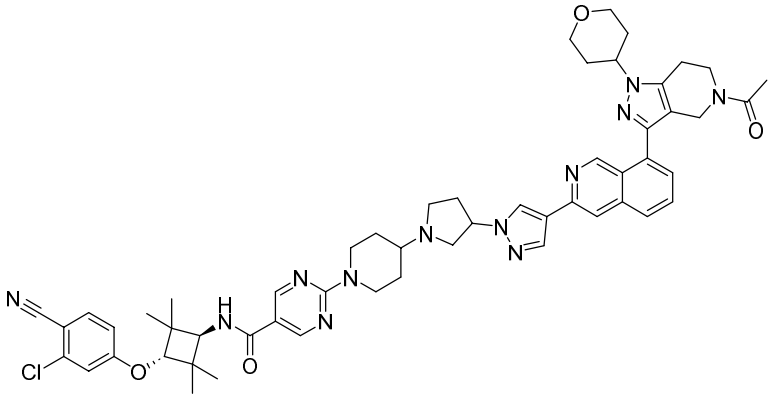
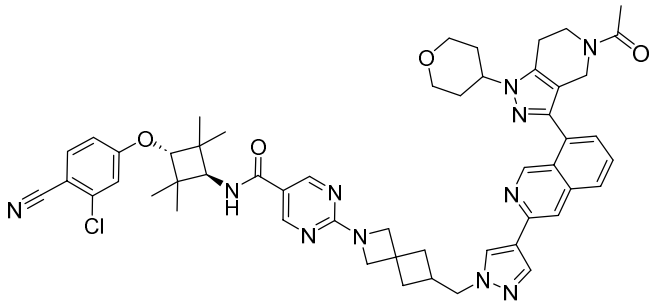
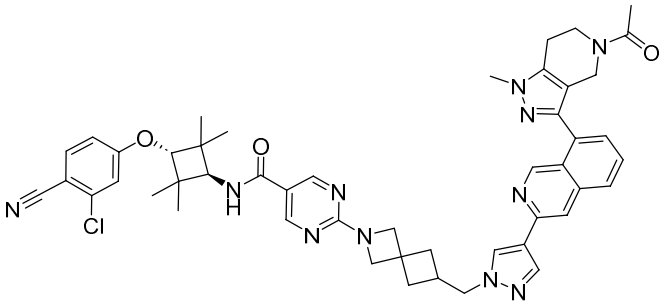
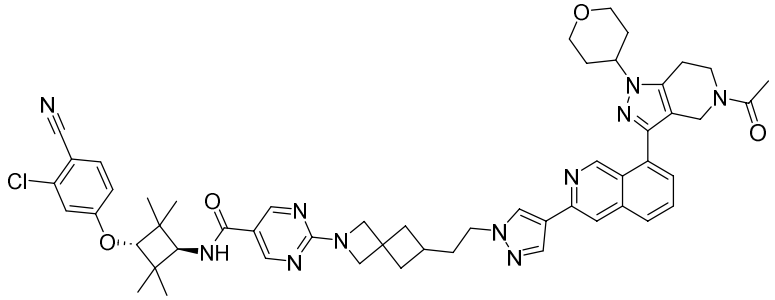
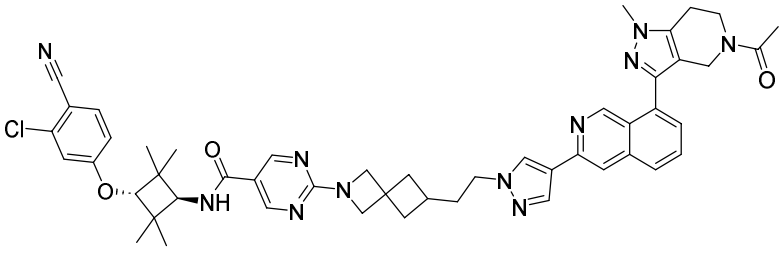
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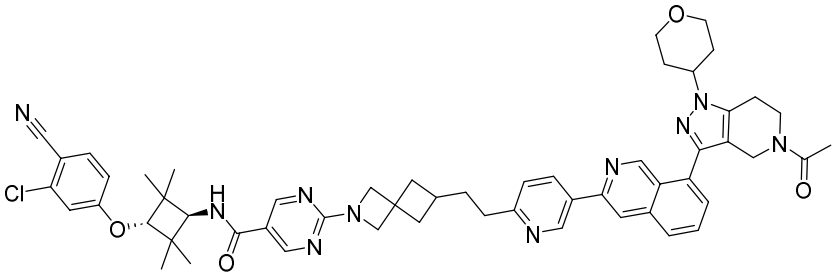
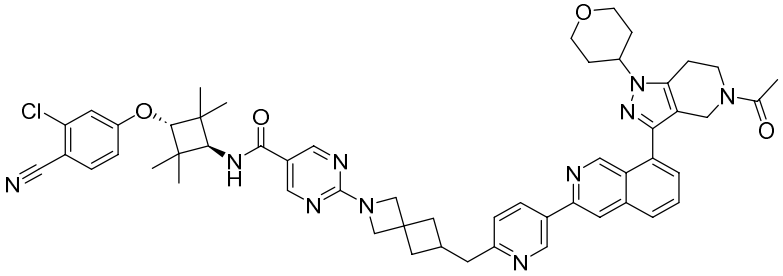
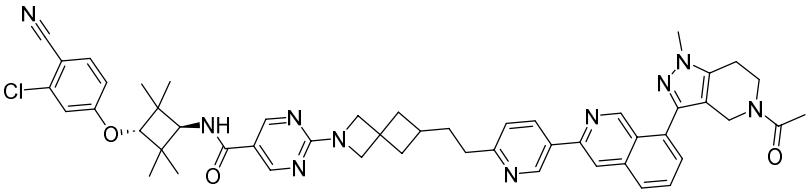
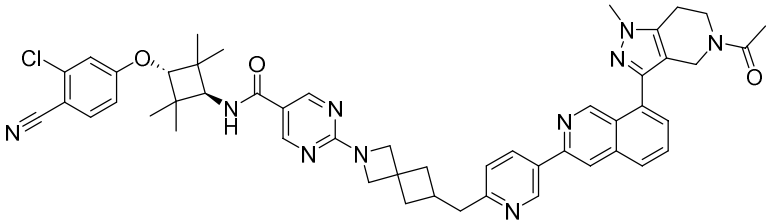
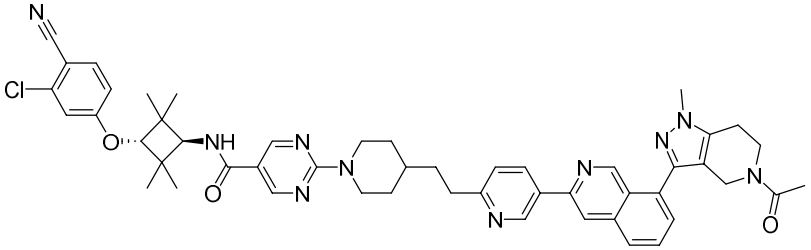
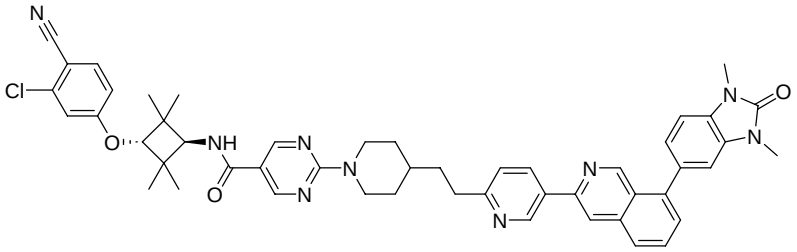
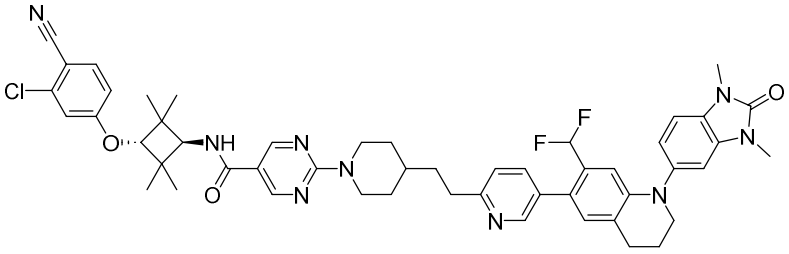
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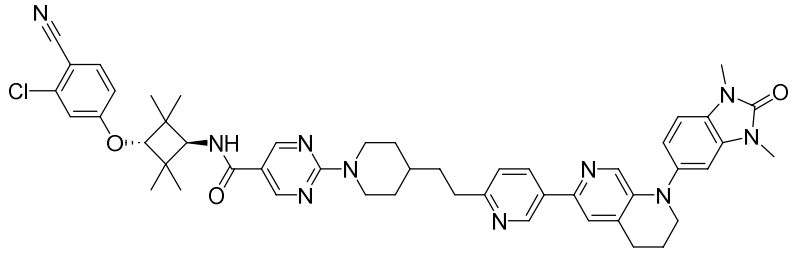
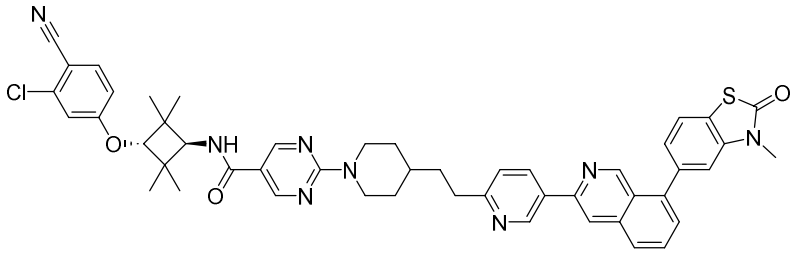
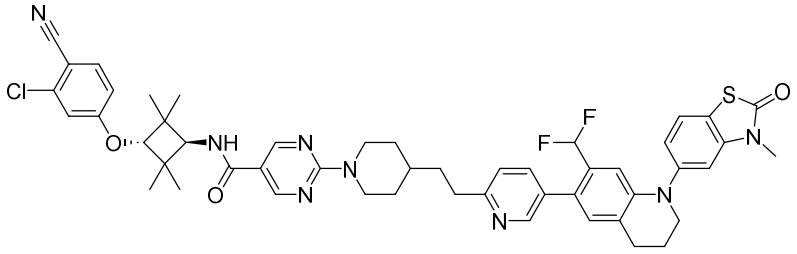
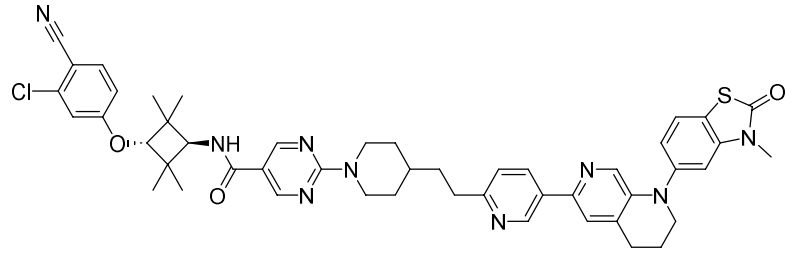
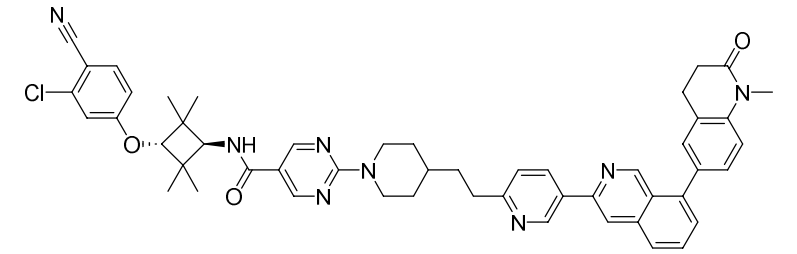
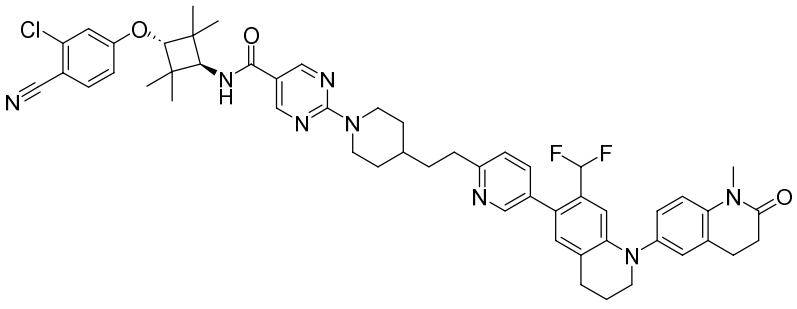
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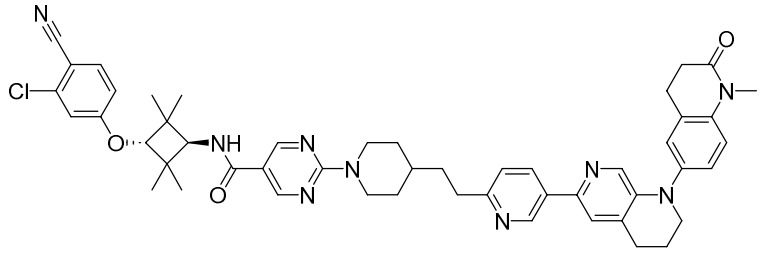
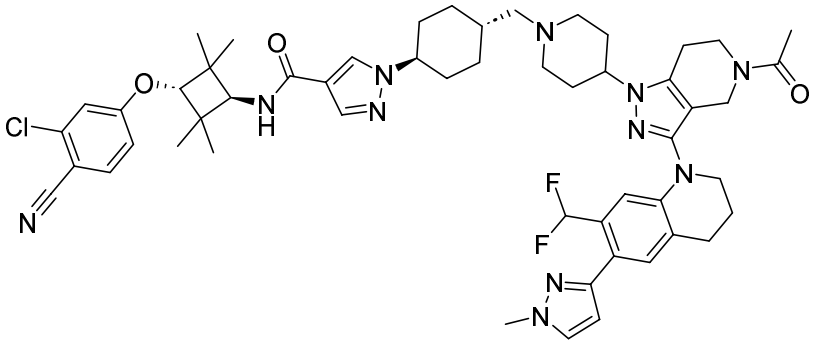
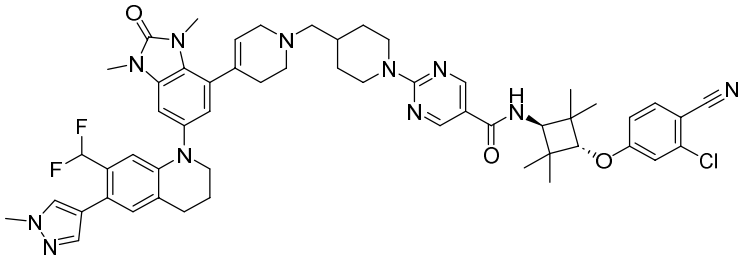
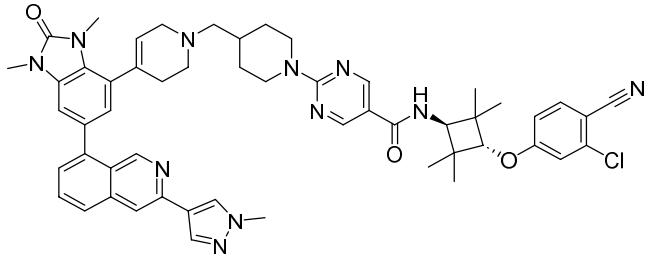
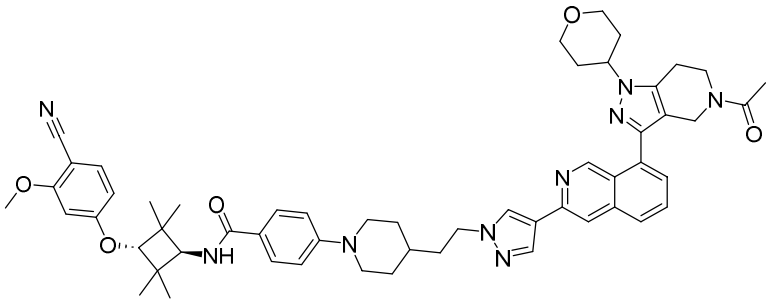
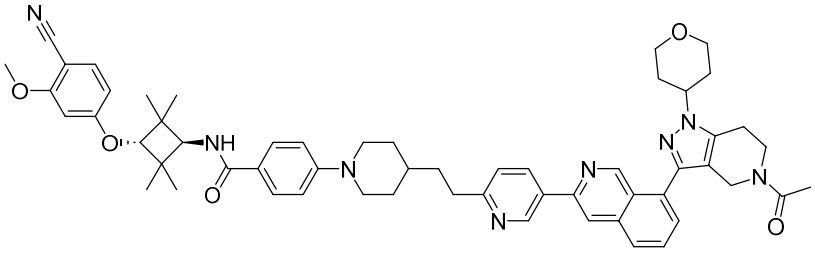
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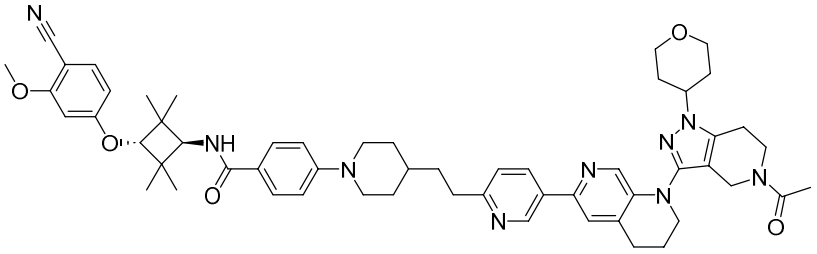
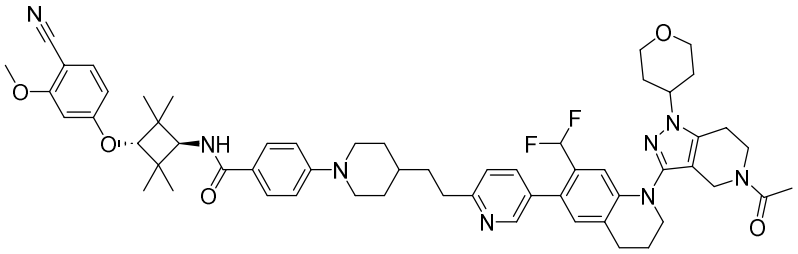
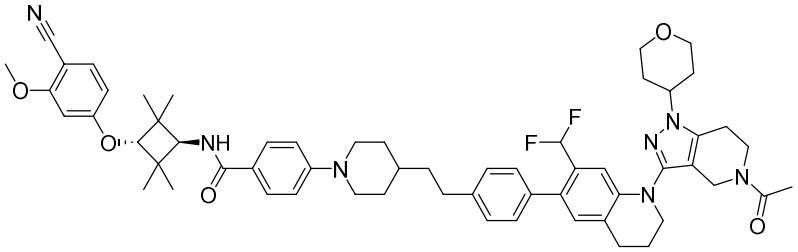
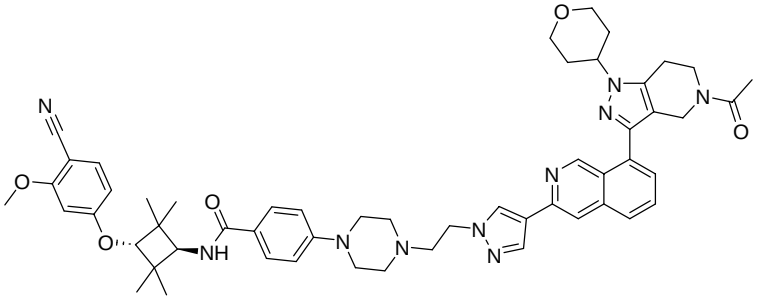
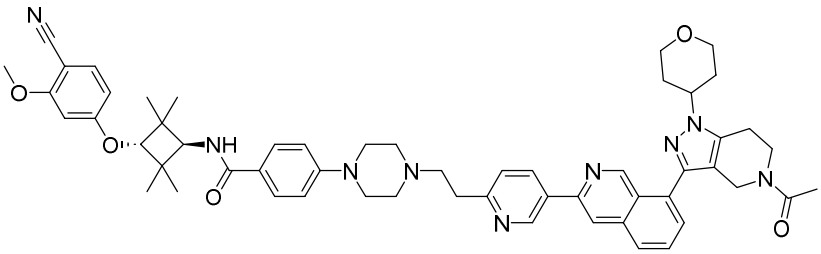
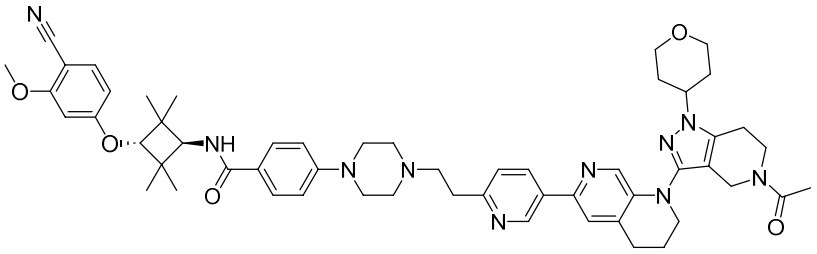
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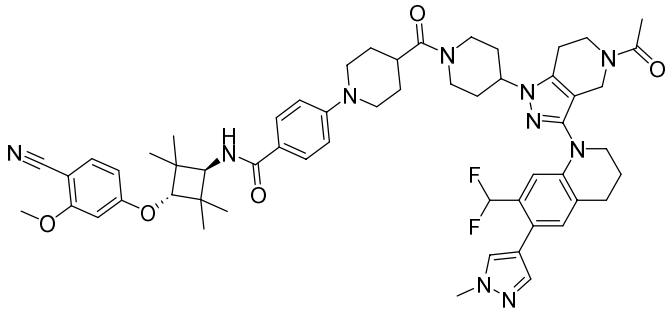
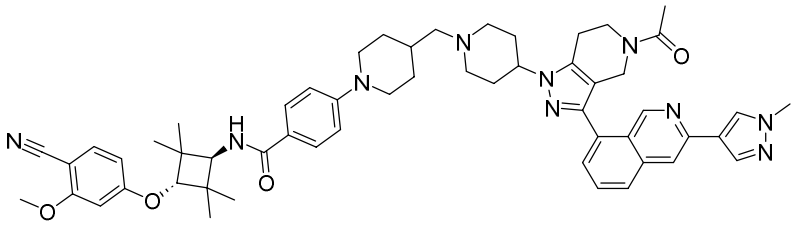
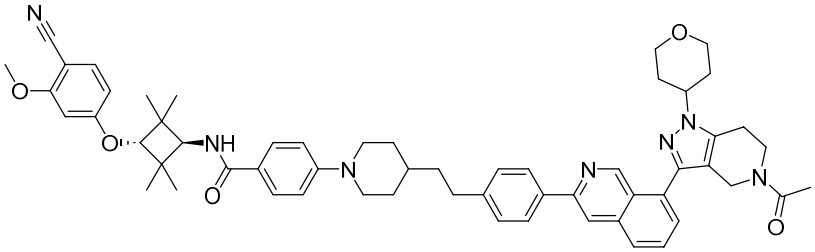
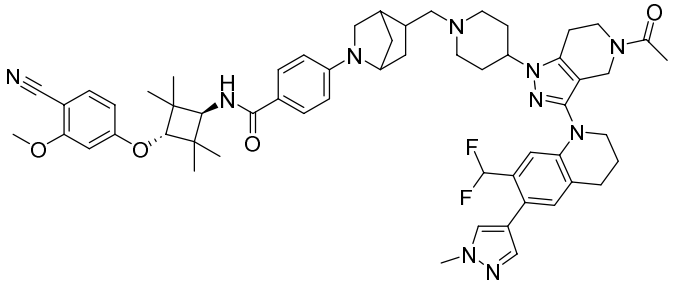
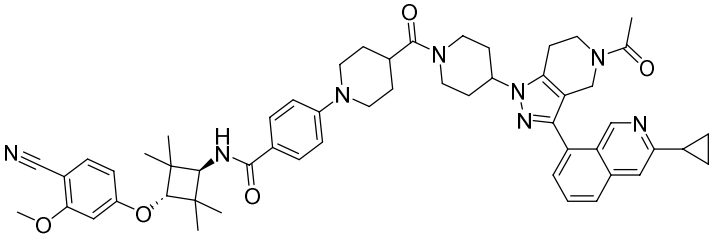
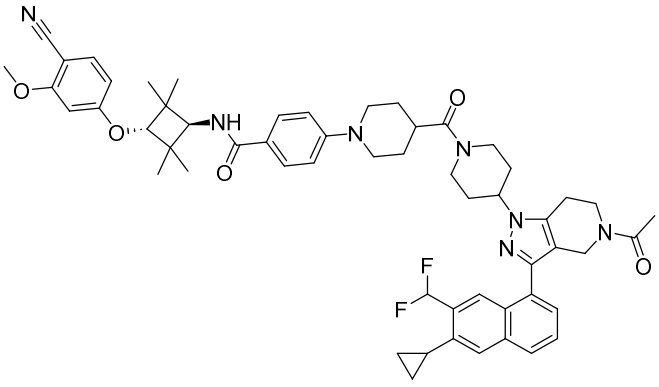
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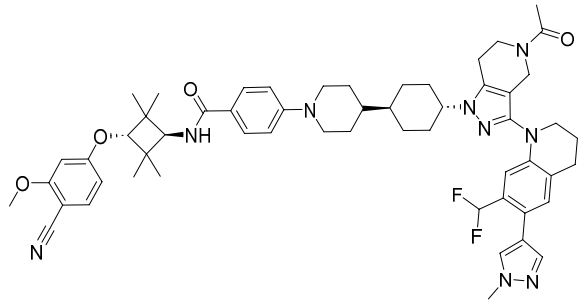
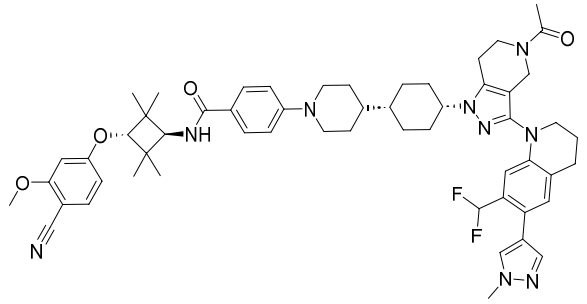
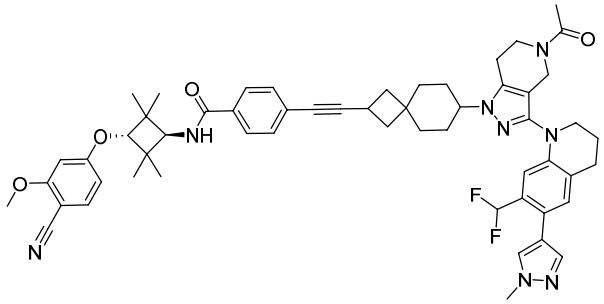
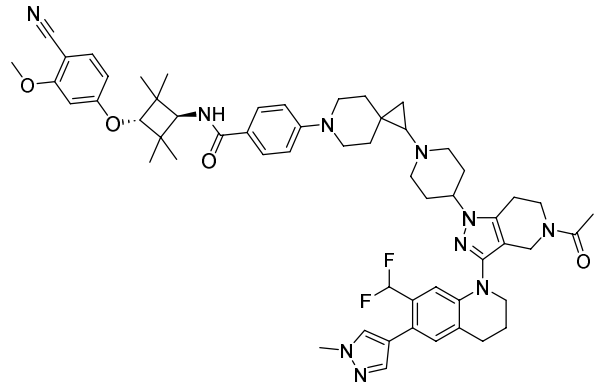
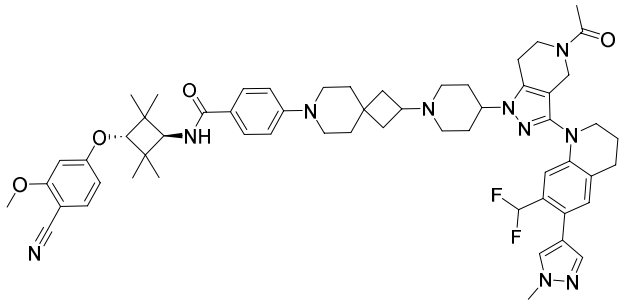
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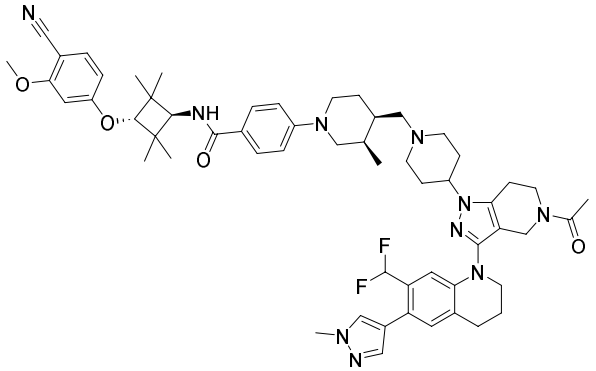
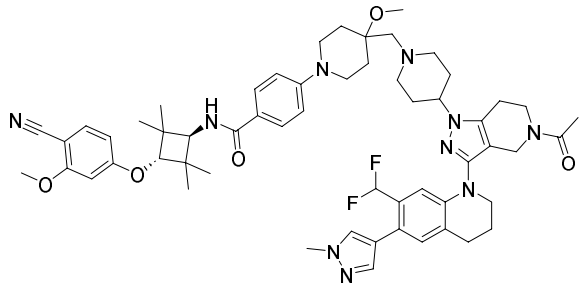
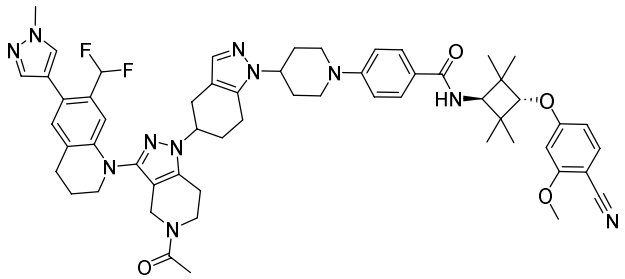
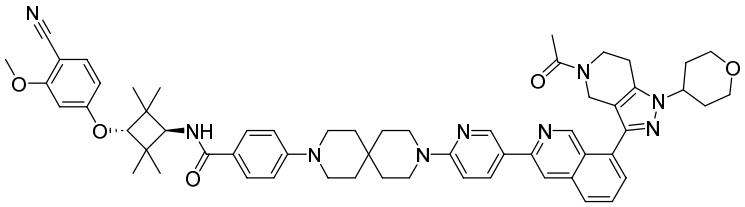
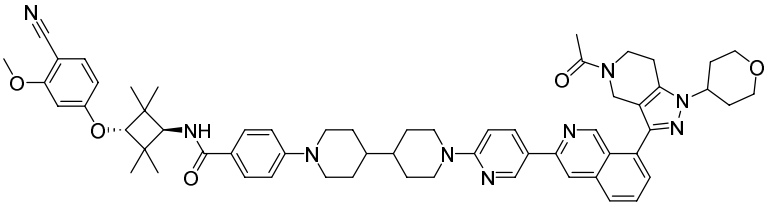
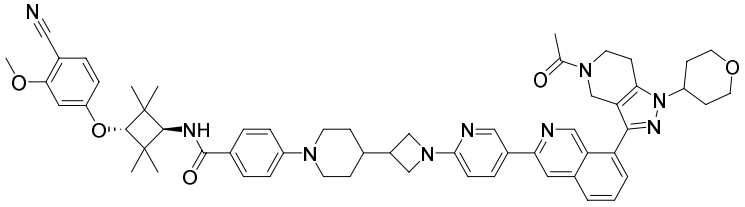
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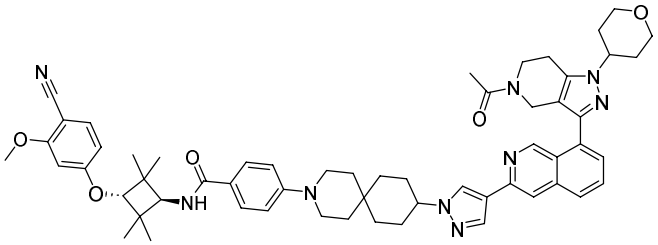
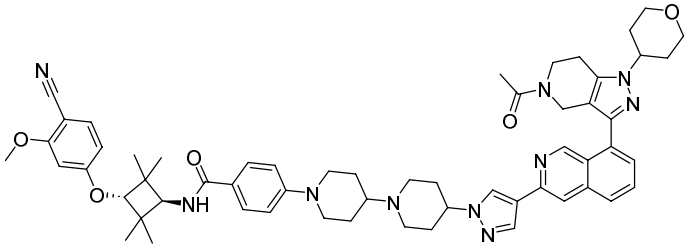
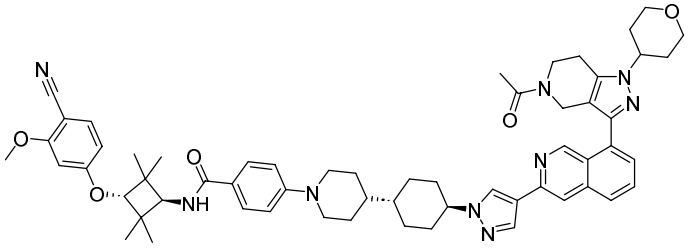
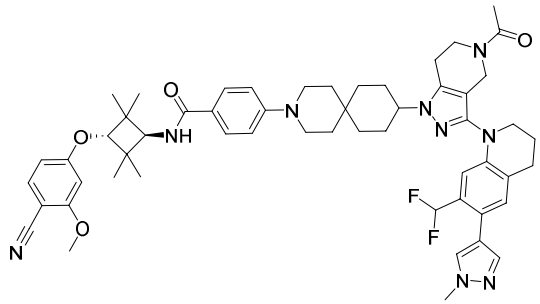
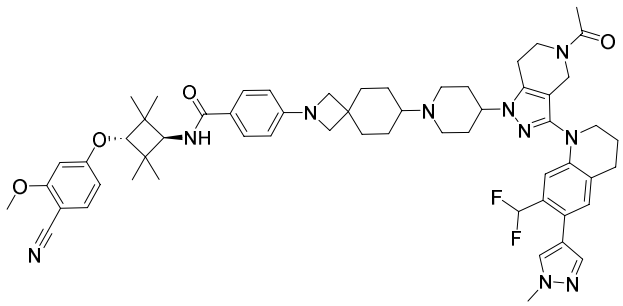
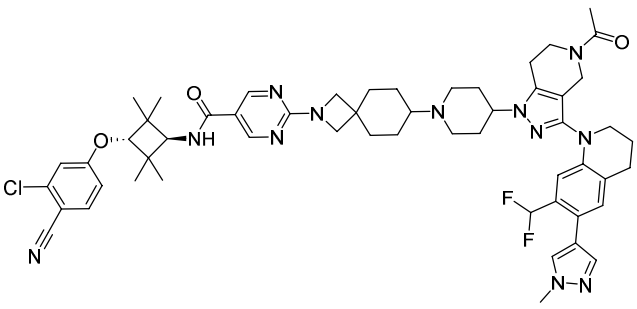
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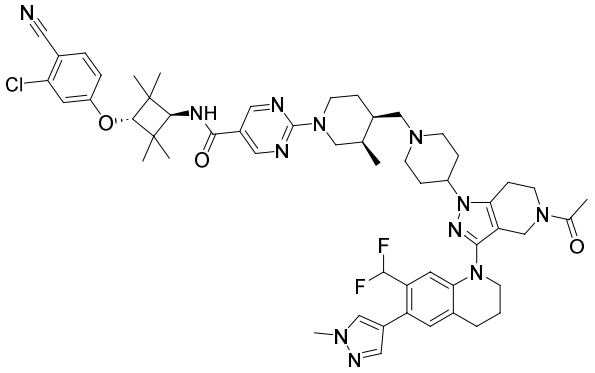
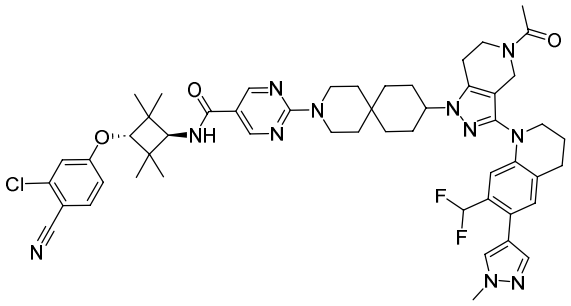
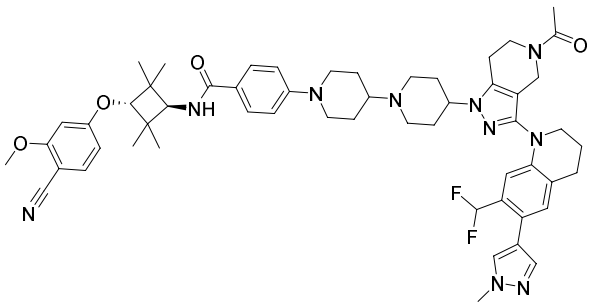
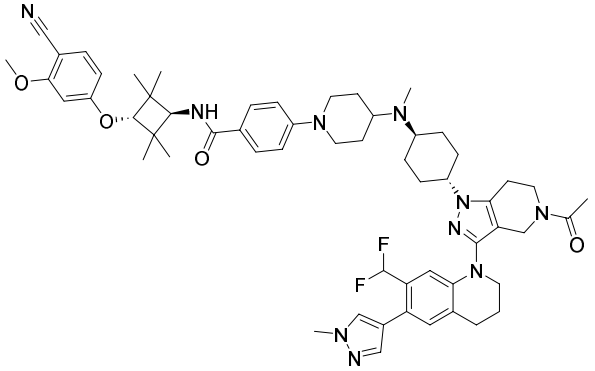
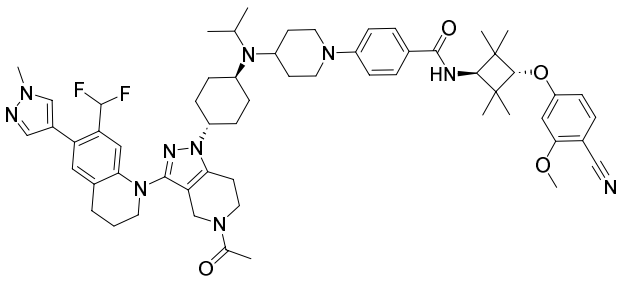
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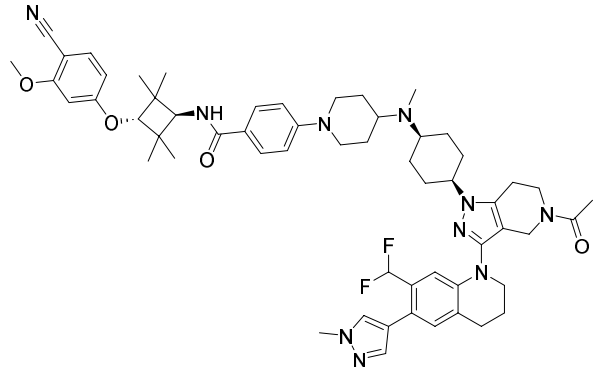
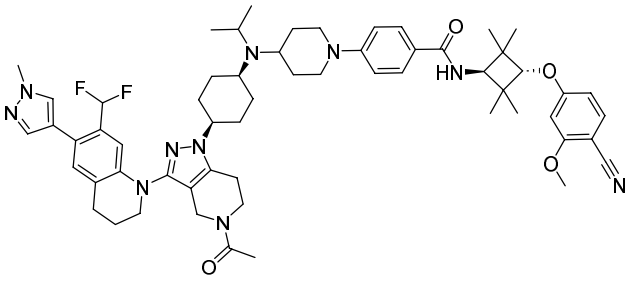
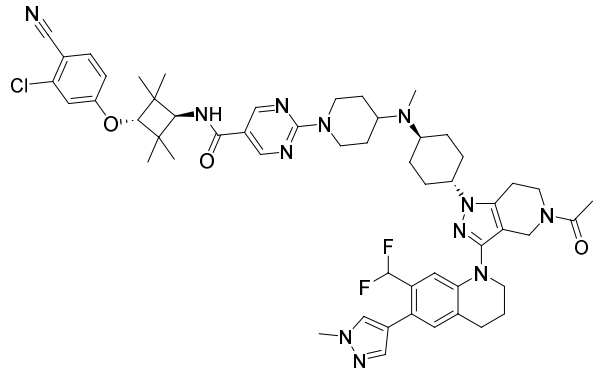
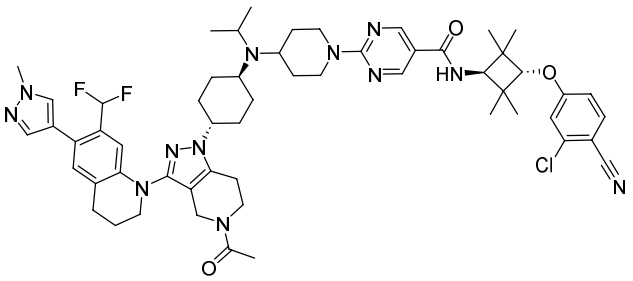
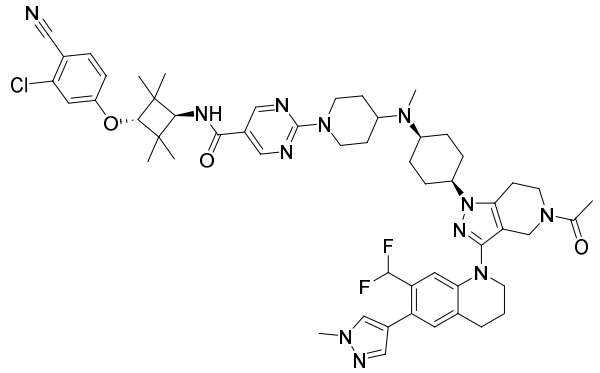
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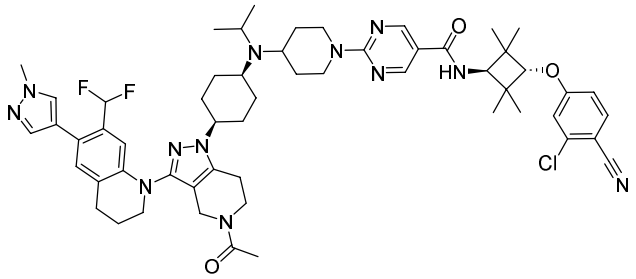
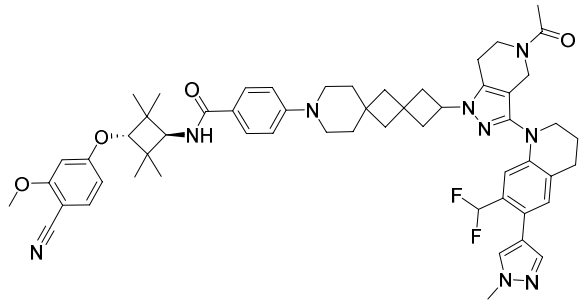
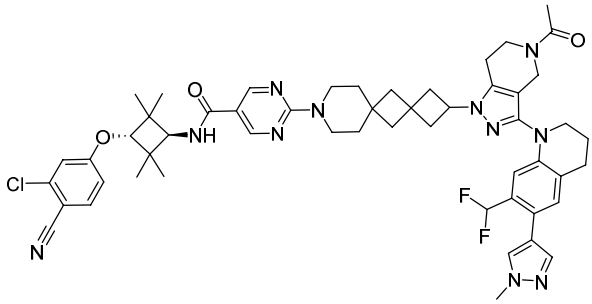
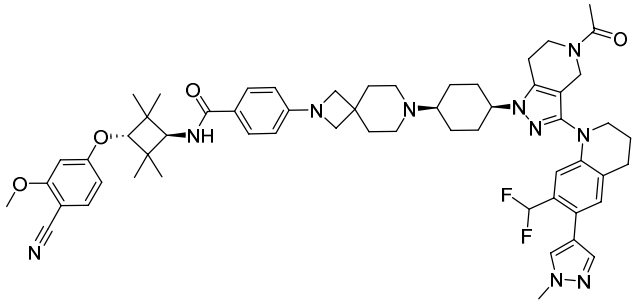
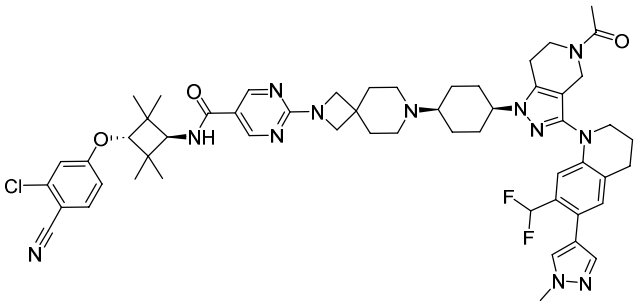
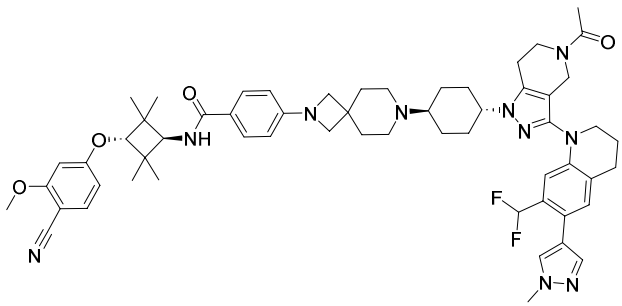
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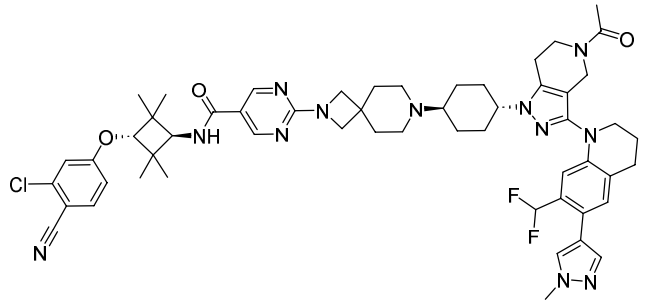
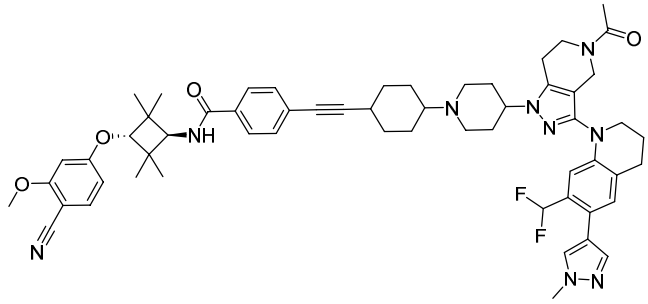
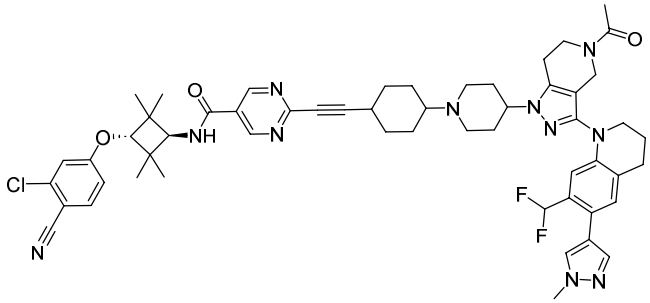
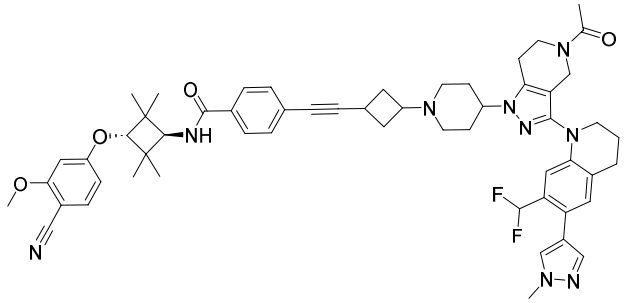
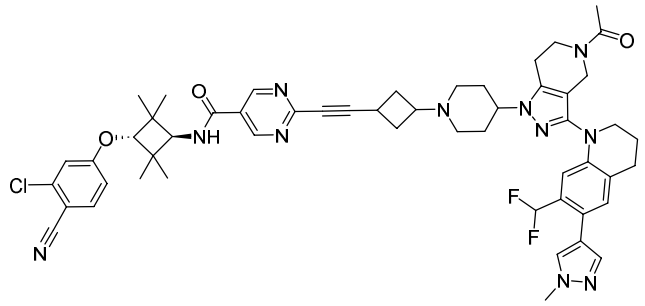
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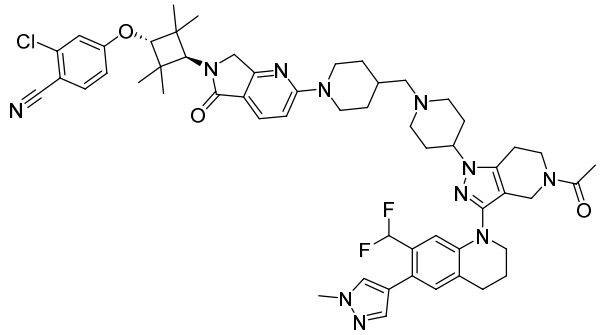
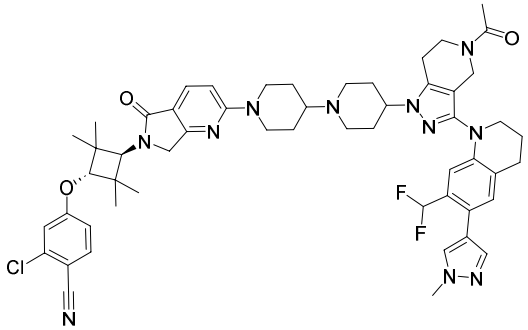
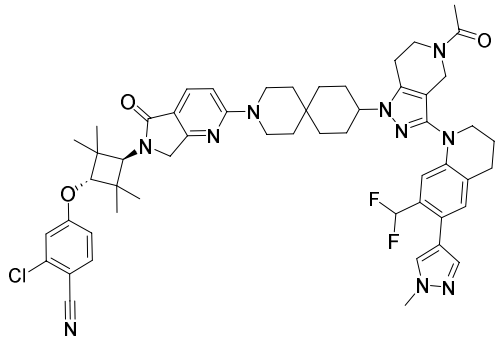
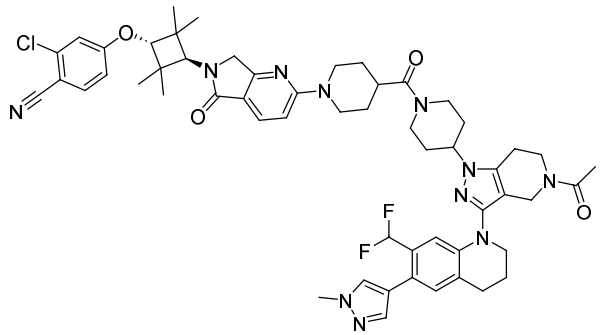
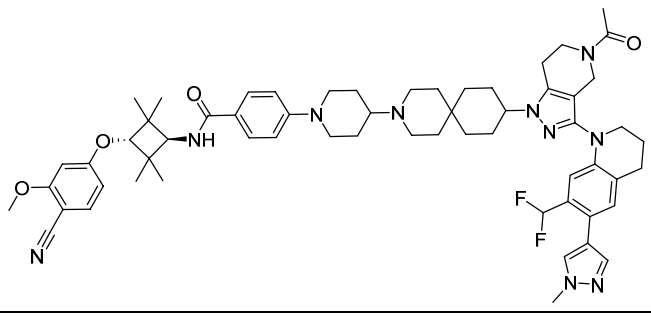
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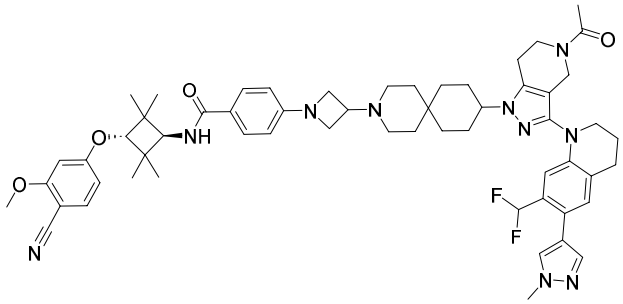
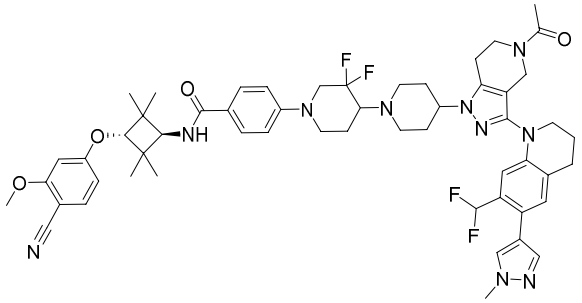
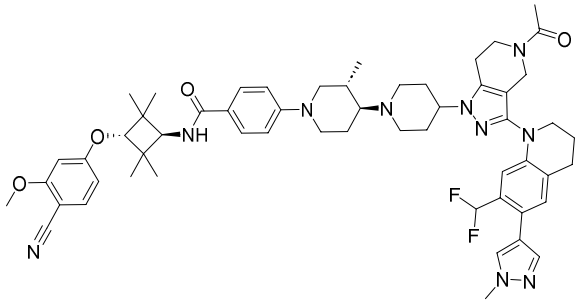
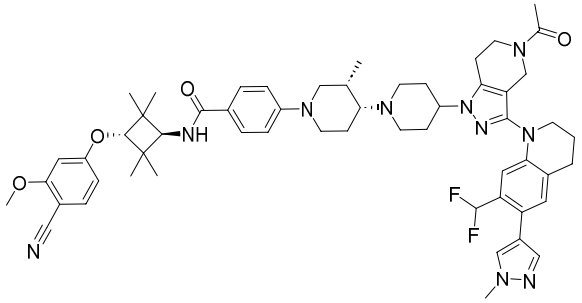
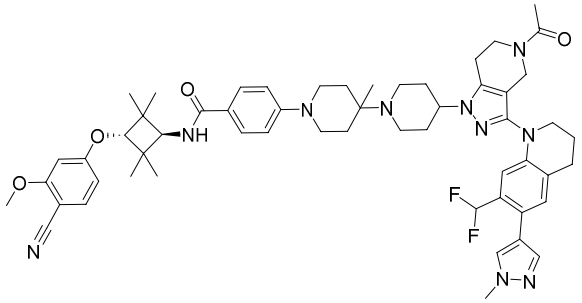
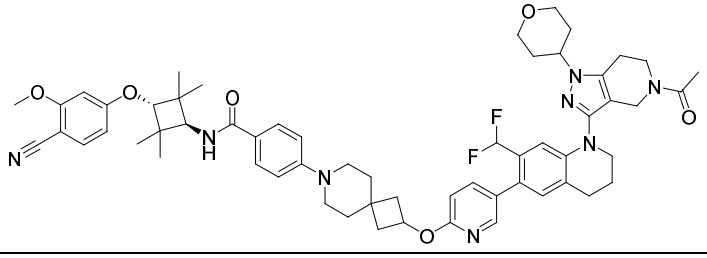
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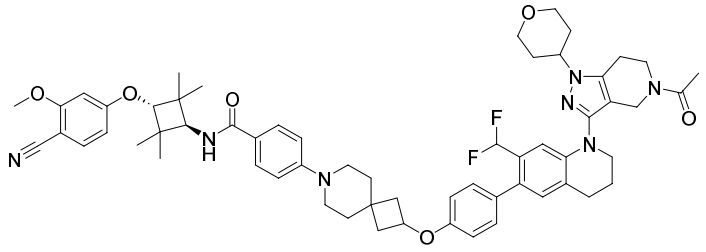
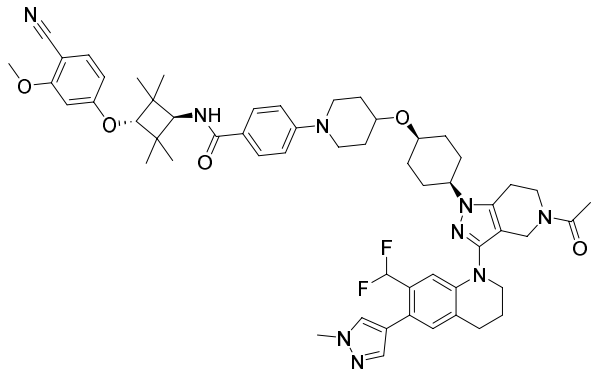
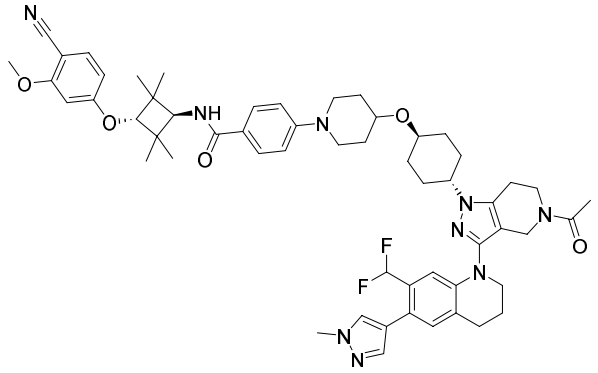
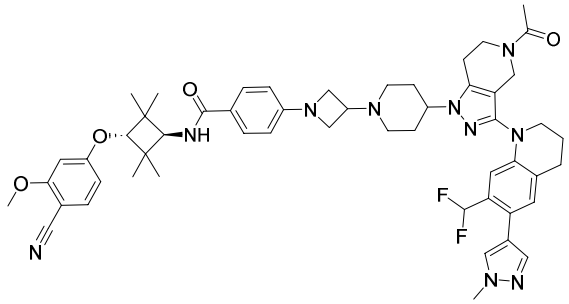
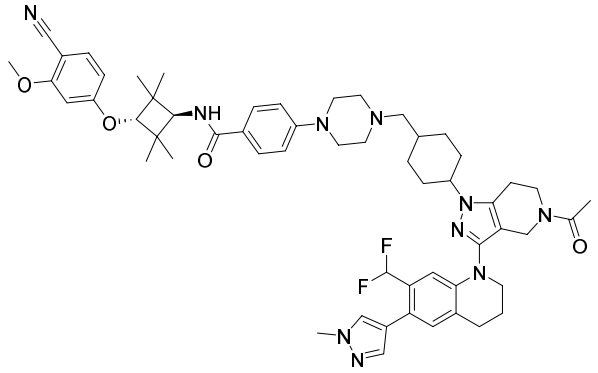
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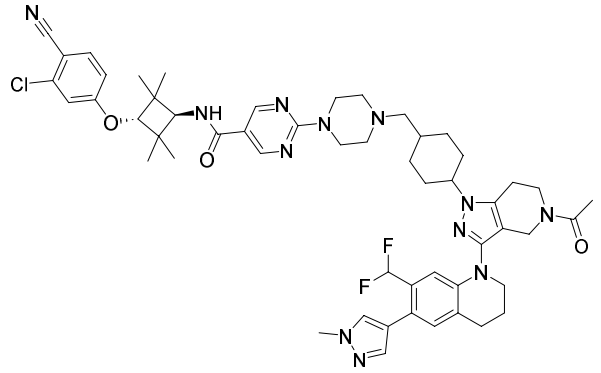
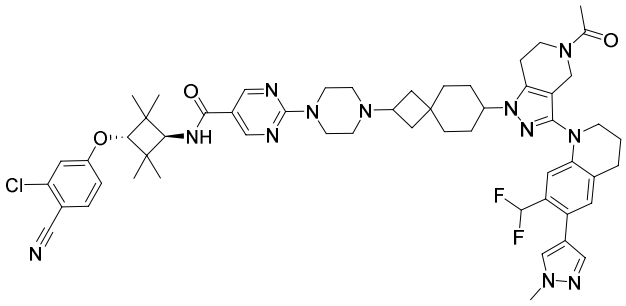
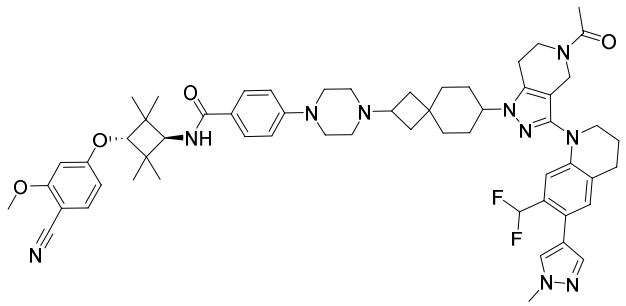
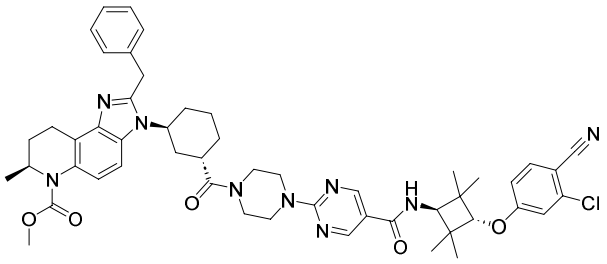
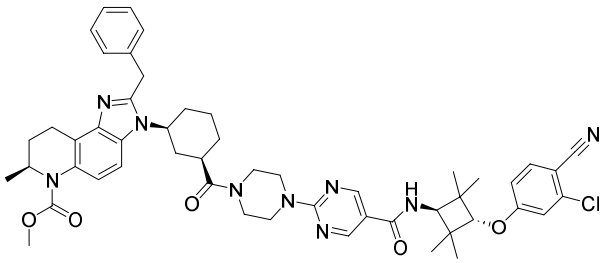
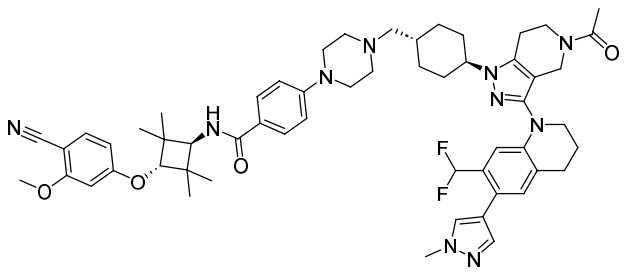
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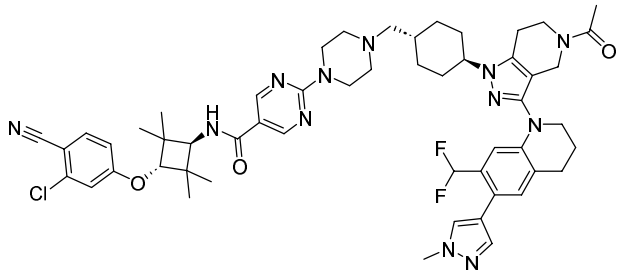
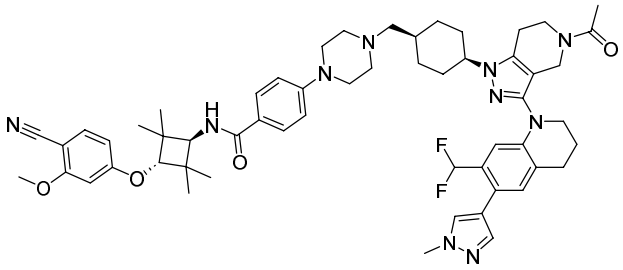
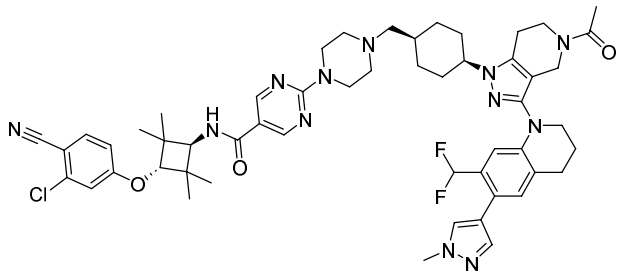
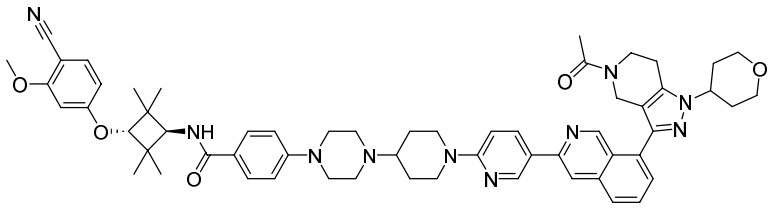
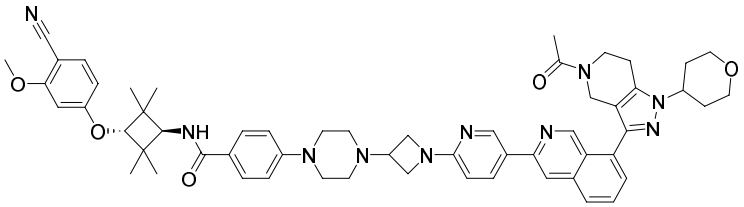
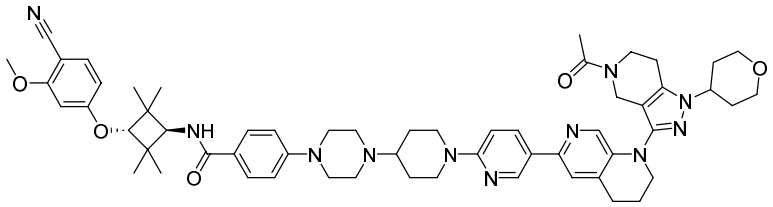
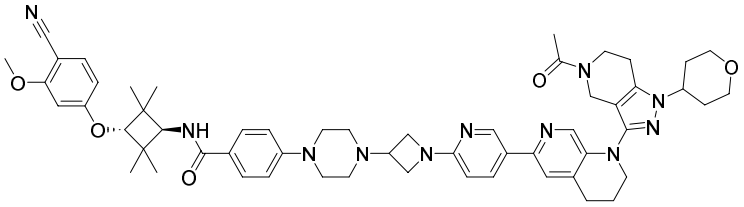
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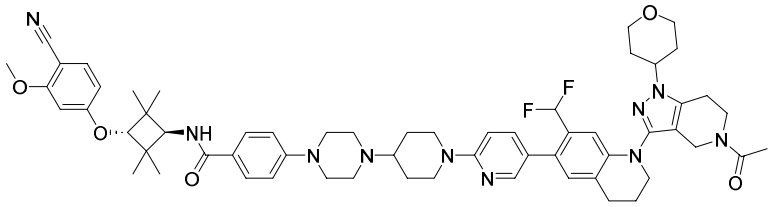
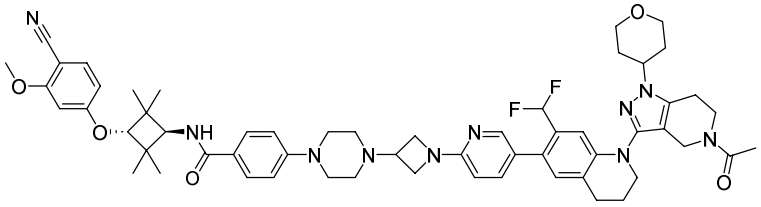
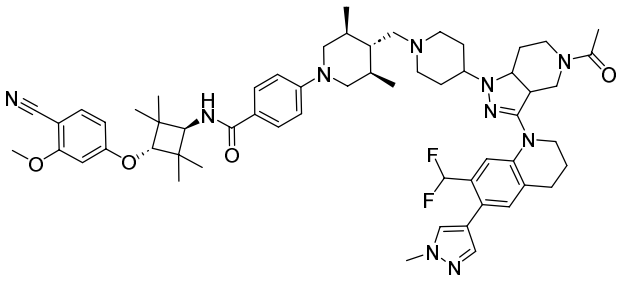
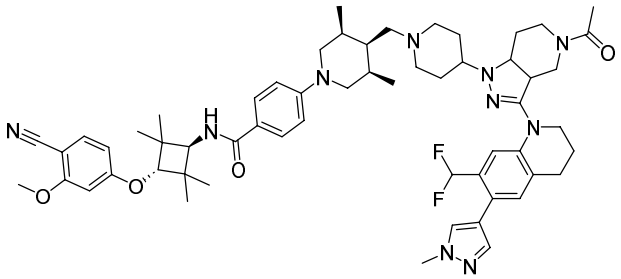
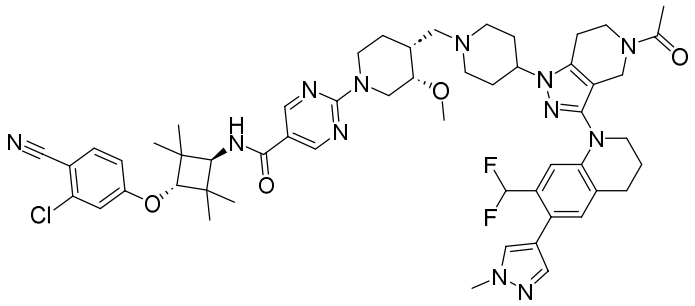
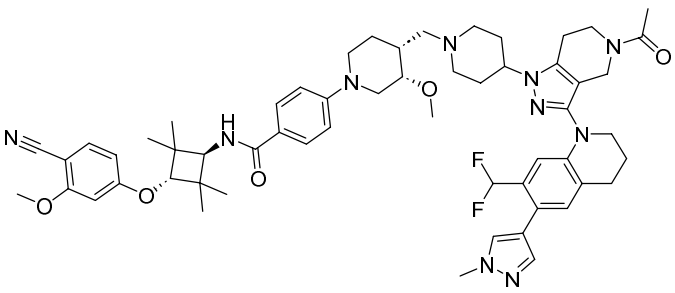
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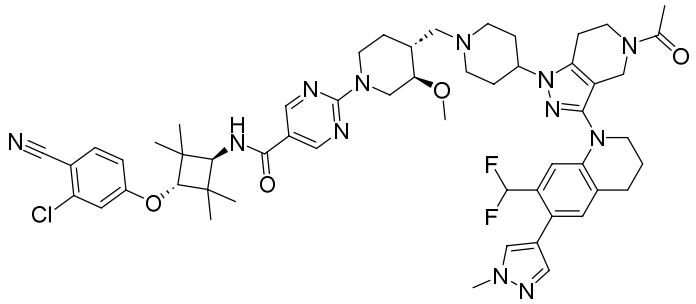
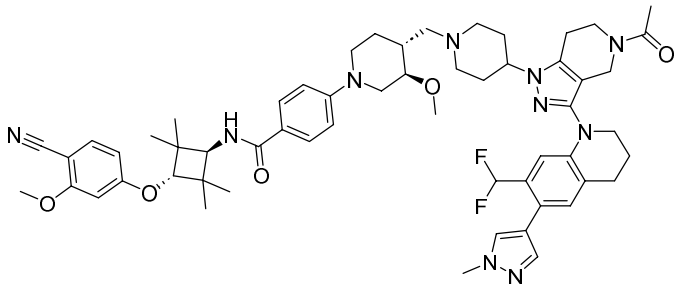
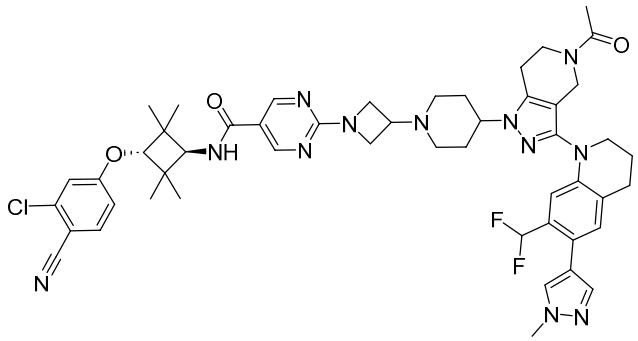
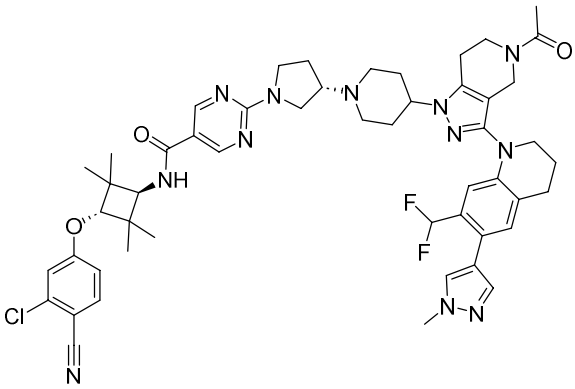
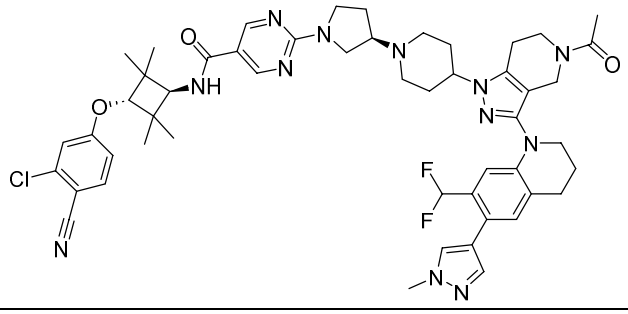
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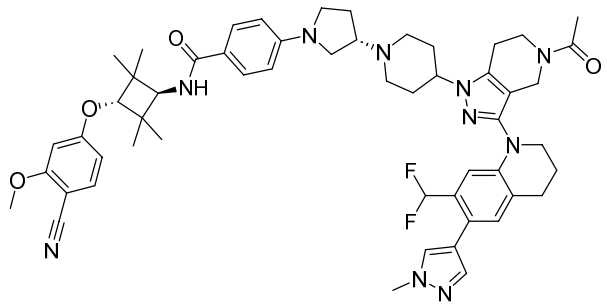
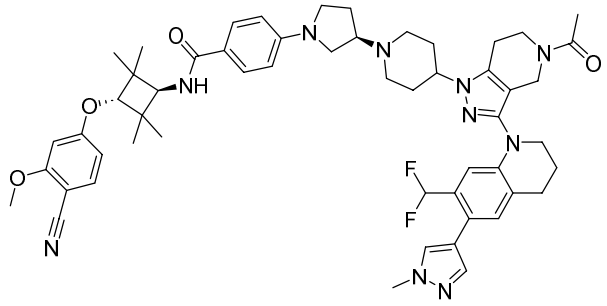
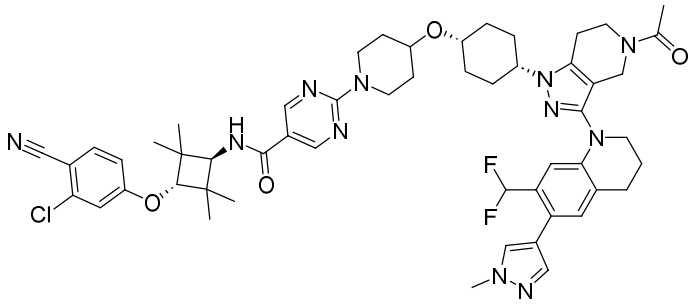
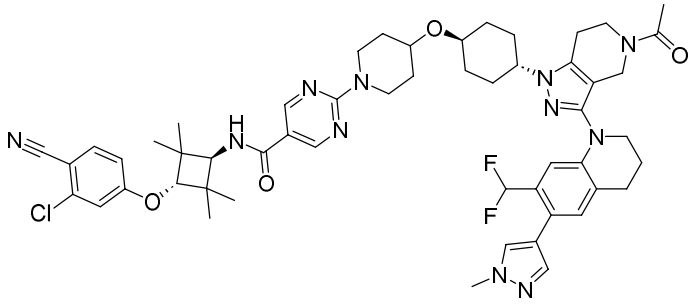
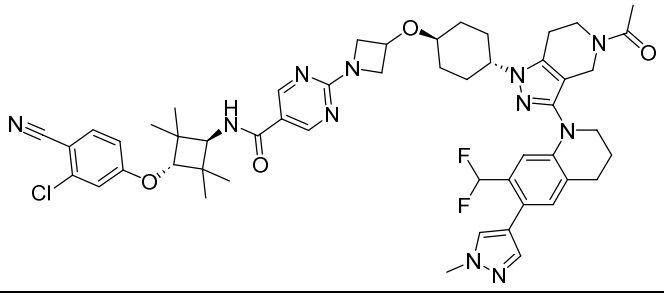
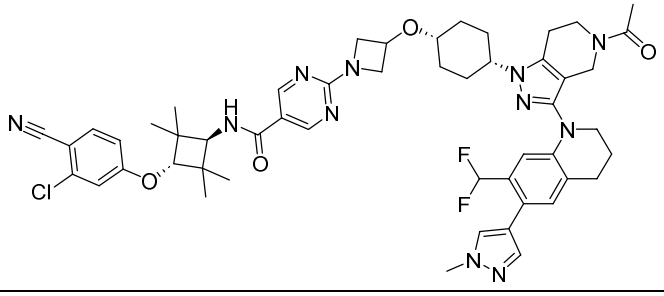
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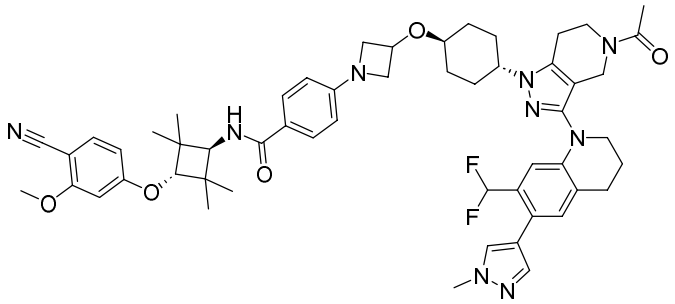
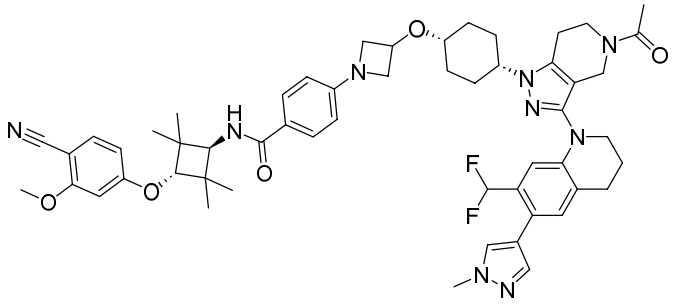
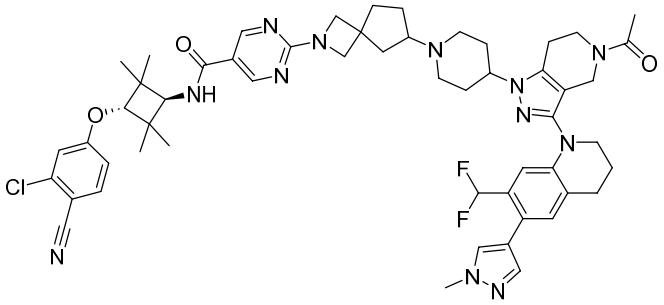
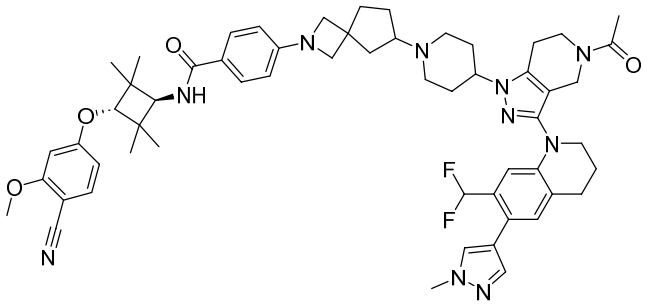
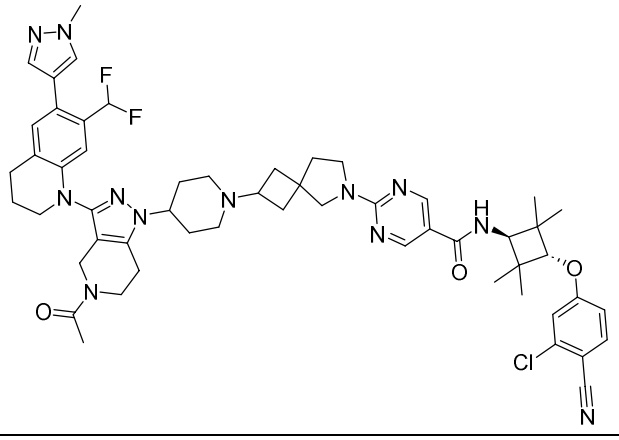
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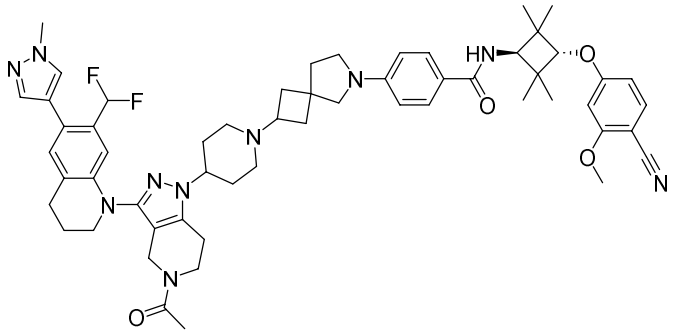
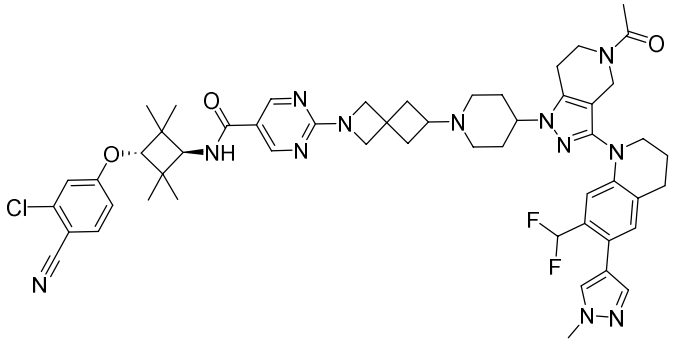
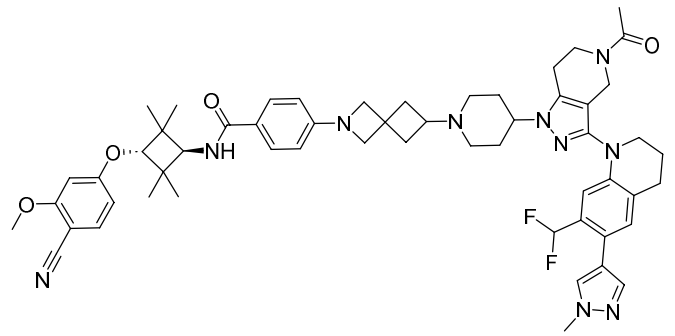
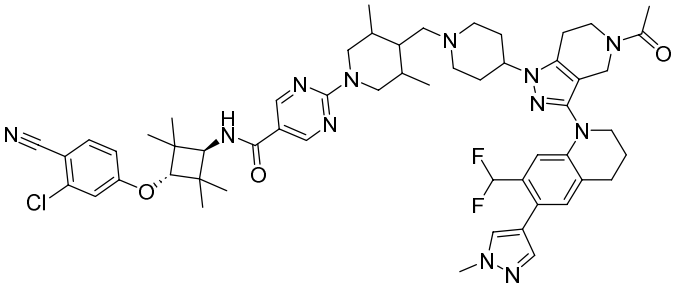
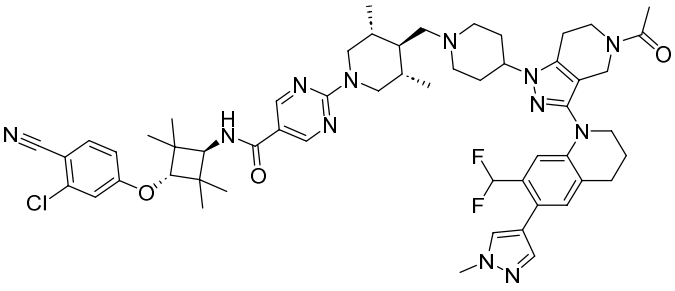
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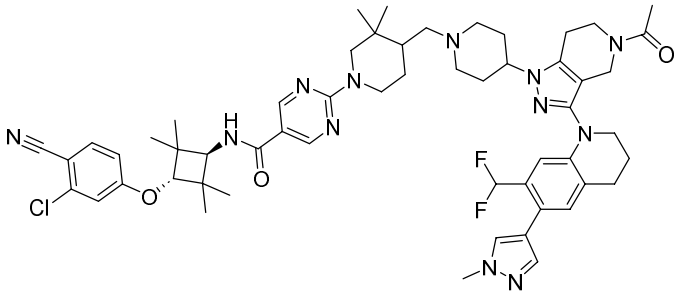
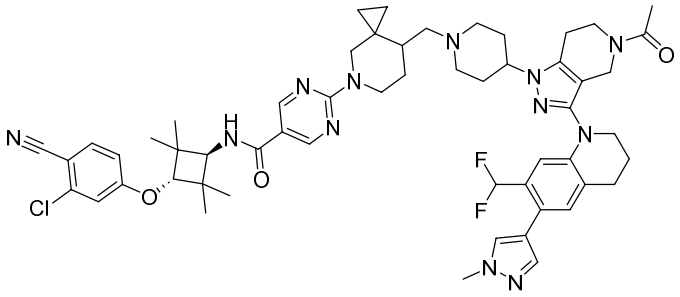
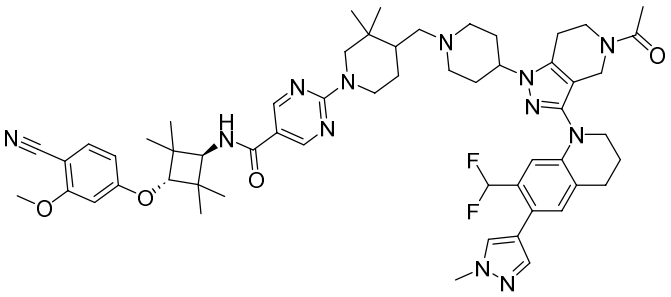
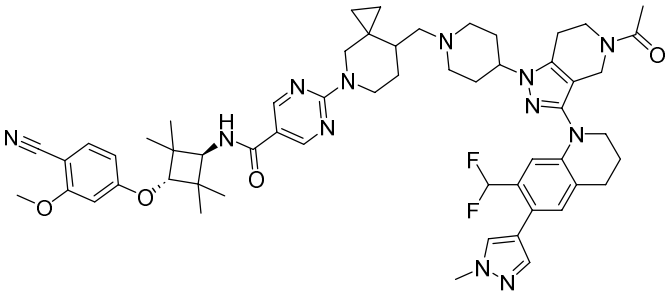
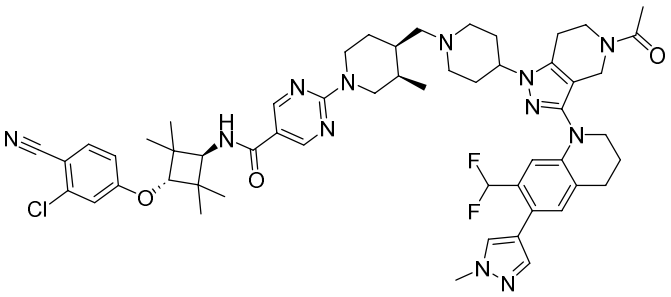
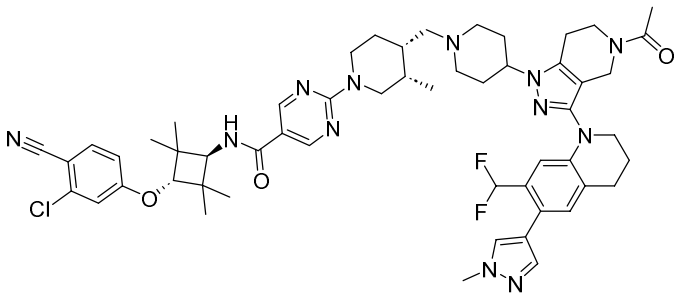
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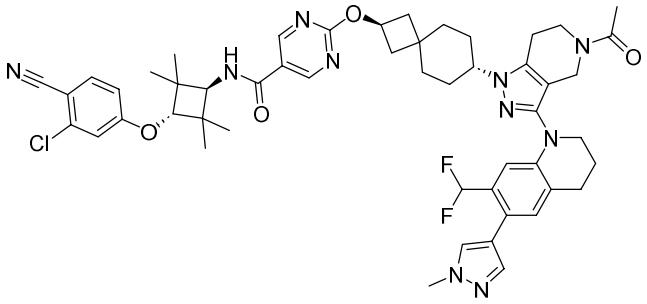
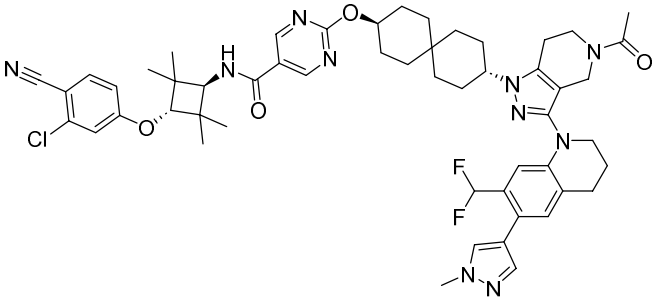
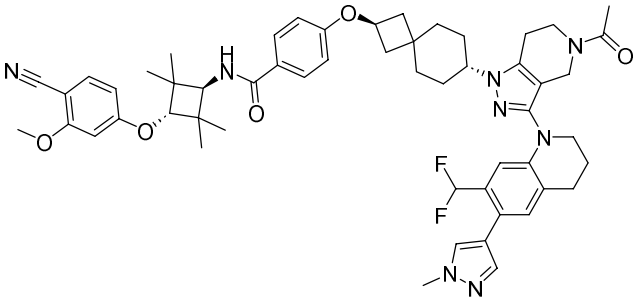
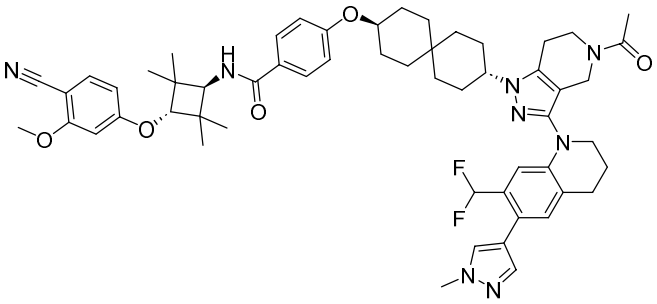
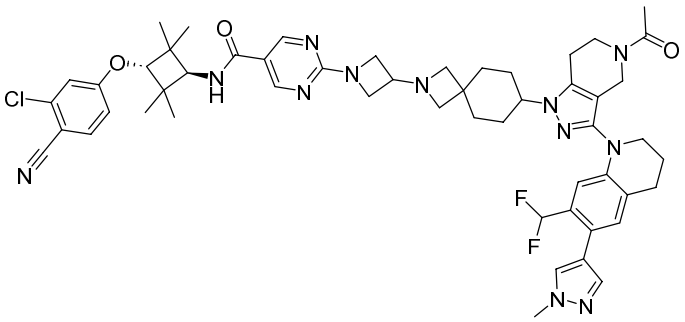
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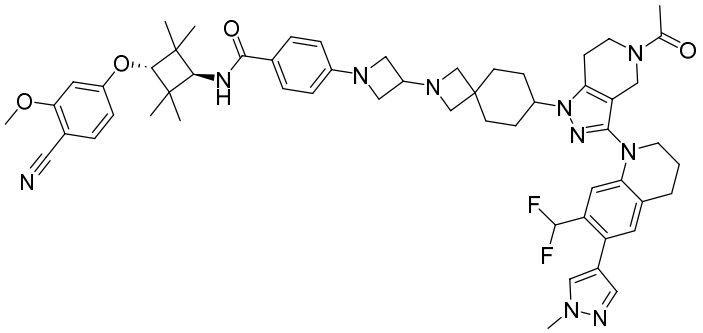
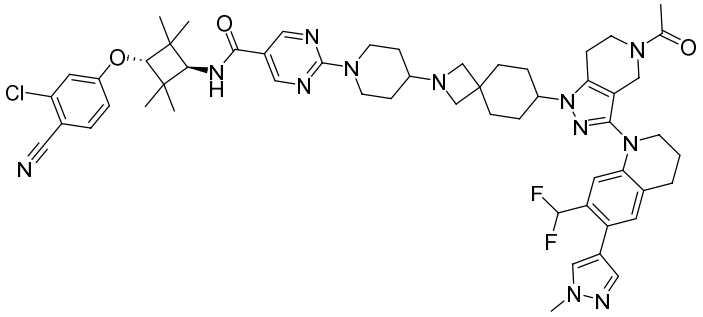
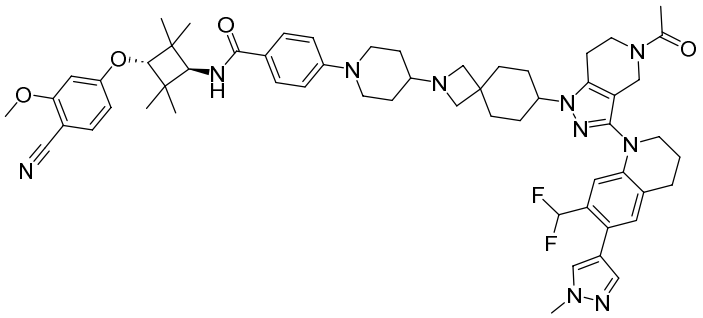
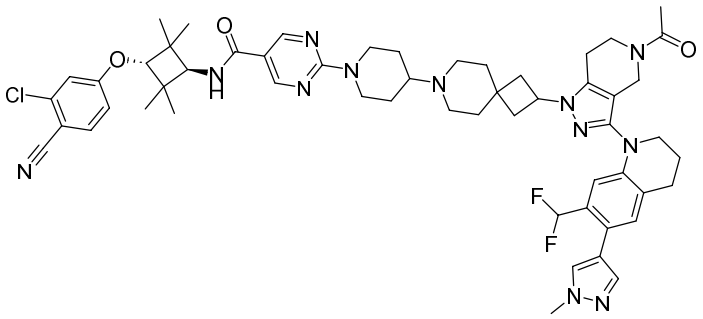
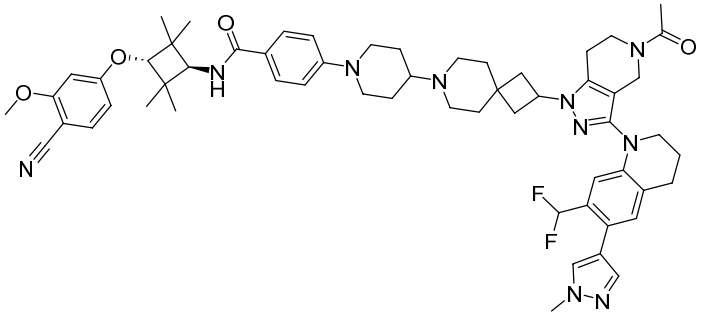
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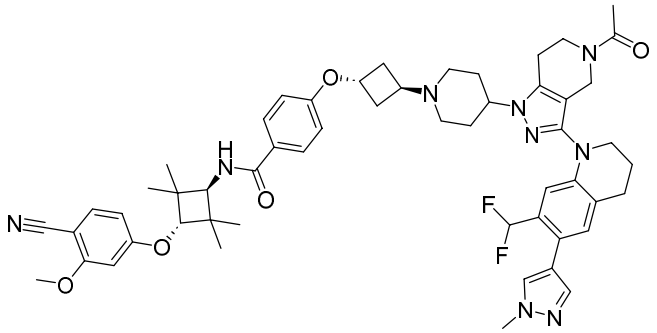
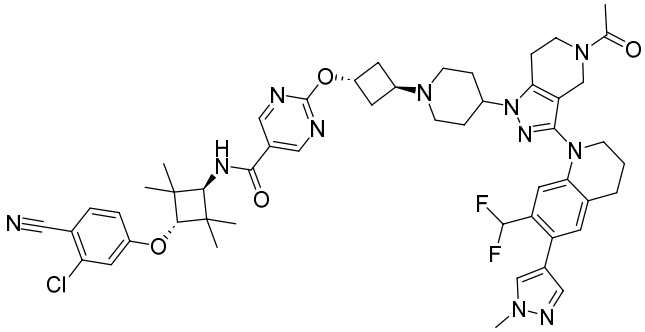
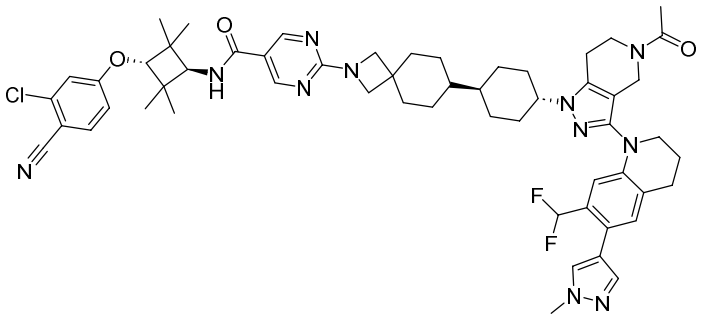
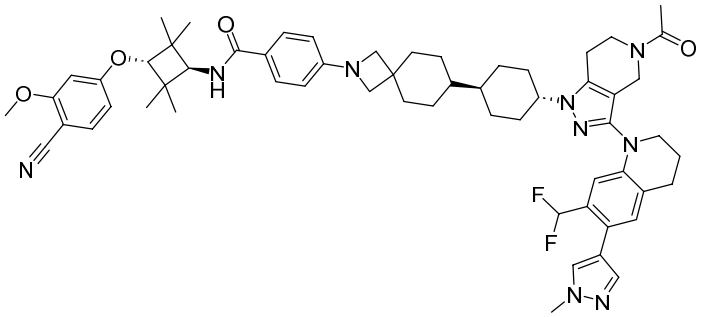
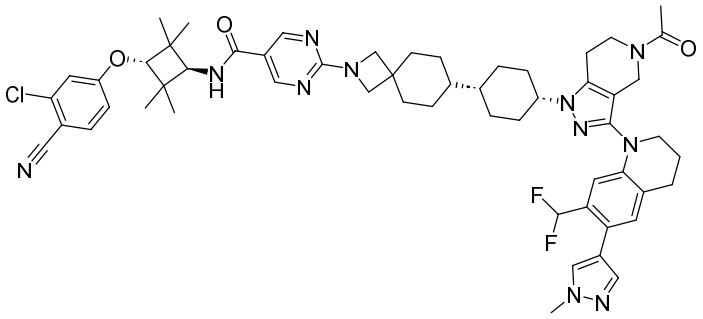
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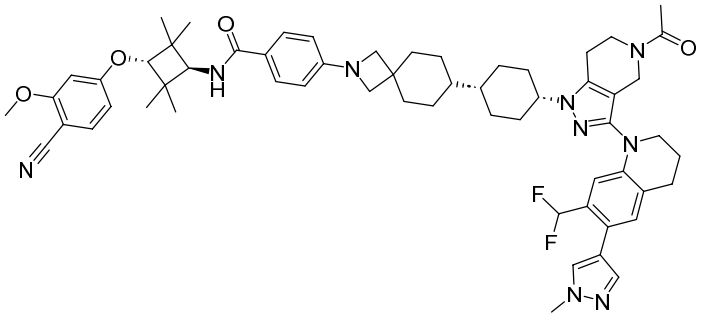
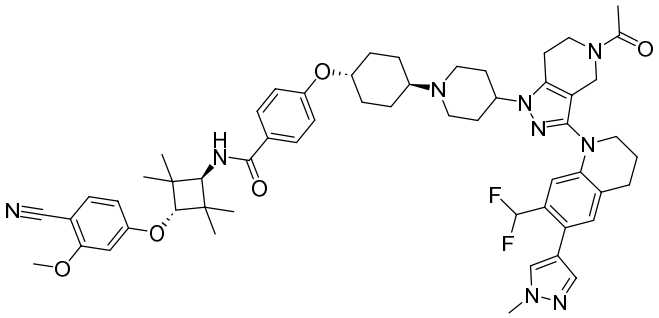
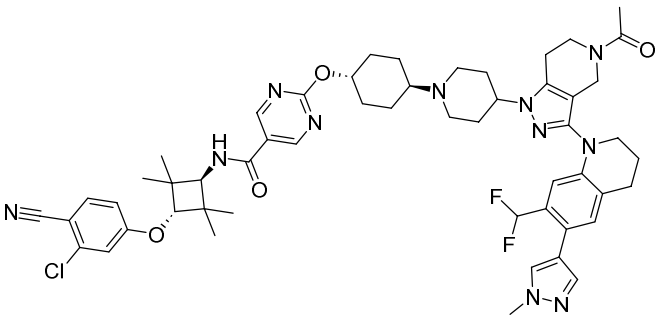
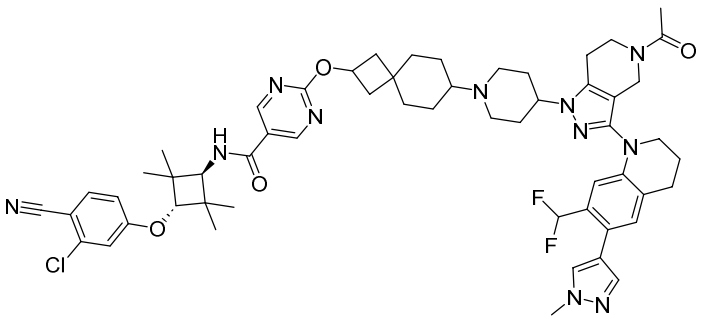
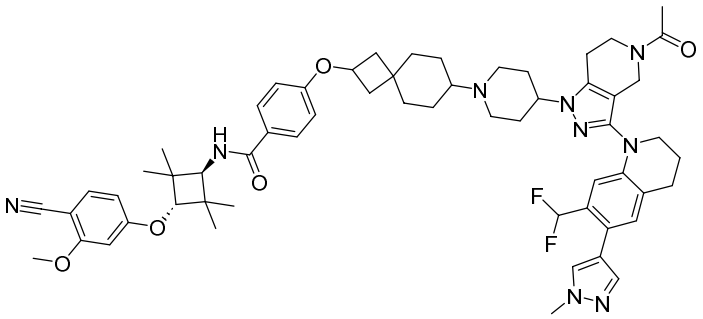
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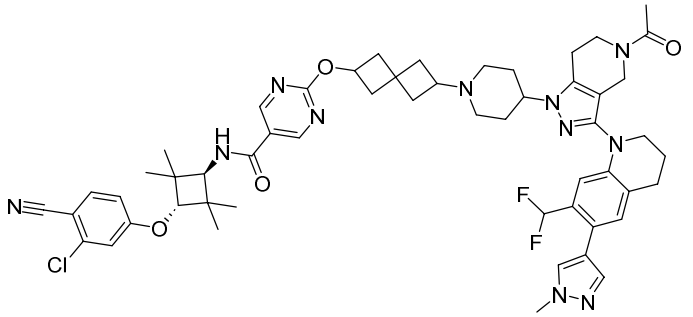
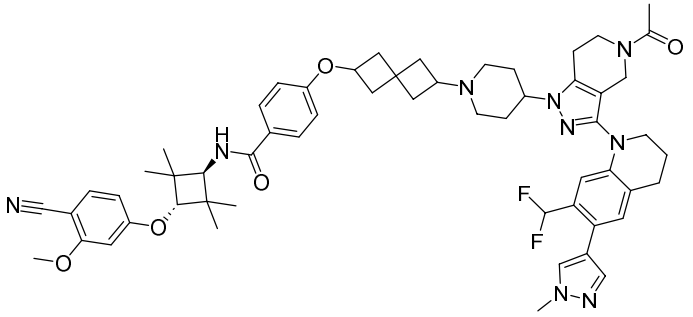
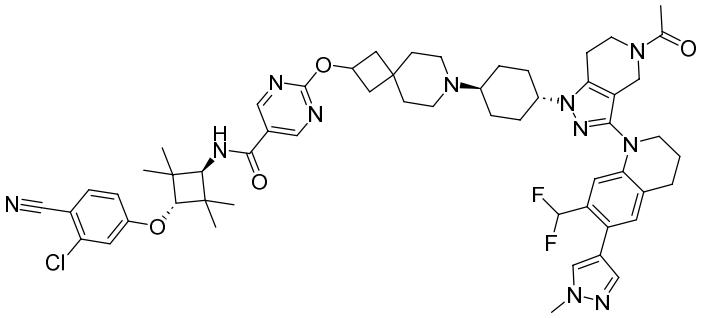
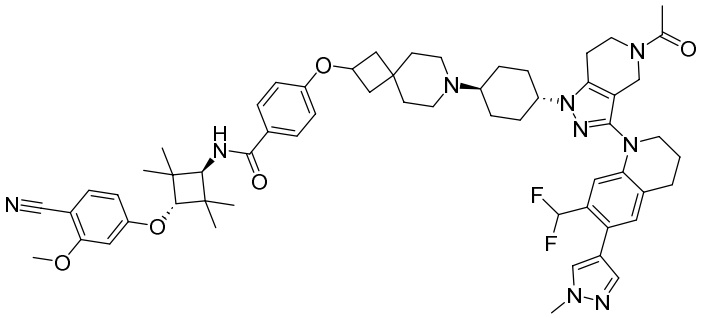
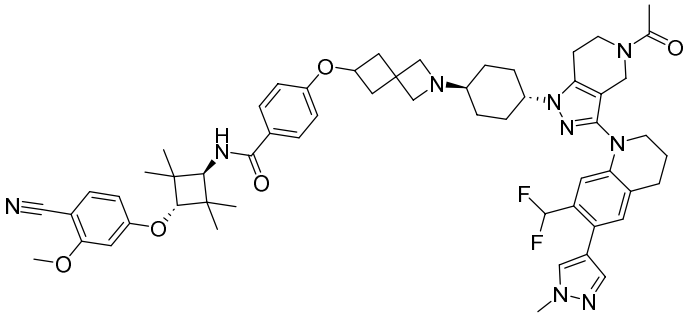
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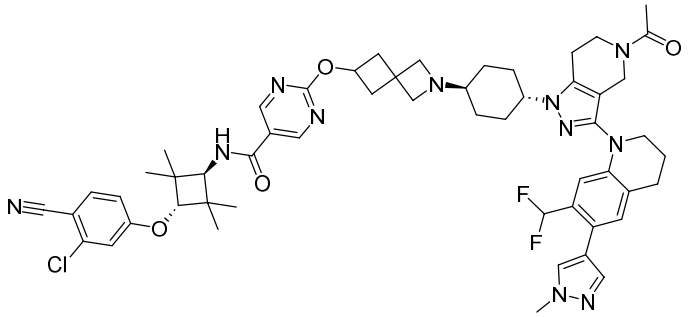
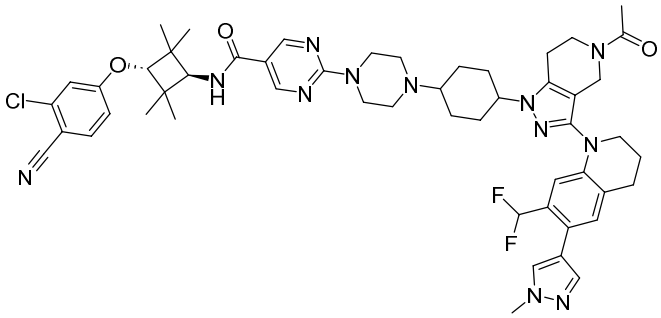
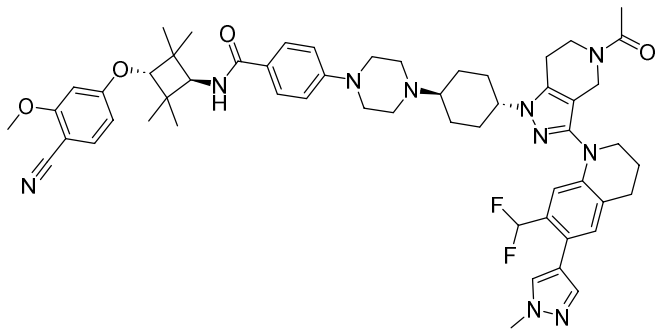
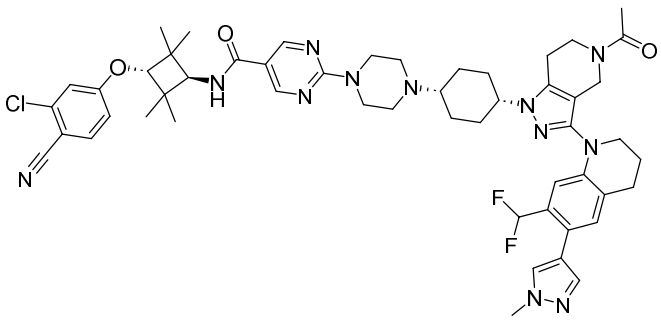
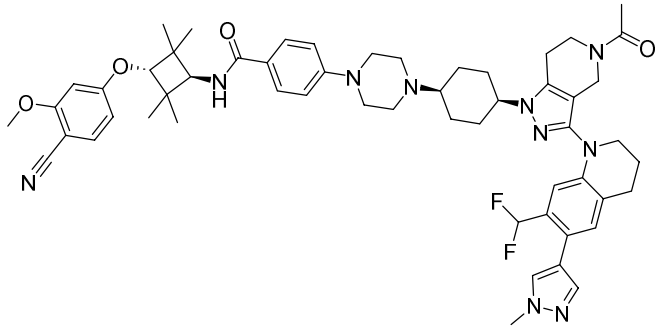
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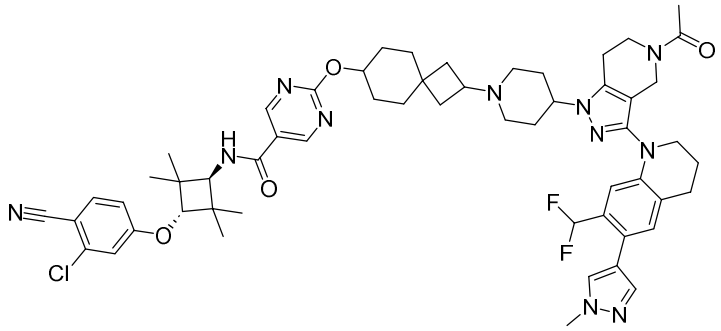
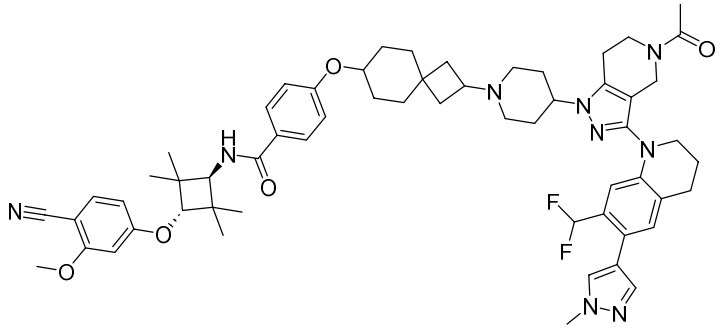
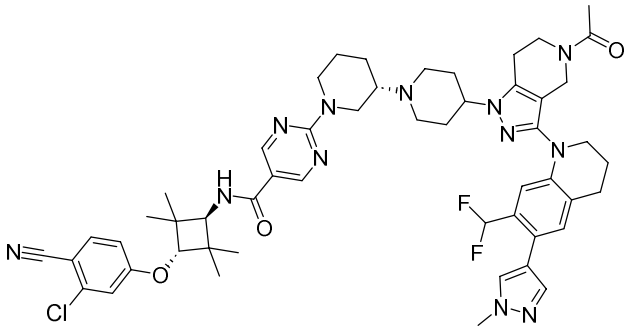
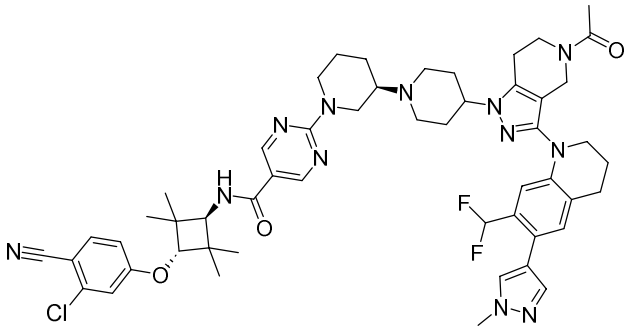
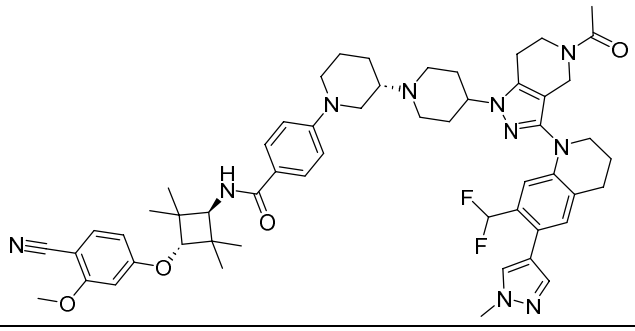
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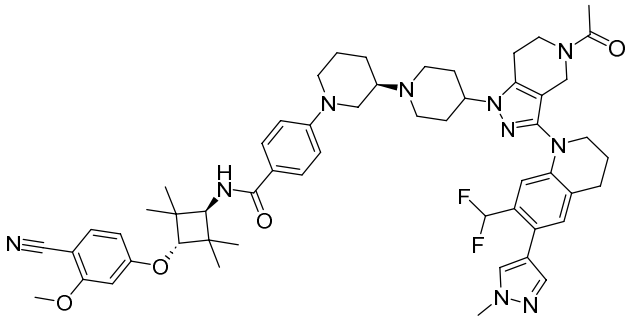
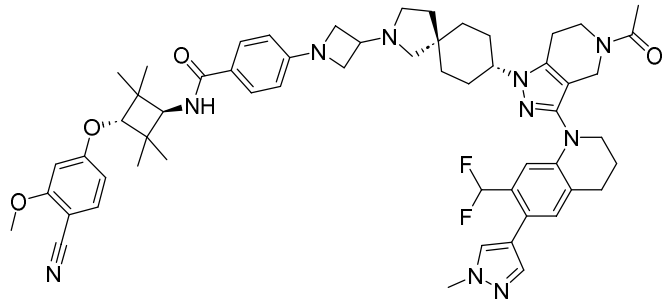
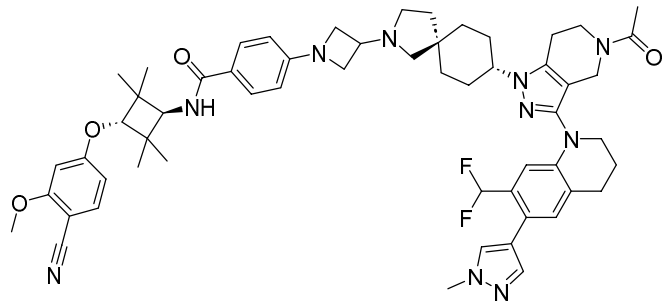
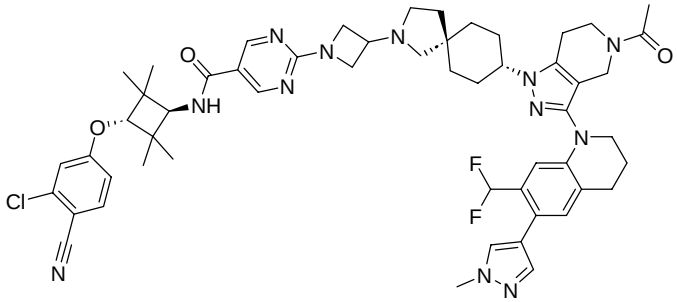
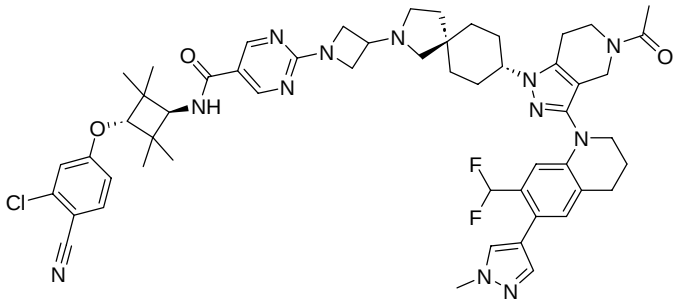
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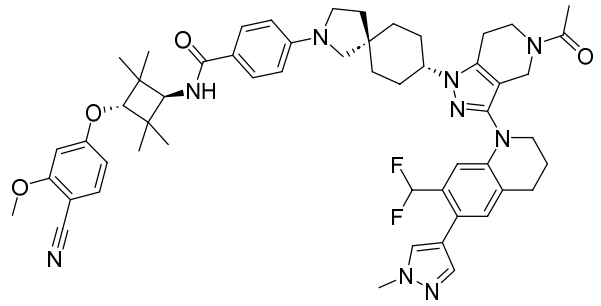
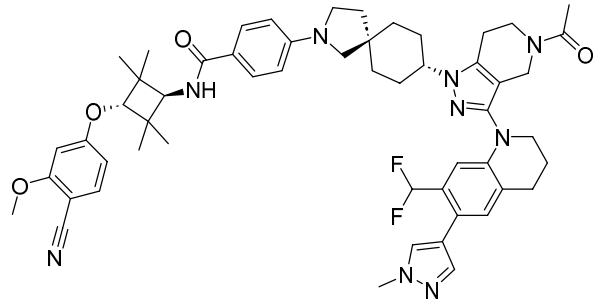
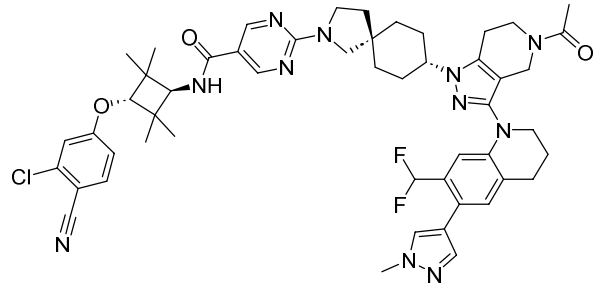
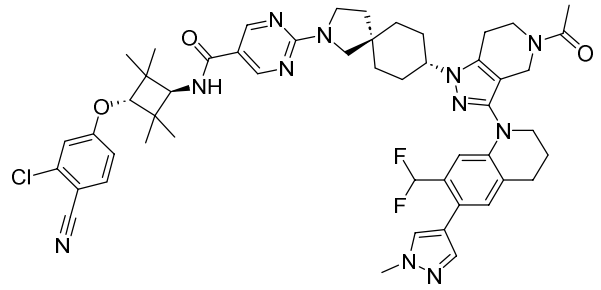
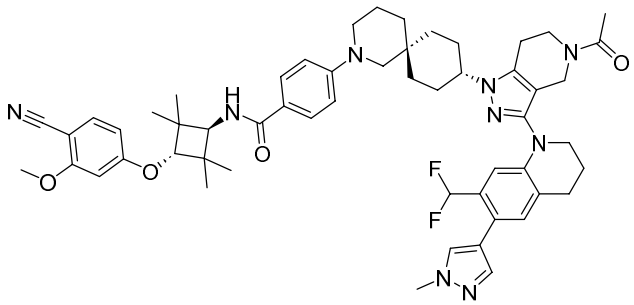
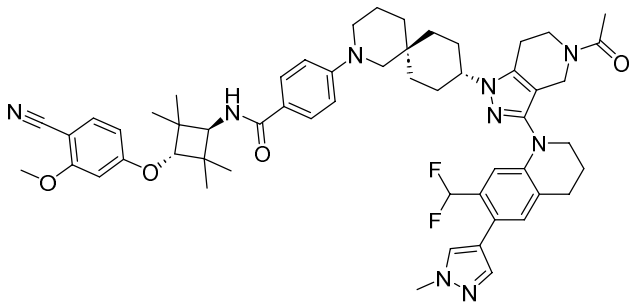
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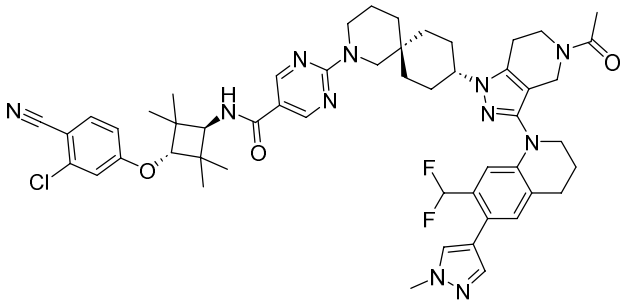
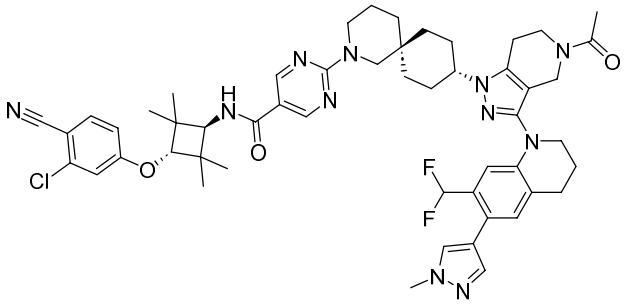
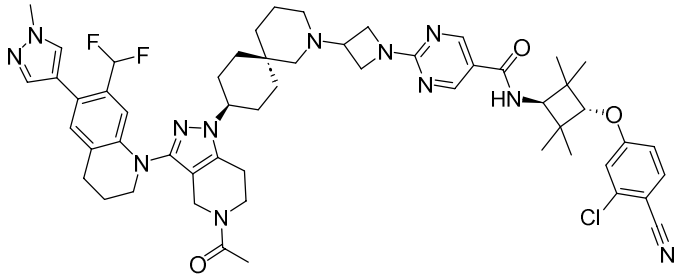
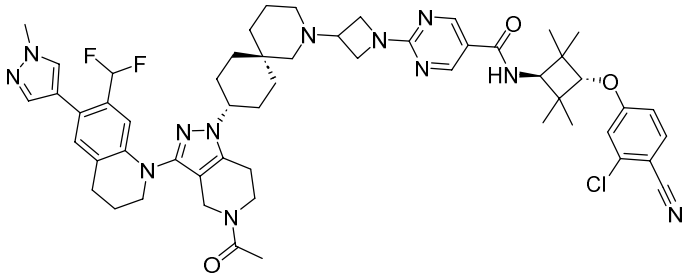
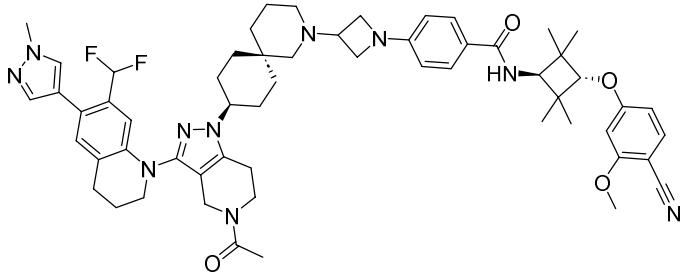
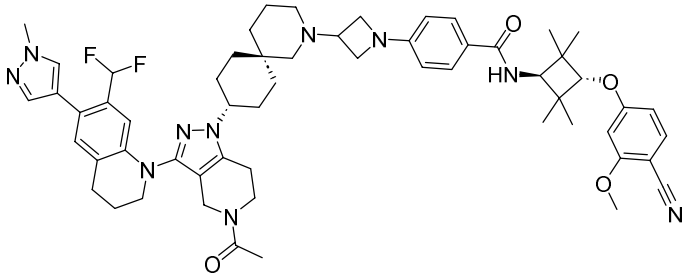
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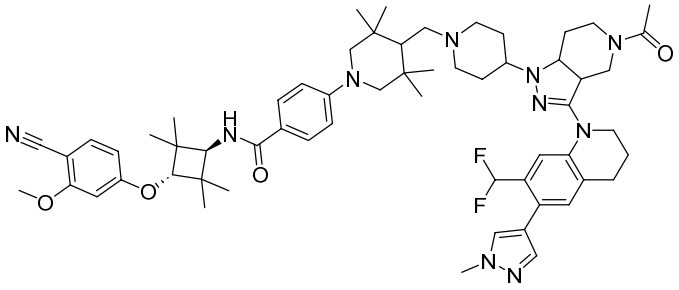
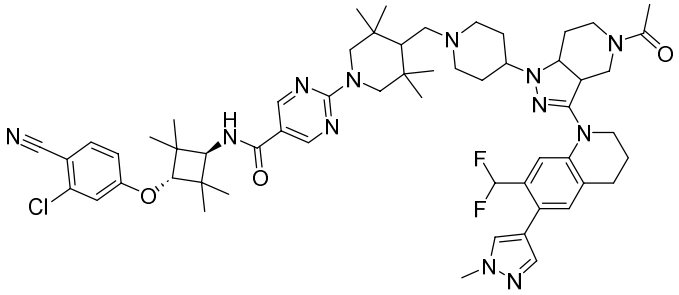
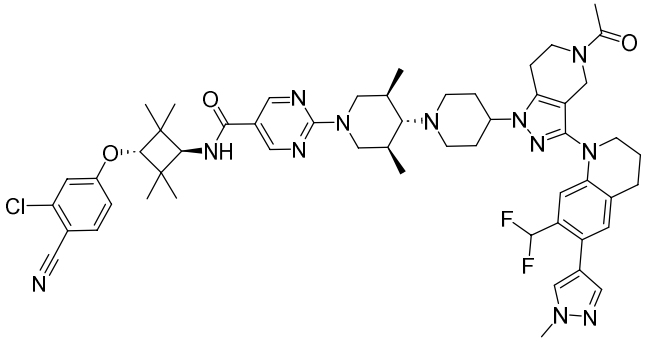
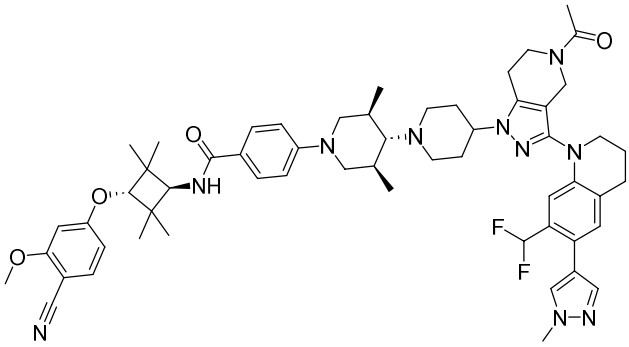
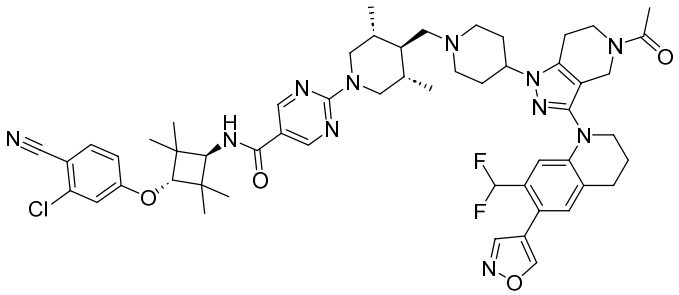
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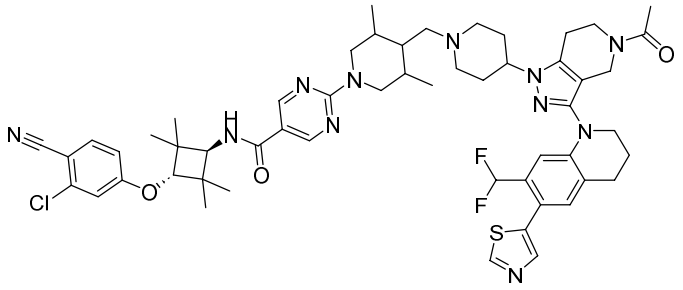
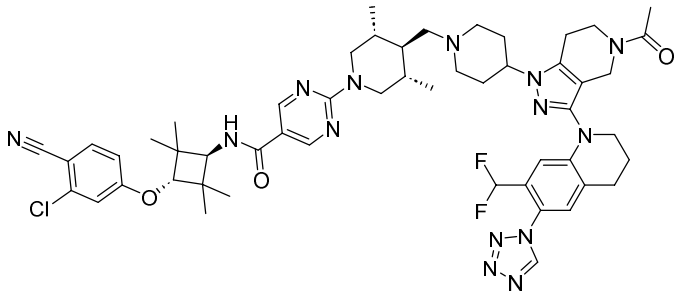
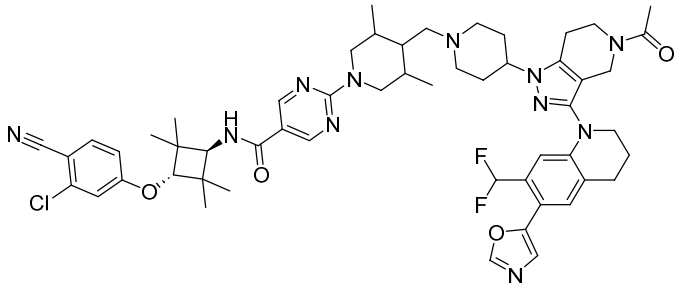
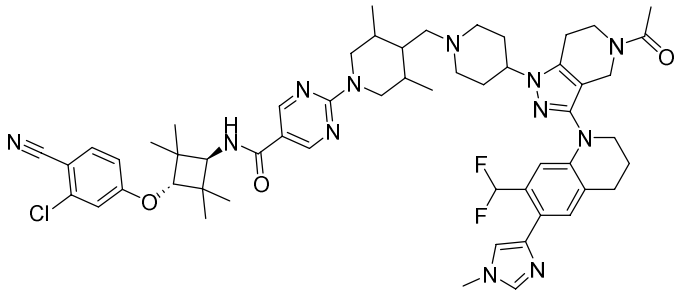
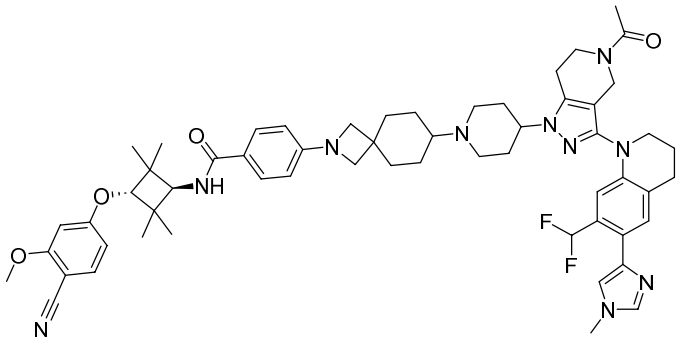
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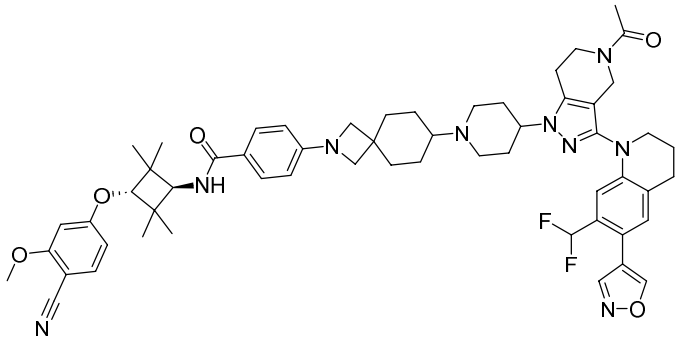
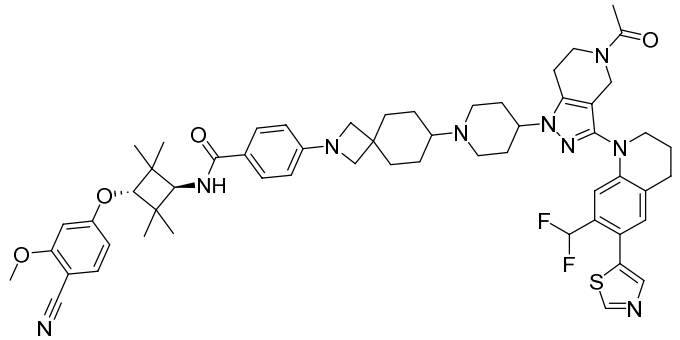
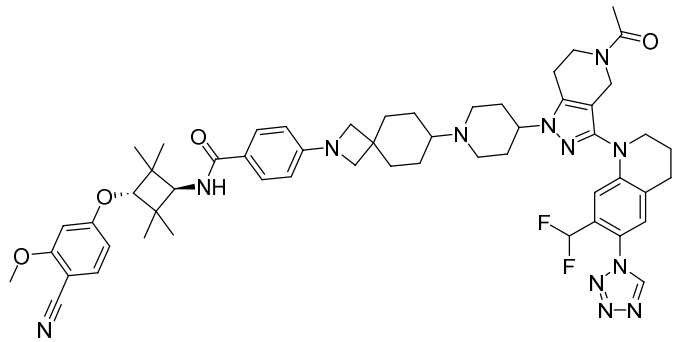
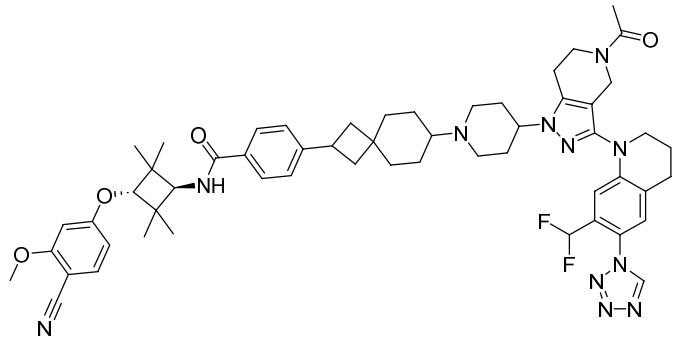
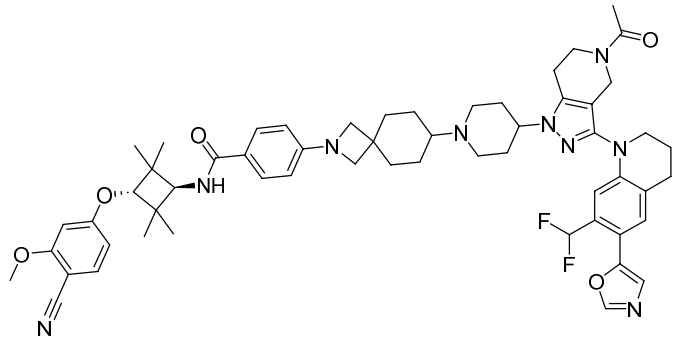
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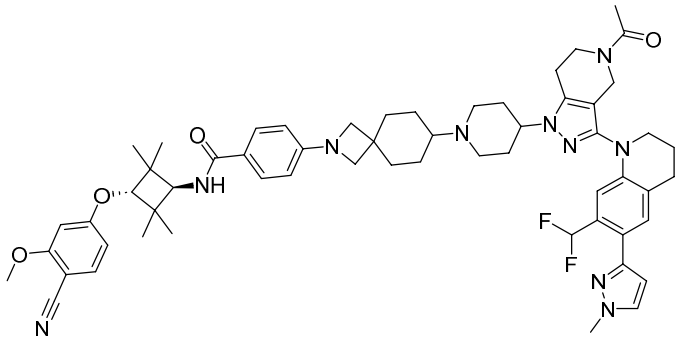
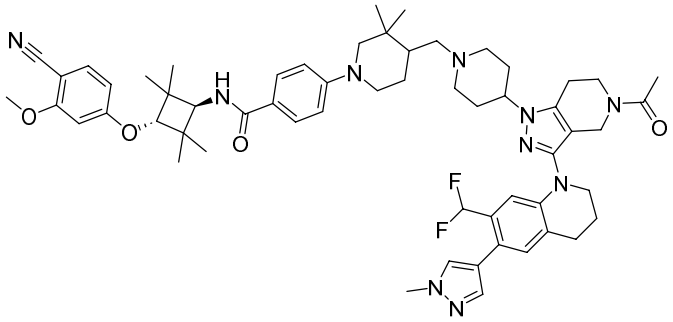
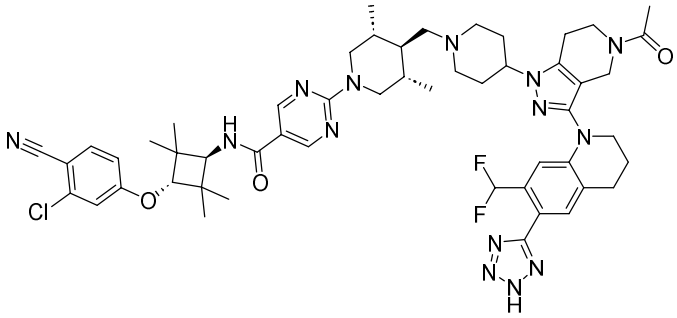
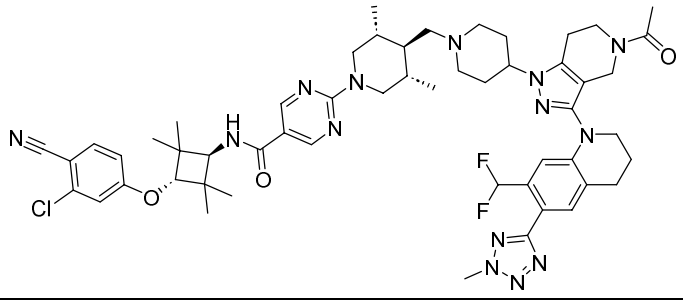
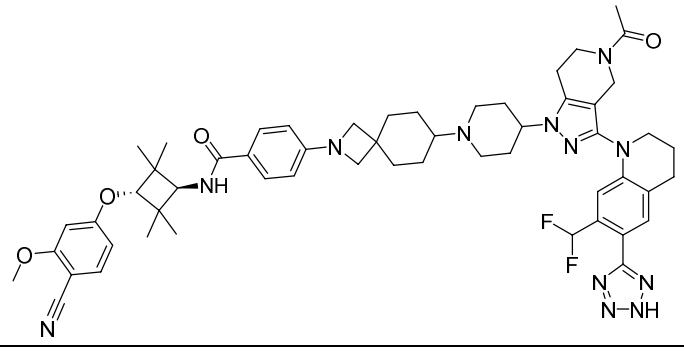
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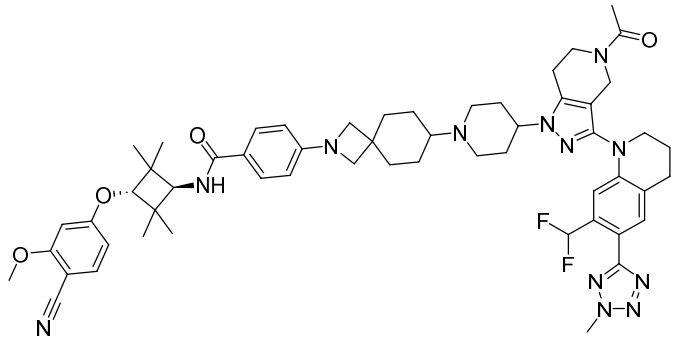
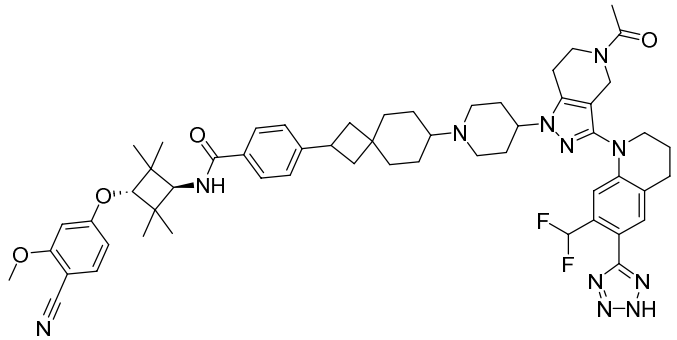
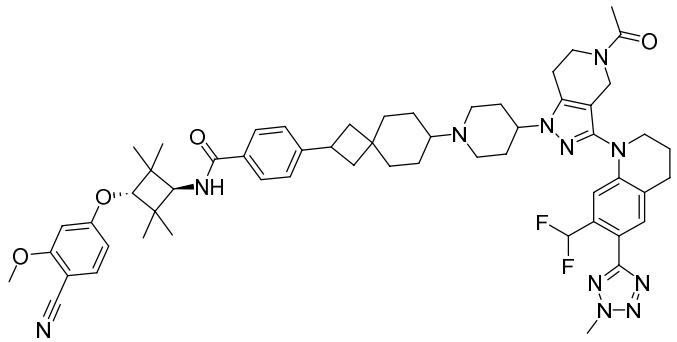
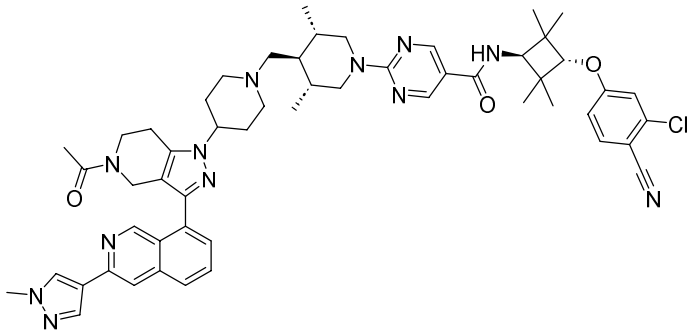
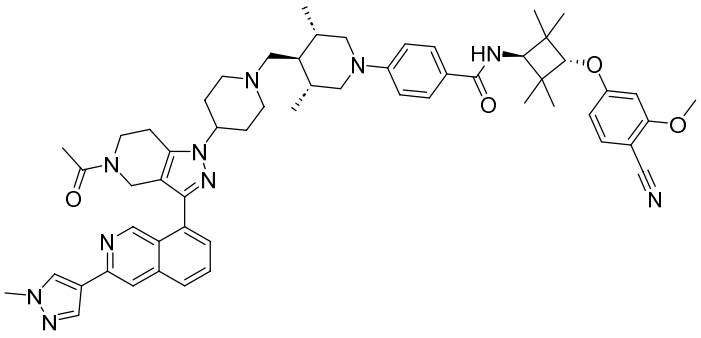
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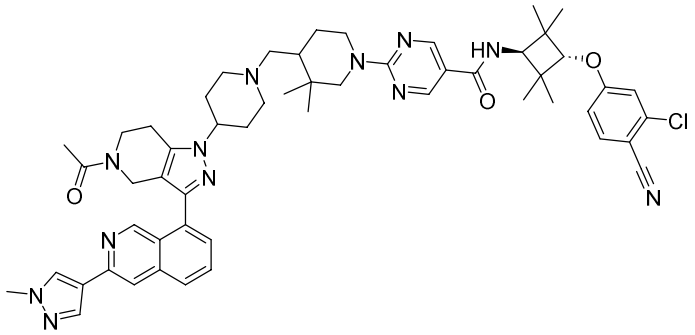
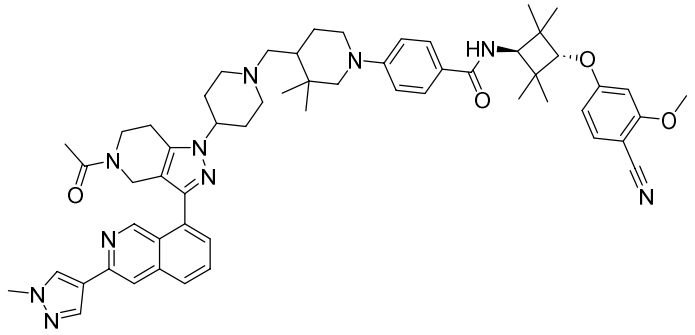
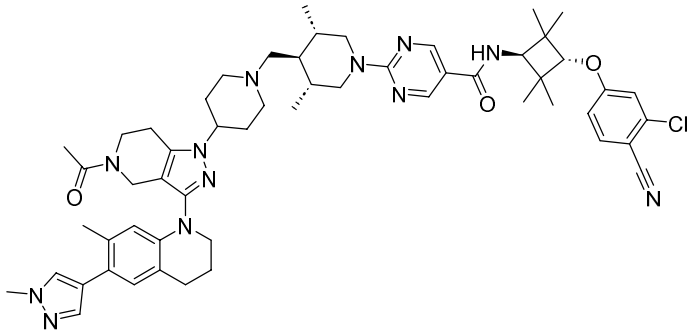
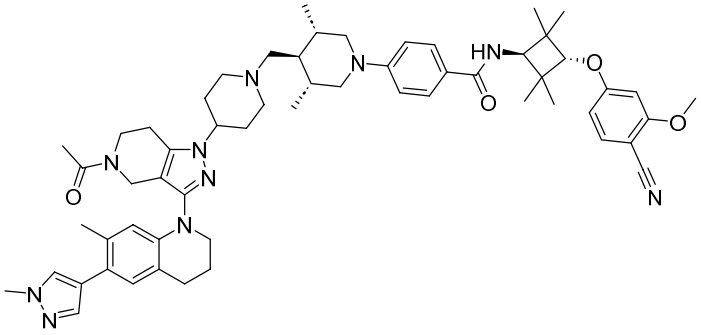
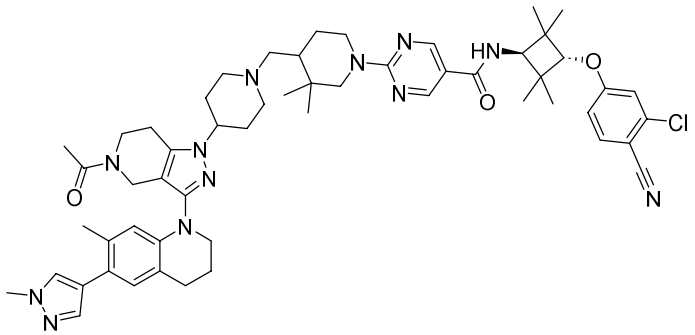
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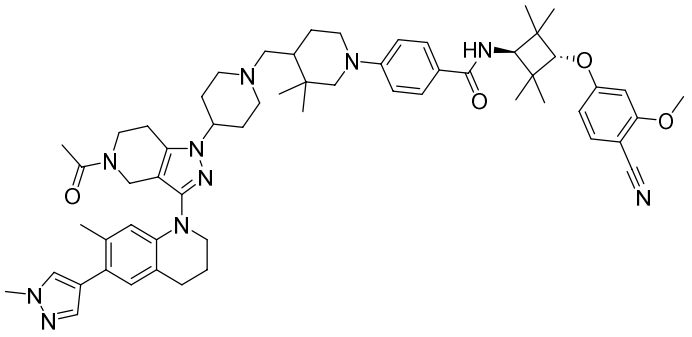
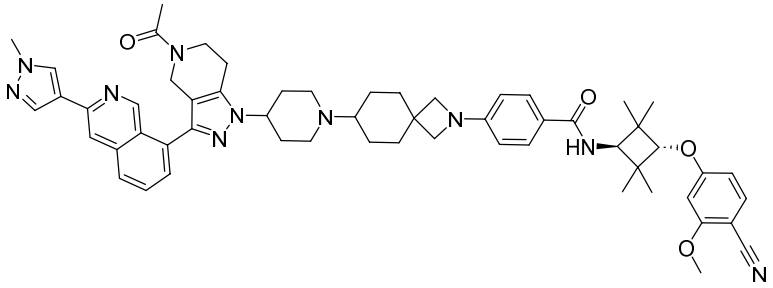
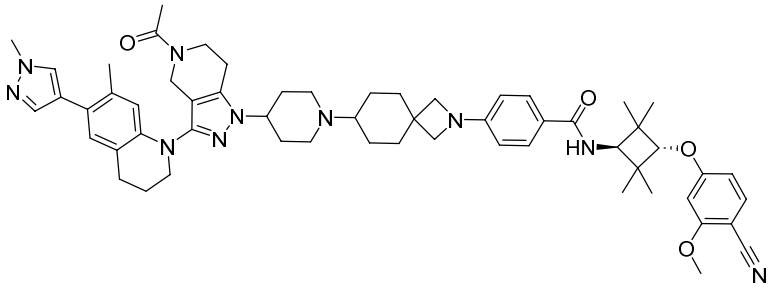
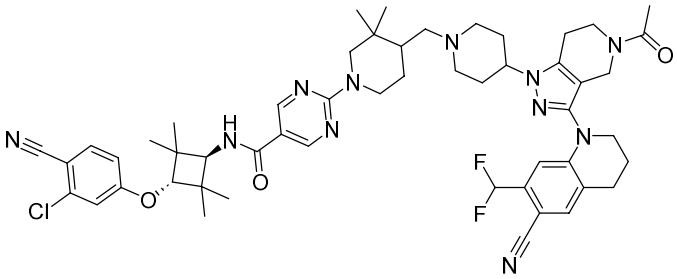
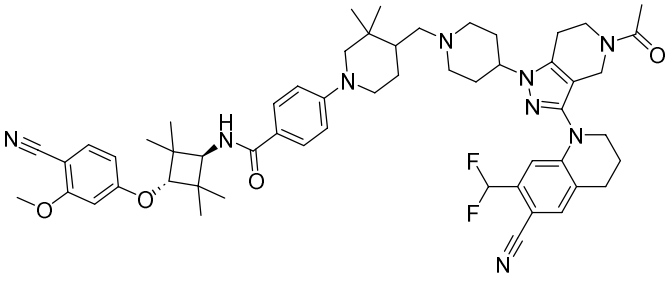
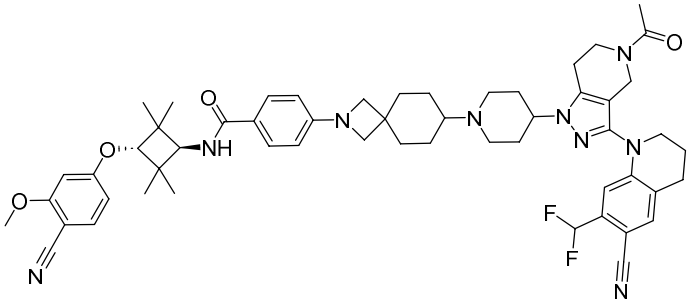
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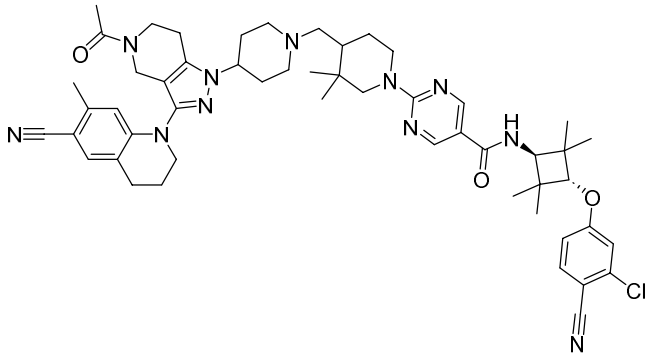
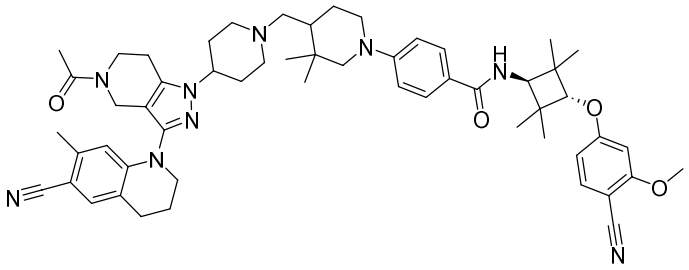
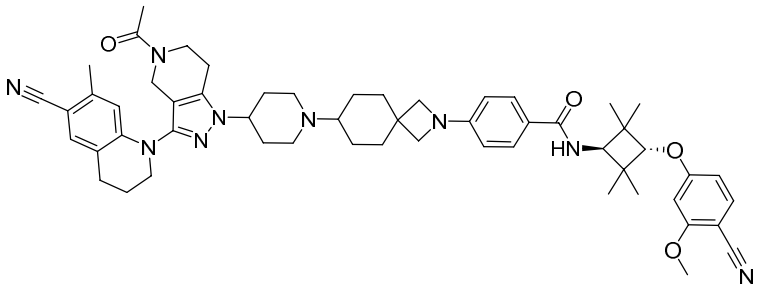
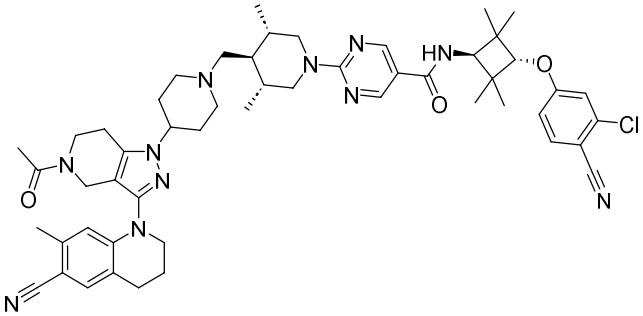
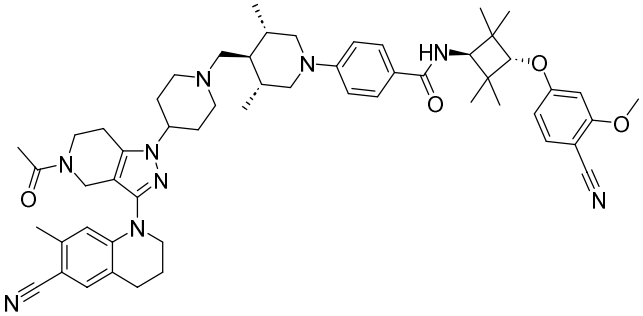
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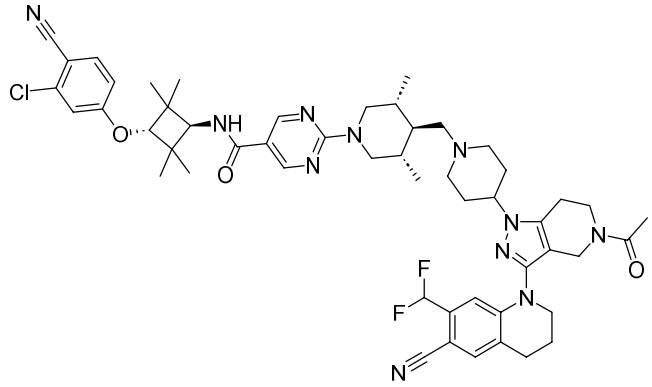
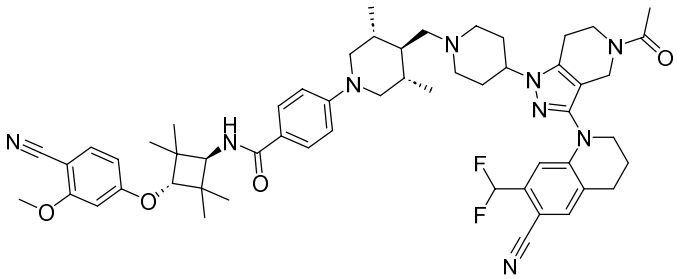
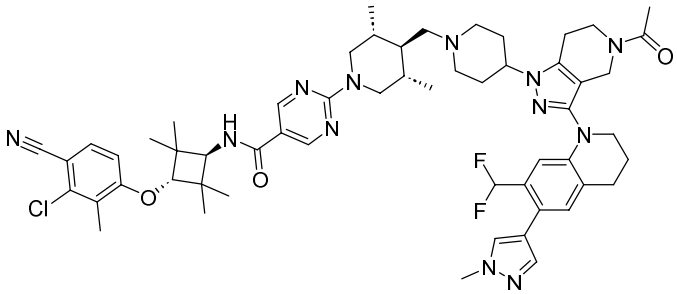
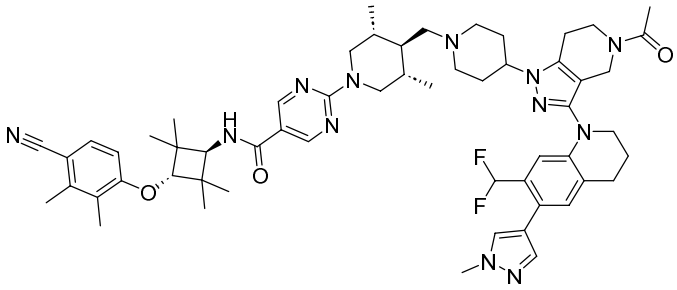
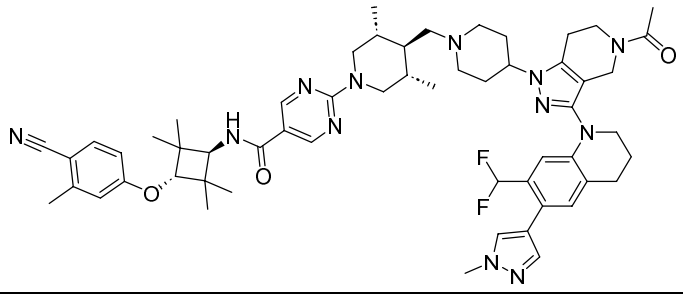
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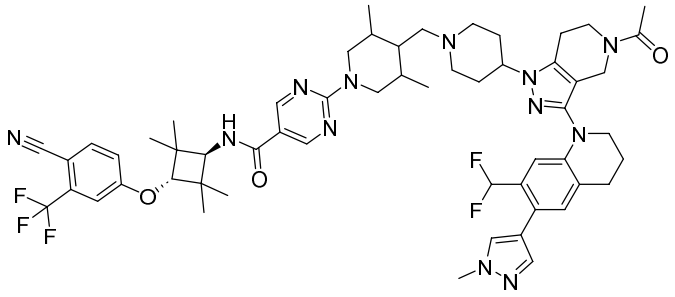
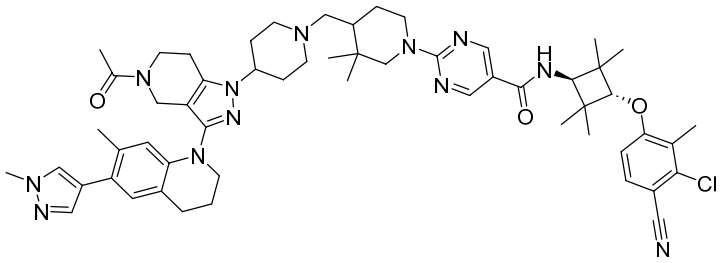
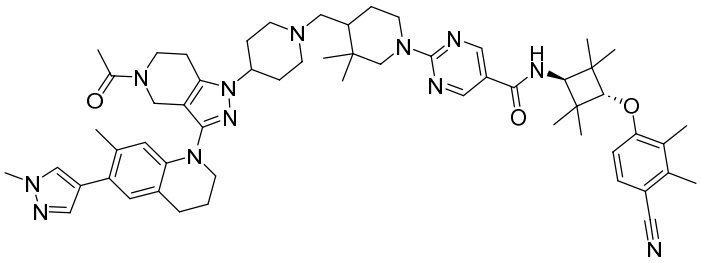
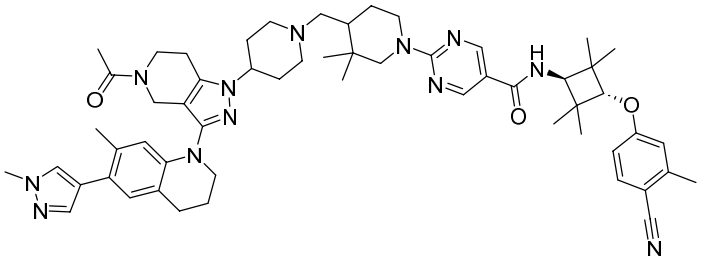
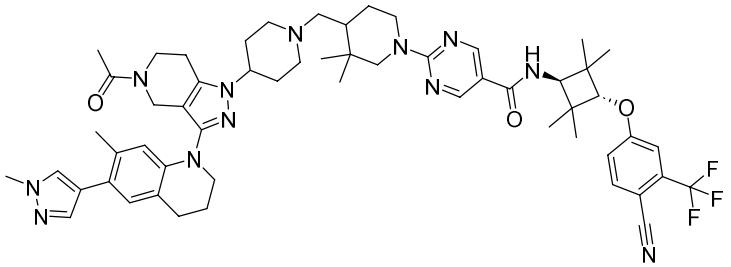
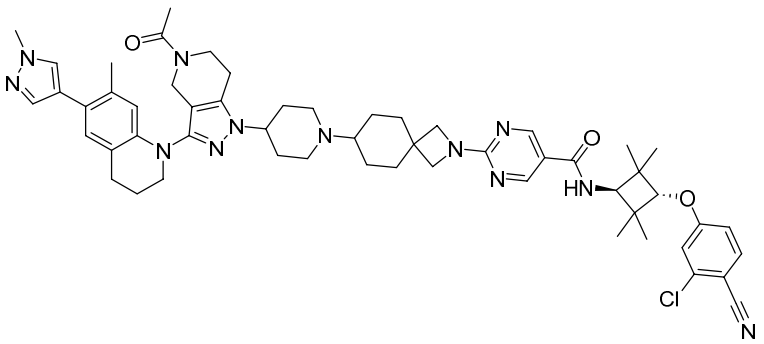
Compound	Structure
437	
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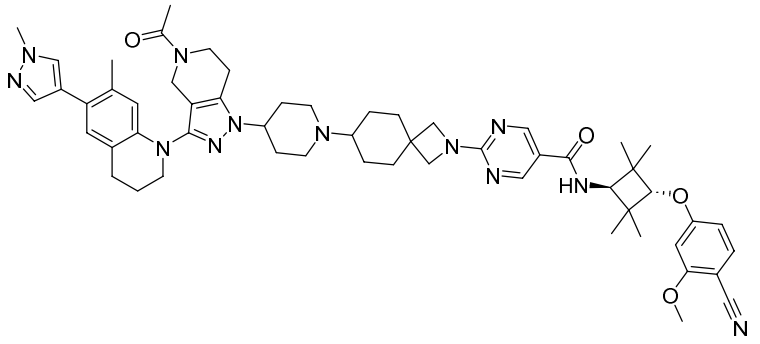
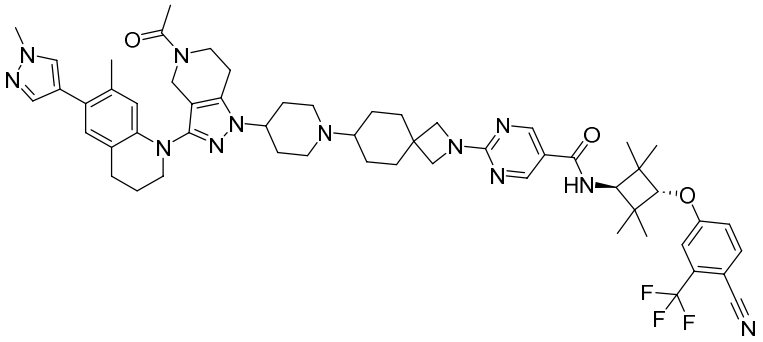
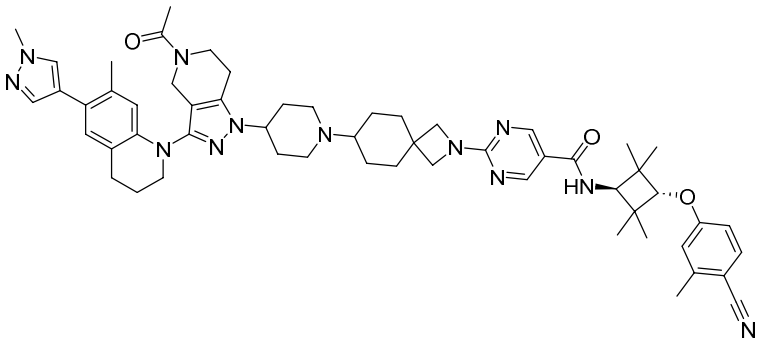
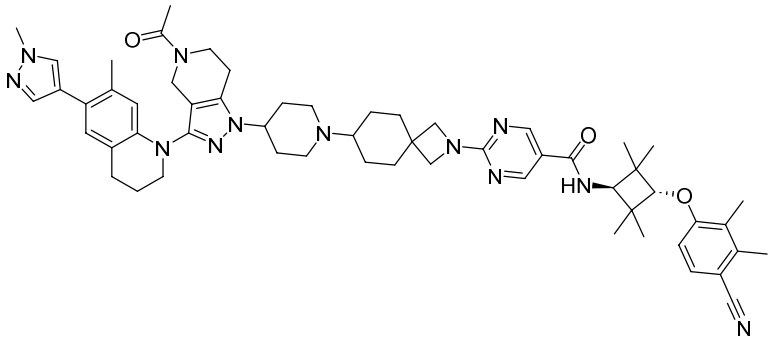
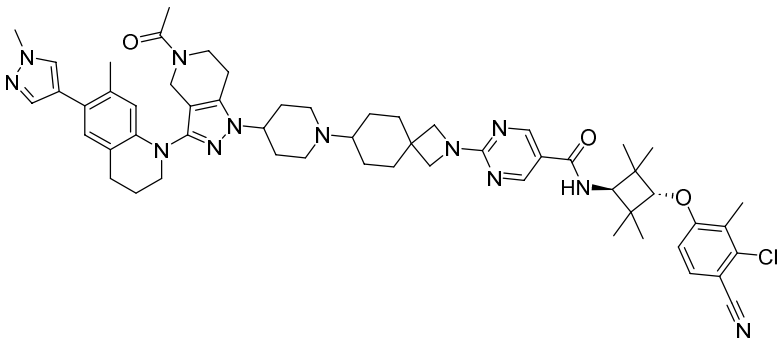
Compound	Structure
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Compound	Structure
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Compound	Structure
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Compound	Structure
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Compound	Structure
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Compound	Structure
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47. A pharmaceutical composition comprising a compound of any one of claims 1-46, or a

pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient.

48. Use of a compound of any one of claims 1-46, or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating prostate cancer in a mammal.

49. Use of a compound of any one of claims 1-46, or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating an androgen receptor dependent or androgen receptor mediated disease or condition in a mammal.

50. The use of claim 49, wherein androgen receptor dependent or androgen receptor mediated disease or condition is selected from benign prostate hyperplasia, hirsutism, adenomas and neoplasms of the prostate, benign or malignant tumor cells containing the androgen receptor, prostate cancer, breast cancer, endometrial cancer, and uterine cancer.

51. A compound of any one of claims 1-46, or a pharmaceutically acceptable salt of solvate thereof, for use in therapy.