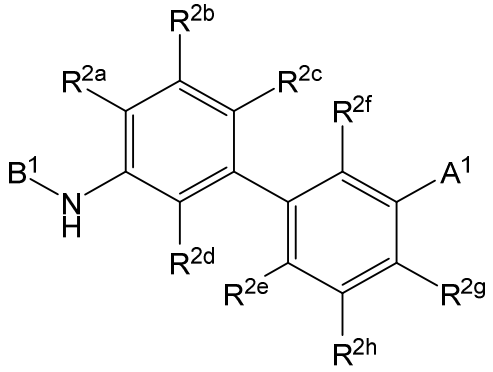
SUMMARY

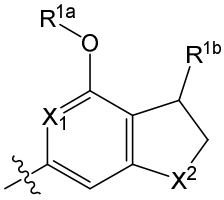
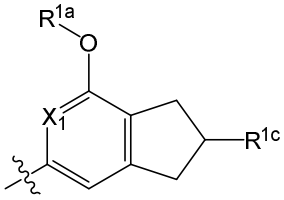
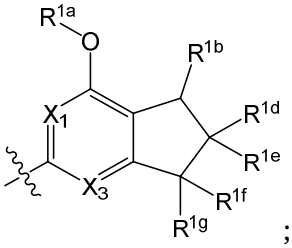
[0004] This disclosure relates to a compound of Formula (I), or a pharmaceutically acceptable salt thereof.

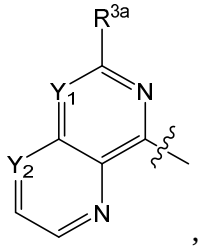
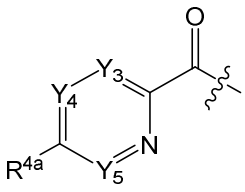
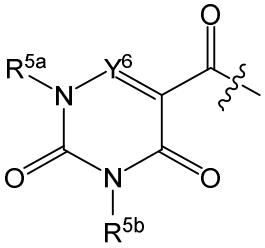
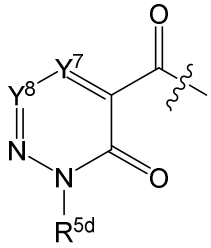
[0004a] In one aspect, there is provided a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having the structure:



(I)

wherein:

A^1 is  ,  , or  ;

B^1 is  ,  ,  , or  ;

each X^1 is selected from the group consisting of CH and N;

X^2 is O;

X^3 is selected from the group consisting of CH, C-halo and N;

Y^1 is selected from the group consisting of N and CH;

Y^2 is selected from the group consisting of N and CH;

Y^3 is selected from the group consisting of N and CH;

Y^4 is selected from the group consisting of N and CH;

Y^5 is selected from the group consisting of N, CH and C–OCH_3;

Y^6 is selected from the group consisting of N and CR^{5c};

Y^7 is CR^{5e};

Y^8 is CR^{5f};

each R^{1a} is selected from the group consisting of $–C_{1-4}$ alkyl, $–C_{1-4}$ haloalkyl, $–CH_2(C_{3-6}$ monocyclic cycloalkyl), $–C_{2-4}$ alkyl(C_{1-4} alkoxy), $–C_{2-4}$ alkyl (C_{1-4} haloalkoxy), $–CH_2$(4-6 membered monocyclic heterocyclyl) and $–CH_2$(5-6 membered monocyclic heteroaryl);

each R^{1b} is selected from the group consisting of $–N(R^{m1})R^{n1}$ and $–R^{x1}$;

R^{1d} is selected from the group consisting of hydrogen,$–CH_3$, $–CH_2CH_3$, –OH, $–OCH_3$ and –F;

R^{1e} is selected from the group consisting of hydrogen, $–CH_3$, $–CH_2CH_3$ and –F;

R^{1f} is selected from the group consisting of hydrogen, $–CH_3$, $–CH_2CH_3$, –OH, $–OCH_3$ and –F;

R^{1g} is selected from the group consisting of hydrogen, $–CH_3$, $–CH_2CH_3$ and –F;

R^{1c} is selected from the group consisting of $–N(R^{m1})R^{n1}$ and $–R^{x1}$;

R^{2a}, R^{2b}, R^{2c}, R^{2e}, R^{2g}, R^{2h} are independently selected from the group consisting of hydrogen and halogen;

R^{2d} and R^{2f} are independently selected from the group consisting of hydrogen, halogen, cyano, $–CH_3$, $–CH_2CH_3$, $–CH_2OH$, $–OCH_3$ and $–SCH_3$;

R^{3a} is selected from the group consisting of H, $–CH_3$, $–CF_3$ and $–CHF_2$;

R^{4a} is selected from the group consisting of H, halogen, $–C_{1-4}$ alkyl, $–C_{1-4}$ haloalkyl, $–CH_2R^{4b}$ and $–C(CH_3)R^{4b}$;

R^{4b} is selected from the group consisting of $–N(R^{m2})R^{n2}$ and $–R^{y1}$;

R^{5a} is selected from the group consisting of hydrogen, $–CH_3$, $–C_{2-4}$ alkyl and $–C_{2-4}$ haloalkyl;

R^{5b} is selected from the group consisting of hydrogen, $–CH_3$, $–C_{2-4}$ alkyl and $–C_{2-4}$ haloalkyl;

R^{5c} is selected from the group consisting of hydrogen, $–CH_3$, $–C_{2-4}$ alkyl and $–C_{2-4}$ haloalkyl;

R^{5d} is selected from the group consisting of hydrogen, $–CH_3$, $–C_{2-4}$ alkyl and $–C_{2-4}$ haloalkyl;

R^{5e} is selected from the group consisting of hydrogen, halogen and $–CH_3$;

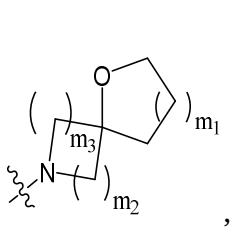
R^{5f} is selected from the group consisting of hydrogen, halogen, -OH, –CN and $–CH_3$;

R^{m1} is selected from the group consisting of hydrogen, $–C_{1-4}$ alkyl, C_{3-6} monocyclic cycloalkyl, C_{5-12} bicyclic cycloalkyl, 5- or 6-membered monocyclic heteroaryl, 4-7 membered monocyclic heterocyclyl, 8-11 membered fused-heteroaryl, 8-11 membered fused-heterocyclyl and $–R^{x2}$; wherein the monocyclic heteroaryl, the bicyclic heteroaryl the monocyclic heterocyclyl and the bicyclic heterocyclyl contain at least one atom or group of atoms independently selected from the group consisting of O (oxygen), S (sulfur), C(=O), S(=O), $S(=O)_2$ and N (nitrogen); wherein the $–C_{1-4}$ alkyl is optionally substituted with one or two or three substituents independently selected from halogen, cyano, hydroxy, $–C_{1-4}$ alkoxy, $–C_{1-4}$ haloalkyl, $–C_{1-4}$ haloalkoxy, $–C(=O)OR^{Z1}$, $–C(=O)NHS(=O)_2R^{Z3}$, $–C(=O)N(R^{Z1})R^{Z2}$, $–S(=O)_2R^{Z3}$, $–S(=O)_2N(R^{Z1})R^{Z2}$, $–N(R^{Z1})C(=O)R^{Z3}$, $–N(R^{Z1})S(=O)R^{Z3}$, $–N(R^{Z1})C(=O)N(R^{Z2})R^{Z3}$ and $–N(R^{Z1})S(=O)N(R^{Z2})R^{Z3}$; wherein the C_{3-6} monocyclic cycloalkyl, the C_{5-12} bicyclic cycloalkyl, the 5- or 6-membered monocyclic heteroaryl, the 4-7 membered monocyclic heterocyclyl, the 8-11 membered fused-heteroaryl and the 8-11 membered fused-heterocyclyl are optionally substituted with one, two, three or four substituents independently selected from halogen, cyano, $–C_{1-4}$ alkyl, hydroxy, $–C_{1-4}$ alkoxy, $–C_{1-4}$ haloalkyl, $–C_{1-4}$ haloalkoxy, $–C(=O)R^{Z1}$, $–C(=O)OR^{Z1}$, $–C(=O)NHS(=O)_2R^{Z3}$, $–C(=O)N(R^{Z1})R^{Z2}$, $–S(=O)_2R^{Z3}$, $–S(=O)_2N(R^{Z1})R^{Z2}$, $–N(R^{Z1})C(=O)R^{Z3}$, $–N(R^{Z1})S(=O)R^{Z3}$, $–N(R^{z1})C(=O)N(R^{Z2})R^{Z3}$ and $–N(R^{Z1})S(=O)N(R^{Z2})R^{Z3}$; and R^{n1} is hydrogen, $–C_{1-4}$ alkyl, $–C_{1-4}$ haloalkyl, C_{3-6} monocyclic cycloalkyl$(CH_2)–$ or $–C(=O)OR^{Z4}$;

R^{m2} is selected from the group consisting of $–CH_3$, $–C_{2-4}$ alkyl, $–C_{1-4}$ haloalkyl and $–R^{y2}$, wherein the $–C_{2-4}$ alkyl is optionally substituted with hydroxy;

R^{n2} is selected from the group consisting of H, $–C_{1-4}$ alkyl and $–C_{1-4}$ haloalkyl;

R^{x1} is selected from the group consisting of: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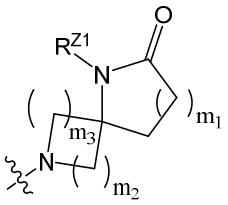
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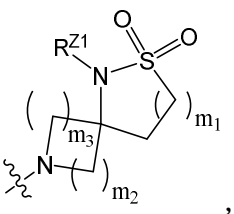
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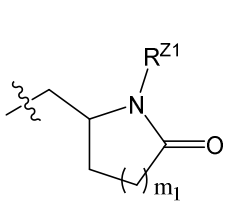
–C(=O)NHS(=O)$_2$R^{Z3}, –C(=O)N(R^{Z1})R^{Z2}, –S(=O)$_2$R^{Z3}, –S(=O)$_2$N(R^{Z1})R^{Z2}, –N(R^{Z1})C(=O)R^{Z3}, –N(R^{Z1})S(=O)R^{Z3}, –N(R^{Z1})C(=O)N(R^{Z1})R^{Z3} and –N(R^{Z1})S(=O)$_2$N(R^{Z2})R^{Z3};

R^{x2} is selected from the group consisting of: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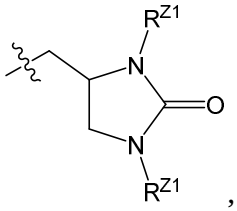
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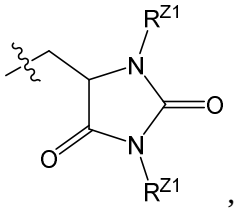
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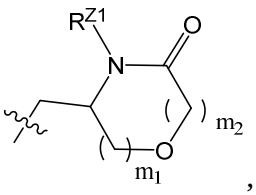
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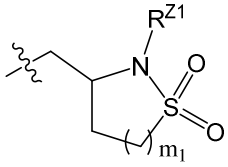
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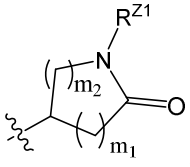
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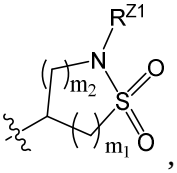
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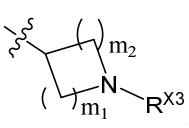
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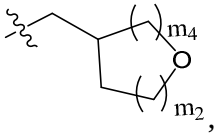
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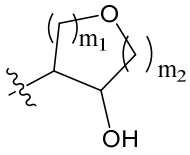
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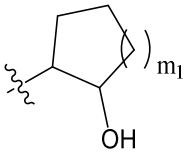
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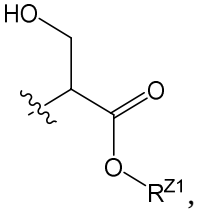
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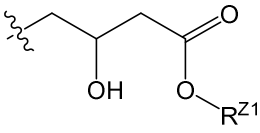
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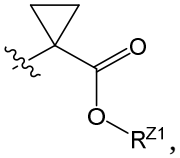
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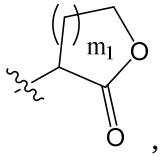
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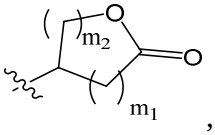
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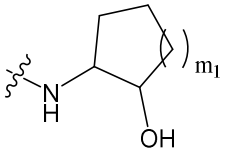
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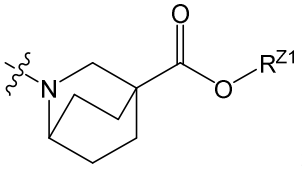
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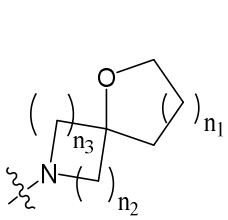
R^{y1} is selected from the group consisting of: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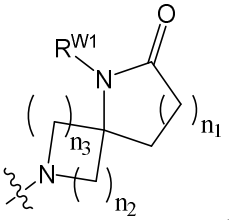
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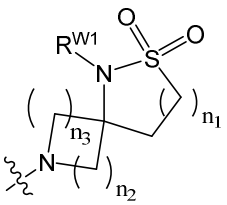
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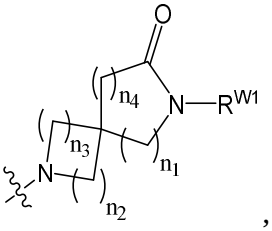
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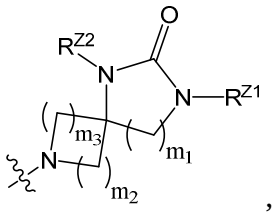
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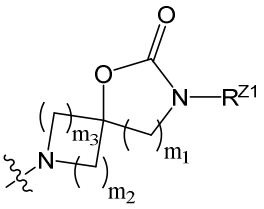
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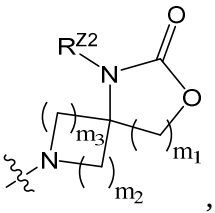
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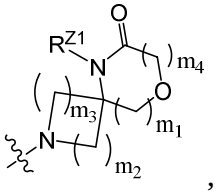
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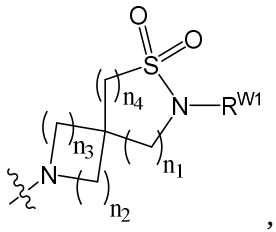
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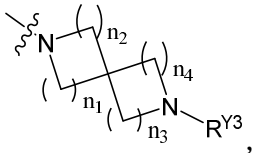
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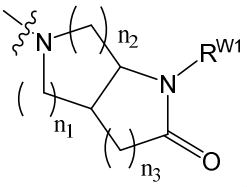
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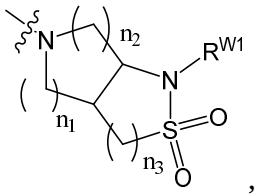
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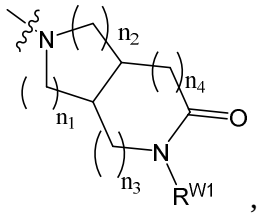
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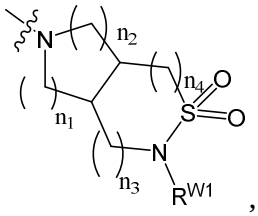
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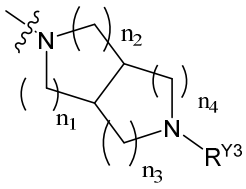
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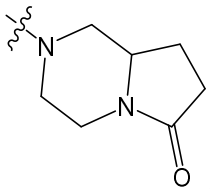
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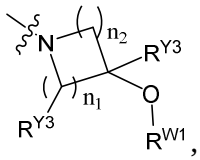
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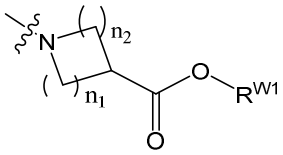
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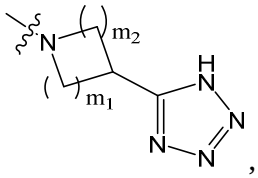
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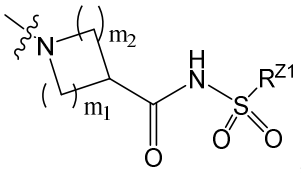
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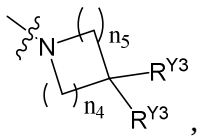
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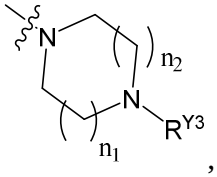
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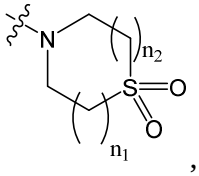
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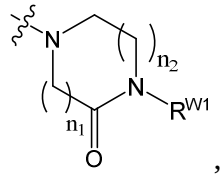
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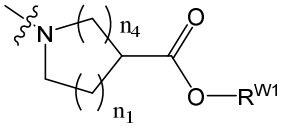
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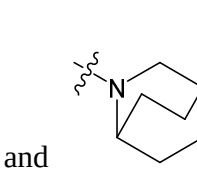
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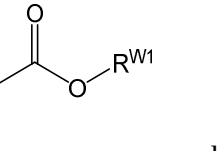
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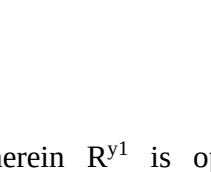
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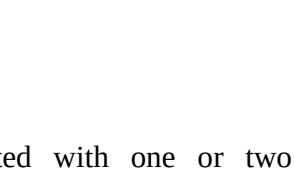
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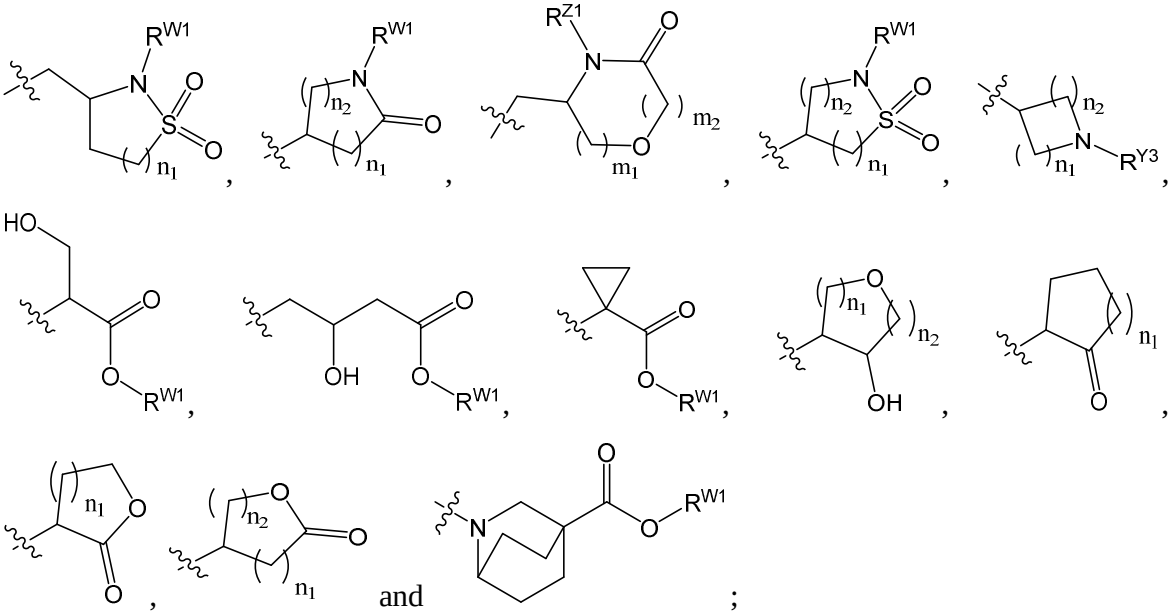
and ; wherein R^{y1} is optionally substituted with one or two substituents independently selected from halogen, cyano, $–C_{1-4}$ alkyl, hydroxy, $–C_{1-4}$ alkoxy, $–C_{1-4}$ haloalkyl, $–C_{1-4}$ haloalkoxy, $–C(=O)OR^{W1}$, $–C(=O)NHS(=O)_2R^{W3}$, $–C(=O)N(R^{W1})R^{W2}$, $–S(=O)_2R^{W3}$, $–S(=O)N(R^{W1})R^{W2}$, $–N(R^{W1})C(=O)R^{W3}$, $–N(R^{W1})S(=O)R^{W3}$, $–N(R^{W1})C(=O)N(R^{W2})R^{W3}$ and $–N(R^{W1})S(=O)N(R^{W2})R^{W3}$;

R^{y2} is selected from the group consisting of:



m_1, m_2, m_3, n_1, n_2 and n_3 are independently 1 or 2;

m_4 and n_4 are independently 0, 1 or 2;

m_5 and n_5 are independently 1, 2, 3 or 4;

each R^{X3} is independently selected from the group consisting of hydrogen, halogen, $–C_{1-4}$ alkyl, $–C_{1-4}$ haloalkyl, $–C(=O)R^{Z3}$, $–C(=O)OR^{Z1}$, $–S(=O)_2R^{Z1}$, $–C(=O)N(R^{Z1})R^{Z2}$ and $–S(=O)N(R^{Z1})R^{Z2}$;

each R^{Y3} is independently selected from the group consisting of hydrogen, halogen, $–C_{1-4}$ alkyl, $–C_{1-4}$ haloalkyl, $–C(=O)R^{W3}$, $–C(=O)OR^{W3}$, $–S(=O)_2R^{W3}$, $–C(=O)N(R^{W1})R^{W2}$ and $–S(=O)N(R^{W1})R^{W2}$;

R^{Z1} and R^{Z2} are independently selected from the group consisting of hydrogen, $–C_{1-4}$ alkyl and $–C_{1-4}$ haloalkyl; or

R^{Z1} and R^{Z2} are taken together to form a monocyclic heterocyclyl when attached to the same nitrogen;

R^{W1} and R^{W2} are independently selected from the group consisting of hydrogen, $–C_{1-4}$ alkyl and $–C_{1-4}$ haloalkyl;

R^{Z3} and R^{W3} are independently selected from the group consisting of hydrogen, $–C_{1-4}$ alkyl and $–C_{1-4}$ haloalkyl; and

R^{Z4} is selected from the group consisting of hydrogen, $–C_{1-4}$ alkyl and 5- to 6-membered monocyclic heterocyclyl$(CH_2)–$ optionally substituted with $–C_{1-4}$ alkyl.

[0005] This disclosure also relates to a pharmaceutical composition that can contain an effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt thereof.

[0005a] In another aspect, there is provided a pharmaceutical composition comprising an effective amount of a compound as defined herein, or a pharmaceutically acceptable salt thereof, and excipient.

[0006] This disclosure also relates to a method of treating a HBV and/or HDV infection that can include administering to a subject identified as suffering from the HBV and/or HDV infection an effective amount of a compound, or a pharmaceutically acceptable salt thereof, as described herein, or a pharmaceutical composition that includes an effective amount of a compound, or a pharmaceutically acceptable salt thereof, as described herein. This disclosure also relates to a compound, or a pharmaceutically acceptable salt thereof, as described herein, or a pharmaceutical composition that includes an effective amount of a compound, or a pharmaceutically acceptable salt thereof, as described herein for the use of treating a HBV and/or HDV infection.

[0007] This disclosure also relates to a method of inhibiting replication of HBV and/or HDV that can include contacting a cell infected with the HBV and/or HDV with an effective amount of a compound, or a pharmaceutically acceptable salt thereof, as described herein, or a pharmaceutical composition that includes an effective amount of a compound, or a pharmaceutically acceptable salt thereof, as described herein. This disclosure also relates to a compound, or a pharmaceutically acceptable salt thereof, as described herein, or a pharmaceutical composition that includes an effective amount of a compound, or a pharmaceutically acceptable salt thereof, as described herein for the use of inhibiting the replication HBV and/or HDV.

[0007a] In another aspect, there is provided a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, for use in treating hepatitis B.

[0007b] In another aspect, there is provided a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, for use in treating hepatocellular carcinoma (HCC).

[0007c] In another aspect, there is provided use of an effective amount of a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating hepatitis B.

[0007d] In another aspect, there is provided use of an effective amount of a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating hepatocellular carcinoma (HCC).

[0007e] In another aspect, there is provided a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, for use in therapy.

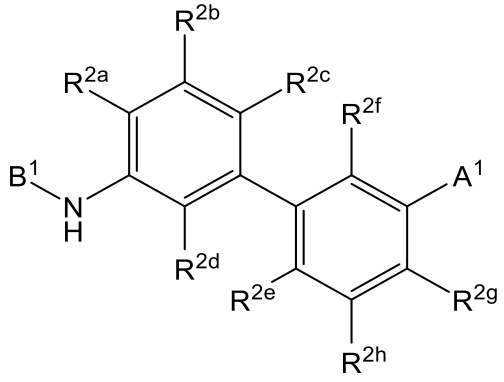
[0008] Other examples are described in greater detail below.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] Figures 1A and 1B show the absolute configuration structure and ORTEP crystal structure of the formate salt of Intermediate 5-1b.

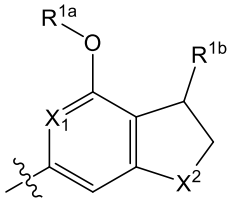
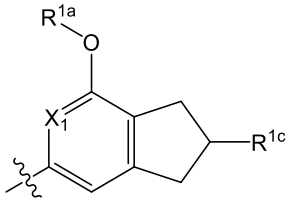
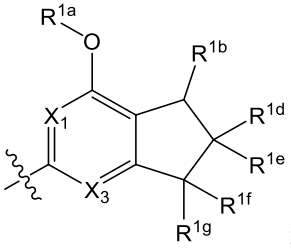
WHAT IS CLAIMED IS:

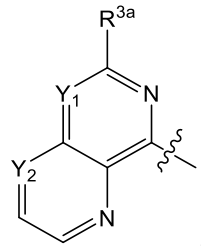
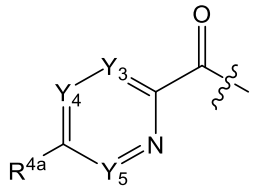
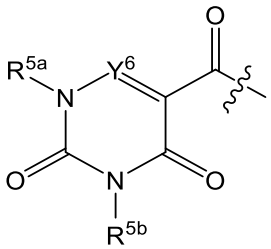
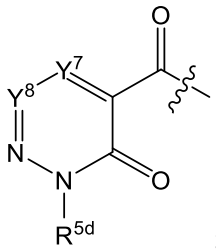
1. A compound of Formula (I), or a pharmaceutically acceptable salt thereof, having the structure:



(I)

wherein:

A^1 is  ,  , or  ;

B^1 is  ,  ,  , or  ;

each X^1 is selected from the group consisting of CH and N;

X^2 is O;

X^3 is selected from the group consisting of CH, C-halo and N;

Y^1 is selected from the group consisting of N and CH;

Y^2 is selected from the group consisting of N and CH;

Y^3 is selected from the group consisting of N and CH;

Y^4 is selected from the group consisting of N and CH;

Y^5 is selected from the group consisting of N, CH and C–OCH_3;

Y^6 is selected from the group consisting of N and CR^{5c};

Y^7 is CR^{5e};

Y^8 is CR^{5f};

each R^{1a} is selected from the group consisting of $–C_{1-4}$ alkyl, $–C_{1-4}$ haloalkyl, $–CH_2$(C_{3-6} monocyclic cycloalkyl), $–C_{2-4}$ alkyl(C_{1-4} alkoxy), $–C_{2-4}$ alkyl (C_{1-4} haloalkoxy), $–CH_2$(4-6 membered monocyclic heterocyclyl) and $–CH_2$(5-6 membered monocyclic heteroaryl);

each R^{1b} is selected from the group consisting of $–N(R^{m1})R^{n1}$ and $–R^{x1}$;

R^{1d} is selected from the group consisting of hydrogen,$–CH_3$, $–CH_2CH_3$, –OH, $–OCH_3$ and –F;

R^{1e} is selected from the group consisting of hydrogen, $–CH_3$, $–CH_2CH_3$ and –F;

R^{1f} is selected from the group consisting of hydrogen, $–CH_3$, $–CH_2CH_3$, –OH, $–OCH_3$ and –F;

R^{1g} is selected from the group consisting of hydrogen, $–CH_3$, $–CH_2CH_3$ and –F;

R^{1c} is selected from the group consisting of $–N(R^{m1})R^{n1}$ and $–R^{x1}$;

R^{2a}, R^{2b}, R^{2c}, R^{2e}, R^{2g}, R^{2h} are independently selected from the group consisting of hydrogen and halogen;

R^{2d} and R^{2f} are independently selected from the group consisting of hydrogen, halogen, cyano, $–CH_3$, $–CH_2CH_3$, $–CH_2OH$, $–OCH_3$ and $–SCH_3$;

R^{3a} is selected from the group consisting of H, $–CH_3$, $–CF_3$ and $–CHF_2$;

R^{4a} is selected from the group consisting of H, halogen, $–C_{1-4}$ alkyl, $–C_{1-4}$ haloalkyl, $–CH_2R^{4b}$ and $–C(CH_3)R^{4b}$;

R^{4b} is selected from the group consisting of $–N(R^{m2})R^{n2}$ and $–R^{y1}$;

R^{5a} is selected from the group consisting of hydrogen, $–CH_3$, $–C_{2-4}$ alkyl and $–C_{2-4}$ haloalkyl;

R^{5b} is selected from the group consisting of hydrogen, $–CH_3$, $–C_{2-4}$ alkyl and $–C_{2-4}$ haloalkyl;

R^{5c} is selected from the group consisting of hydrogen, $–CH_3$, $–C_{2-4}$ alkyl and $–C_{2-4}$ haloalkyl;

R^{5d} is selected from the group consisting of hydrogen, $–CH_3$, $–C_{2-4}$ alkyl and $–C_{2-4}$ haloalkyl;

R^{5e} is selected from the group consisting of hydrogen, halogen and $–CH_3$;

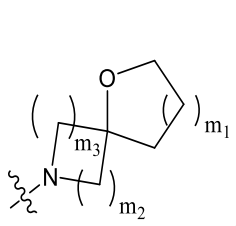
R^{5f} is selected from the group consisting of hydrogen, halogen, -OH, –CN and $–CH_3$;

R^{m1} is selected from the group consisting of hydrogen, $–C_{1-4}$ alkyl, C_{3-6} monocyclic cycloalkyl, C_{5-12} bicyclic cycloalkyl, 5- or 6-membered monocyclic heteroaryl, 4-7 membered monocyclic heterocyclyl, 8-11 membered fused-heteroaryl, 8-11 membered fused-heterocyclyl and $–R^{x2}$; wherein the monocyclic heteroaryl, the bicyclic heteroaryl the monocyclic heterocyclyl and the bicyclic heterocyclyl contain at least one atom or group of atoms independently selected from the group consisting of O (oxygen), S (sulfur), C(=O), S(=O), $S(=O)_2$ and N (nitrogen); wherein the $–C_{1-4}$ alkyl is optionally substituted with one or two or three substituents independently selected from halogen, cyano, hydroxy, $–C_{1-4}$ alkoxy, $–C_{1-4}$ haloalkyl, $–C_{1-4}$ haloalkoxy, $–C(=O)OR^{Z1}$, $–C(=O)NHS(=O)_2R^{Z3}$, $–C(=O)N(R^{Z1})R^{Z2}$, $–S(=O)_2R^{Z3}$, $–S(=O)_2N(R^{Z1})R^{Z2}$, $–N(R^{Z1})C(=O)R^{Z3}$, $–N(R^{Z1})S(=O)R^{Z3}$, $–N(R^{Z1})C(=O)N(R^{Z2})R^{Z3}$ and $–N(R^{Z1})S(=O)N(R^{Z2})R^{Z3}$; wherein the C_{3-6} monocyclic cycloalkyl, the C_{5-12} bicyclic cycloalkyl, the 5- or 6-membered monocyclic heteroaryl, the 4-7 membered monocyclic heterocyclyl, the 8-11 membered fused-heteroaryl and the 8-11 membered fused-heterocyclyl are optionally substituted with one, two, three or four substituents independently selected from halogen, cyano, $–C_{1-4}$ alkyl, hydroxy, $–C_{1-4}$ alkoxy, $–C_{1-4}$ haloalkyl, $–C_{1-4}$ haloalkoxy, $–C(=O)R^{Z1}$, $–C(=O)OR^{Z1}$, $–C(=O)NHS(=O)_2R^{Z3}$, $–C(=O)N(R^{Z1})R^{Z2}$, $–S(=O)_2R^{Z3}$, $–S(=O)_2N(R^{Z1})R^{Z2}$, $–N(R^{Z1})C(=O)R^{Z3}$, $–N(R^{Z1})S(=O)R^{Z3}$, $–N(R^{z1})C(=O)N(R^{Z2})R^{Z3}$ and $–N(R^{Z1})S(=O)N(R^{Z2})R^{Z3}$; and R^{n1} is hydrogen, $–C_{1-4}$ alkyl, $–C_{1-4}$ haloalkyl, C_{3-6} monocyclic cycloalkyl$(CH_2)–$ or $–C(=O)OR^{Z4}$;

R^{m2} is selected from the group consisting of $–CH_3$, $–C_{2-4}$ alkyl, $–C_{1-4}$ haloalkyl and $–R^{y2}$, wherein the $–C_{2-4}$ alkyl is optionally substituted with hydroxy;

R^{n2} is selected from the group consisting of H, $–C_{1-4}$ alkyl and $–C_{1-4}$ haloalkyl;

R^{x1} is selected from the group consisting of: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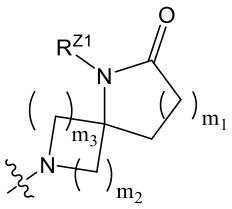
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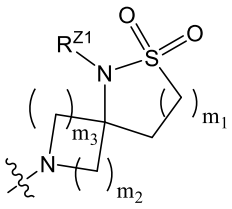
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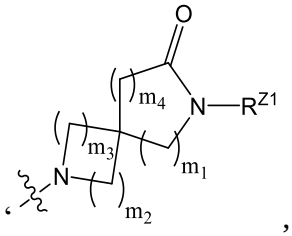
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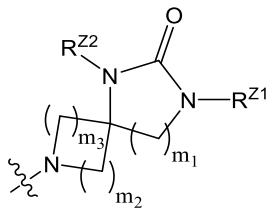
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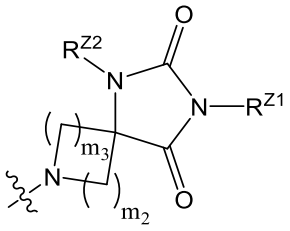
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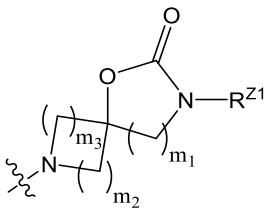
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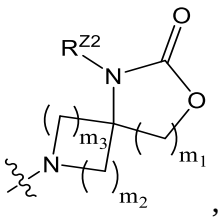
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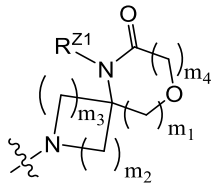
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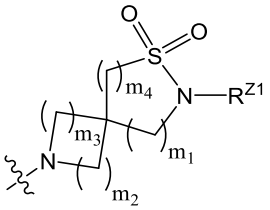
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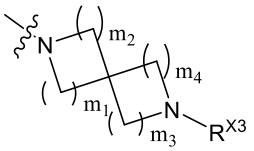
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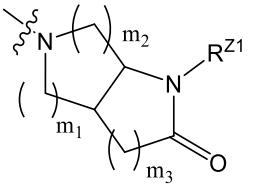
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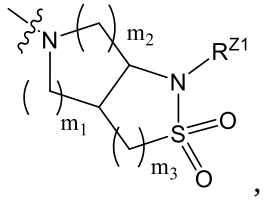
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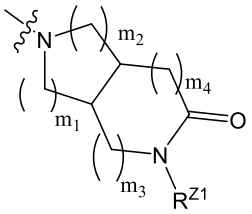
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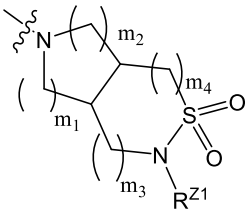
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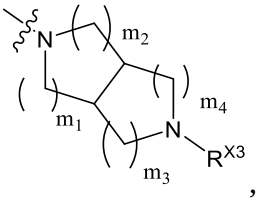
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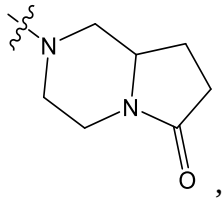
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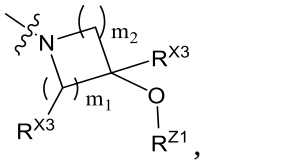
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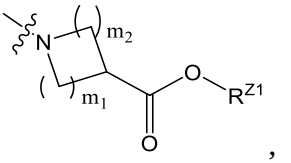
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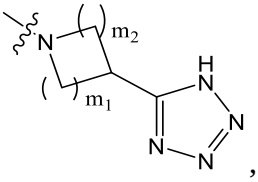
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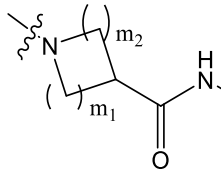
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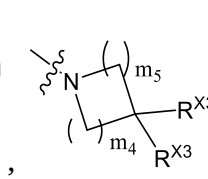
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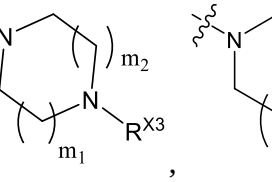
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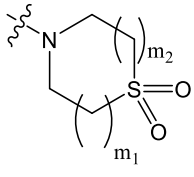
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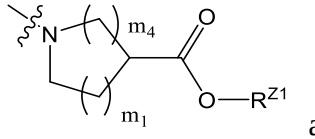
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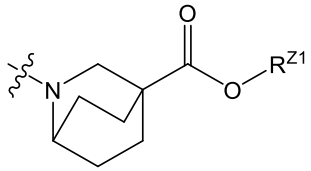
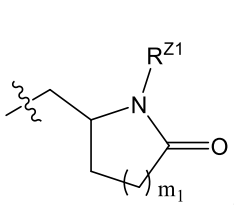

; wherein R^{x1} is optionally substituted with one or two substituents independently selected from halogen, cyano, –C_{1-4} alkyl, hydroxy, –C_{1-4} alkoxy, –C_{1-4} haloalkyl, –C_{1-4} haloalkoxy, –C(=O)OR^{Z1},

–C(=O)NHS(=O)$_2$R^{Z3}, –C(=O)N(R^{Z1})R^{Z2}, –S(=O)$_2$R^{Z3}, –S(=O)$_2$N(R^{Z1})R^{Z2}, –N(R^{Z1})C(=O)R^{Z3}, –N(R^{Z1})S(=O)R^{Z3}, –N(R^{Z1})C(=O)N(R^{Z1})R^{Z3} and –N(R^{Z1})S(=O)$_2$N(R^{Z2})R^{Z3};

R^{x2} is selected from the group consisting of: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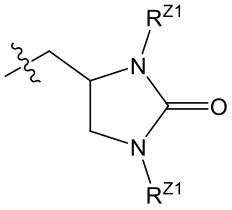
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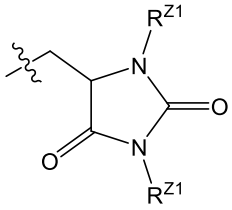
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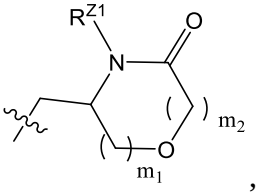
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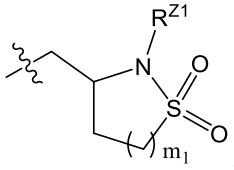
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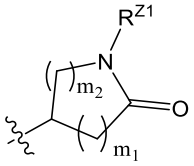
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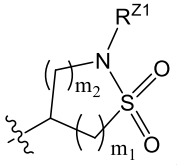
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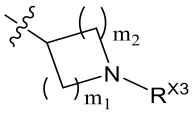
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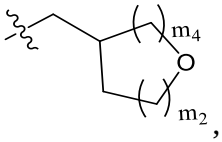
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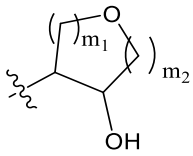
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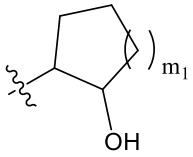
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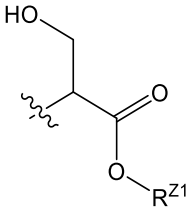
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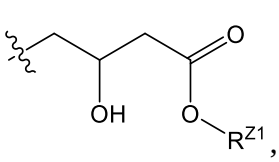
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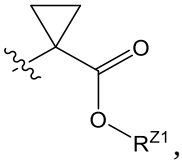
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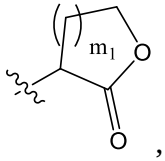
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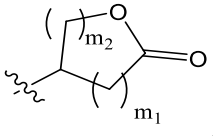
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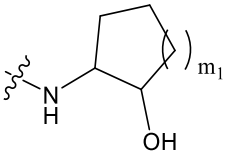
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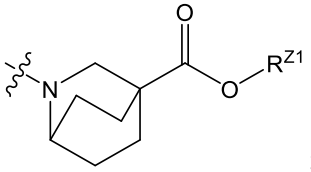
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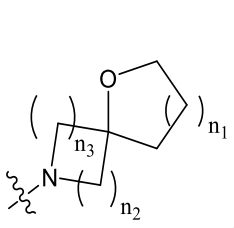
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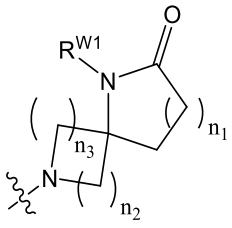
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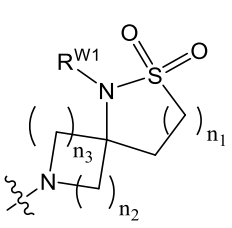
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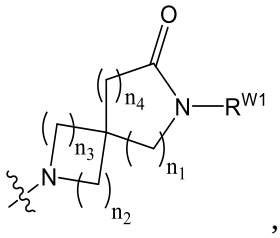
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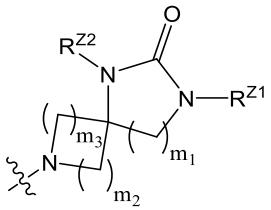
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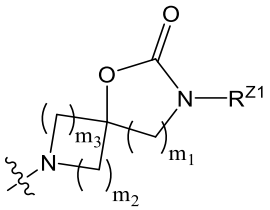
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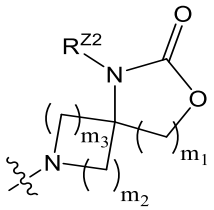
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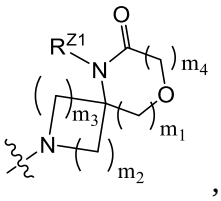
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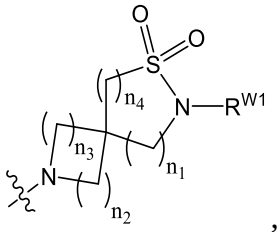
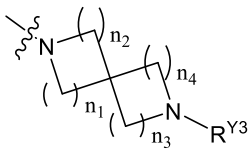
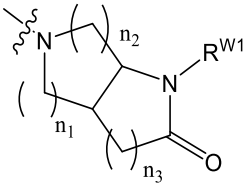
 ,  ,  ,

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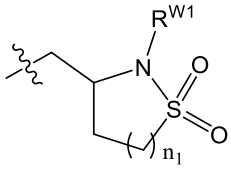
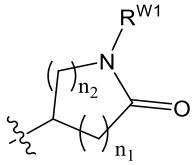
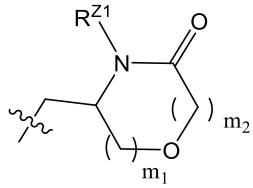
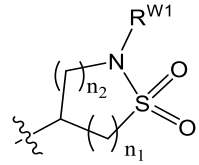
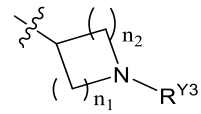
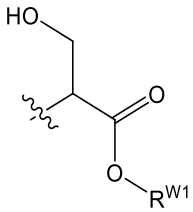
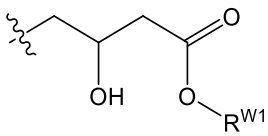
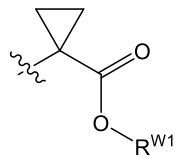
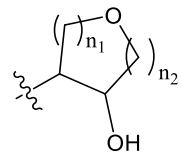
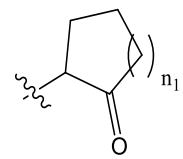
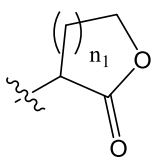
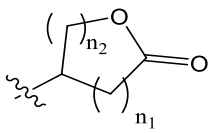
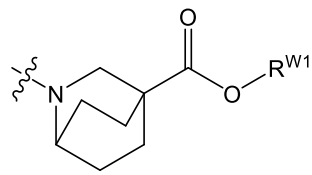
 ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,

 ,  and  ;

m_1, m_2, m_3, n_1, n_2 and n_3 are independently 1 or 2;

m_4 and n_4 are independently 0, 1 or 2;

m_5 and n_5 are independently 1, 2, 3 or 4;

each R^{X3} is independently selected from the group consisting of hydrogen, halogen, $–C_{1-4}$ alkyl, $–C_{1-4}$ haloalkyl, $–C(=O)R^{Z3}$, $–C(=O)OR^{Z1}$, $–S(=O)_2R^{Z1}$, $–C(=O)N(R^{Z1})R^{Z2}$ and $–S(=O)N(R^{Z1})R^{Z2}$;

each R^{Y3} is independently selected from the group consisting of hydrogen, halogen, $–C_{1-4}$ alkyl, $–C_{1-4}$ haloalkyl, $–C(=O)R^{W3}$, $–C(=O)OR^{W3}$, $–S(=O)_2R^{W3}$, $–C(=O)N(R^{W1})R^{W2}$ and $–S(=O)N(R^{W1})R^{W2}$;

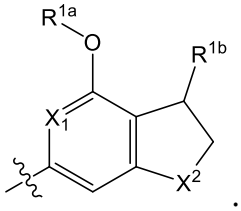
R^{Z1} and R^{Z2} are independently selected from the group consisting of hydrogen, $–C_{1-4}$ alkyl and $–C_{1-4}$ haloalkyl; or

R^{Z1} and R^{Z2} are taken together to form a monocyclic heterocyclyl when attached to the same nitrogen;

R^{W1} and R^{W2} are independently selected from the group consisting of hydrogen, $–C_{1-4}$ alkyl and $–C_{1-4}$ haloalkyl;

R^{Z3} and R^{W3} are independently selected from the group consisting of hydrogen, $–C_{1-4}$ alkyl and $–C_{1-4}$ haloalkyl; and

R^{Z4} is selected from the group consisting of hydrogen, $–C_{1-4}$ alkyl and 5- to 6-membered monocyclic heterocyclyl(CH_2)– optionally substituted with $–C_{1-4}$ alkyl.

2. The compound of Claim 1, wherein A^1 is 

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3. The compound of Claim 2, wherein X^1 is CH.

4. The compound of Claim 2, wherein X^1 is N.

5. The compound of any one of Claims 2-4, wherein R^{1a} is $–C_{1-4}$ alkyl.

6. The compound of any one of Claims 2-4, wherein R^{1a} is $–C_{1-4}$ haloalkyl.

7. The compound of any one of Claims 2-4, wherein R^{1a} is $–C_{2-4}$ alkyl(C_{1-4} alkoxy) or $–C_{2-4}$ alkyl (C_{1-4} haloalkoxy).

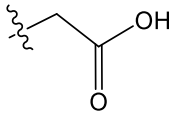
8. The compound of any one of Claims 2-4, wherein R^{1a} is selected from the group consisting of $–CH_2$(C_{3-6} monocyclic cycloalkyl), $–CH_2$(4-6 membered monocyclic heterocyclyl) and $–CH_2$(5-6 membered monocyclic heteroaryl).

9. The compound of any one of Claims 2-8, wherein R^{1b} is $–N(R^{m1})R^{n1}$.

10. The compound of Claim 9, wherein R^{n1} is hydrogen.

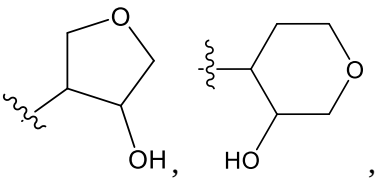
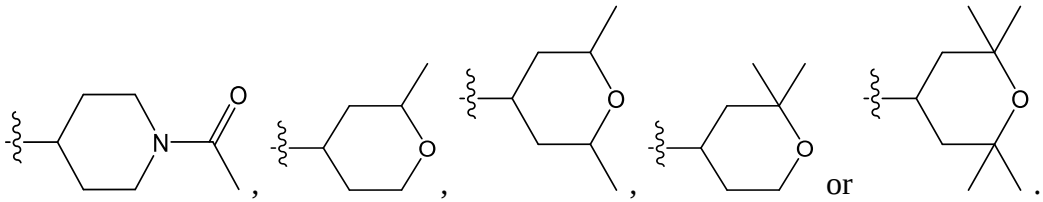
11. The compound of Claim 9, wherein R^{n1} is $–C(=O)OR^{Z4}$.

12. The compound of any one of Claims 9-11, wherein R^{m1} is $–C_{1-4}$ alkyl optionally substituted with $–C(=O)OR^{Z1}$ or 4-7 membered monocyclic heterocyclyl optionally substituted with hydroxy.

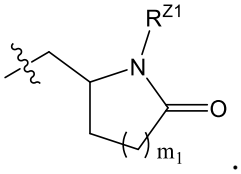
13. The compound of Claim 12, wherein R^{m1} is 

.

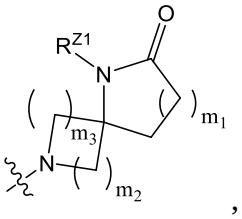
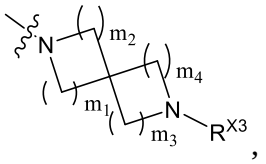
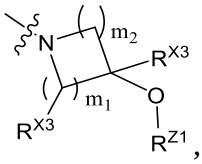
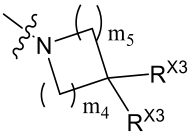
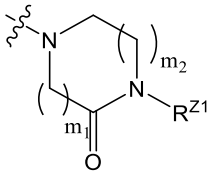
14. The compound of Claim 12, wherein R^{m1} is tetrahydrofuran or tetrahydro-2H-pyran, each optionally substituted with hydroxy or C_{1-4} alkyl.

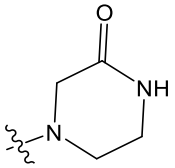
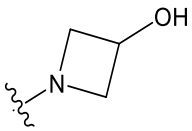
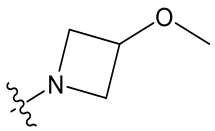
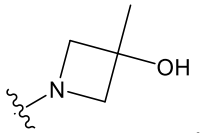
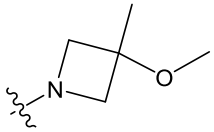
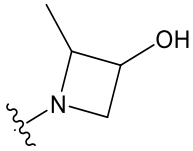
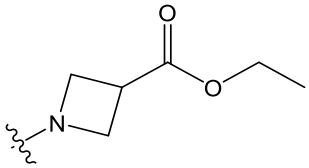
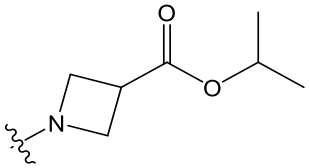
15. The compound of Claim 14, wherein R^{m1} is  ,  , or .

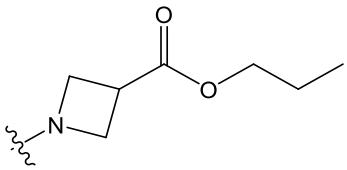
16. The compound of any one of Claims 9-11, wherein R^{m1} is $-R^{x2}$.

17. The compound of Claim 16, wherein $-R^{x2}$ is  .

18. The compound of any one of Claims 2-8, wherein R^{1b} is $-R^{x1}$.

19. The compound of Claim 18, wherein $-R^{x1}$ is selected from the group consisting of:  ,  ,  ,  , and  .

20. The compound of Claim 19, wherein $-R^{x1}$ is selected from the group consisting of:  ,  ,  ,  ,  ,  ,  ,  .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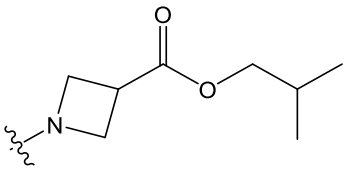
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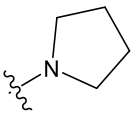
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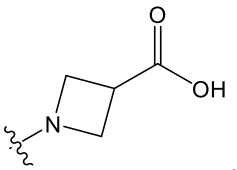
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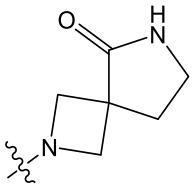
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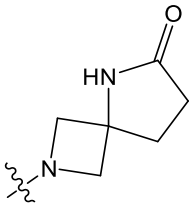
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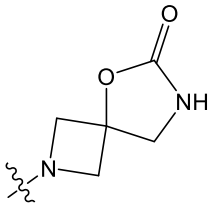
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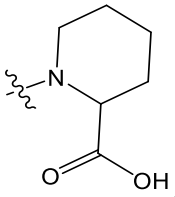
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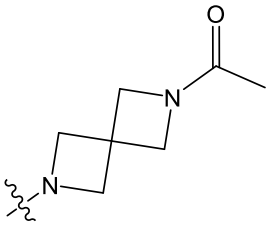
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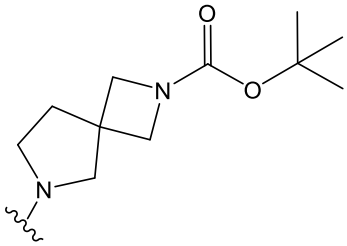
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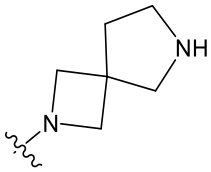
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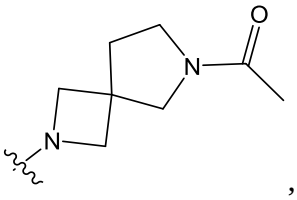
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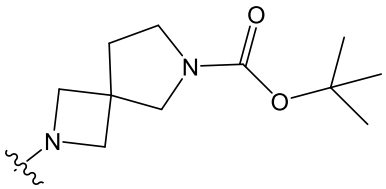
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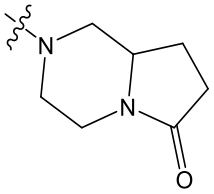
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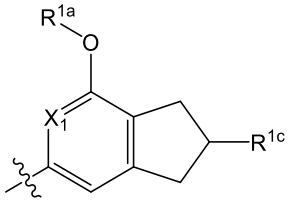
21. The compound of Claim 1, wherein A^1 is  .

22. The compound of Claim 21, wherein X^1 is CH.

23. The compound of Claim 21, wherein X^1 is N.

24. The compound of any one of Claims 21-23, wherein R^{1a} is $-C_{1-4}$ alkyl.

25. The compound of any one of Claims 21-23, wherein R^{1a} is $-C_{1-4}$ haloalkyl.

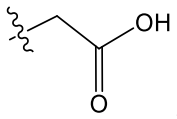
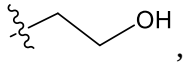
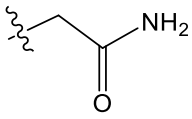
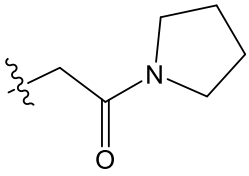
26. The compound of any one of Claims 21-23, wherein R^{1a} is selected from the group consisting of $-CH_2$(C_{3-6} monocyclic cycloalkyl), $-CH_2$(4-6 membered monocyclic heterocyclyl) and $-CH_2$(5-6 membered monocyclic heteroaryl).

27. The compound of any one of Claims 21-26, wherein R^{1c} is $-N(R^{m1})R^{n1}$.

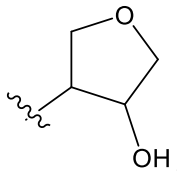
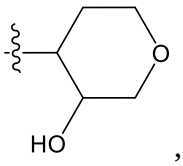
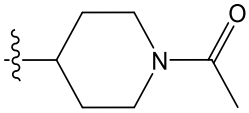
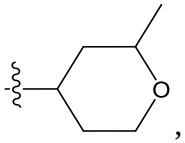
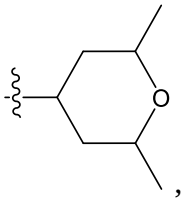
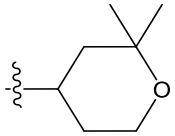
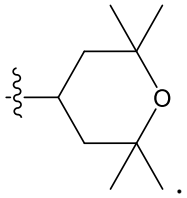
28. The compound of Claim 27, wherein R^{n1} is hydrogen.

29. The compound of Claim 27, wherein R^{n1} is $-C(=O)OR^{Z4}$.

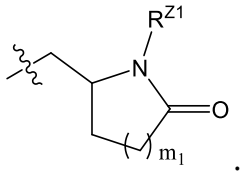
30. The compound of any one of Claims 27-29, wherein R^{m1} is C_{3-6} monocyclic cycloalkyl, $-C_{1-4}$ alkyl optionally substituted with $-C(=O)OR^{Z1}$ or 4-7 membered monocyclic heterocyclyl optionally substituted with hydroxy.

31. The compound of Claim 30, wherein R^{m1} is  ,  ,  or  .

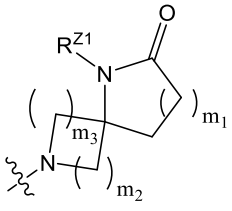
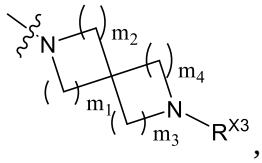
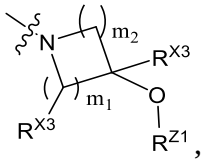
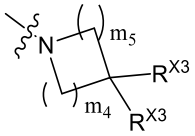
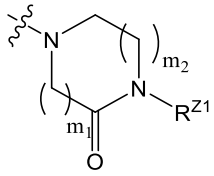
32. The compound of Claim 30, wherein R^{m1} is tetrahydrofuran or tetrahydro-2H-pyran, each optionally substituted with hydroxy.

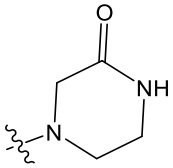
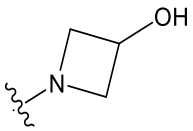
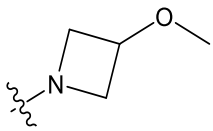
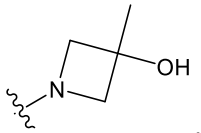
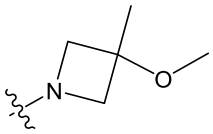
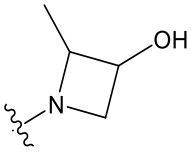
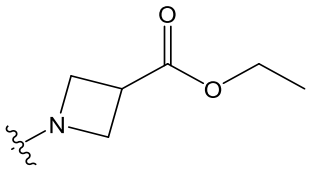
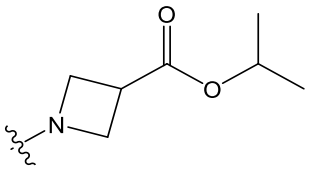
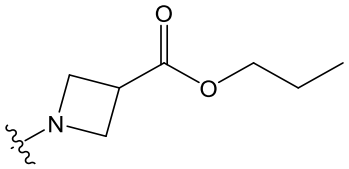
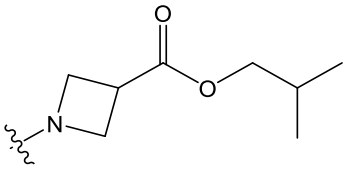
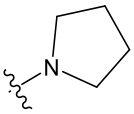
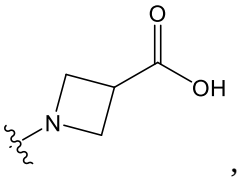
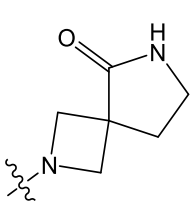
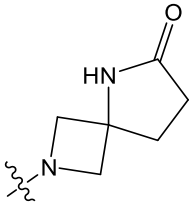
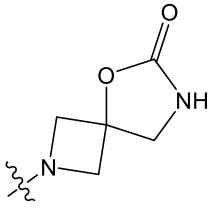
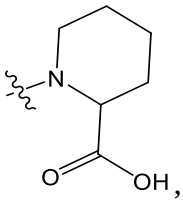
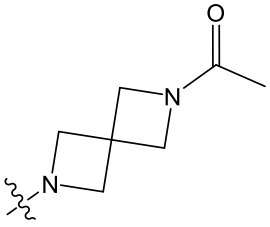
33. The compound of Claim 32, wherein R^{m1} is  ,  ,  ,  ,  ,  or  .

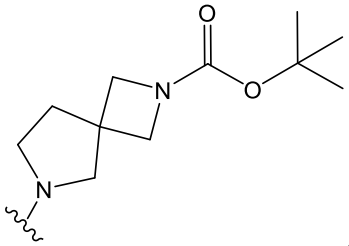
34. The compound of any one of Claims 27-29, wherein R^{m1} is $-R^{x2}$.

35. The compound of Claim 34, wherein $-R^{x2}$ is  .

36. The compound of any one of Claims 21-26, wherein R^{1c} is $-R^{x1}$.

37. The compound of Claim 36, wherein $-R^{x1}$ is selected from the group consisting of:  ,  ,  ,  , and  .

38. The compound of Claim 37, wherein $-R^{x1}$ is selected from the group consisting of:  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  .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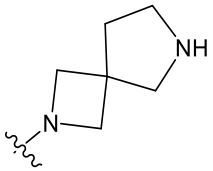
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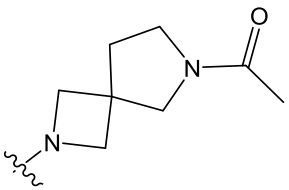
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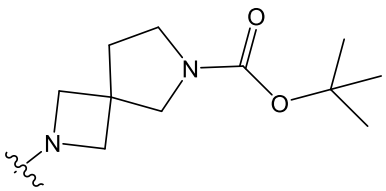
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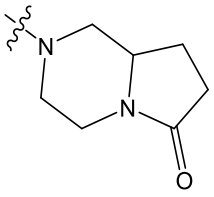
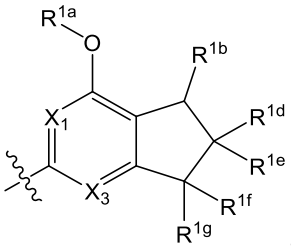

.

39. The compound of Claim 1, wherein A^1 is  .

40. The compound of Claim 39, wherein X^1 is CH.

41. The compound of Claim 39, wherein X^1 is N.

42. The compound of any one of Claims 39-41, wherein X^3 is CH.

43. The compound of any one of Claims 39-41, wherein X^3 is C-halo.

44. The compound of any one of Claims 39-41, wherein X^3 is N.

45. The compound of any one of Claims 39-44, wherein R^{1a} is $–C_{1-4}$ alkyl.

46. The compound of any one of Claims 39-44, wherein R^{1a} is $–C_{1-4}$ haloalkyl.

47. The compound of any one of Claims 39-44, wherein R^{1a} is selected from the group consisting of $–CH_2$(C_{3-6} monocyclic cycloalkyl), $–CH_2$(4-6 membered monocyclic heterocyclyl) and $–CH_2$(5-6 membered monocyclic heteroaryl).

48. The compound of any one of Claims 39-47, wherein R^{1b} is $–N(R^{m1})R^{n1}$.

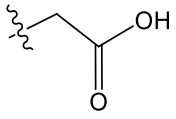
49. The compound of any one of Claims 39-47, wherein R^{n1} is hydrogen.

50. The compound of any one of Claims 39-47, wherein R^{n1} is $–C(=O)OR^{Z4}$.

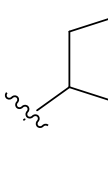
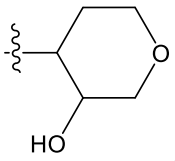
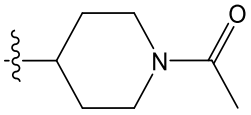
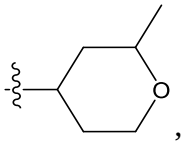
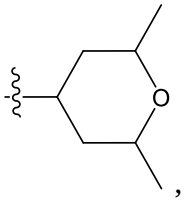
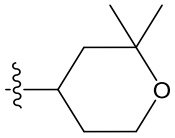
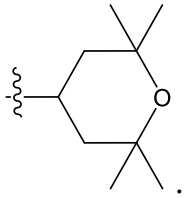
51. The compound of any one of Claims 39-50, wherein R^{m1} is hydrogen.

52. The compound of any one of Claims 39-50, wherein R^{m1} is $–C_{1-4}$ alkyl optionally substituted with $–C(=O)OR^{Z1}$ or 4-7 membered monocyclic heterocyclyl optionally substituted with hydroxy.

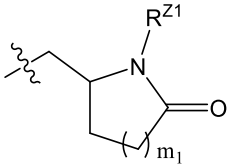
53. The compound of any one of Claims 39-50, wherein R^{m1} is C_5 monocyclic cycloalkyl or C_6 monocyclic cycloalkyl.

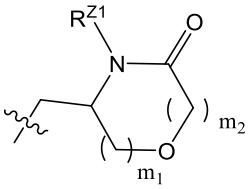
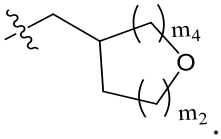
54. The compound of Claim 52, wherein R^{m1} is  .

55. The compound of Claim 52, wherein R^{m1} is tetrahydrofuran or tetrahydro-2H-pyran, each optionally substituted with hydroxy, or piperidine optionally substituted with $–C(=O)R^{Z1}$.

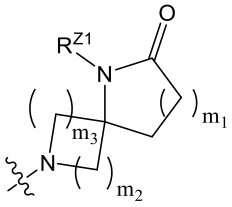
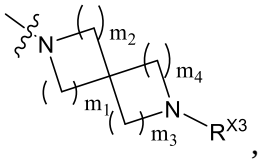
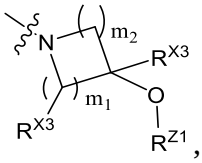
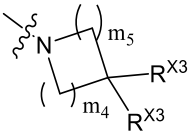
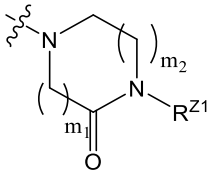
56. The compound of Claim 55, wherein R^{m1} is  ,  ,  ,  ,  ,  or  .

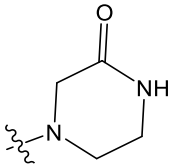
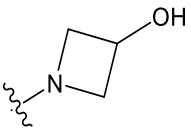
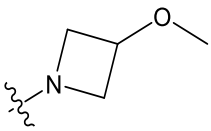
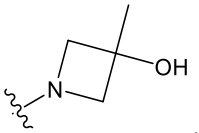
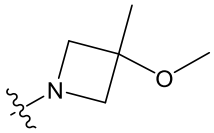
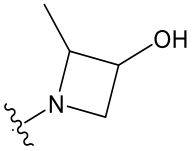
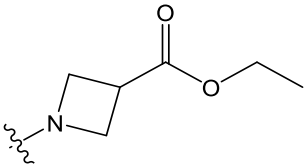
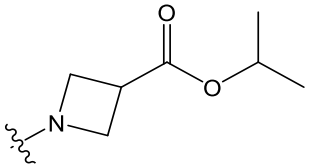
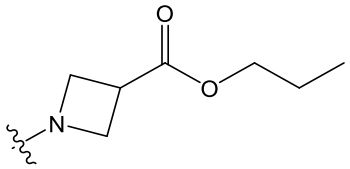
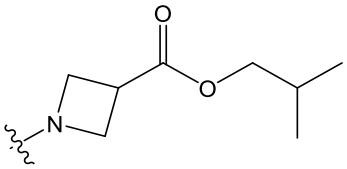
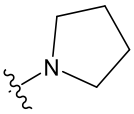
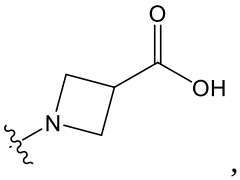
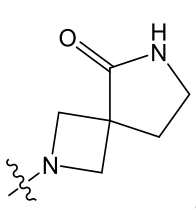
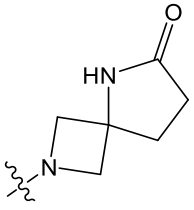
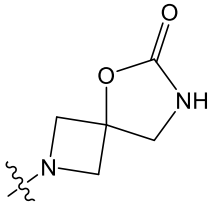
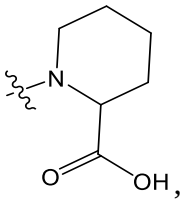
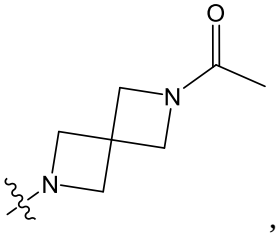
57. The compound of any one of Claims 39-50, wherein R^{m1} is $–R^{x2}$.

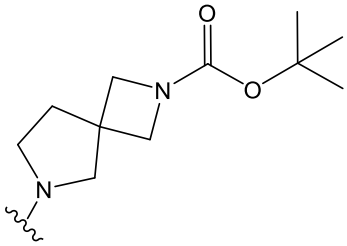
58. The compound of Claim 57, wherein $–R^{x2}$ is  .

59. The compound of Claim 57, wherein $–R^{x2}$ is  or  .

60. The compound of any one of Claims 39-47, wherein R^{1b} is $–R^{x1}$.

61. The compound of Claim 60, wherein $-R^{x1}$ is selected from the group consisting of:  ,  ,  ,  , and  .

62. The compound of Claim 61, wherein $-R^{x1}$ is selected from the group consisting of:  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  .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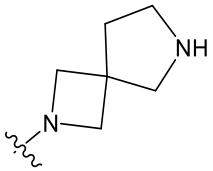
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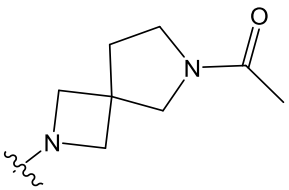
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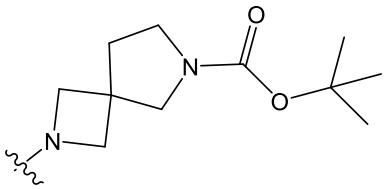
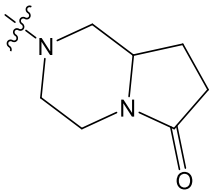
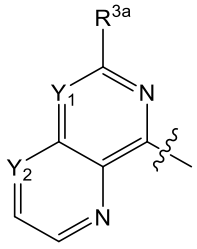
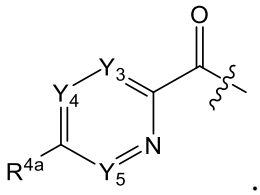


and .

63. The compound of any one of Claims 39-62, wherein R^{1d} is hydrogen.
64. The compound of any one of Claims 39-62, wherein R^{1d} is –OH.
65. The compound of any one of Claims 39-62, wherein R^{1d} is $–CH_3$.
66. The compound of any one of Claims 39-62, wherein R^{1d} is –F.
67. The compound of any one of Claims 63-66, wherein R^{1e} is hydrogen.
68. The compound of any one of Claims 63-66, wherein R^{1e} is $–CH_3$.
69. The compound of any one of Claims 63-68, wherein R^{1f} is hydrogen.
70. The compound of any one of Claims 63-68, wherein R^{1f} is $–CH_3$.
71. The compound of any one of Claims 63-70, wherein R^{1g} is hydrogen.
72. The compound of any one of Claims 1-71, wherein B^1 is  .
73. The compound of Claim 72, wherein Y^1 is N.
74. The compound of Claim 72, wherein Y^1 is CH.
75. The compound of any one of Claims 72-74, wherein Y^2 is N.
76. The compound of any one of Claims 72-74, wherein Y^2 is CH.
77. The compound of any one of Claims 72-76, wherein R^{3a} is H.
78. The compound of any one of Claims 72-76, wherein R^{3a} is $–CH_3$.
79. The compound of any one of Claims 72-76, wherein R^{3a} is $–CF_3$.
80. The compound of any one of Claims 72-76, wherein R^{3a} is $–CHF_2$.

81. The compound of any one of Claims 1-71, wherein B^1 is  .

82. The compound of Claim 81, wherein Y^3 is N.

83. The compound of Claim 81, wherein Y^3 is CH.

84. The compound of any one of Claims 81-83, wherein Y^4 is N.

85. The compound of any one of Claims 81-83, wherein Y^4 is CH.

86. The compound of any one of Claims 81-85, wherein Y^5 is N.

87. The compound of any one of Claims 81-85, wherein Y^5 is CH.

88. The compound of any one of Claims 81-85, wherein Y^5 is C–OCH_3.

89. The compound of any one of Claims 81-88, wherein R^{4a} is H.

90. The compound of any one of Claims 81-88, wherein R^{4a} is halogen.

91. The compound of any one of Claims 81-88, wherein R^{4a} is –C_{1-4} alkyl.

92. The compound of any one of Claims 81-88, wherein R^{4a} is –C_{1-4} haloalkyl.

93. The compound of any one of Claims 81-88, wherein R^{4a} is –CH_2R^{4b}.

94. The compound of any one of Claims 81-88, wherein R^{4a} is –$C(CH_3)R^{4b}$.

95. The compound of Claim 93 or 94, wherein R^{4b} is –$N(R^{m2})R^{n2}$.

96. The compound of Claim 95, wherein R^{m2} is –CH_3.

97. The compound of Claim 95, wherein R^{m2} is –C_{2-4} alkyl.

98. The compound of Claim 95, wherein R^{m2} is–C_{1-4} haloalkyl.

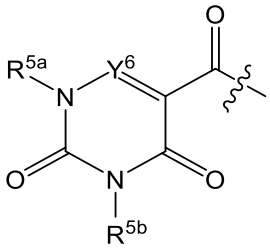
99. The compound of Claim 95, wherein R^{m2} is –C_{2-4} alkyl substituted with hydroxy.

100. The compound of any one of Claims 95-99, wherein R^{n2} is H.

101. The compound of any one of Claims 95-99, wherein R^{n2} is –C_{1-4} alkyl.

102. The compound of any one of Claims 95-99, wherein R^{n2} is –C_{1-4} haloalkyl.

103. The compound of Claim 93 or 94, wherein R^{4b} is –R^{y1}.

104. The compound of any one of Claims 1-71, wherein B^1 is  .

105. The compound of Claim 104, R^{5a} is hydrogen.

106. The compound of Claim 104, R^{5a} is $–CH_3$.

107. The compound of Claim 104, R^{5a} is $–C_{2-4}$ alkyl.

108. The compound of Claim 104, R^{5a} is $–C_{2-4}$ haloalkyl.

109. The compound of any one of Claims 104-108, wherein R^{5b} is hydrogen.

110. The compound of any one of Claims 104-108, wherein R^{5b} is $–CH_3$.

111. The compound of any one of Claims 104-108, wherein R^{5b} is $–C_{2-4}$ alkyl.

112. The compound of any one of Claims 104-108, wherein R^{5b} is $–C_{2-4}$ haloalkyl.

113. The compound of any one of Claims 104-112, wherein Y^6 is N.

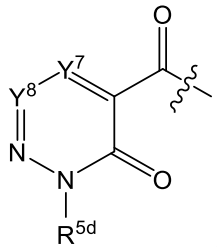
114. The compound of any one of Claims 104-112, wherein Y^6 is CR^{5c}.

115. The compound of Claim 114, wherein R^{5c} is hydrogen.

116. The compound of Claim 114, wherein R^{5c} is $–CH_3$.

117. The compound of Claim 114, wherein R^{5c} is $–C_{2-4}$ alkyl.

118. The compound of Claim 114, wherein R^{5c} is $–C_{2-4}$ haloalkyl.

119. The compound of any one of Claims 1-71, wherein B^1 is  .

120. The compound of Claim 119, wherein R^{5d} is hydrogen.

121. The compound of Claim 119, wherein R^{5d} is $–CH_3$.

122. The compound of Claim 119, wherein R^{5d} is $–C_{2-4}$ alkyl.

123. The compound of Claim 119, wherein R^{5d} is $–C_{2-4}$ haloalkyl.

124. The compound of any one of Claims 119-123, wherein Y^7 is CR^{5e}, wherein R^{5e} is hydrogen.

125. The compound of any one of Claims 119-123, wherein Y^7 is CR^{5e}, wherein R^{5e} is halogen.

126. The compound of any one of Claims 119-123, wherein Y^7 is CR^{5e}, wherein R^{5e} is $–CH_3$.

127. The compound of any one of Claims 119-126, wherein Y^8 is CR^{5f}, wherein R^{5f} is hydrogen.

128. The compound of any one of Claims 119-126, wherein Y^8 is CR^{5f}, wherein R^{5f} is halogen.

129. The compound of any one of Claims 119-126, wherein Y^8 is CR^{5f}, wherein R^{5f} is -OH.

130. The compound of any one of Claims 119-126, wherein Y^8 is CR^{5f}, wherein R^{5f} is CN.

131. The compound of any one of Claims 119-126, wherein Y^8 is CR^{5f}, wherein R^{5f} is $–CH_3$.

132. The compound of any one of Claims 1-131, wherein R^{2a}, R^{2b}, R^{2c}, R^{2e}, R^{2g} and R^{2h} are each hydrogen.

133. The compound of any one of Claims 1-131, wherein R^{2a}, R^{2c}, R^{2e}, R^{2g} and R^{2h} are each hydrogen; and R^{2b} halogen.

134. The compound of any one of Claims 1-131, wherein R^{2b}, R^{2c}, R^{2e}, R^{2g} and R^{2h} are each hydrogen; and R^{2a} halogen.

135. The compound of any one of Claims 1-134, wherein R^{2d} and R^{2f} are each halogen.

136. The compound of any one of Claims 1-134, wherein R^{2d} and R^{2f} are each $–CH_3$.

137. The compound of any one of Claims 1-134, wherein R^{2d} is halogen; and R^{2f} is $–CH_3$.

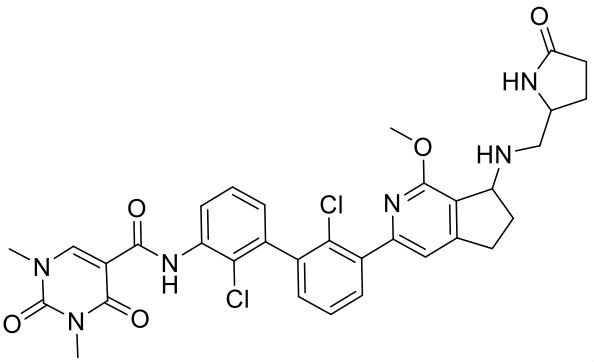
138. The compound of any one of Claims 1-134, wherein R^{2d} is $–CH_3$; and R^{2f} is halogen.

139. The compound of any one of Claims 1-134, wherein R^{2d} is cyano; and R^{2f} is halogen.

140. The compound of any one of Claims 1-134, wherein R^{2d} is $–OCH_3$; and R^{2f} is halogen.

141. The compound of any one of Claims 133-135 or 137-140, wherein the halogen is chloro or fluoro.

142. The compound of Claim 1 selected from the group consisting of: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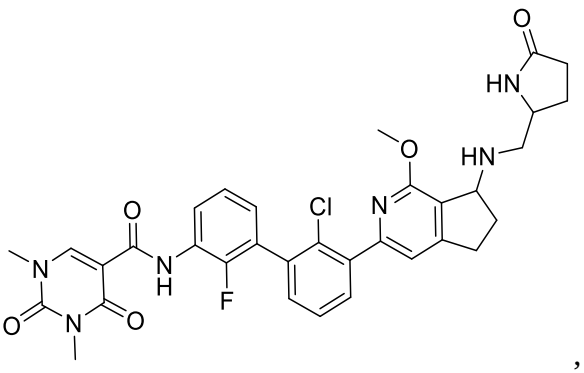
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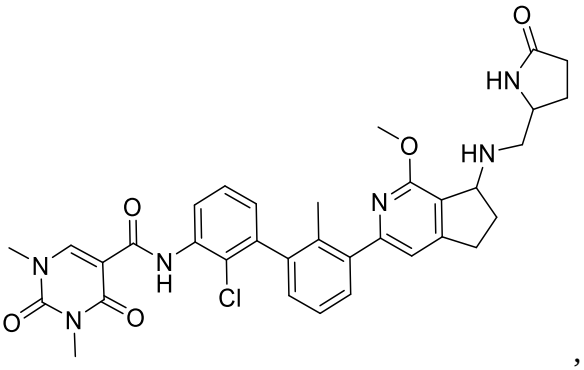
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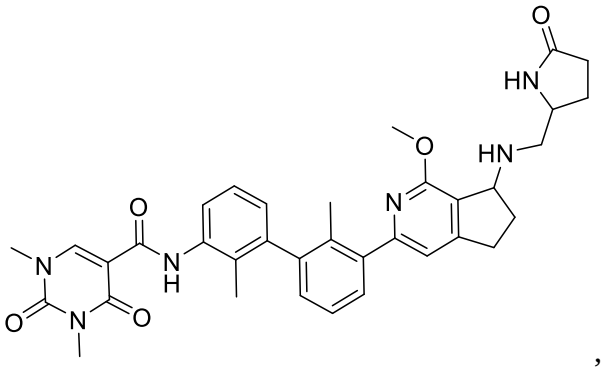
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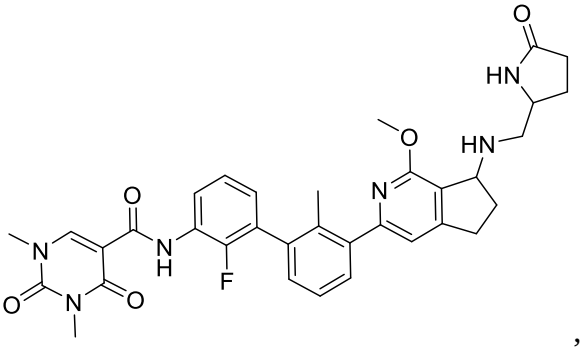
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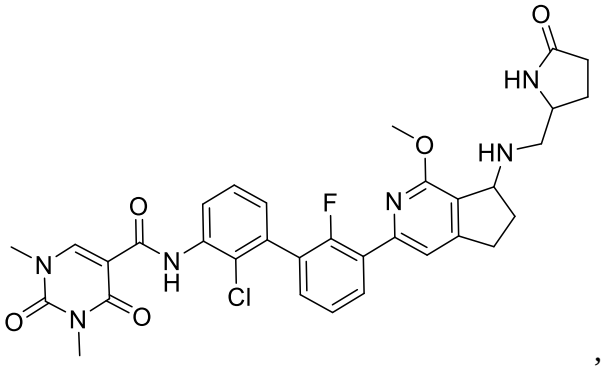
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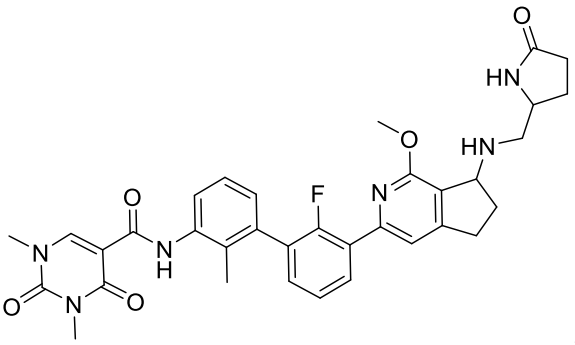
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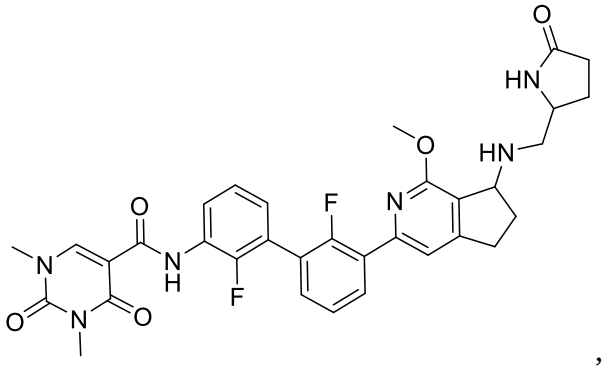
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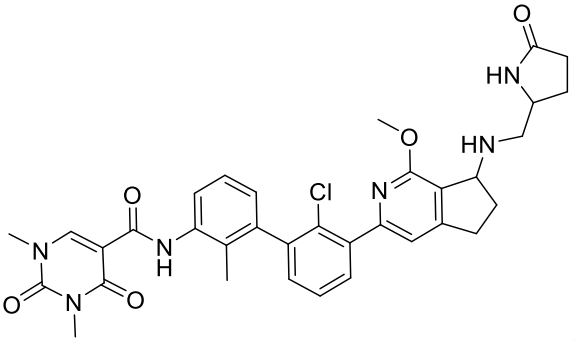
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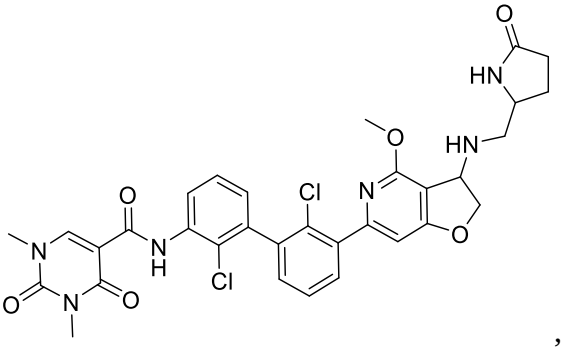
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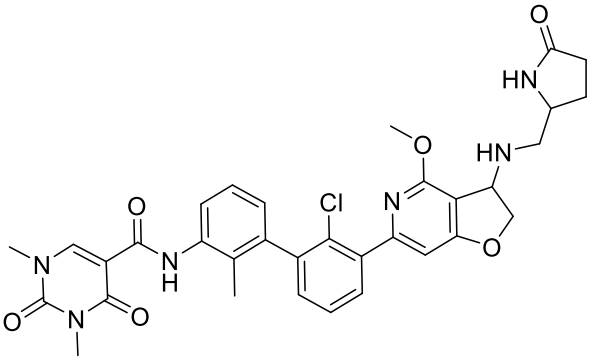
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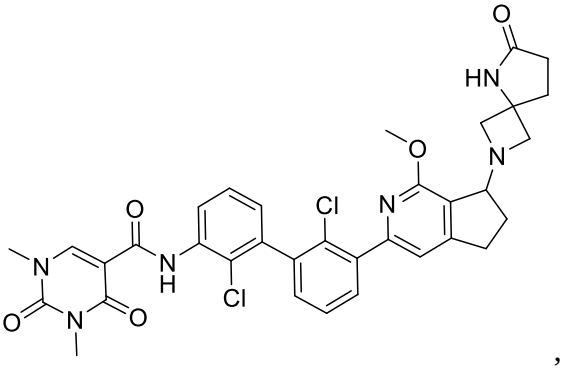
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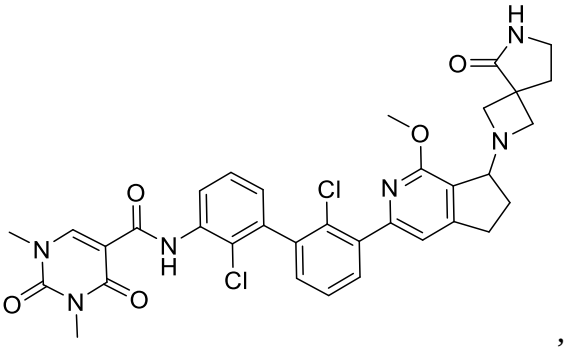
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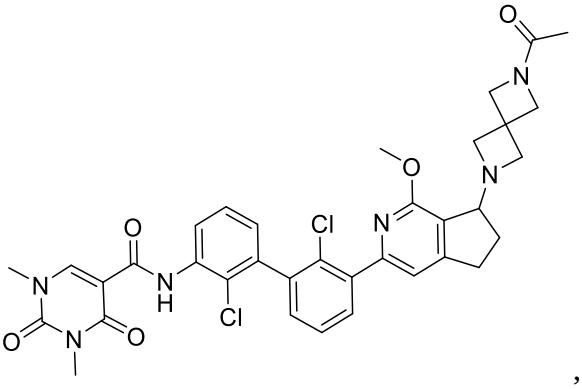
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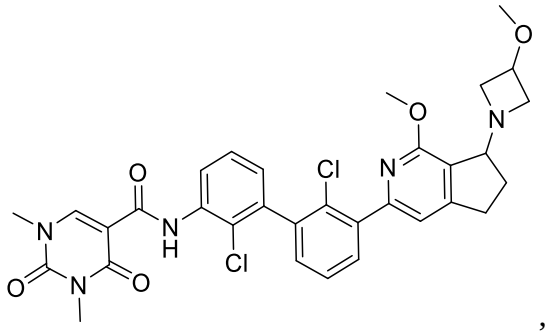
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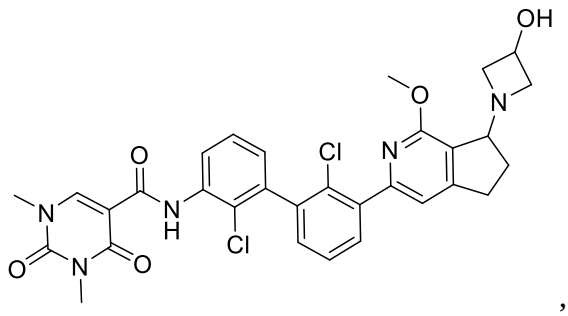
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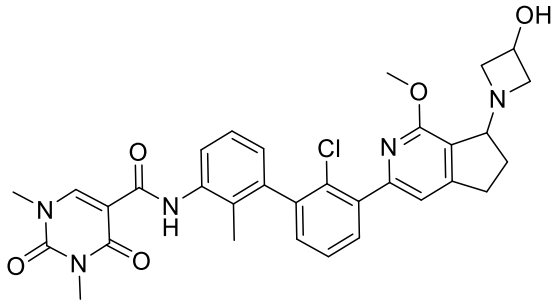
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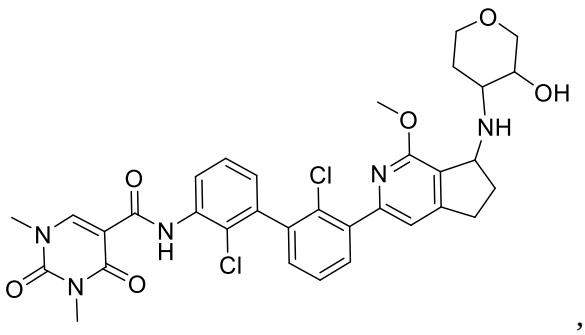
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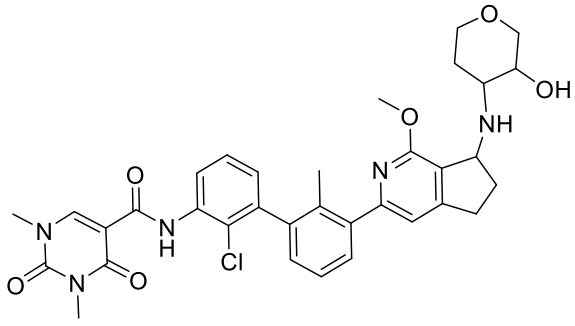
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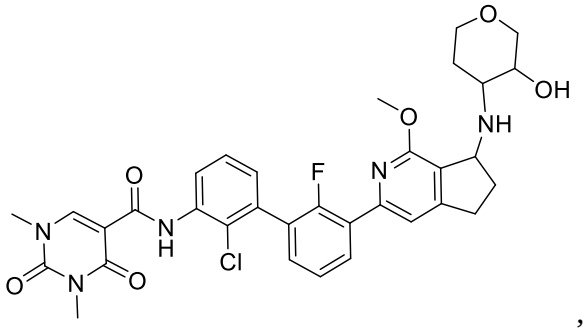
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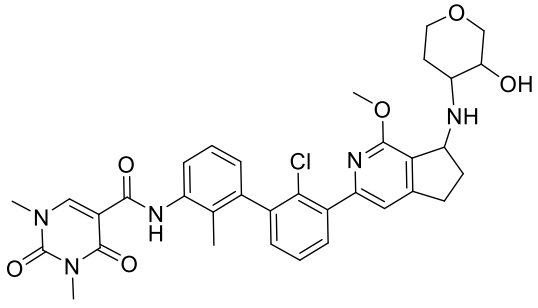
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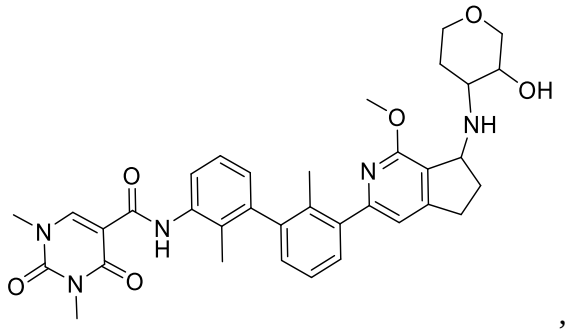
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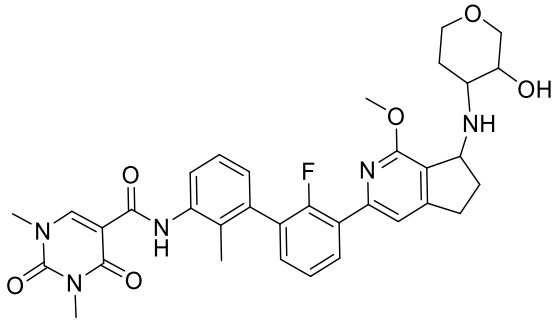
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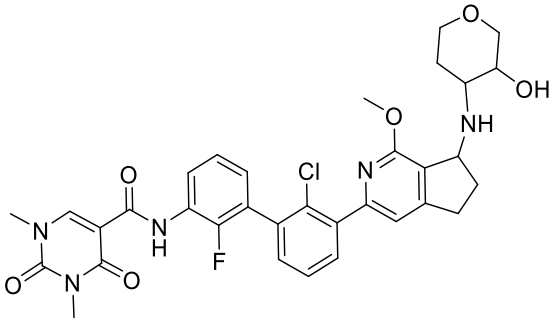
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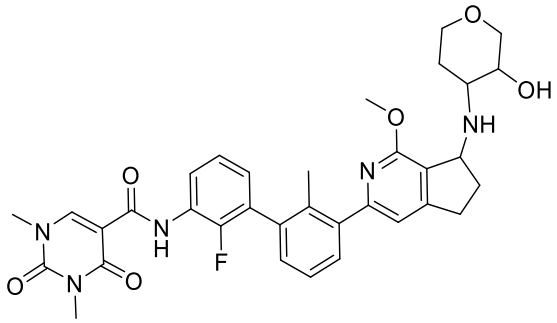
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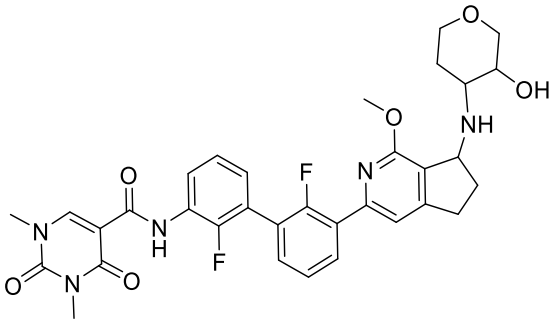
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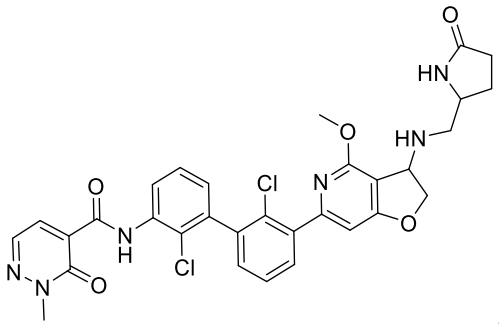
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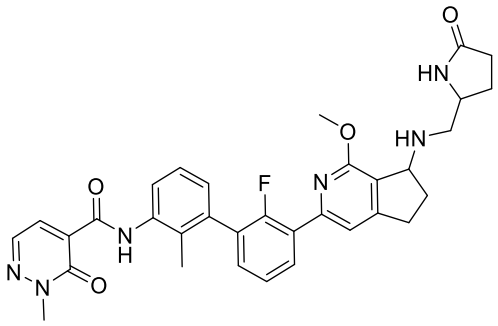
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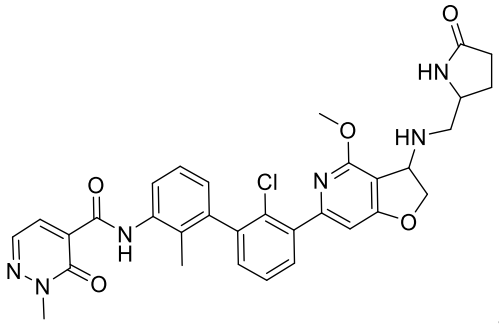
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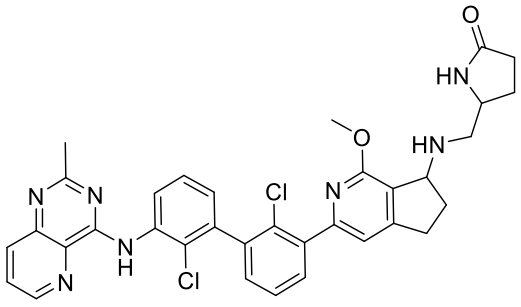
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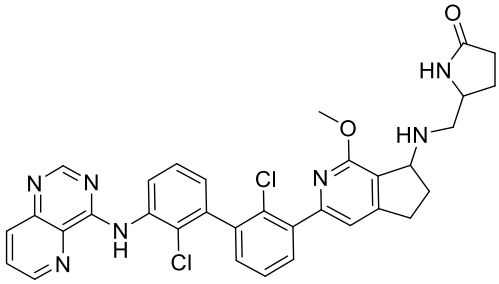
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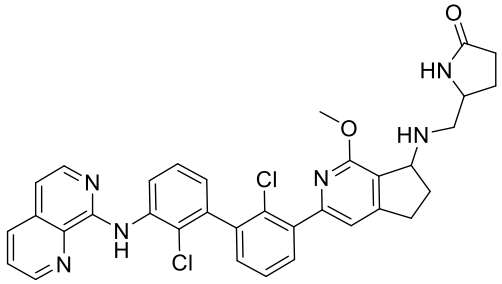
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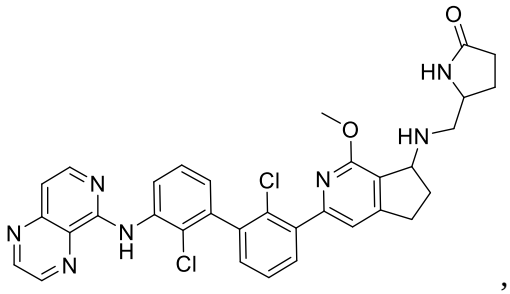
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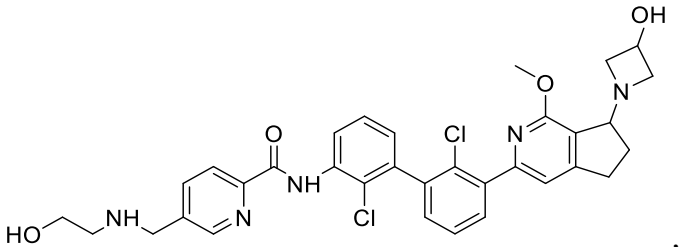
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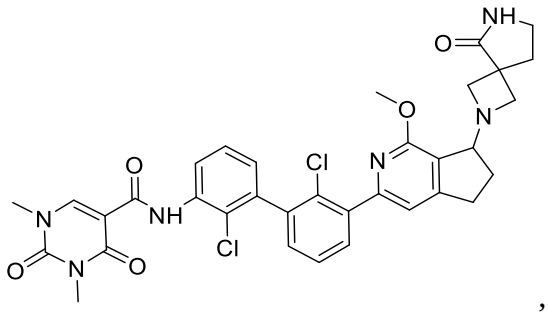
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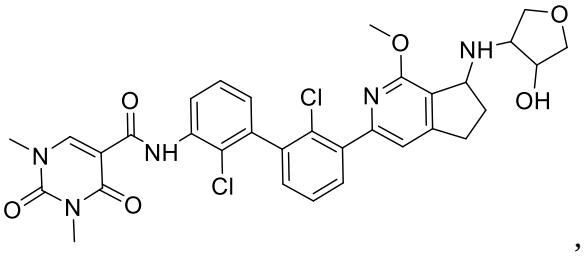
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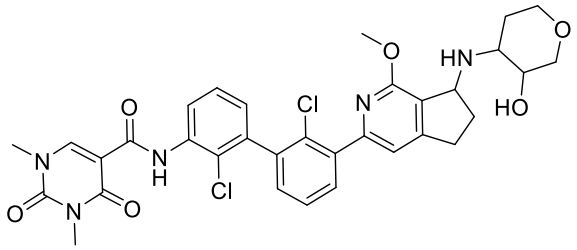
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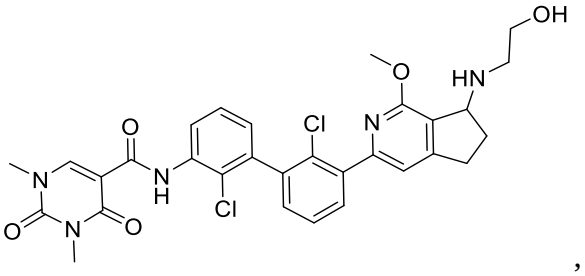
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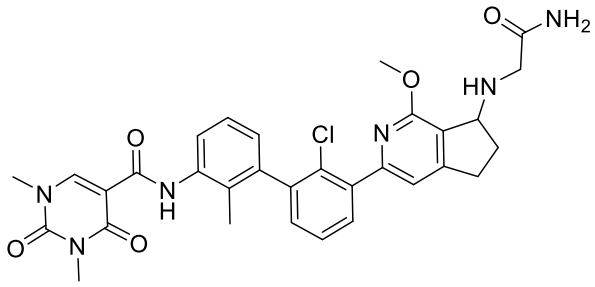
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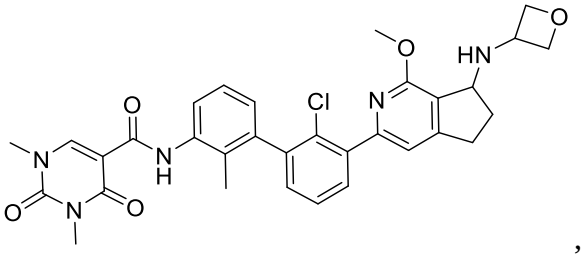
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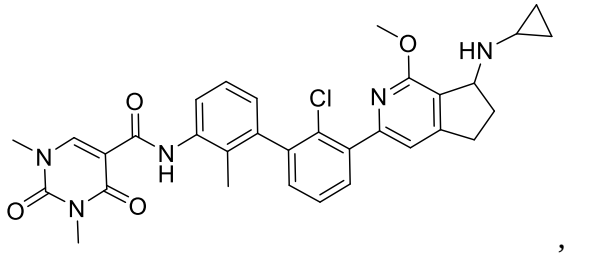
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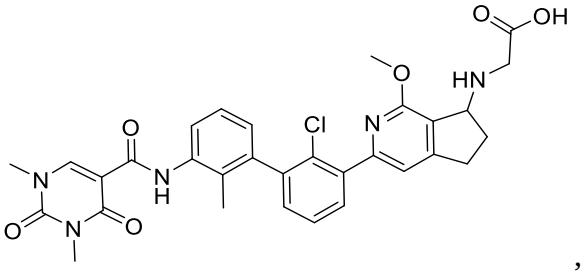
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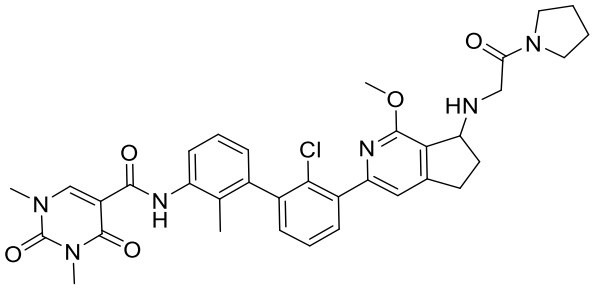
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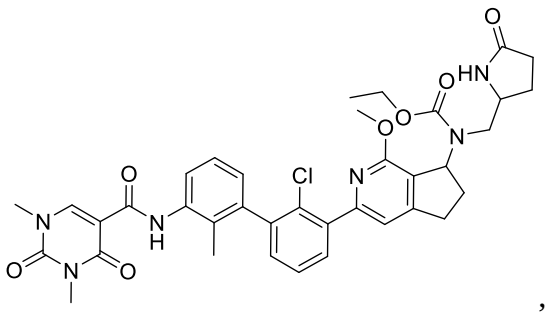
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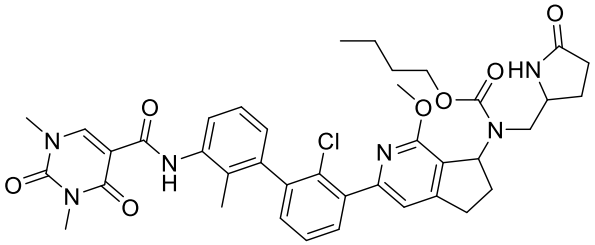
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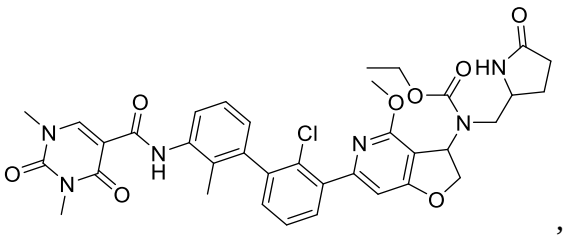
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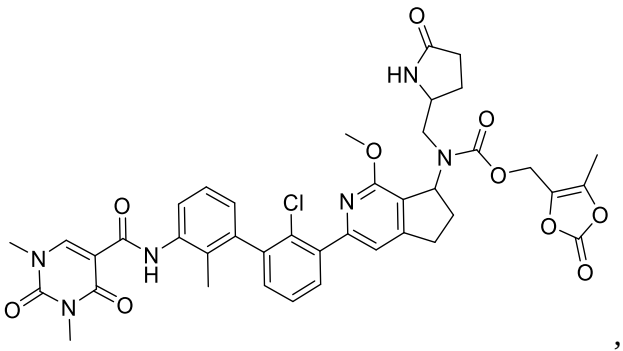
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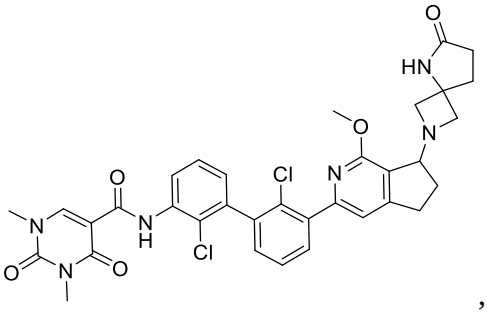
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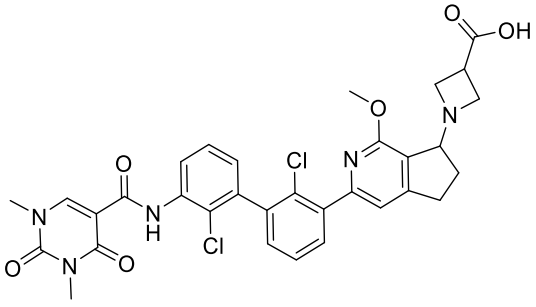
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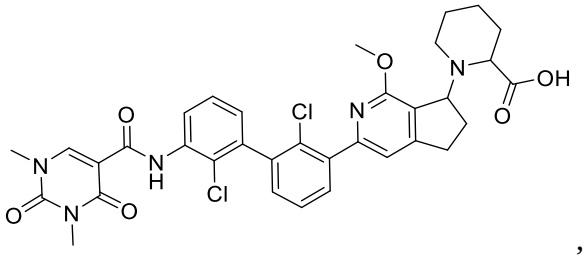
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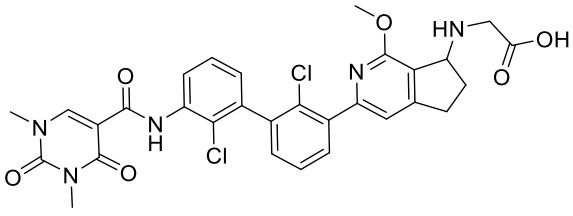
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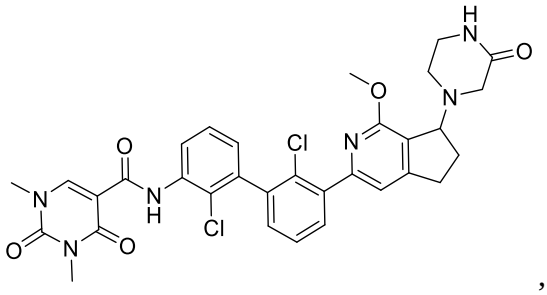
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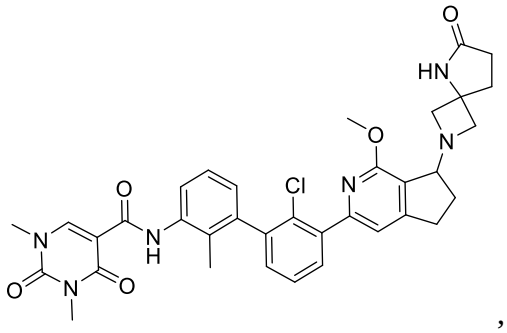
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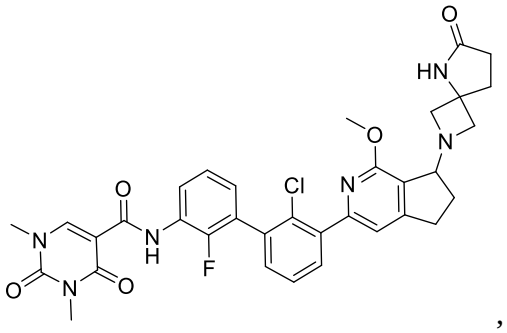
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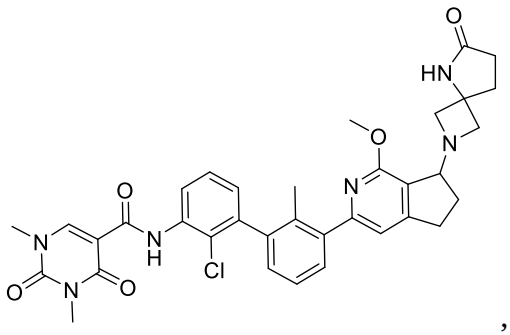
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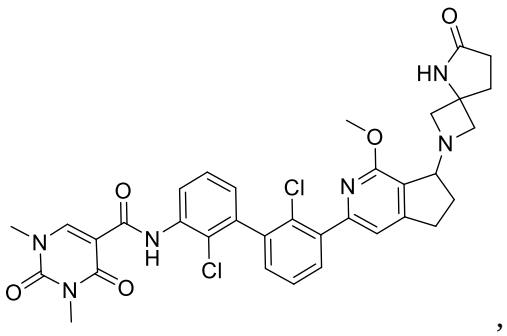
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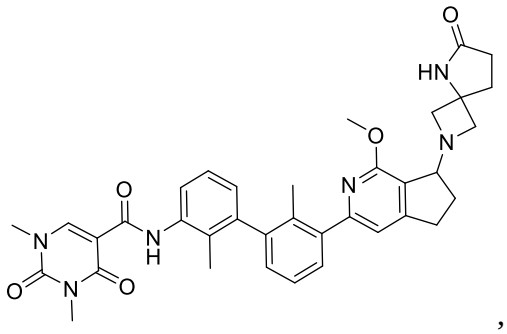
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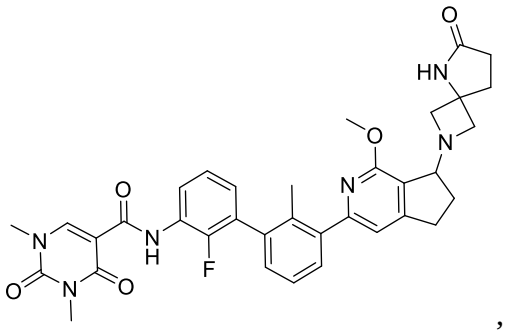
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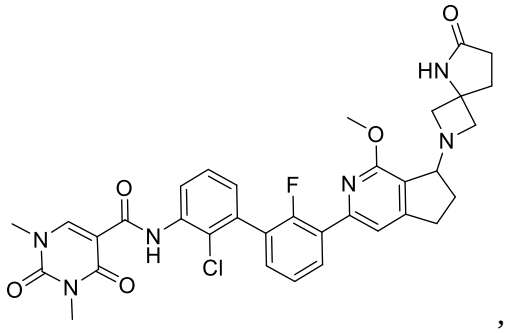
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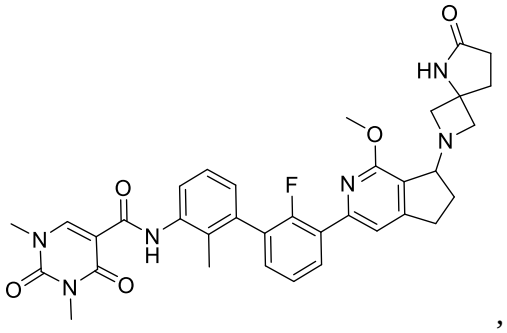
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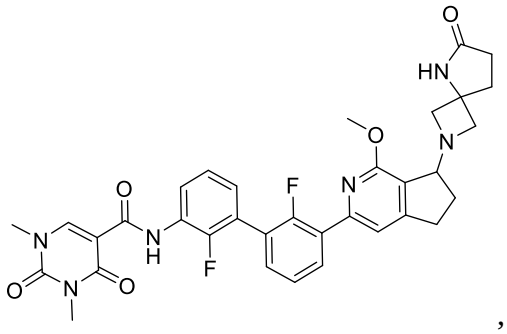
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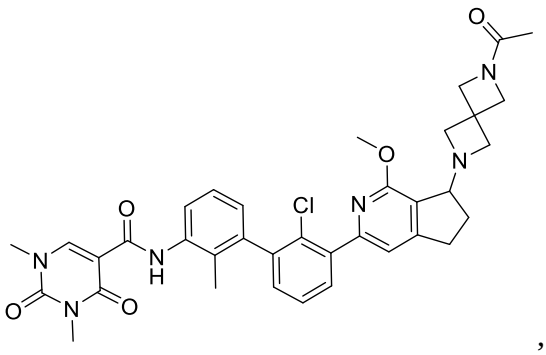
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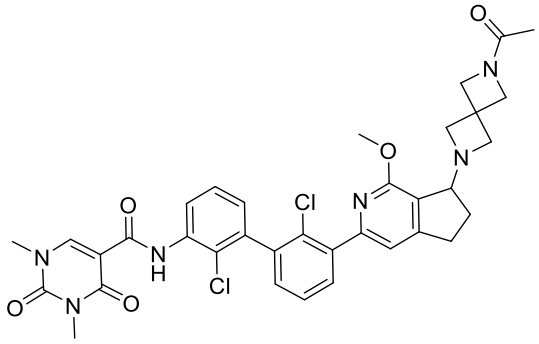
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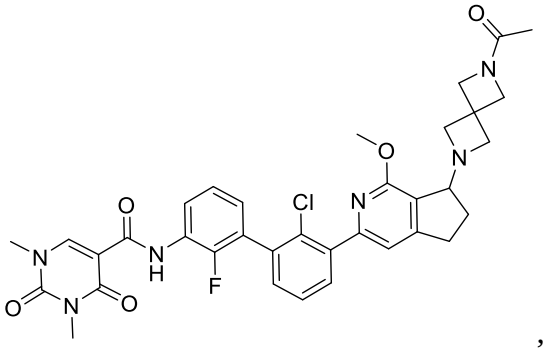
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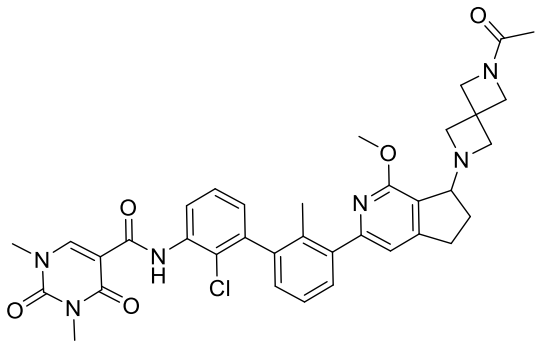
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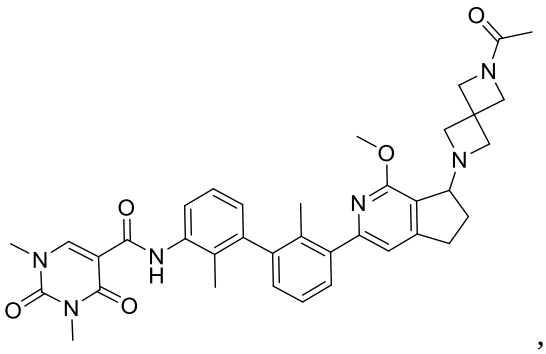
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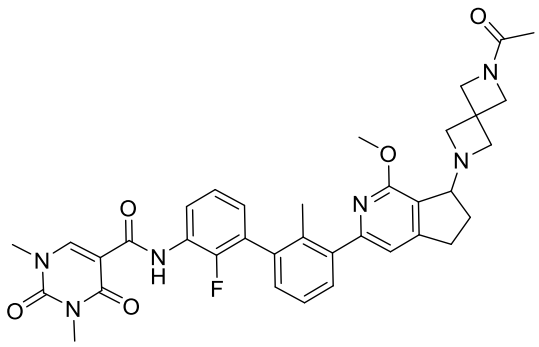
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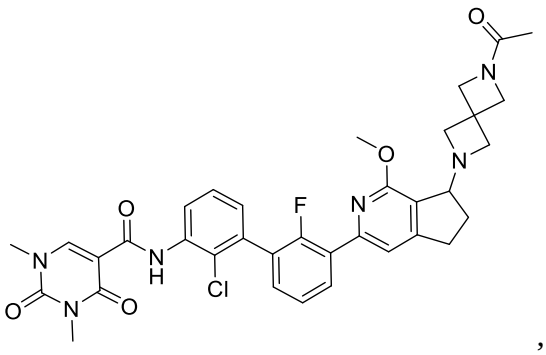
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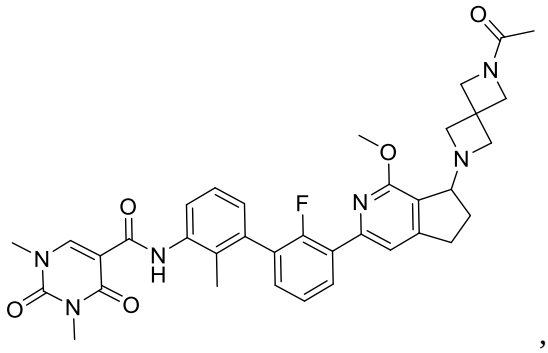
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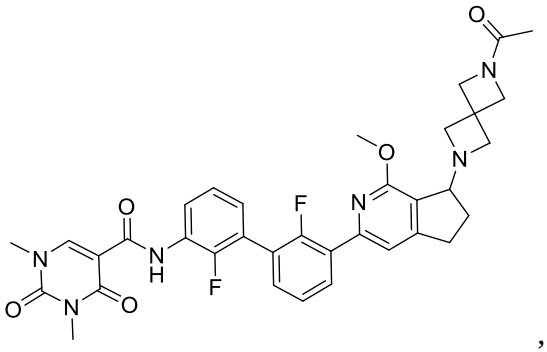
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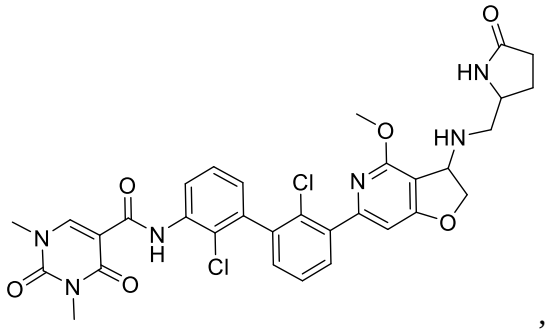
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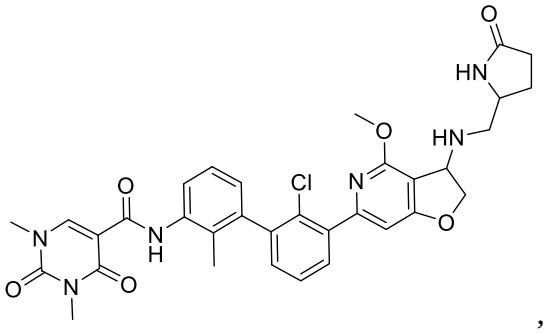
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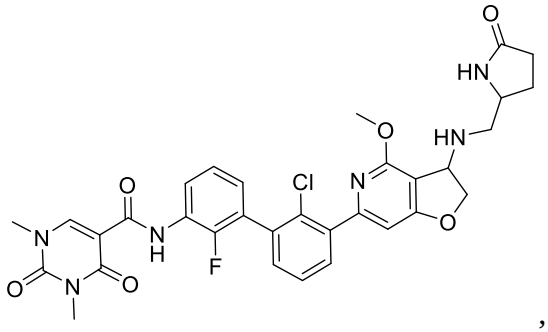
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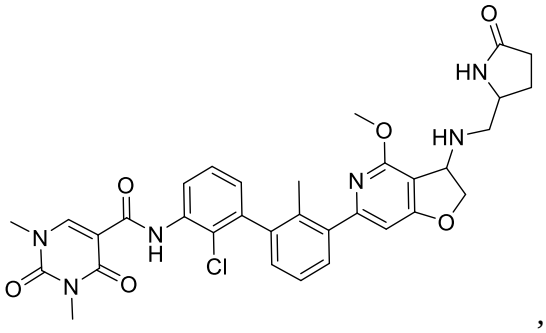
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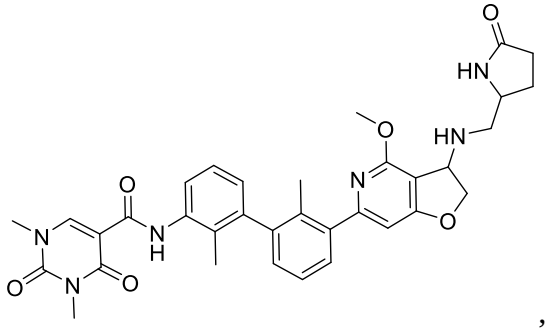
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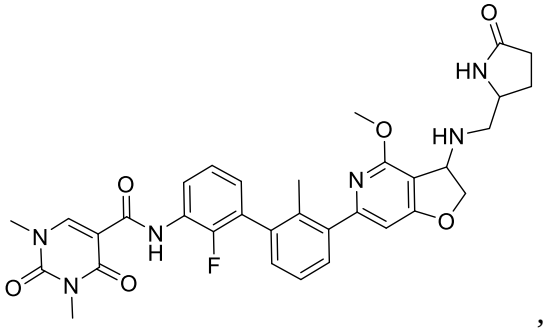
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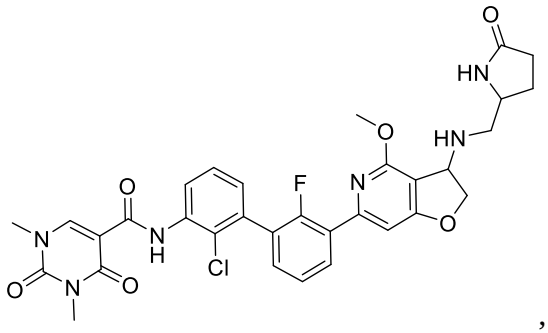
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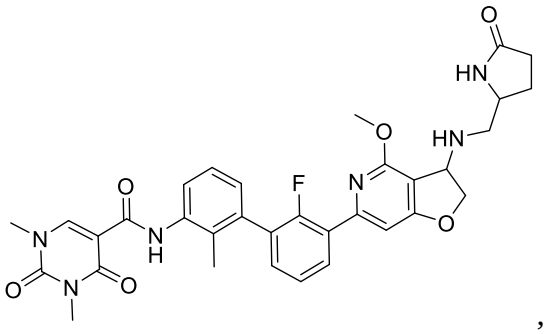
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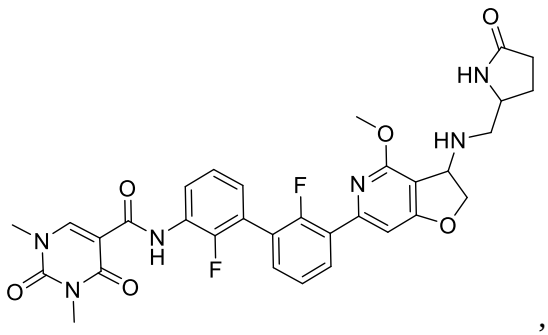
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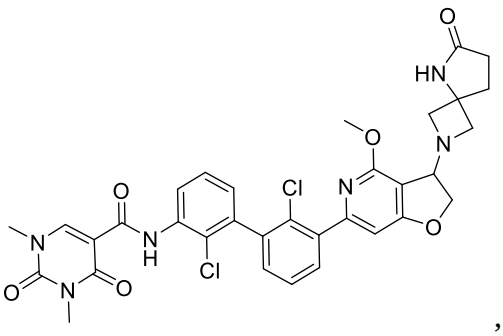
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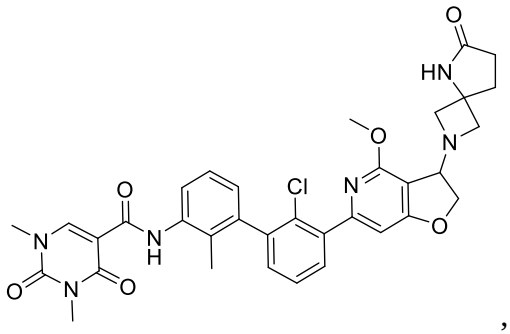
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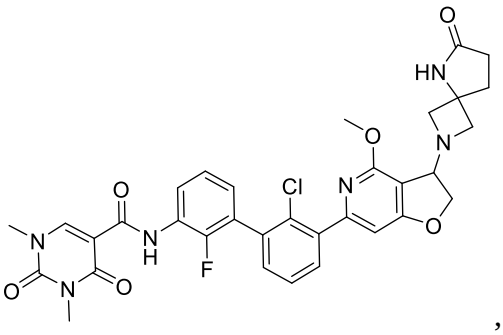
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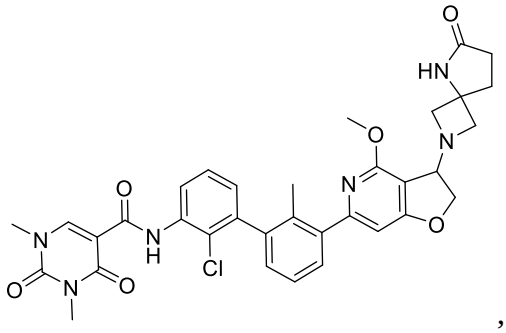
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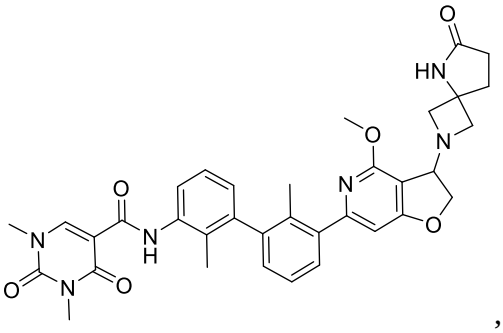
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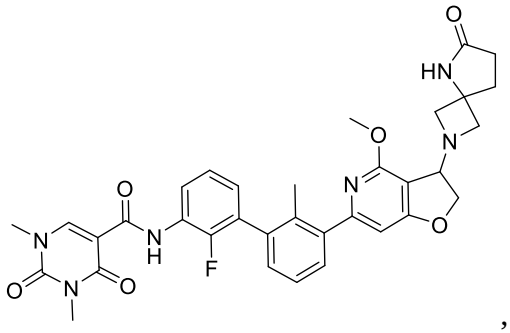
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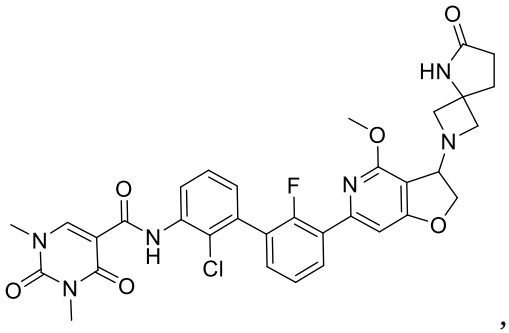
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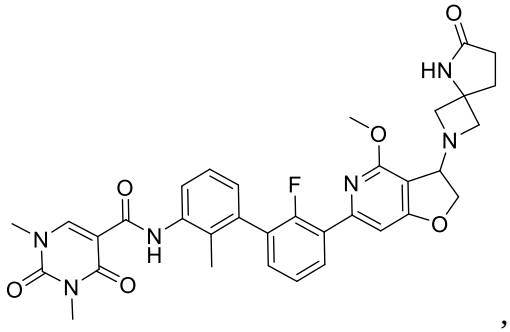
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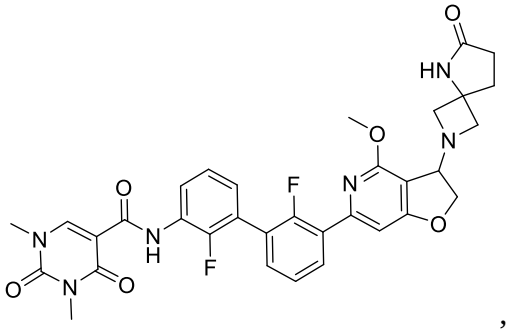
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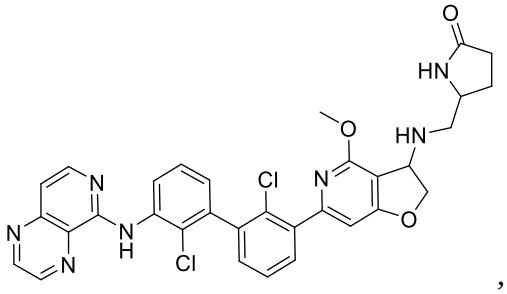
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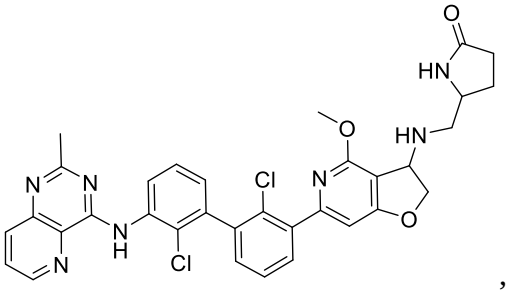
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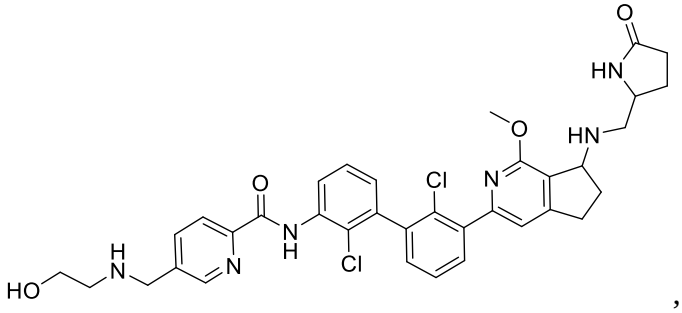
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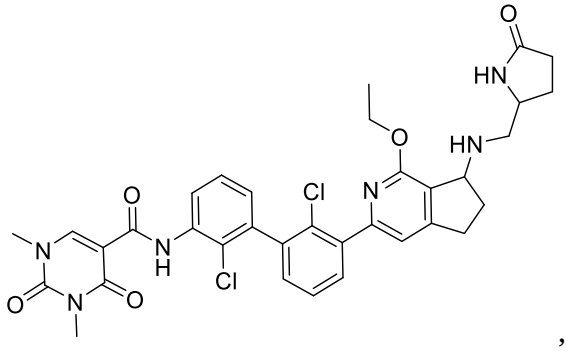
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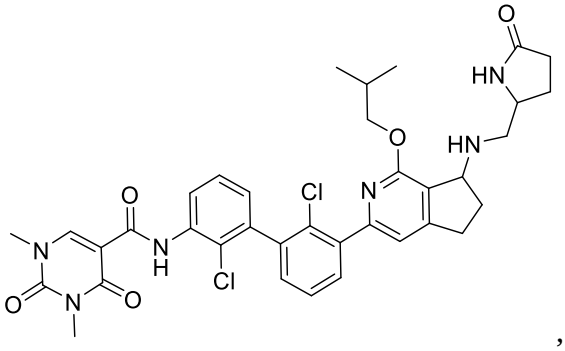
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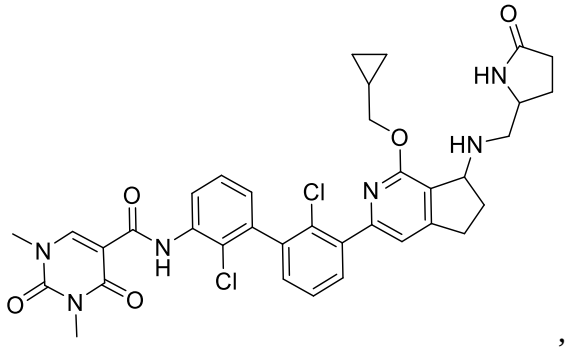
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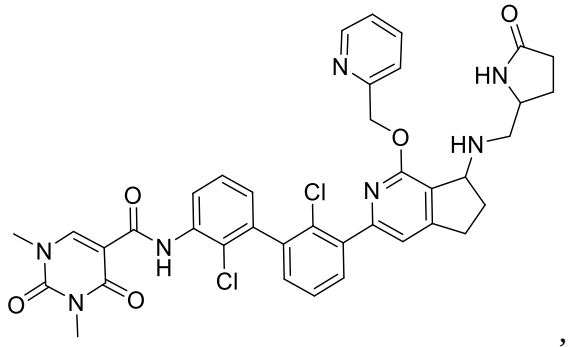
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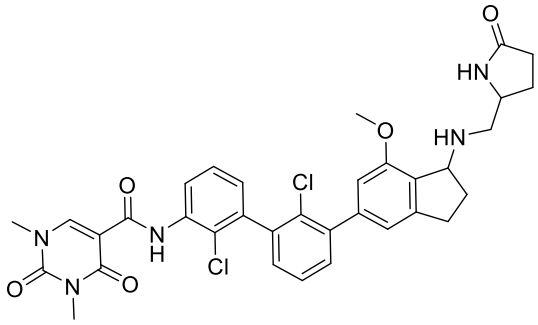
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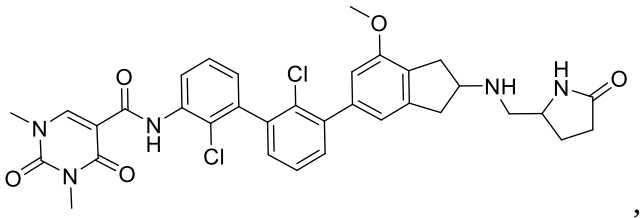
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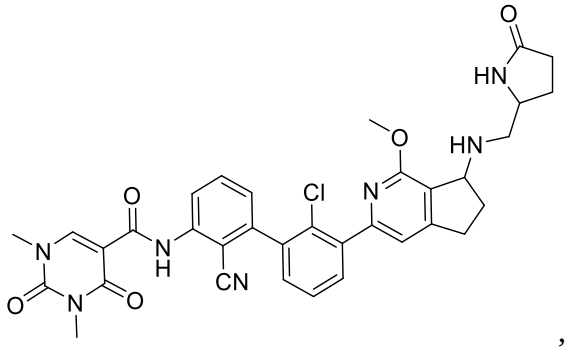
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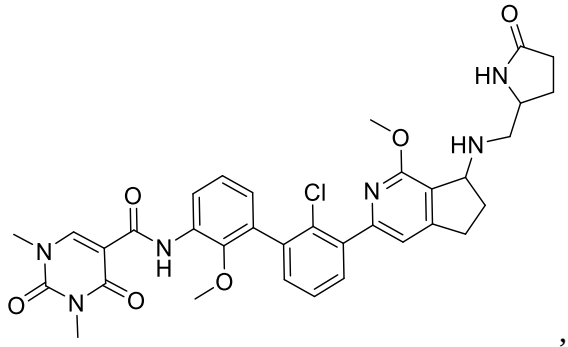
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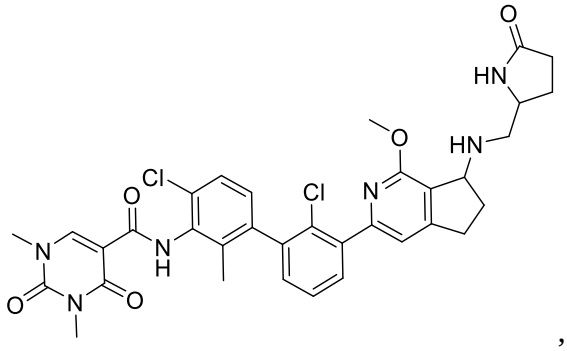
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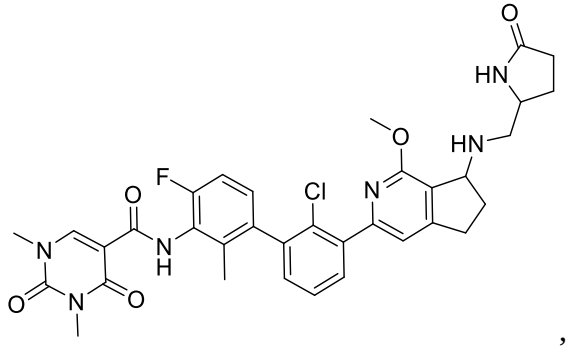
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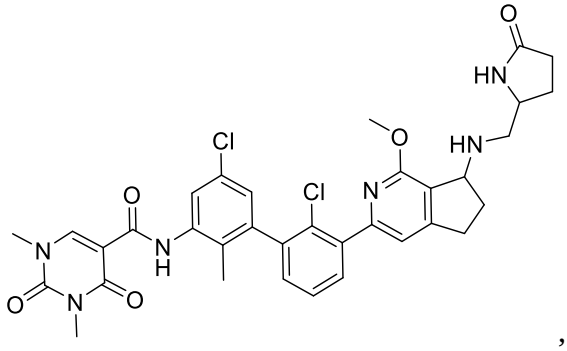
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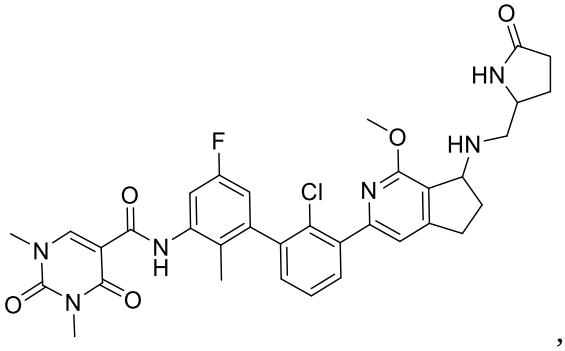
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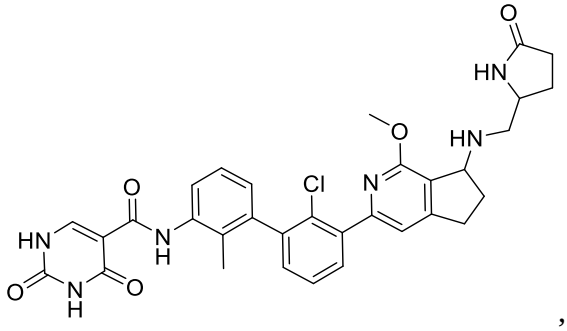
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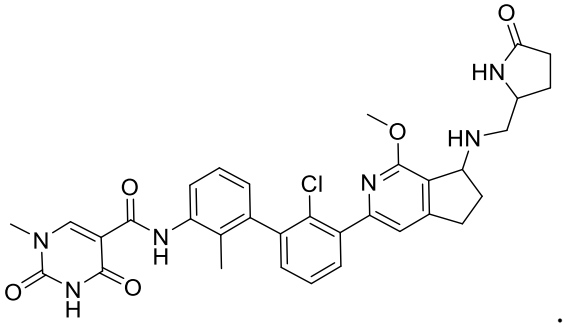
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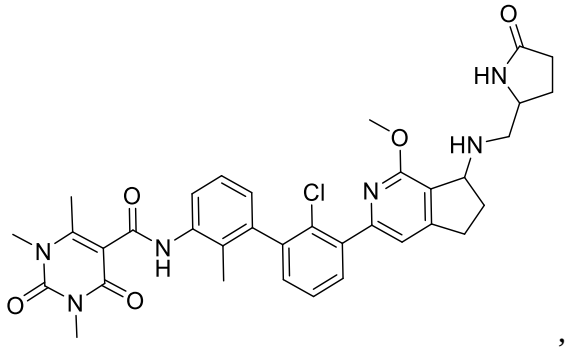
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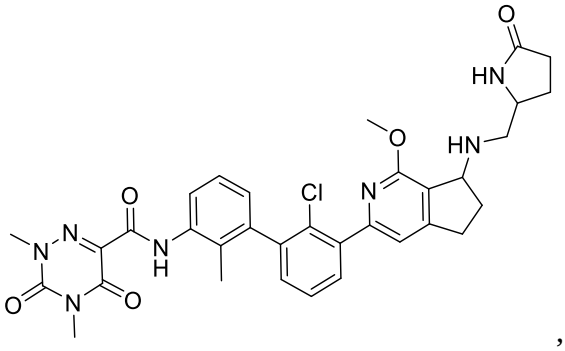
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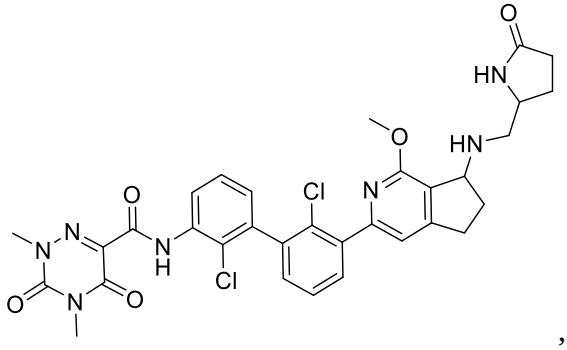
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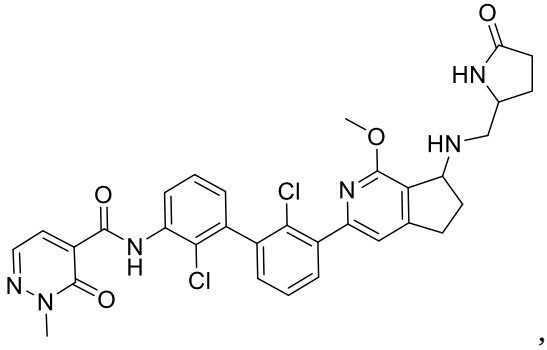
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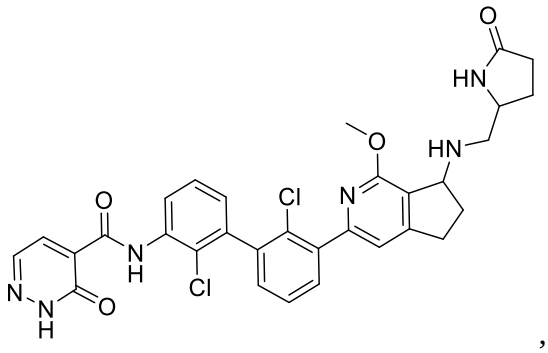
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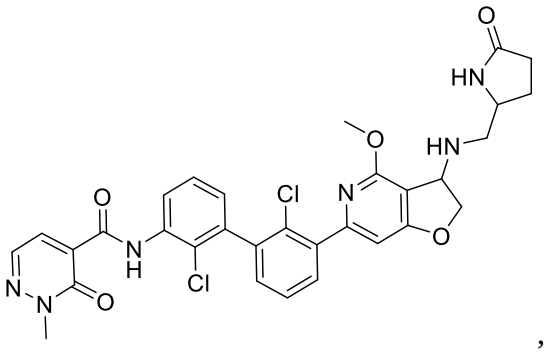
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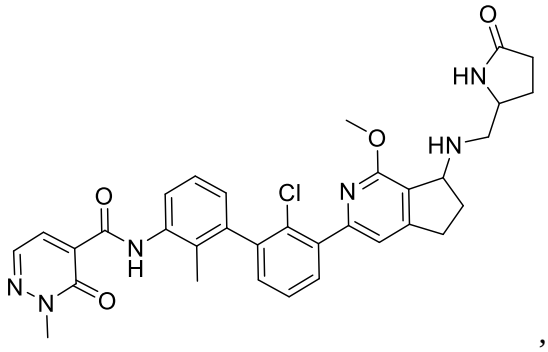
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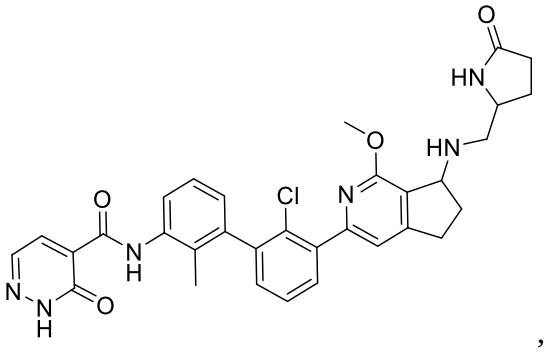
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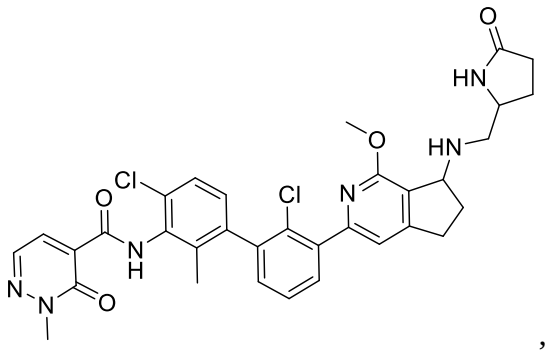
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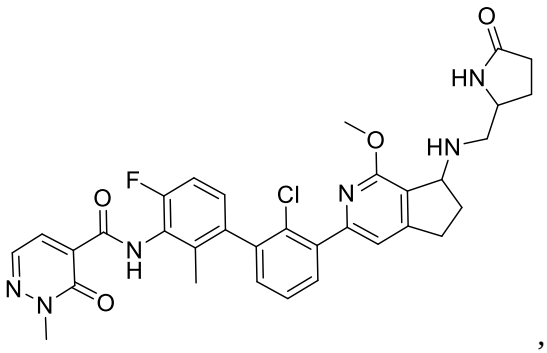
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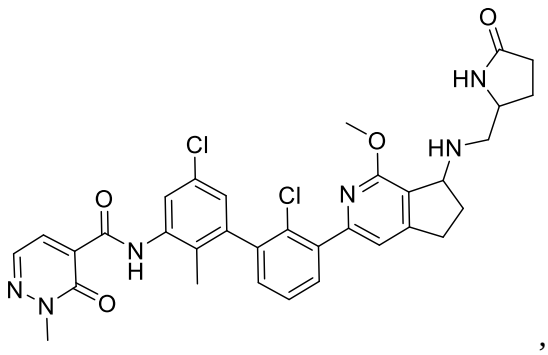
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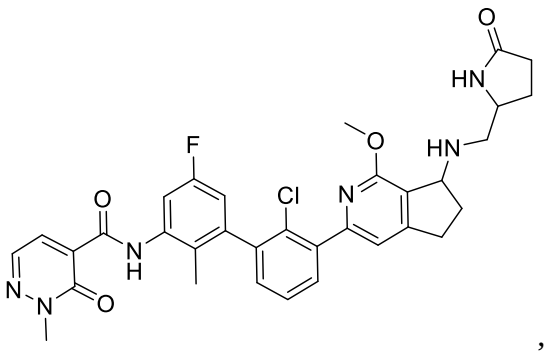
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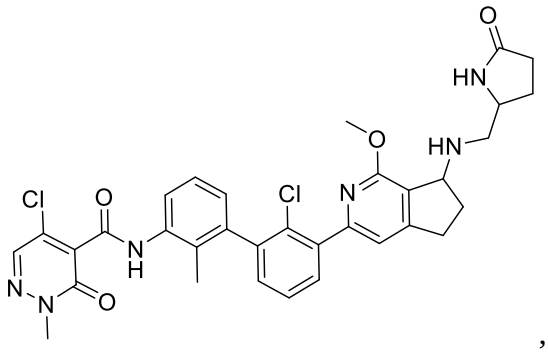
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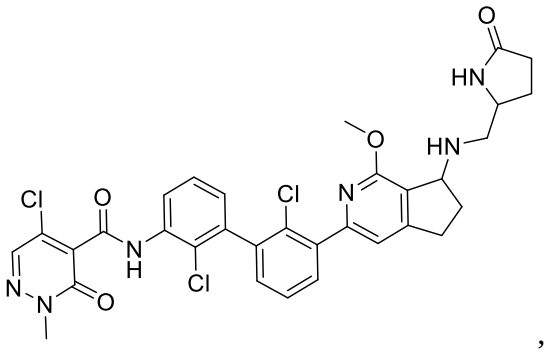
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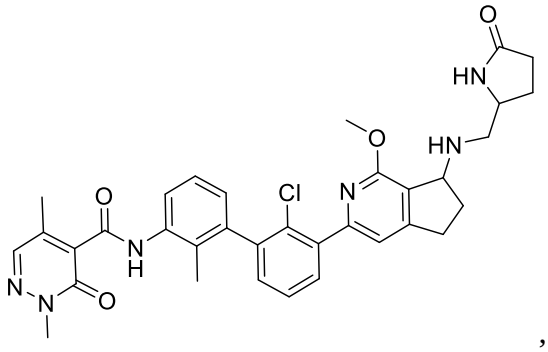
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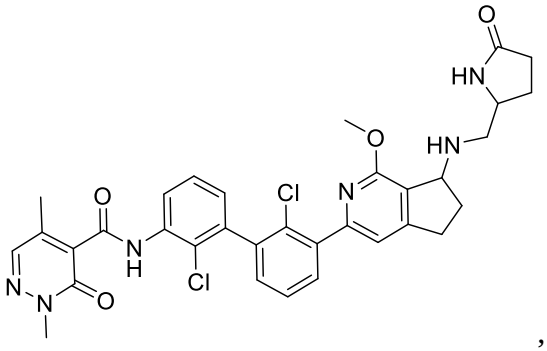
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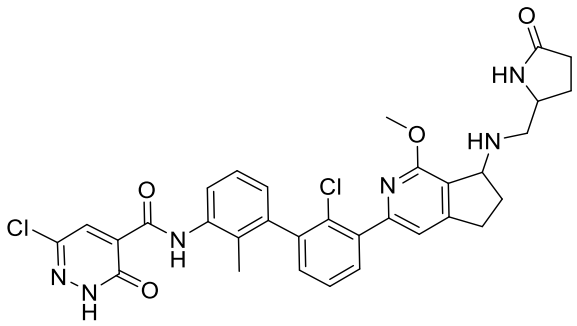
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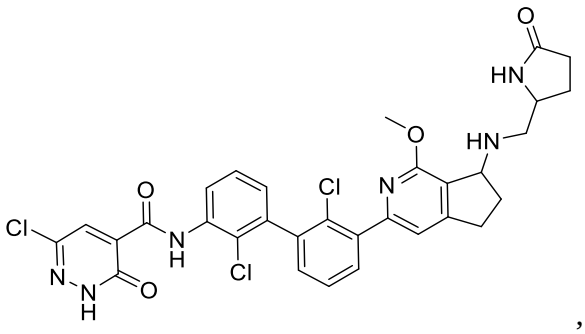
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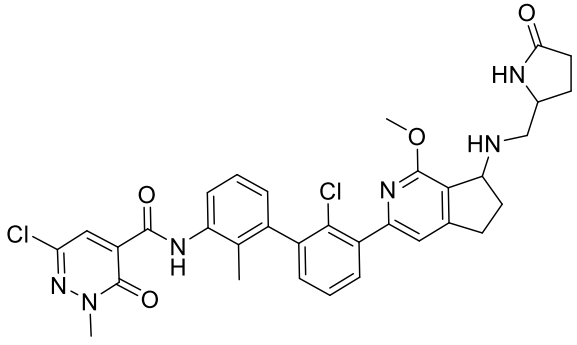
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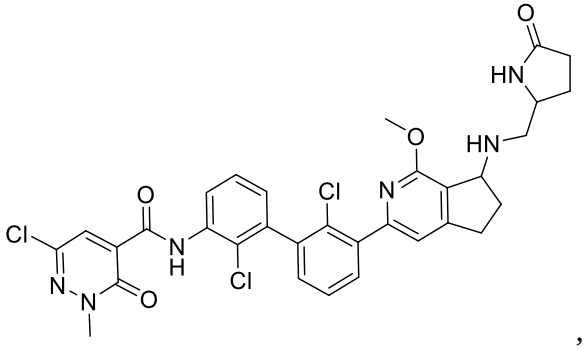
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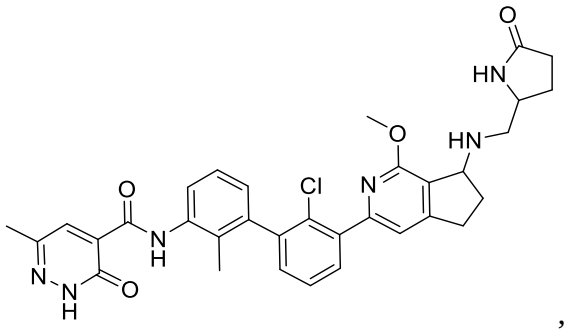
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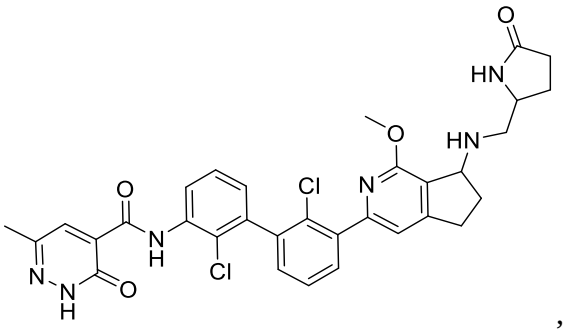
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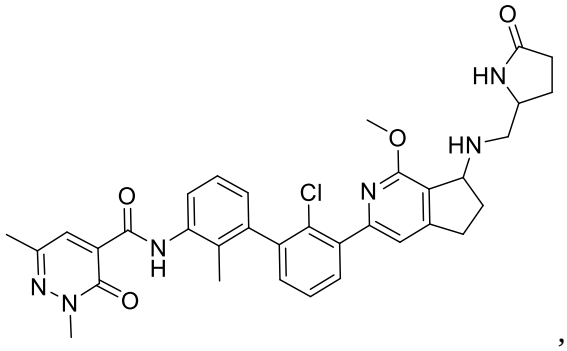
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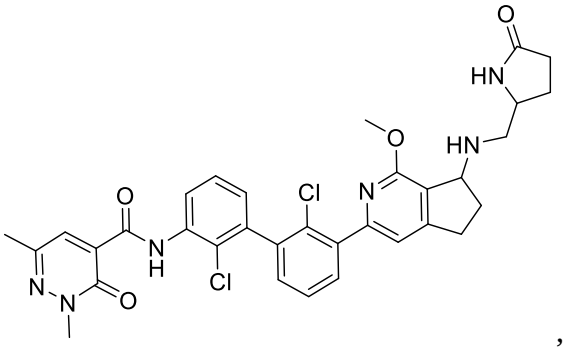
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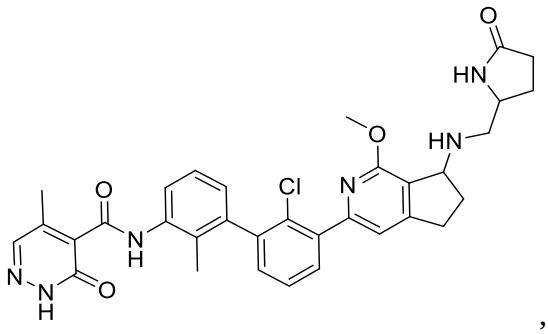
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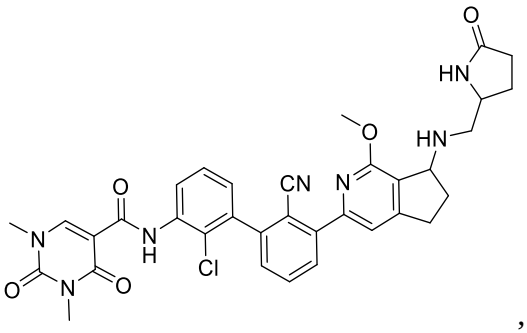
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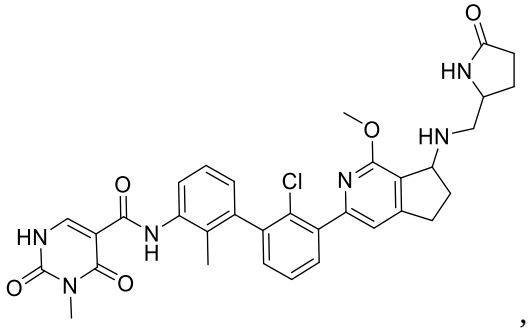
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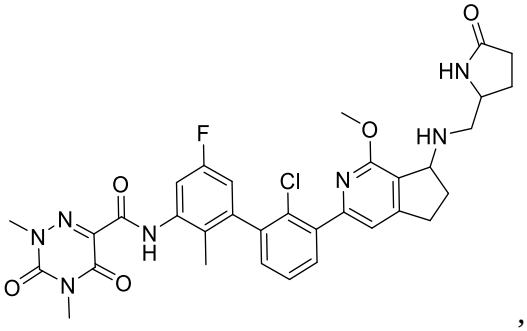
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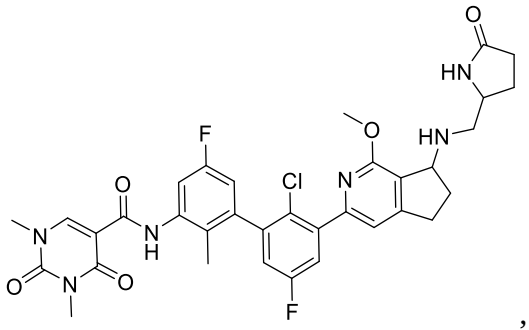
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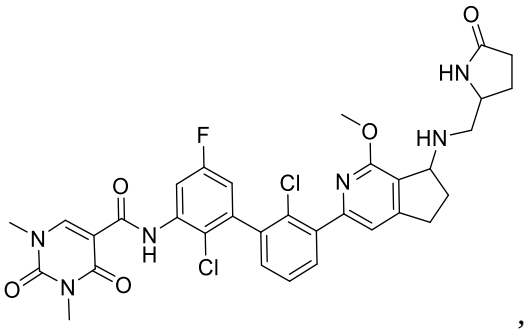
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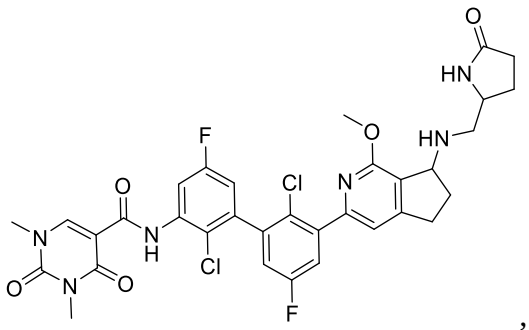
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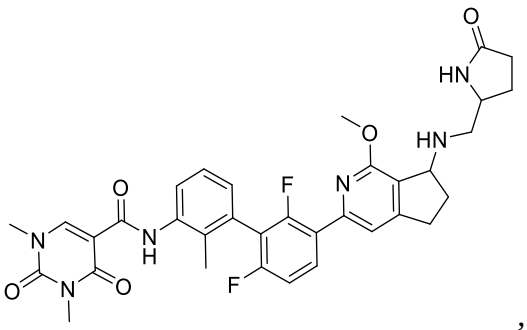
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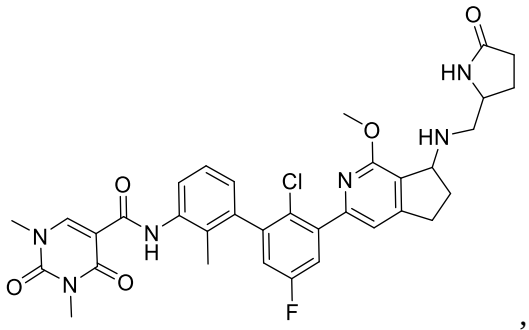
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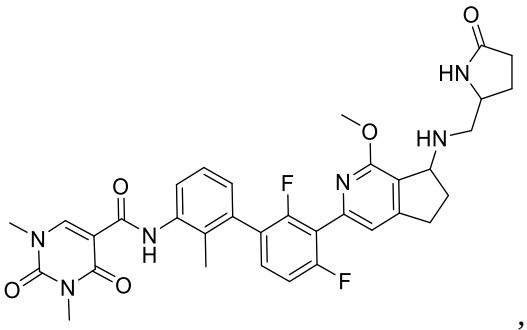
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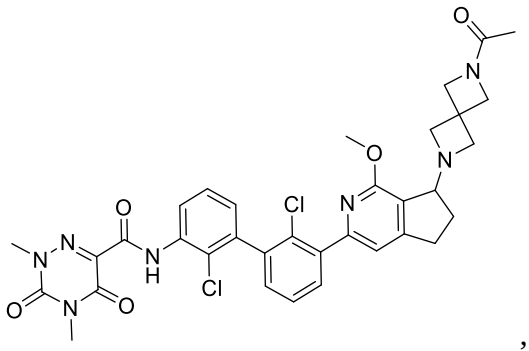
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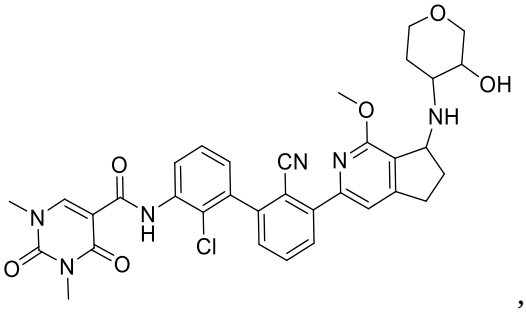
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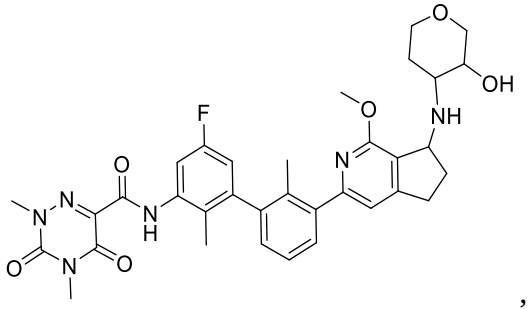
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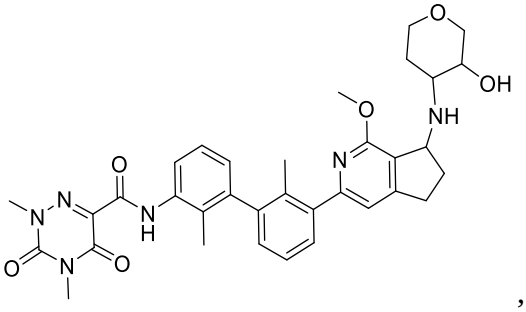
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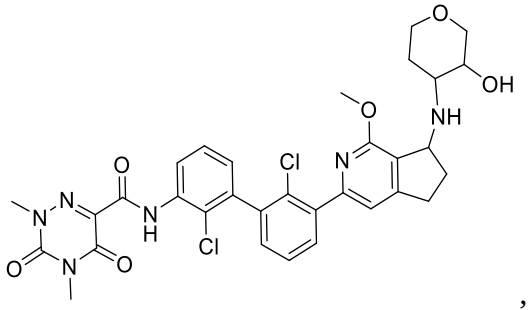
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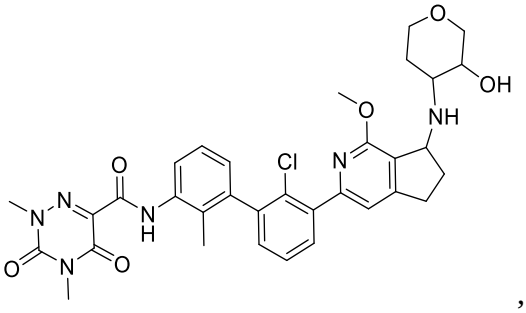
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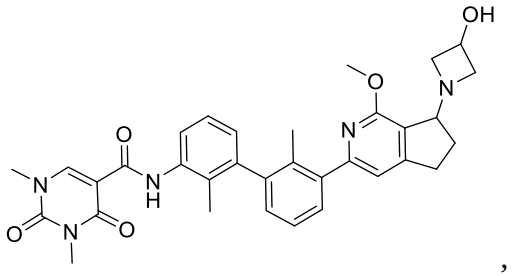
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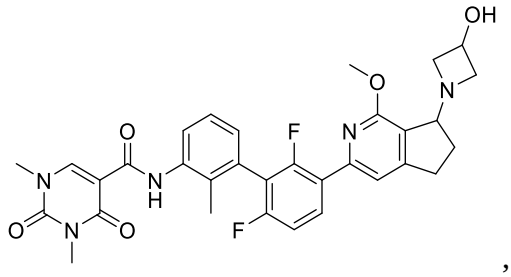
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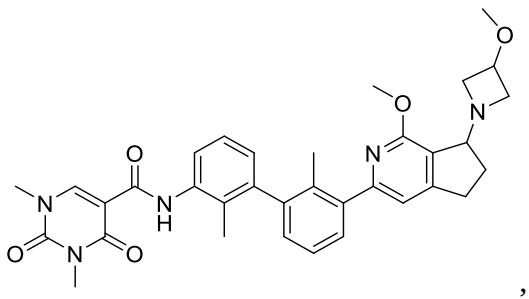
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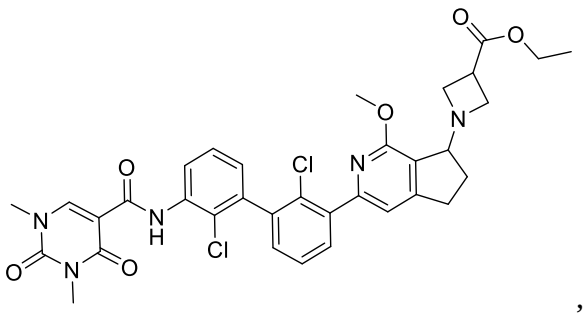
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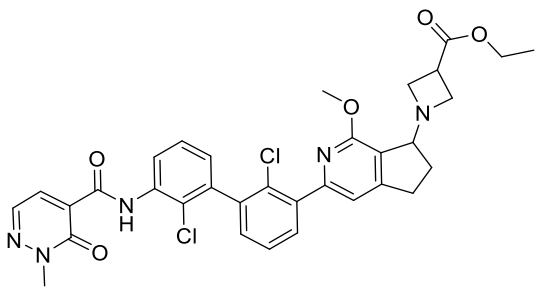
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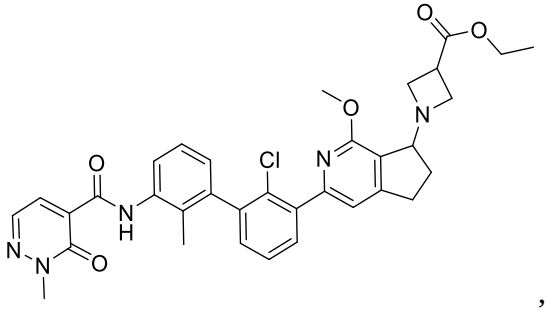
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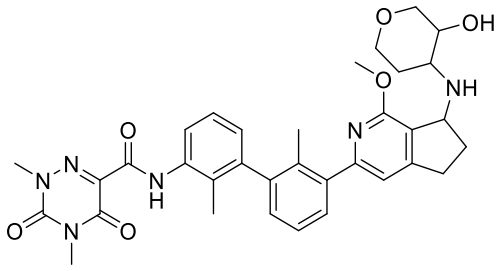
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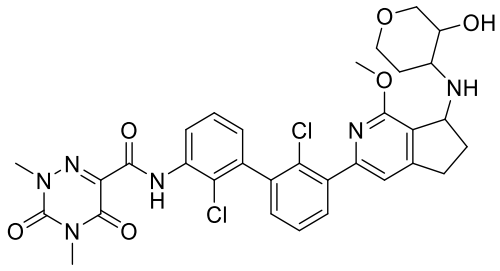
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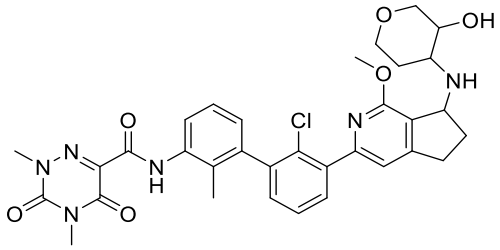
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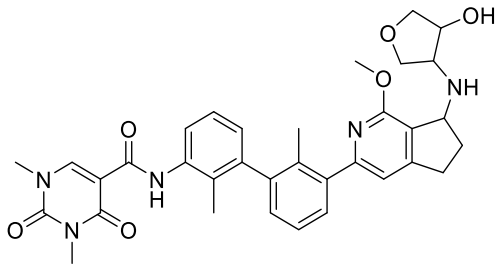
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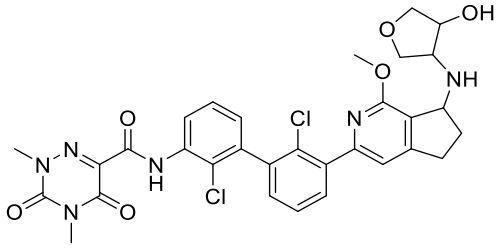
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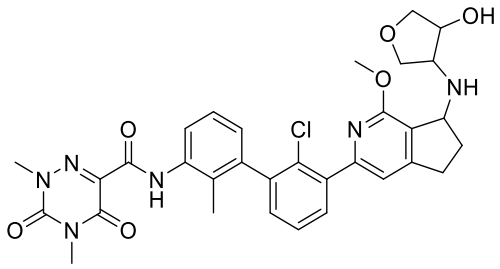
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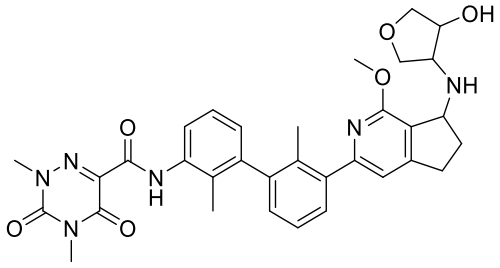
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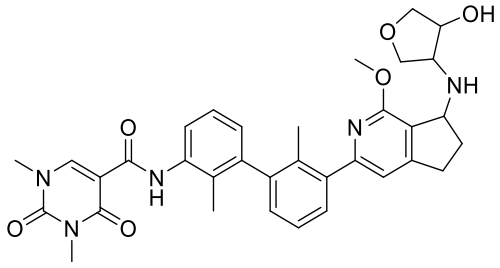
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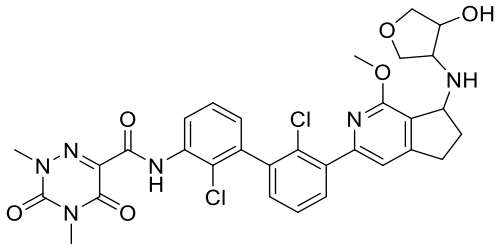
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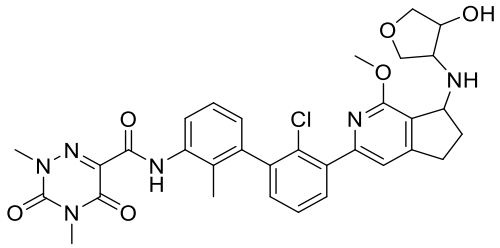
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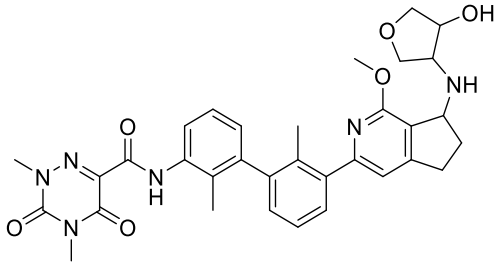
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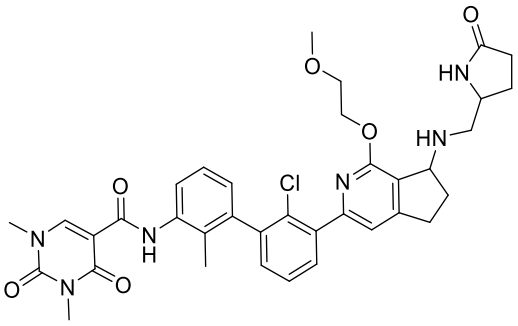
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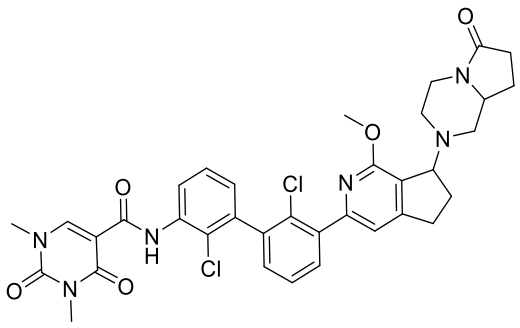
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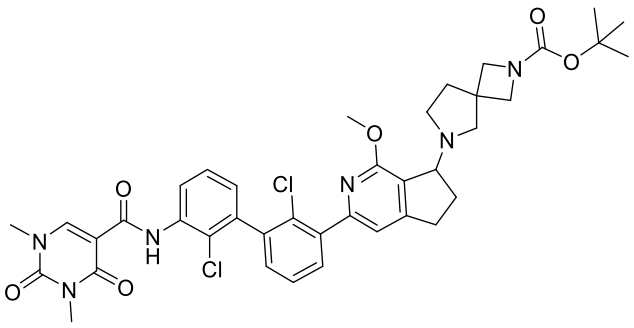
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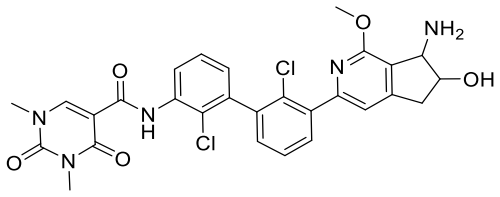
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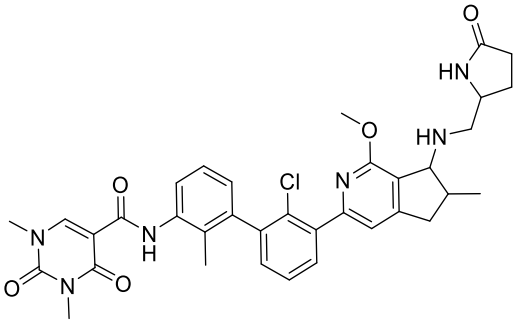
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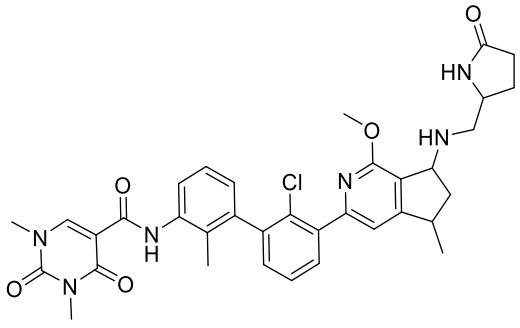
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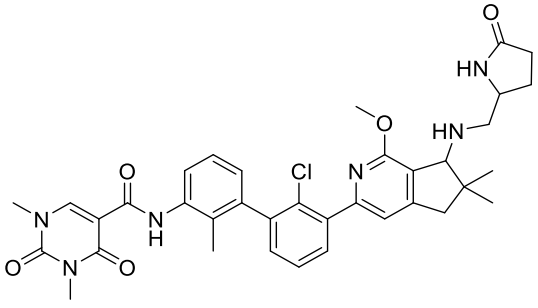
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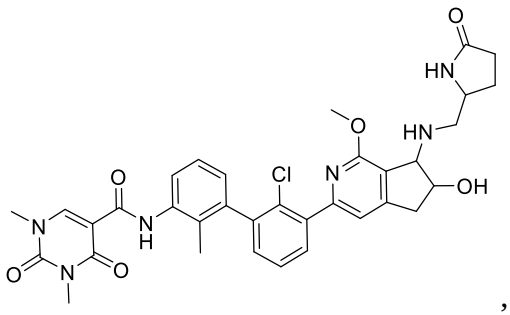
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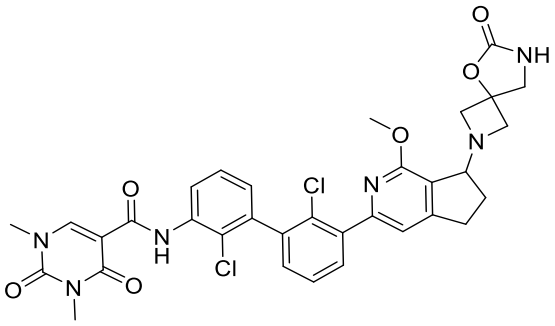
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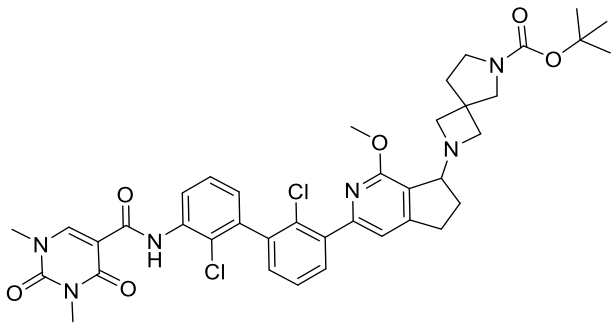
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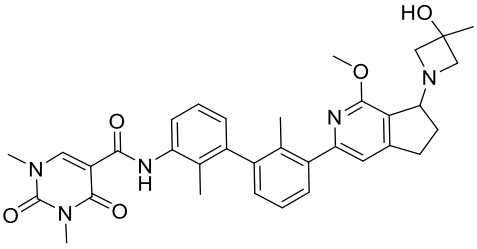
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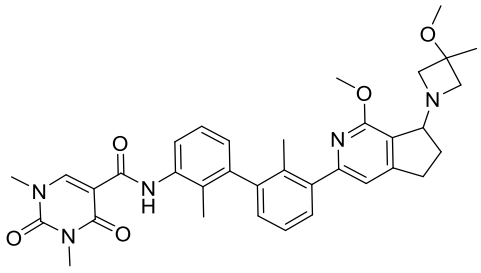
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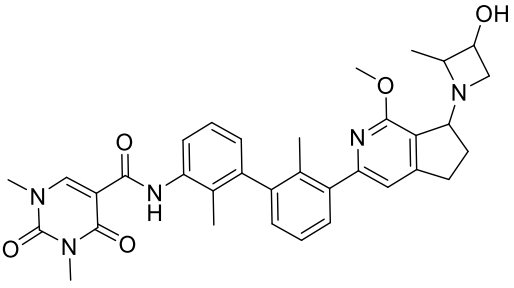
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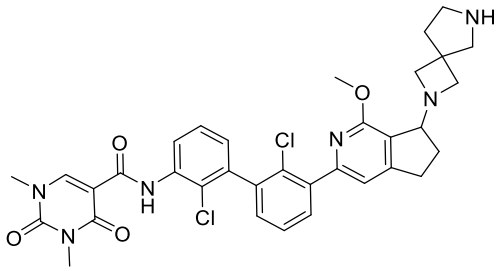
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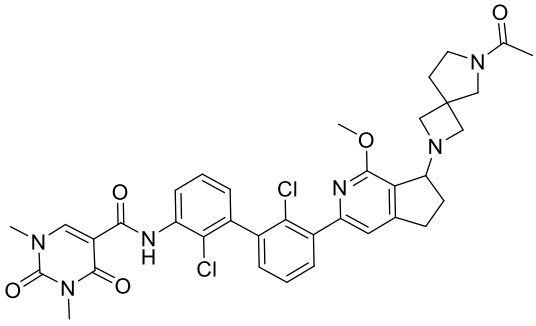
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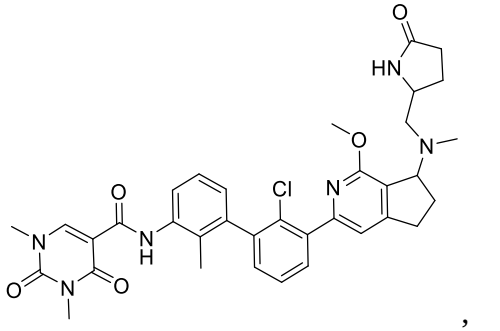
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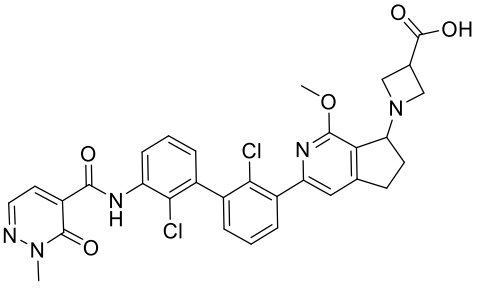
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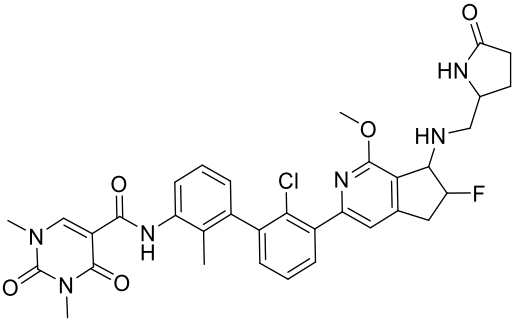
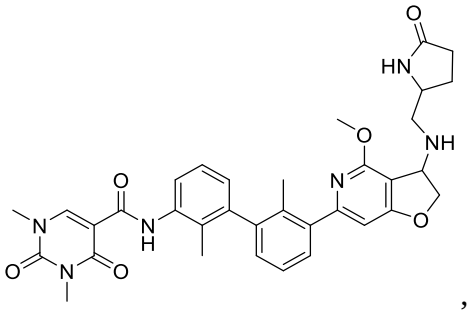
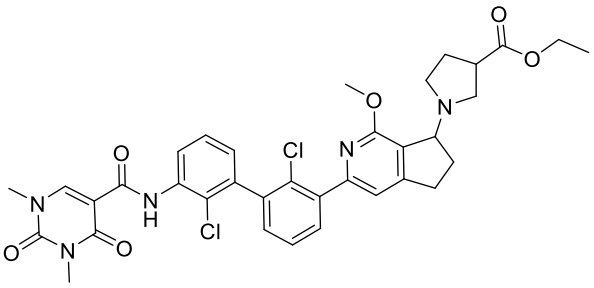
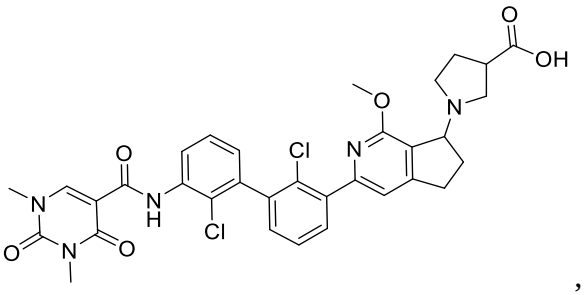
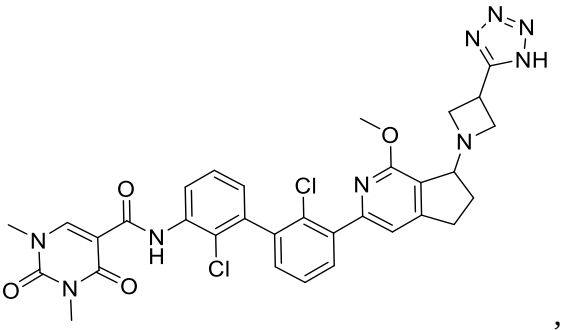
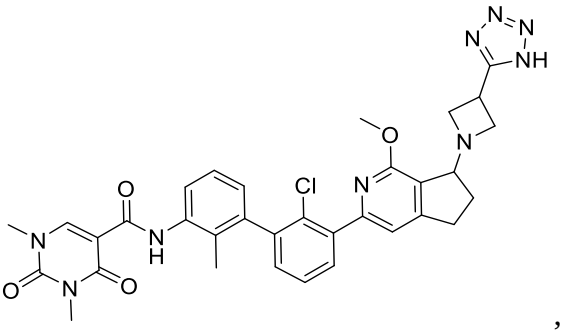
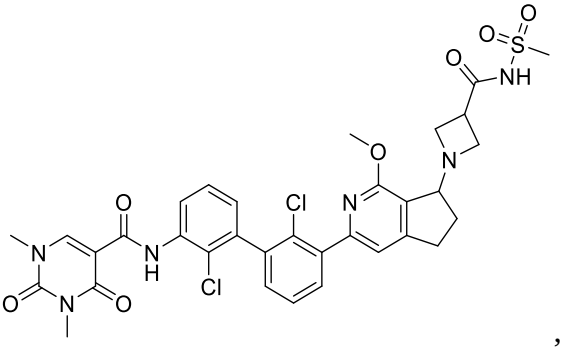
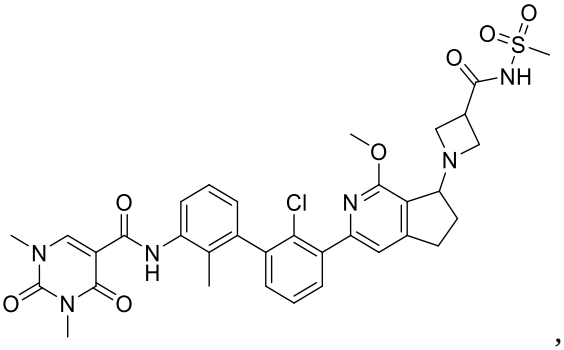
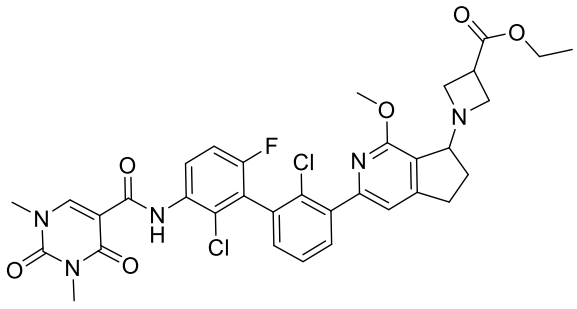
 and  , or a pharmaceutically acceptable salt of any of the foregoing.

143. The compound of Claim 1 selected from the group consisting of:

 ,  ,

 ,  ,

 ,  ,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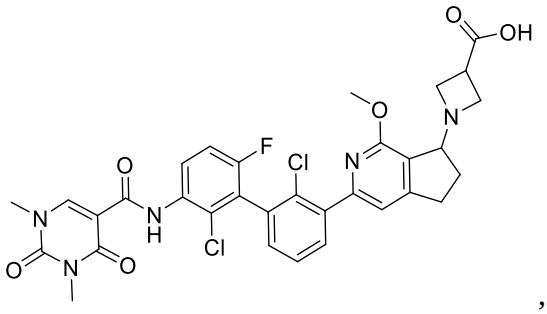
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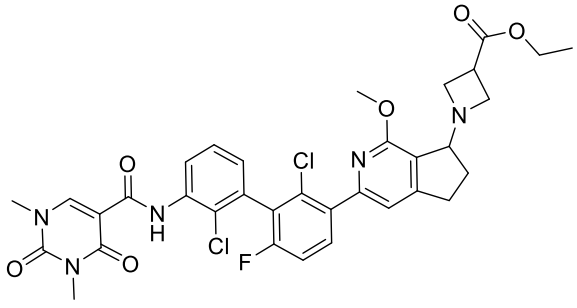
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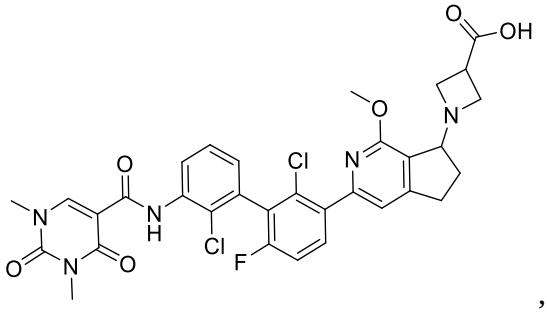
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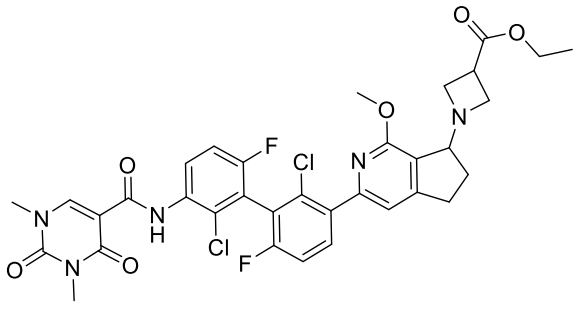
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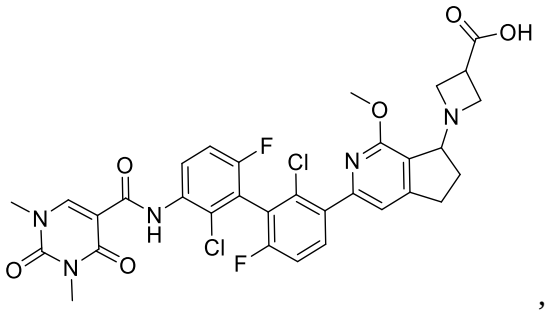
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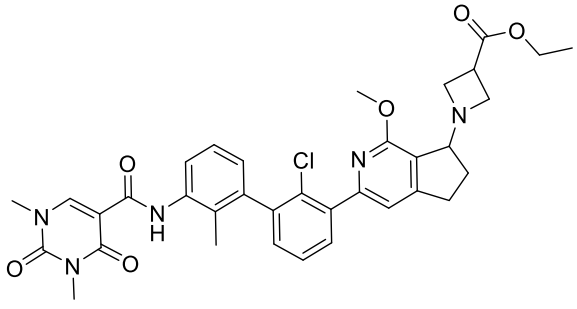
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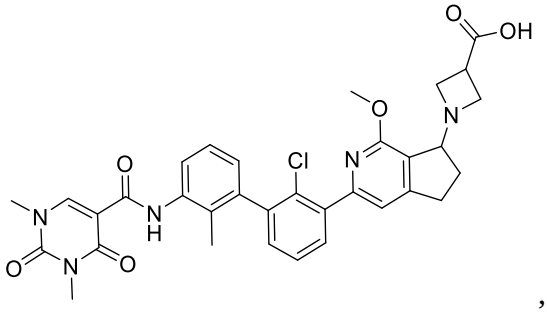
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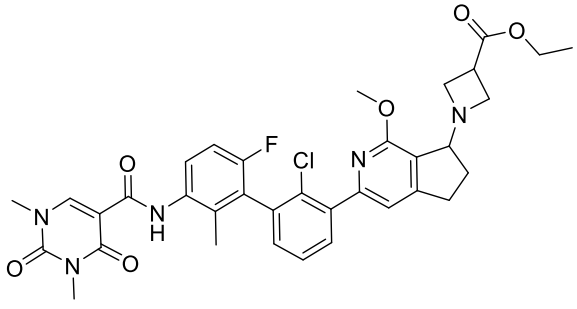
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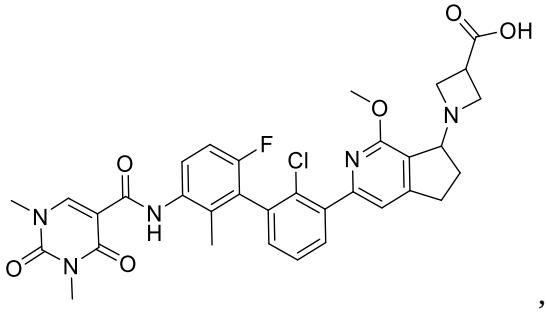
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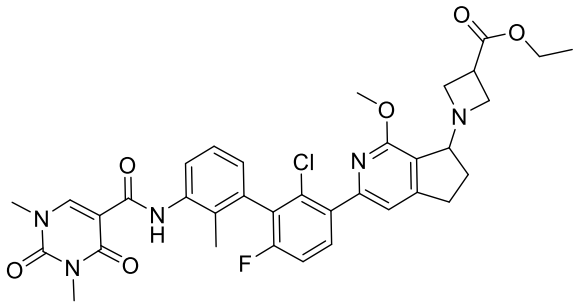
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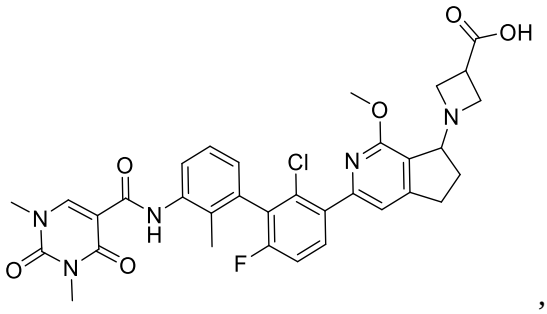
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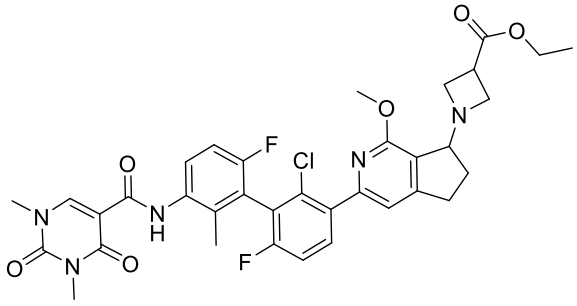
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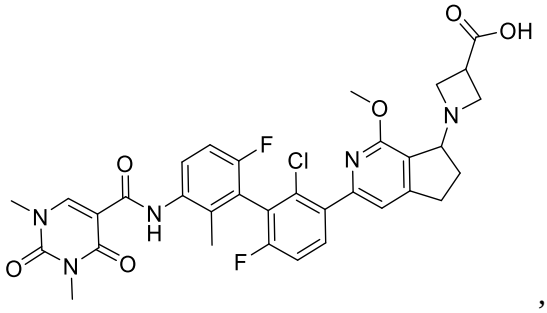
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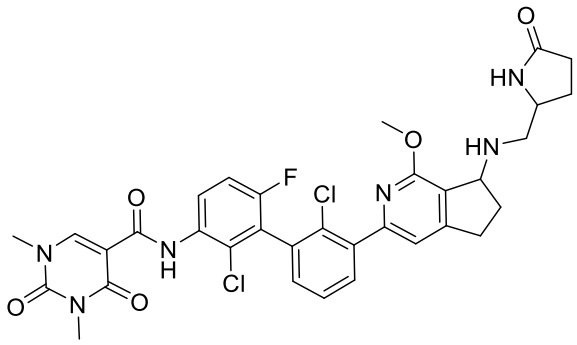
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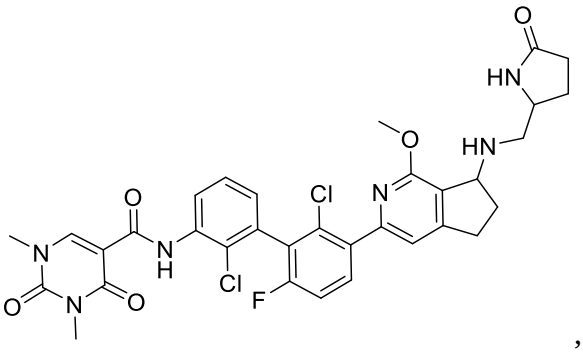
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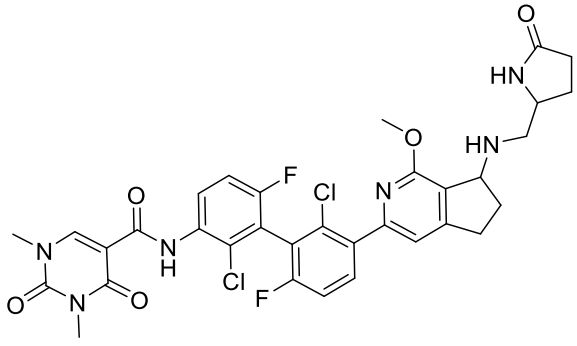
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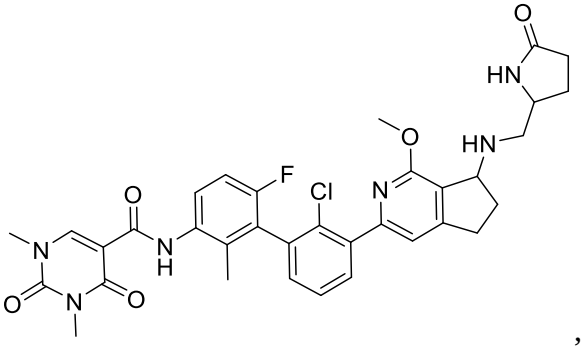
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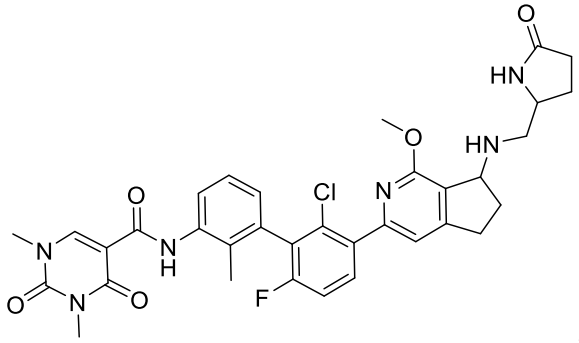
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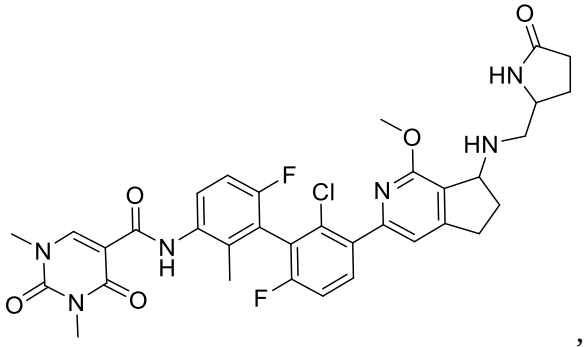
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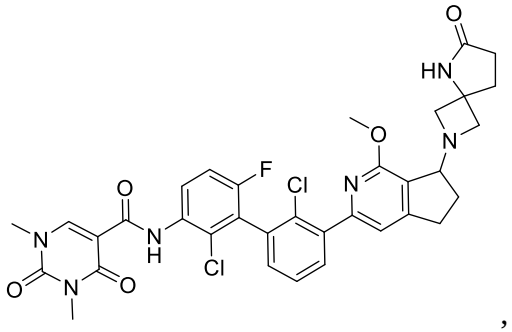
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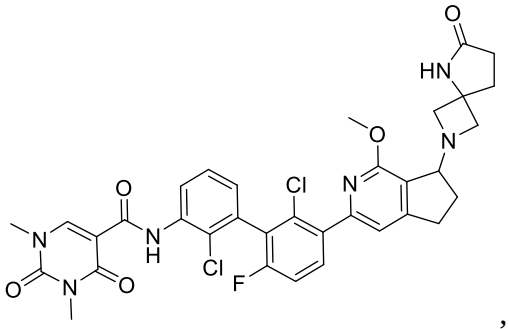
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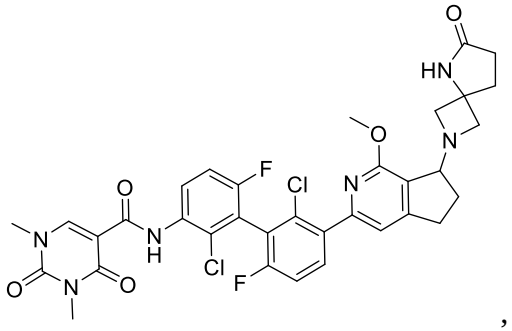
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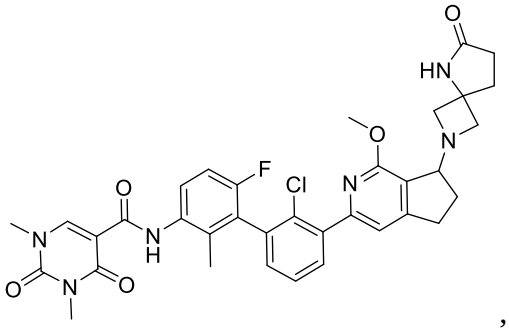
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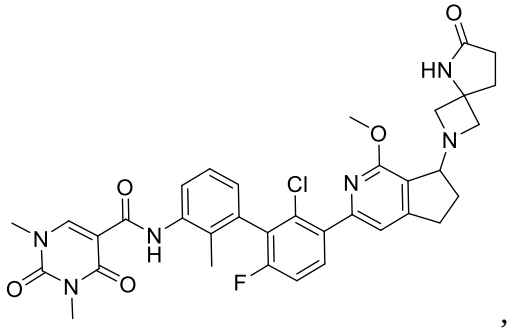
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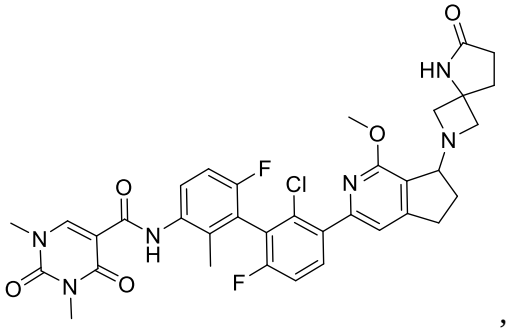
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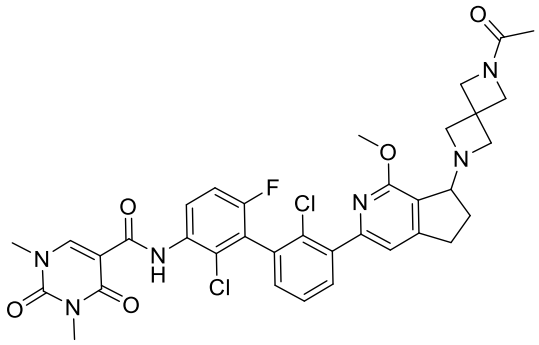
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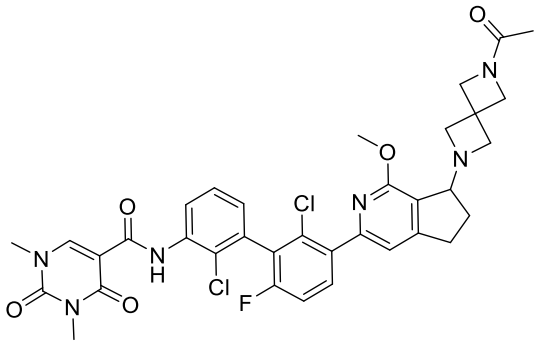
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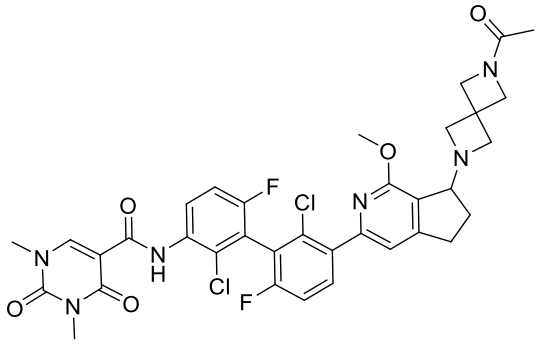
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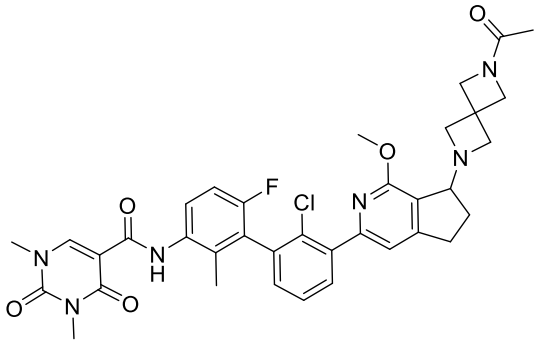
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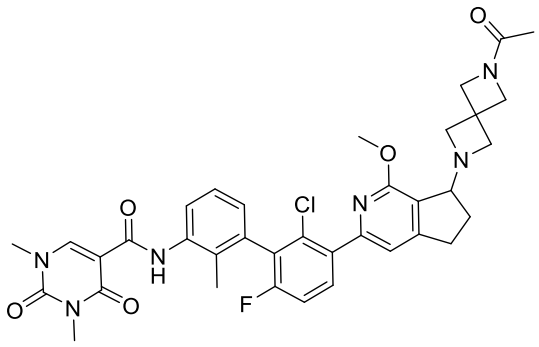
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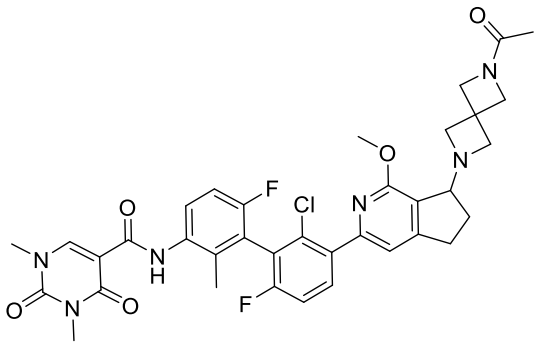
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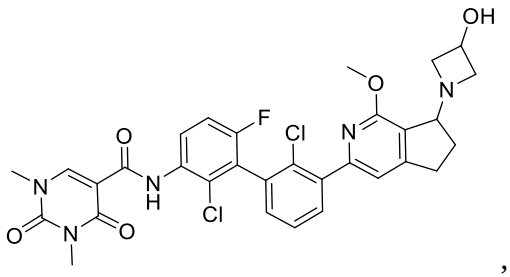
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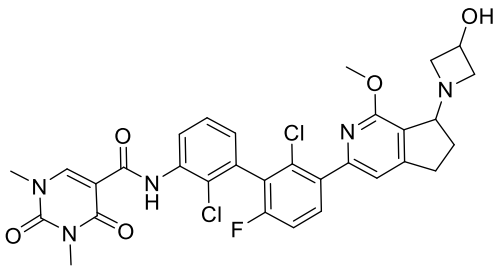
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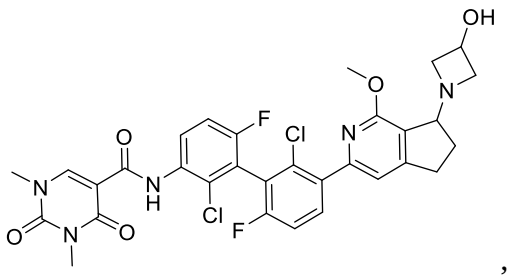
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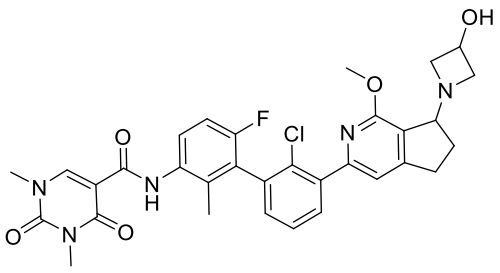
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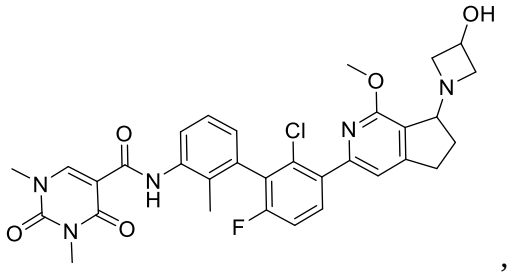
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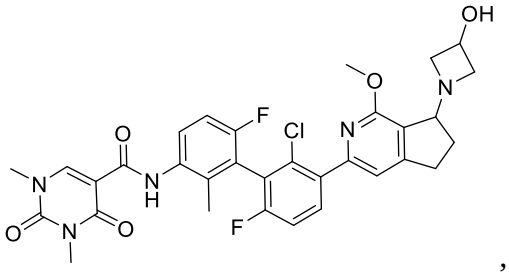
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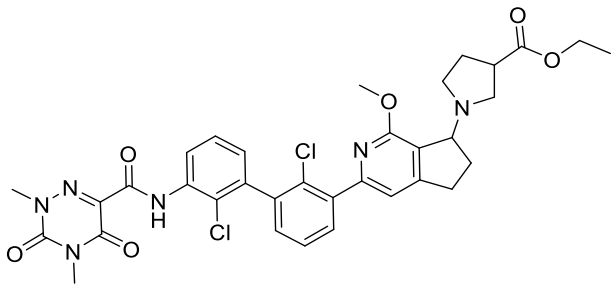
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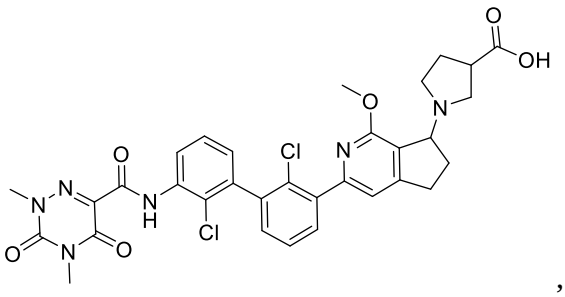
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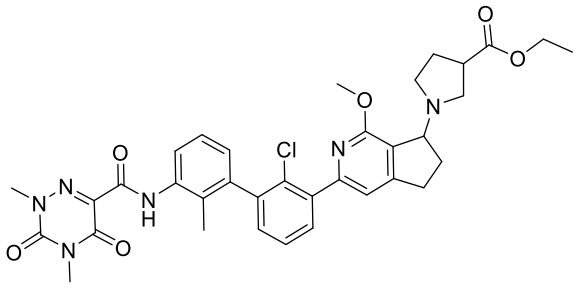
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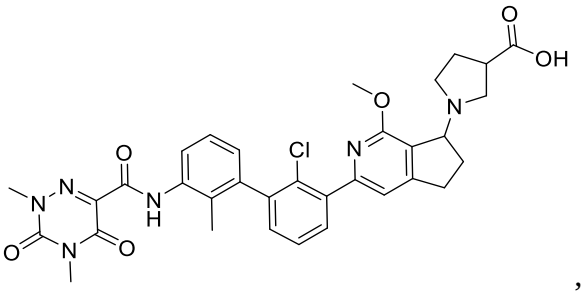
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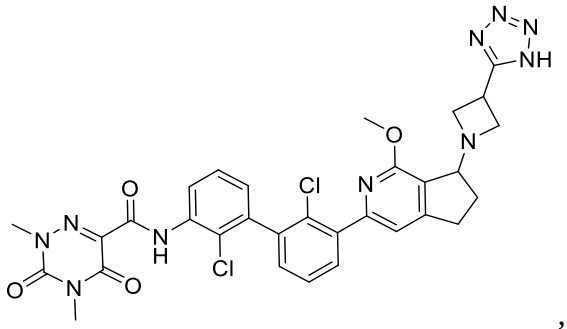
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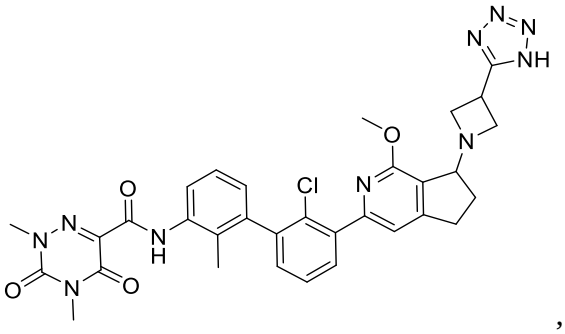
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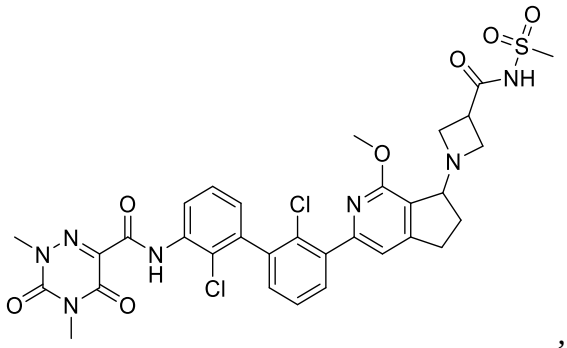
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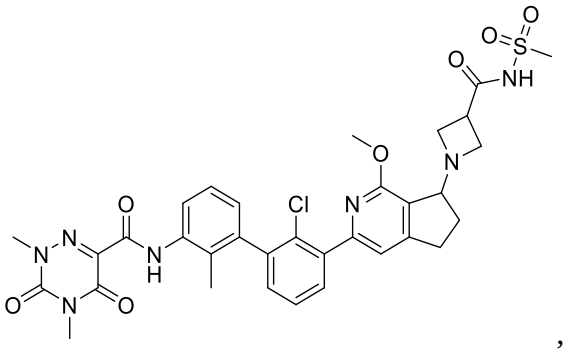
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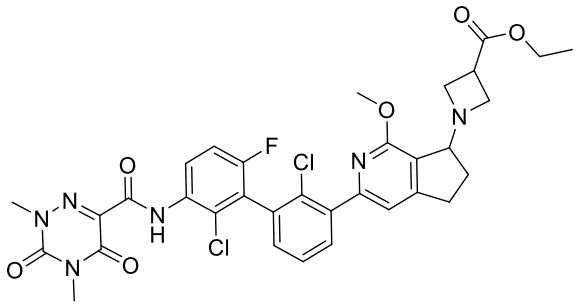
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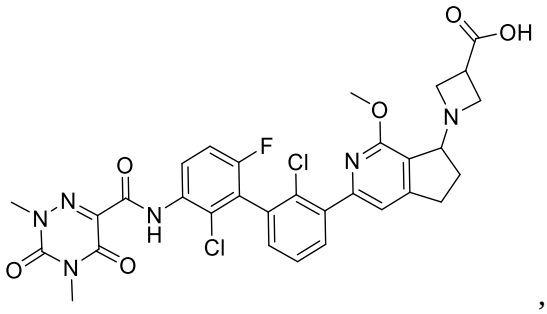
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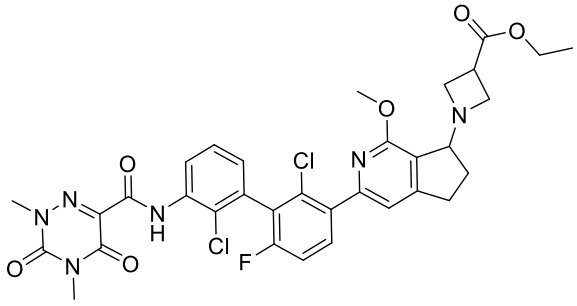
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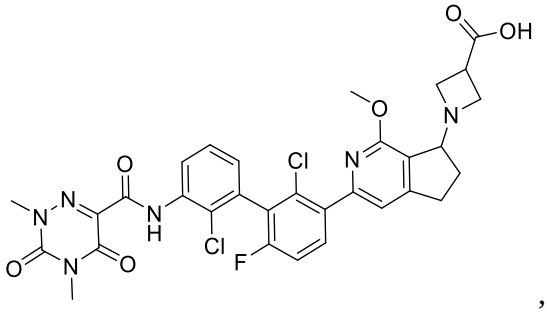
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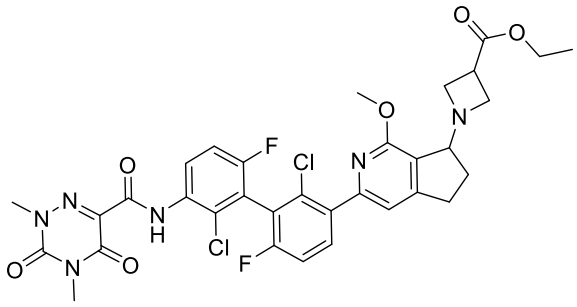
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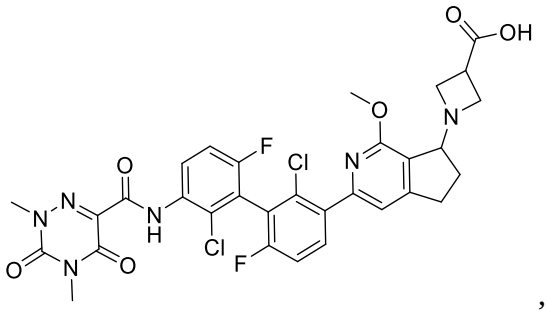
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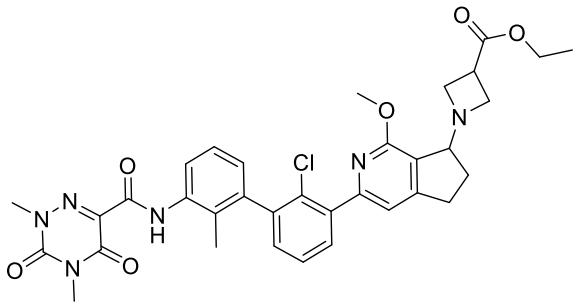
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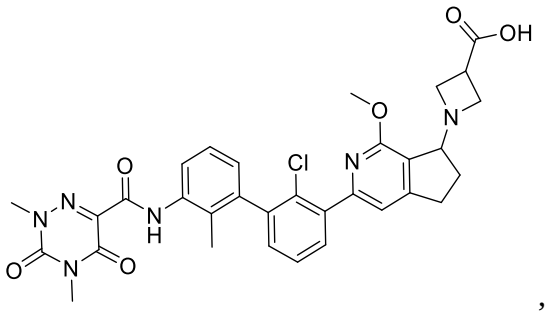
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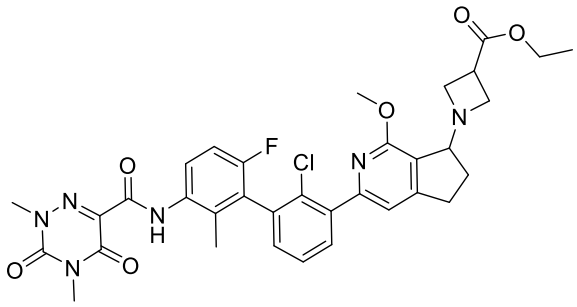
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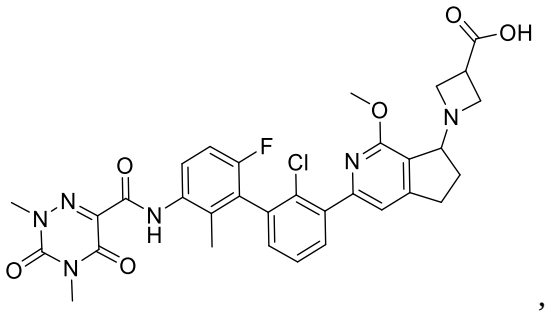
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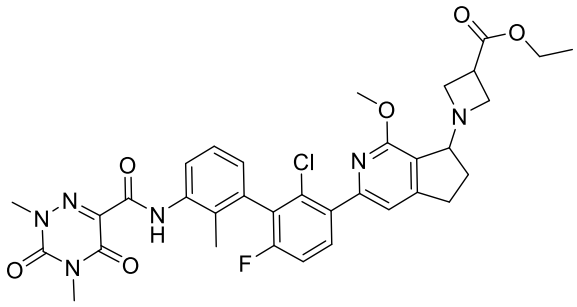
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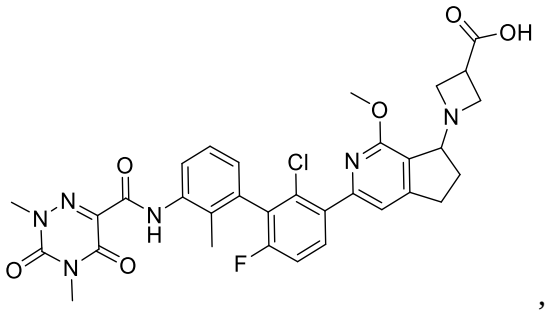
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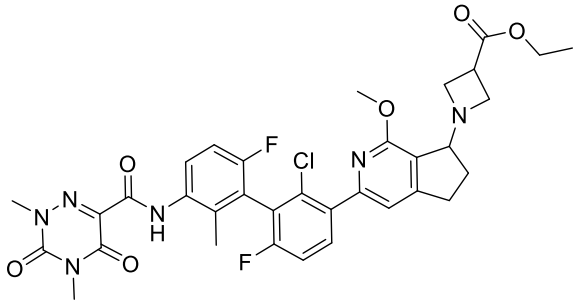
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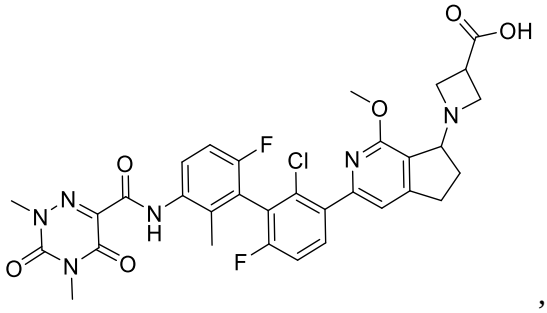
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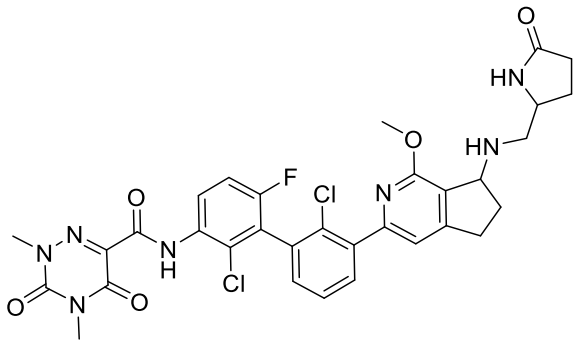
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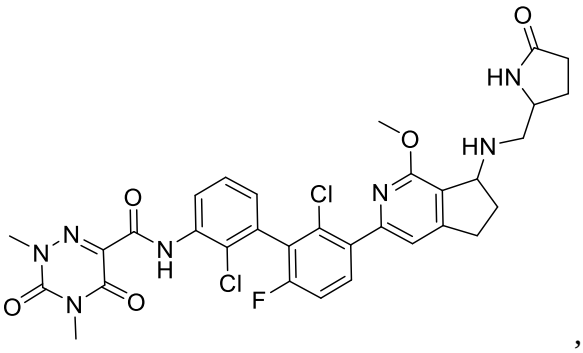
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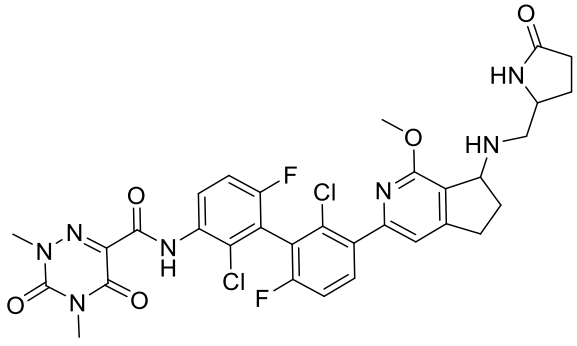
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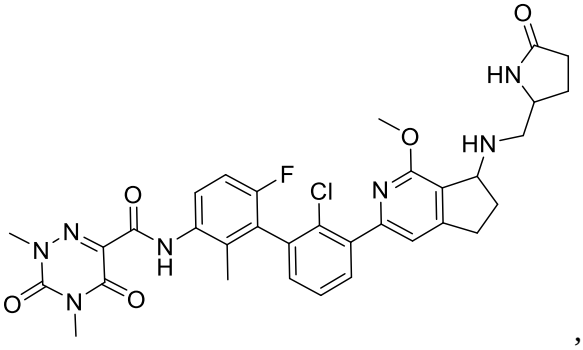
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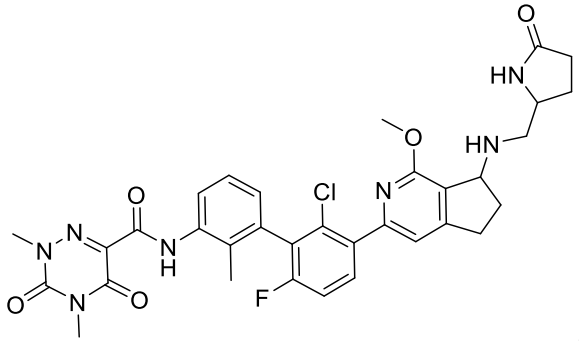
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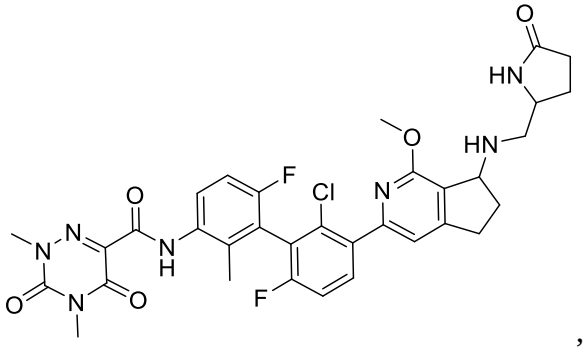
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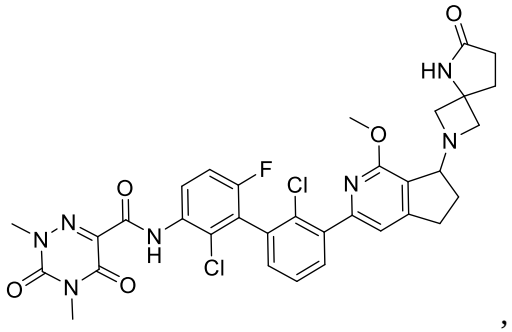
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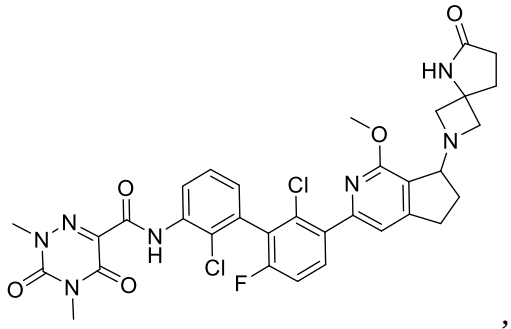
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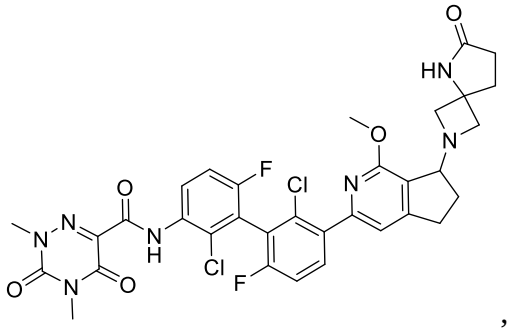
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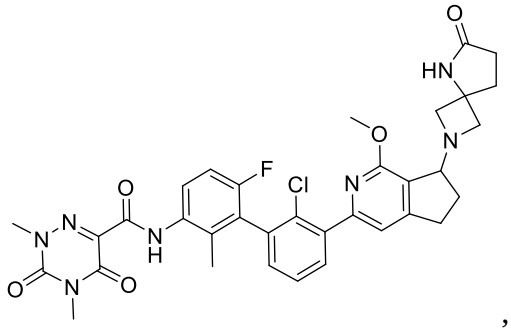
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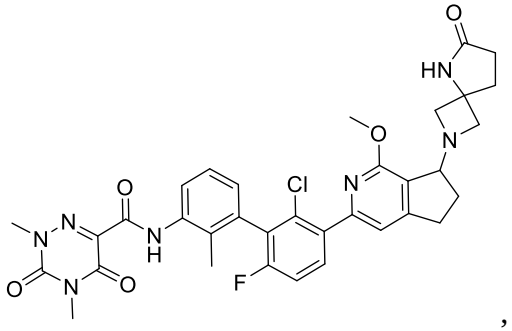
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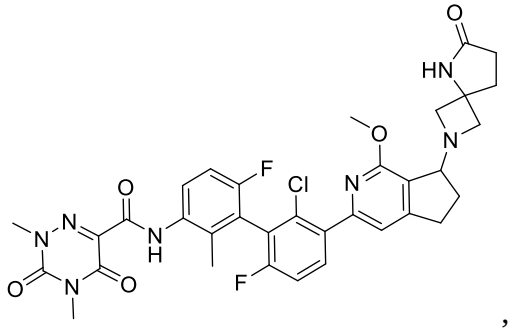
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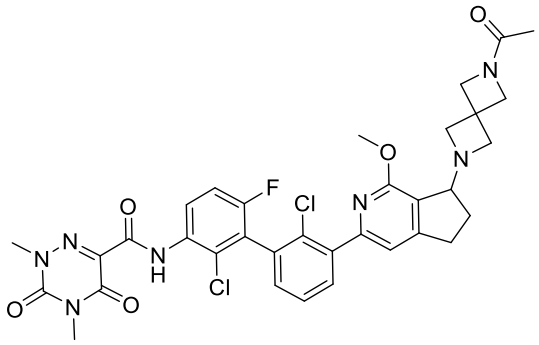
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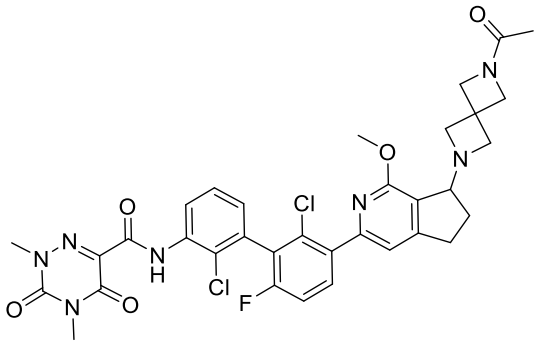
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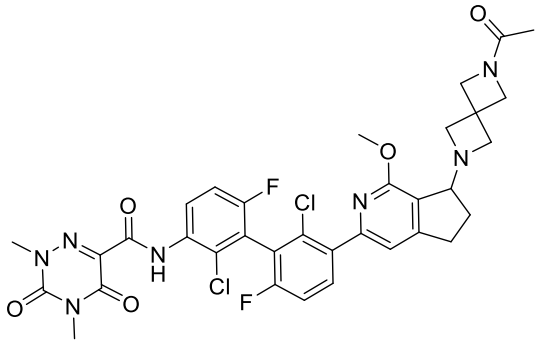
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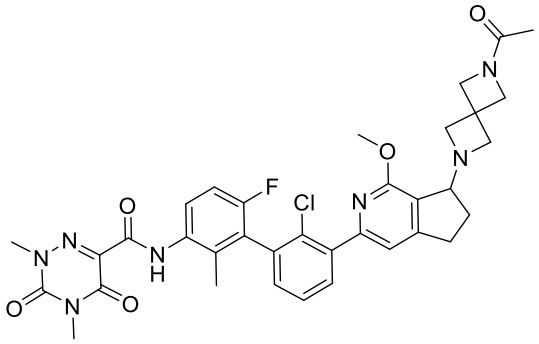
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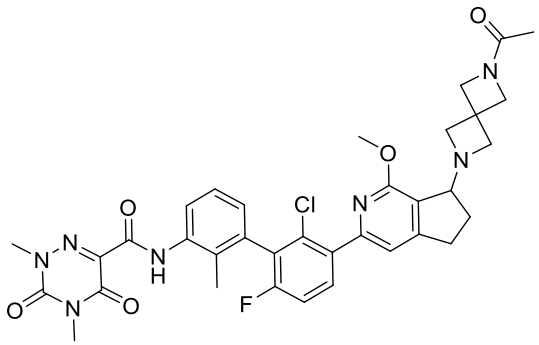
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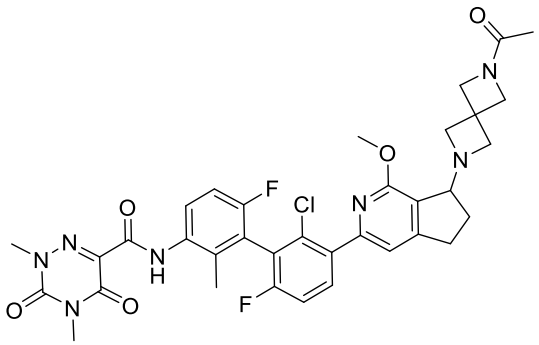
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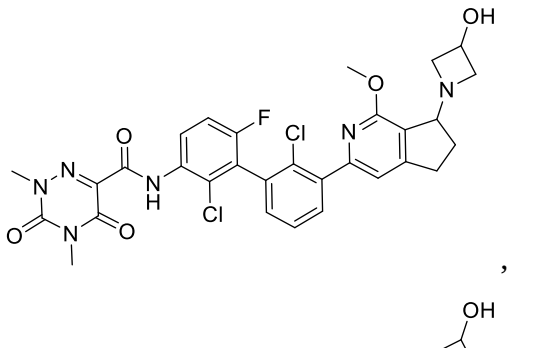
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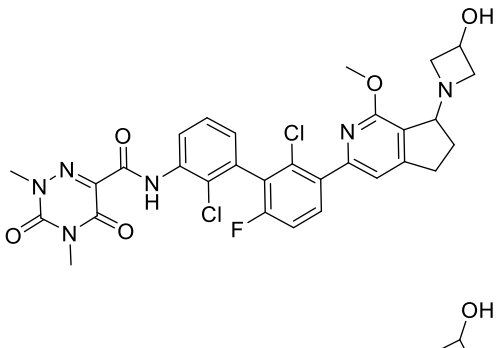
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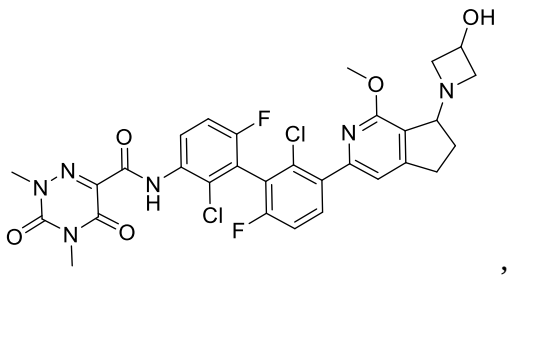
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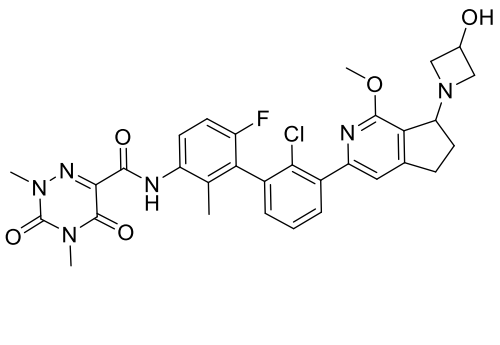
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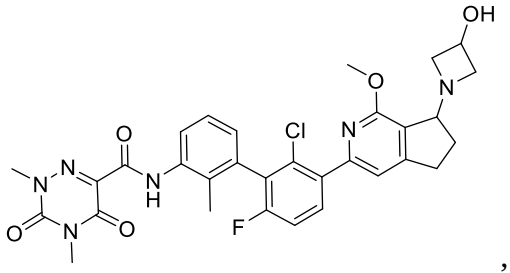
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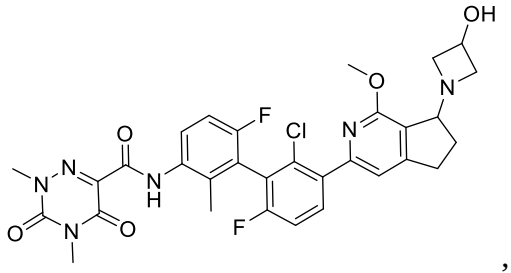
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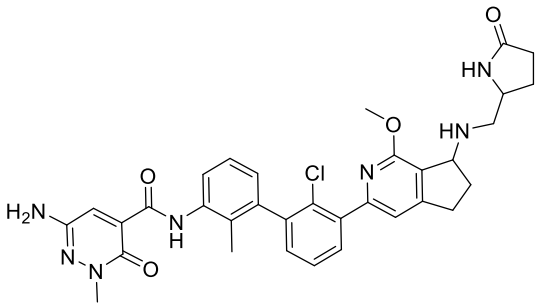
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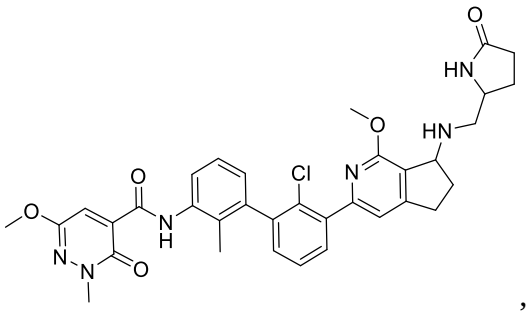
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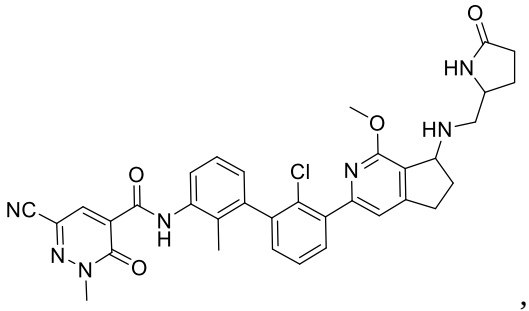
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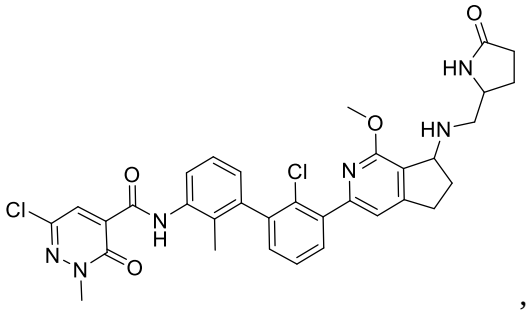
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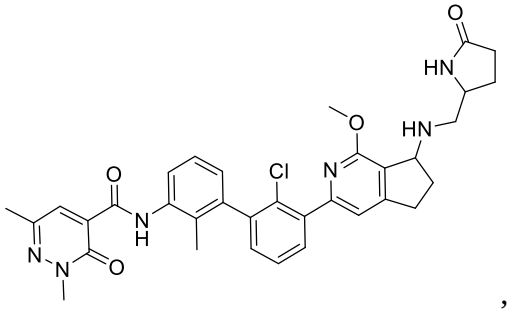
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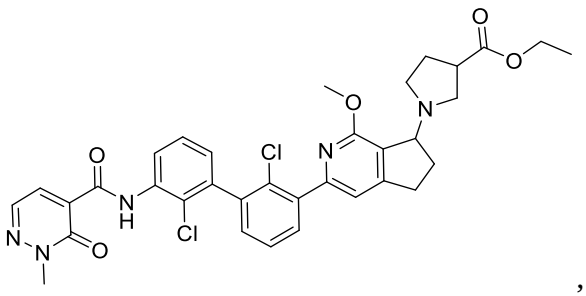
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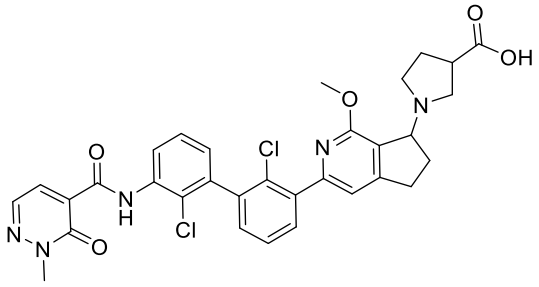
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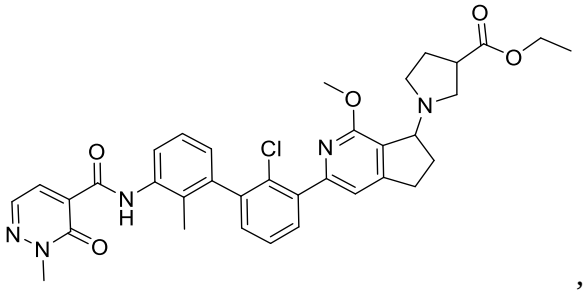
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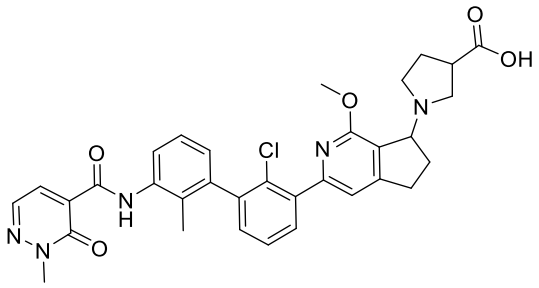
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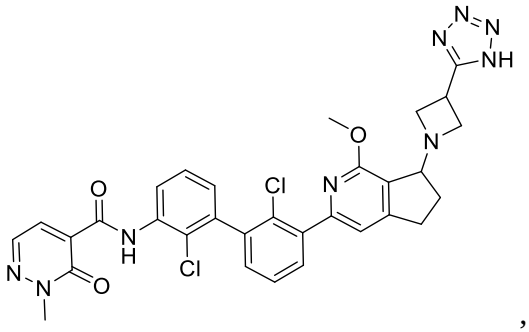
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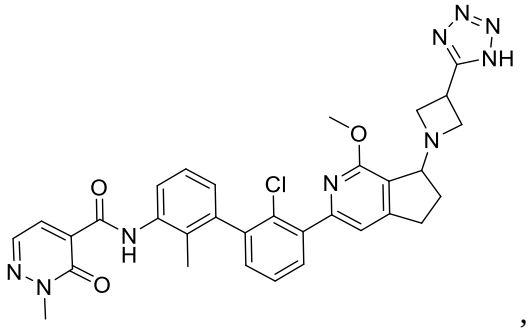
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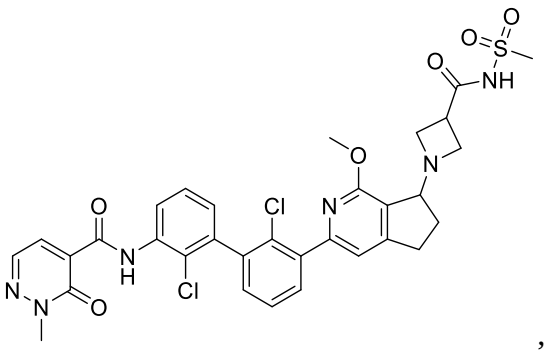
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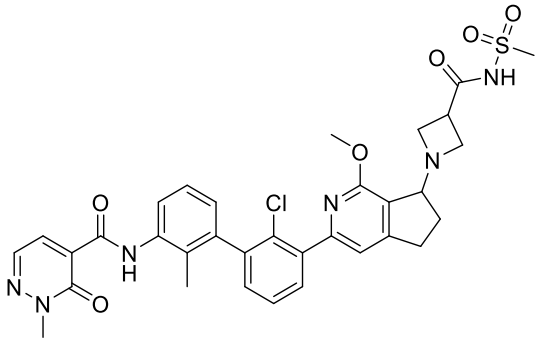
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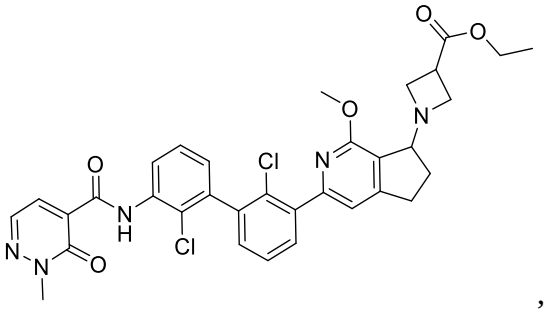
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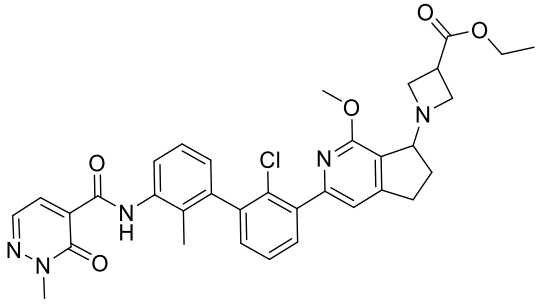
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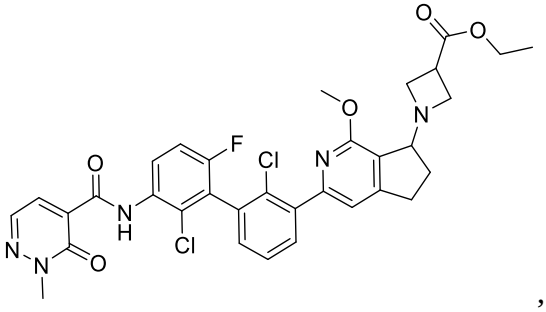
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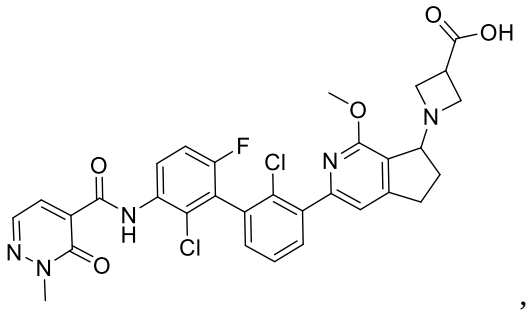
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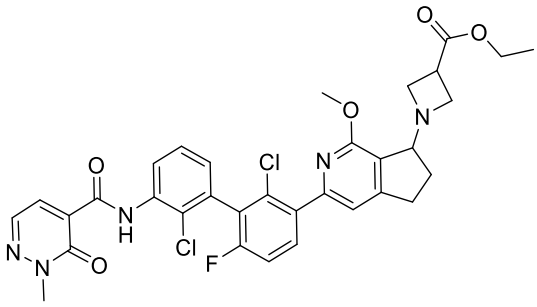
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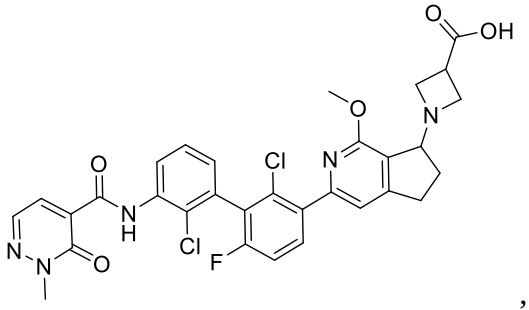
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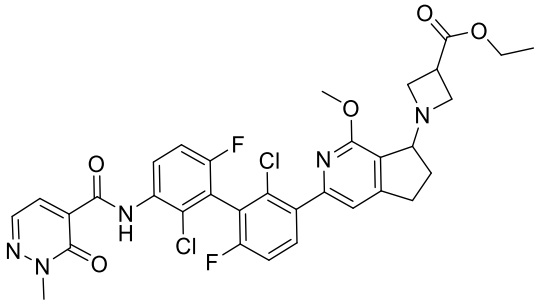
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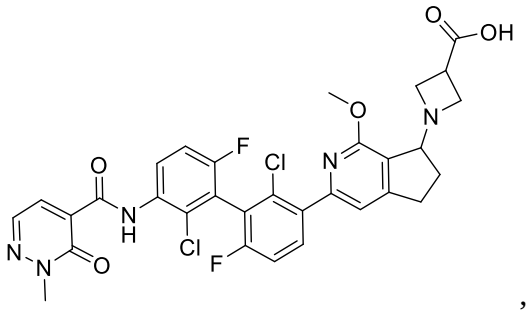
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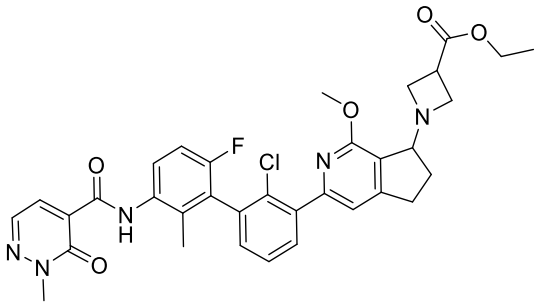
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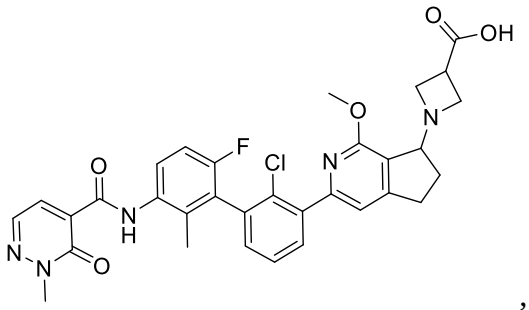
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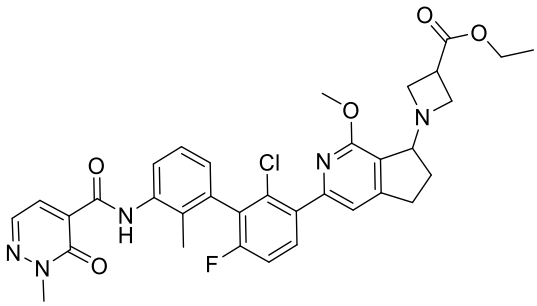
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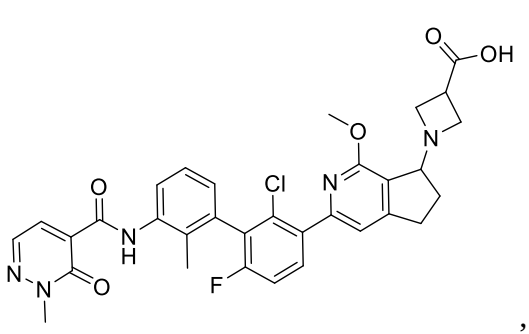
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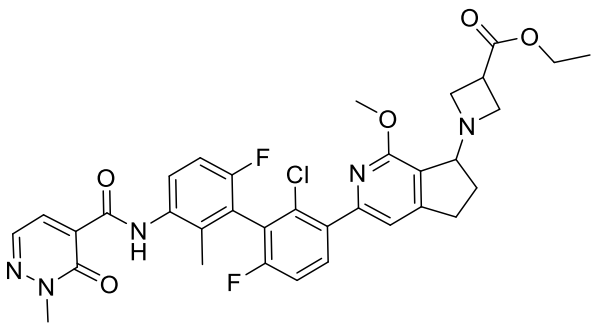
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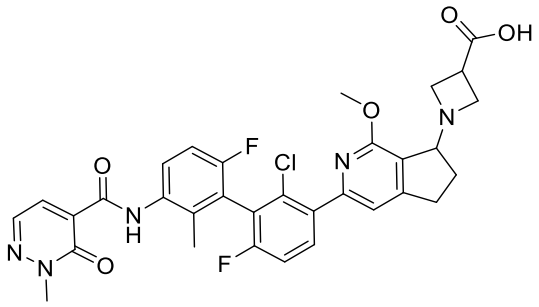
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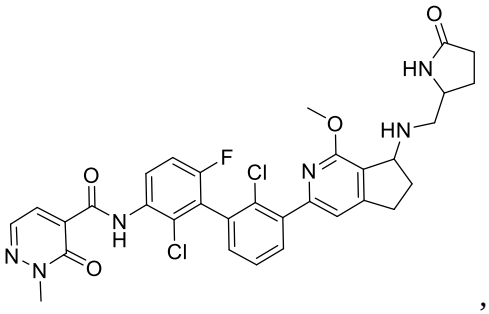
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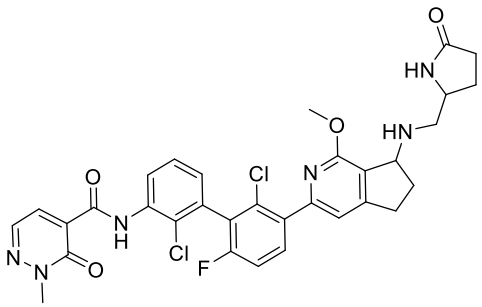
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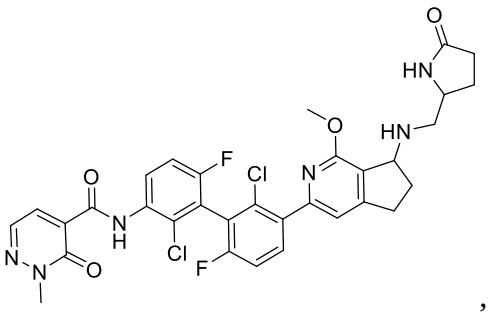
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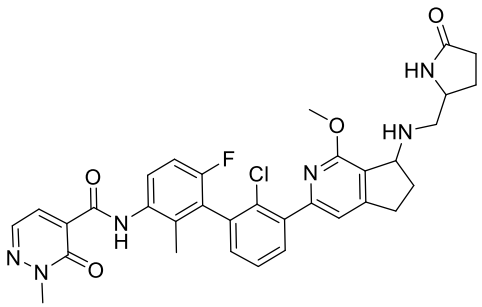
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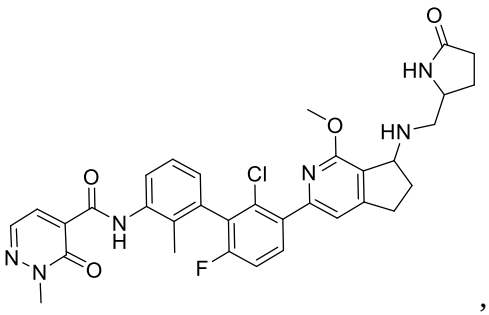
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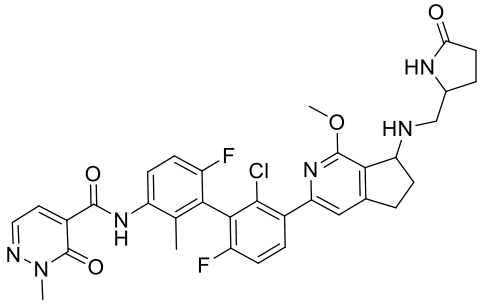
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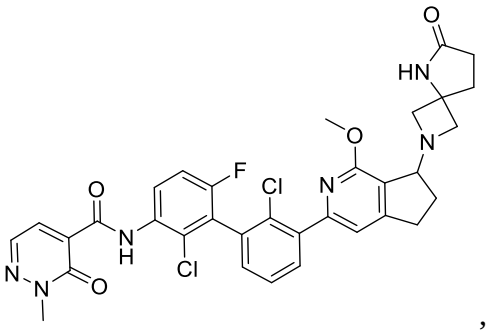
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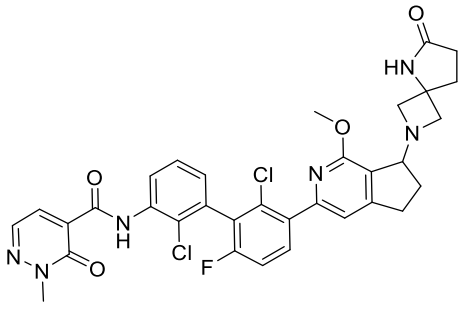
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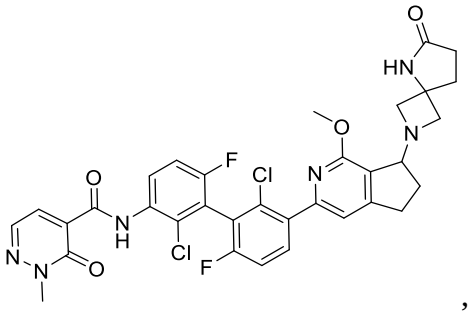
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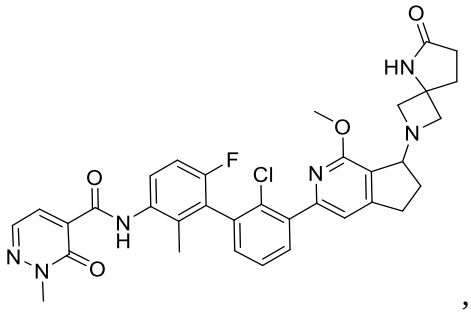
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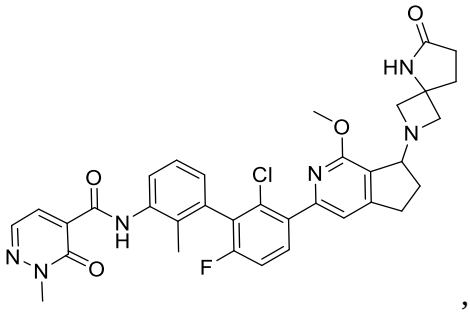
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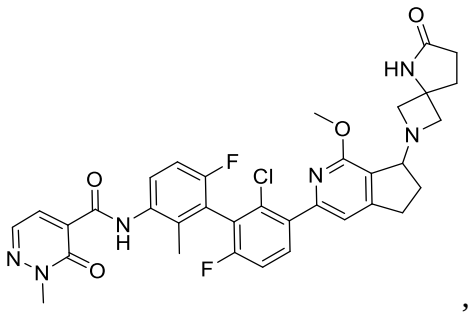
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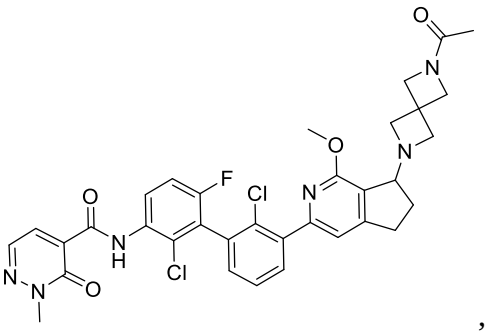
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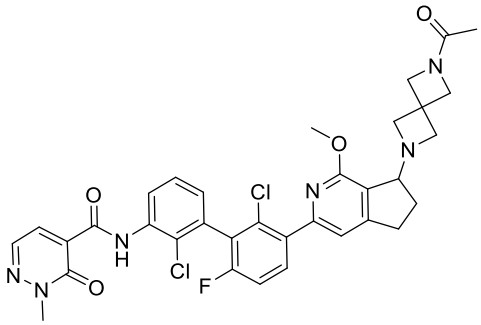
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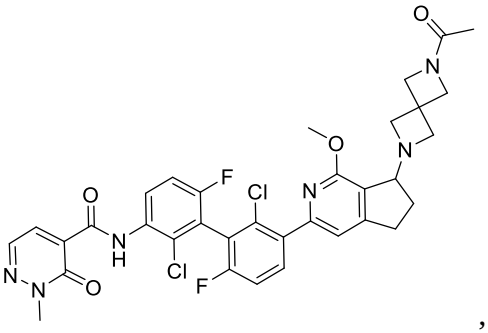
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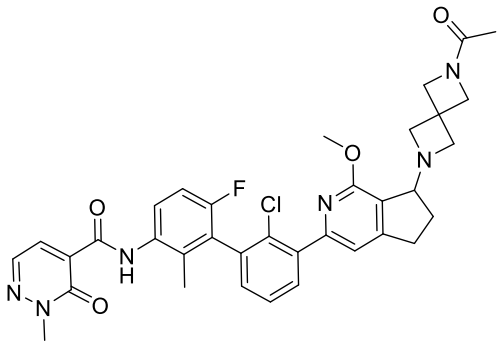
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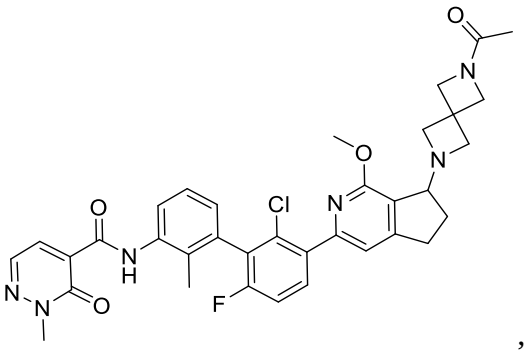
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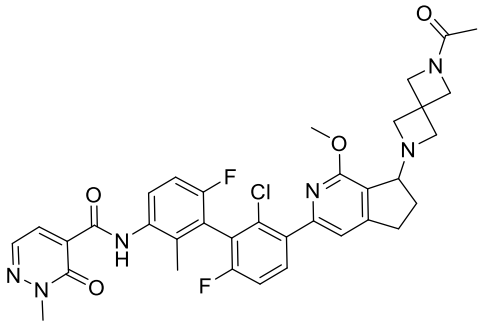
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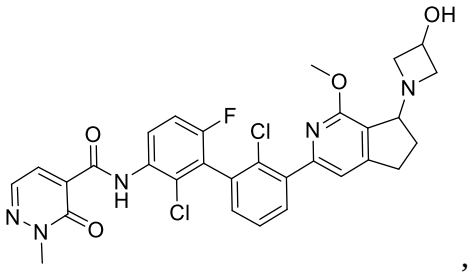
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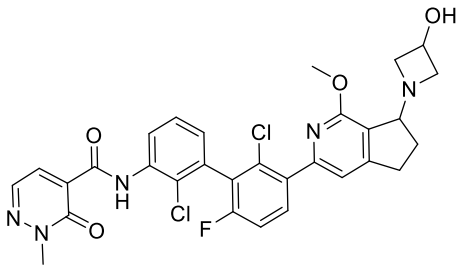
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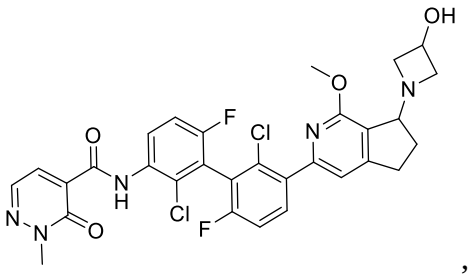
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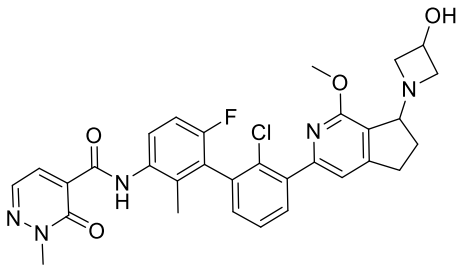
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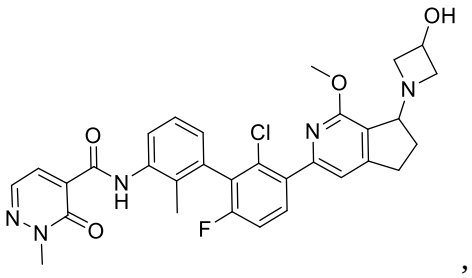
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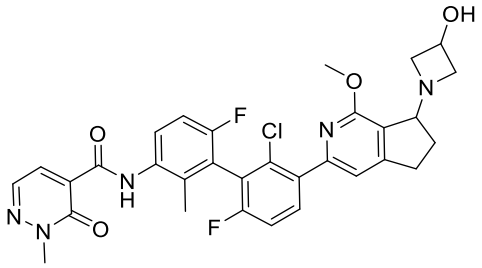
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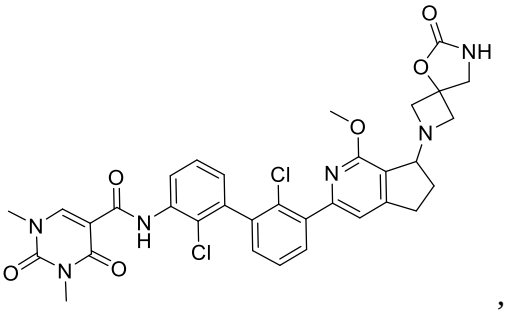
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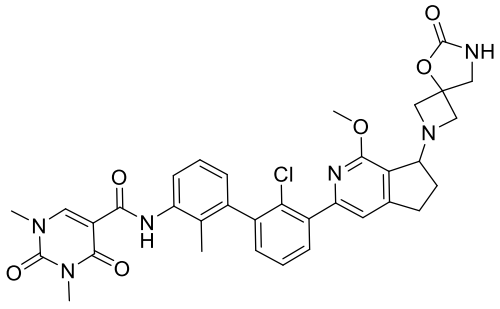
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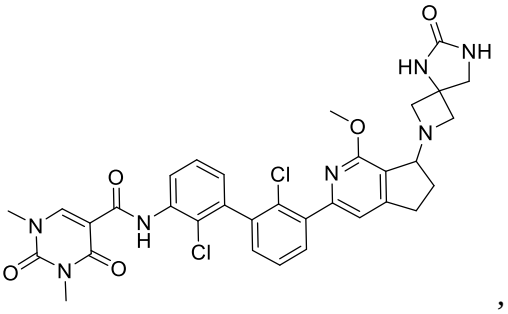
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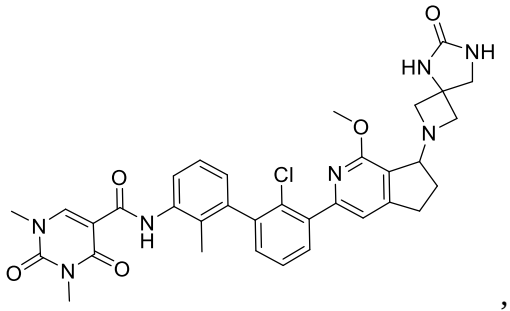
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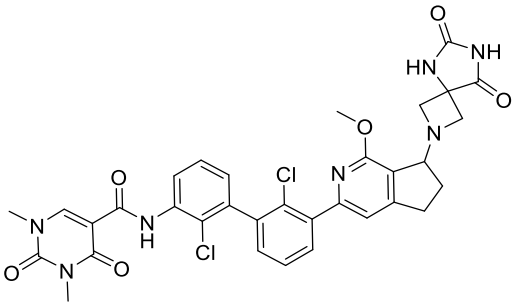
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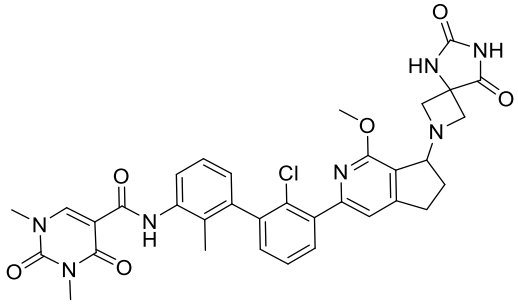
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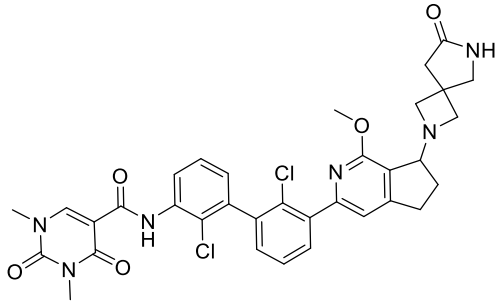
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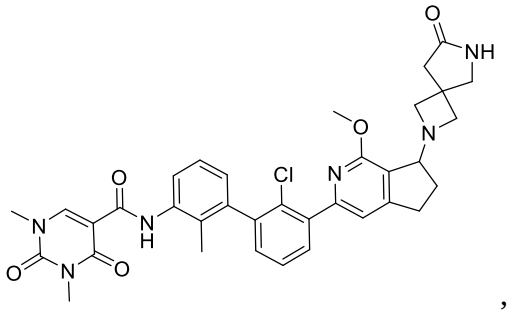
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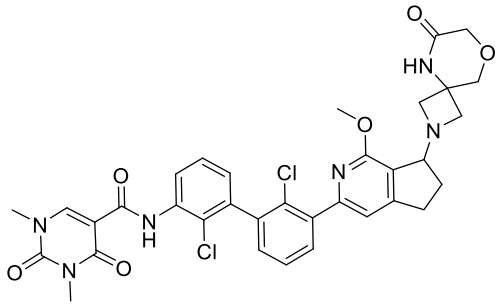
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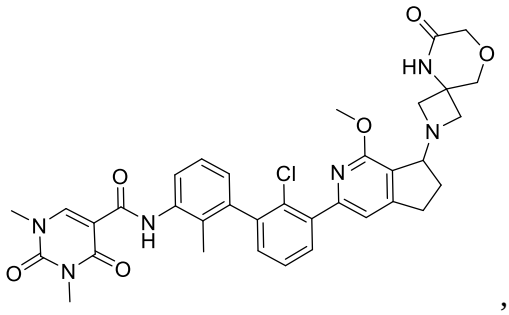
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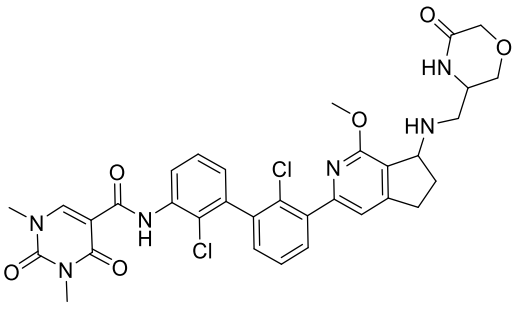
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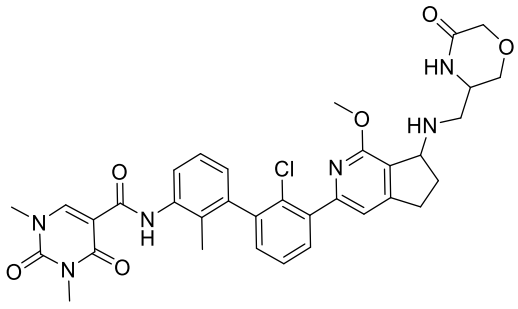
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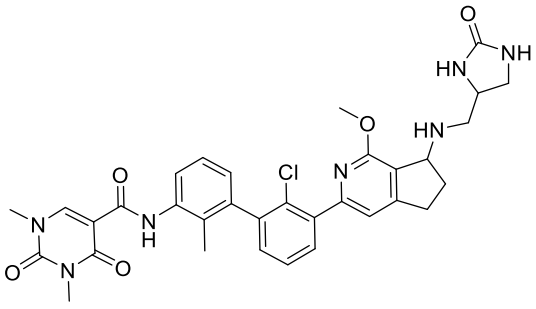
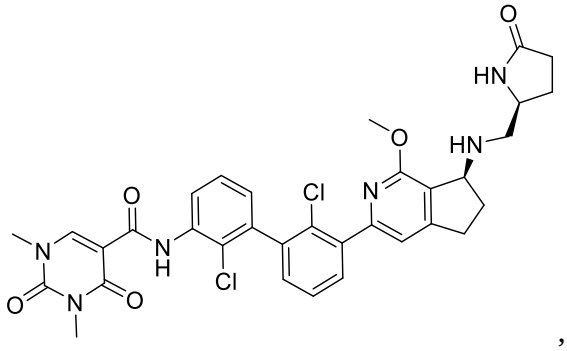

, or a pharmaceutically acceptable salt of any of the foregoing.

144. The compound of Claim 1 selected from the group consisting of: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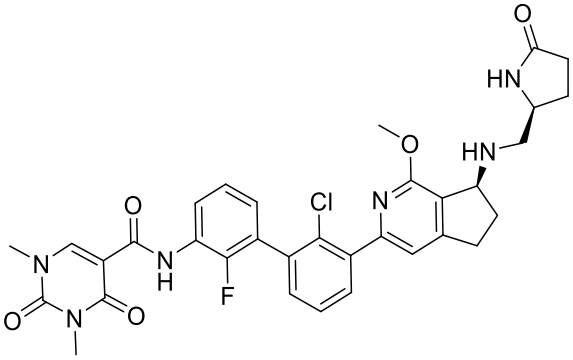
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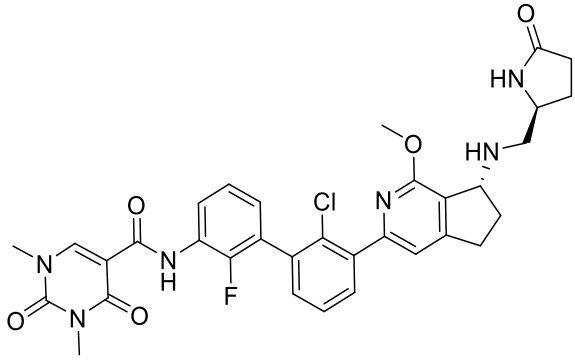
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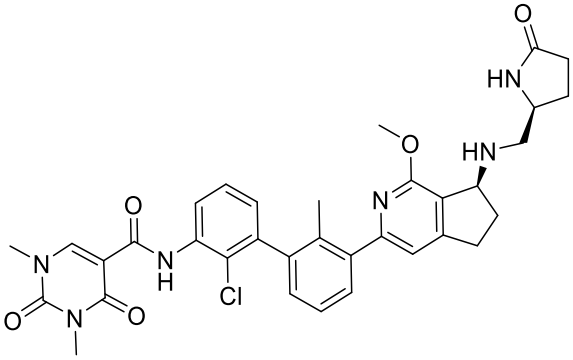
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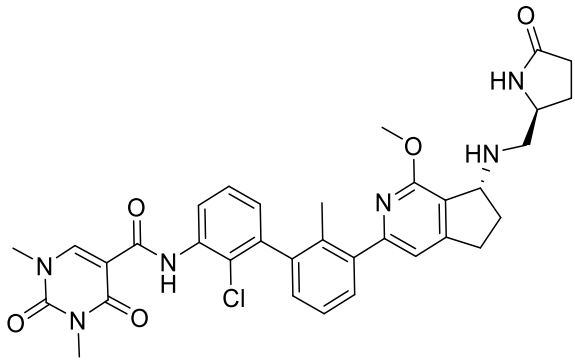
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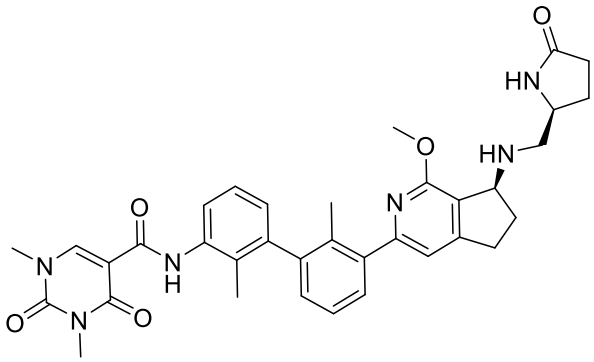
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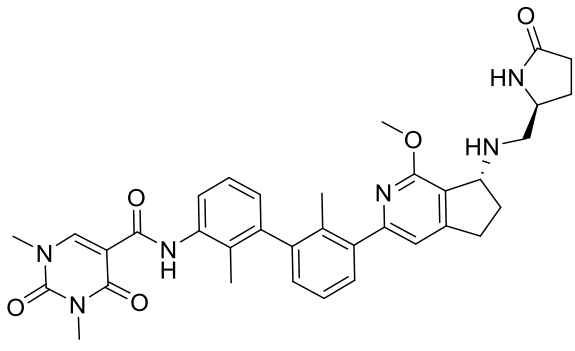
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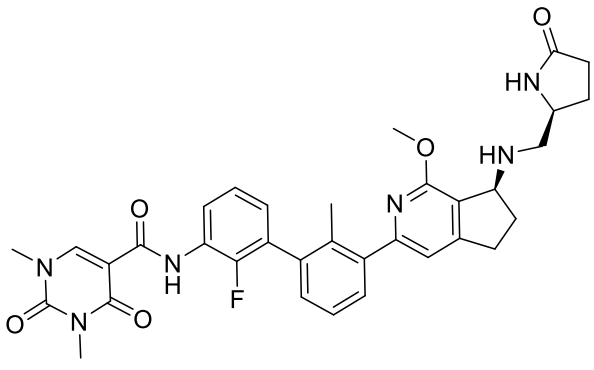
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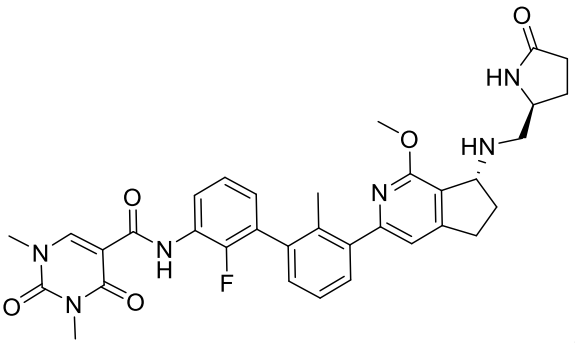
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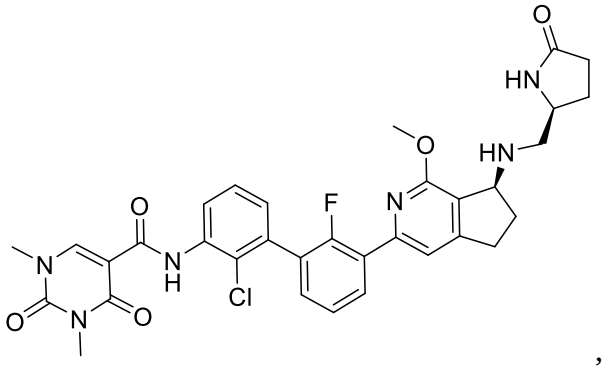
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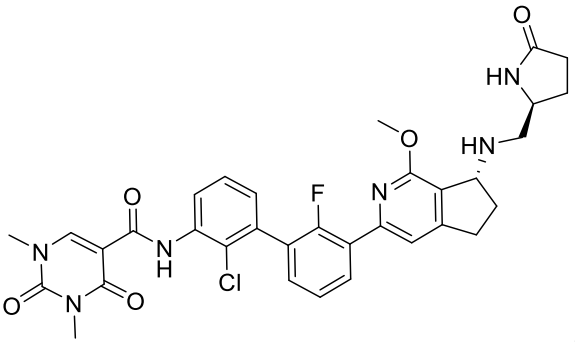
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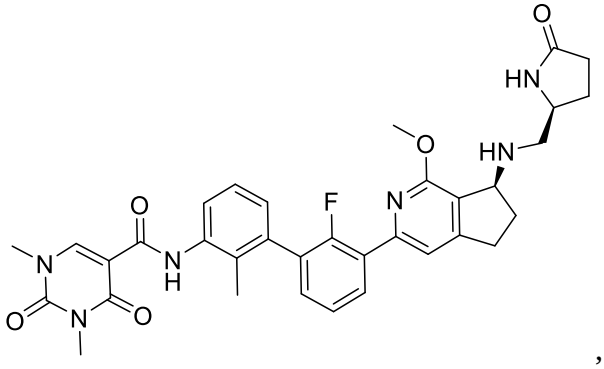
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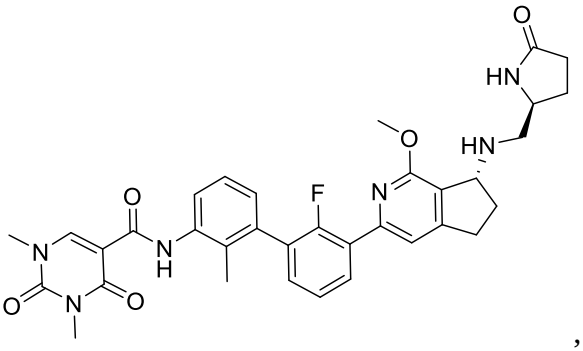
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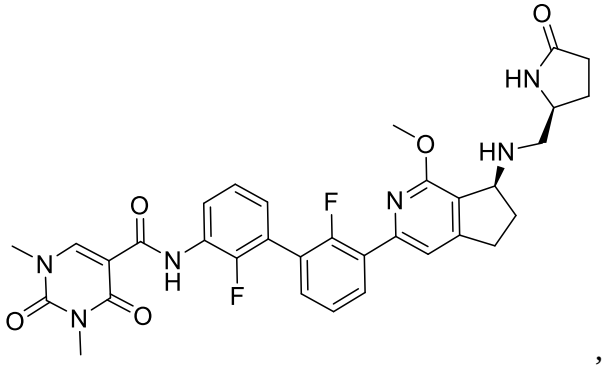
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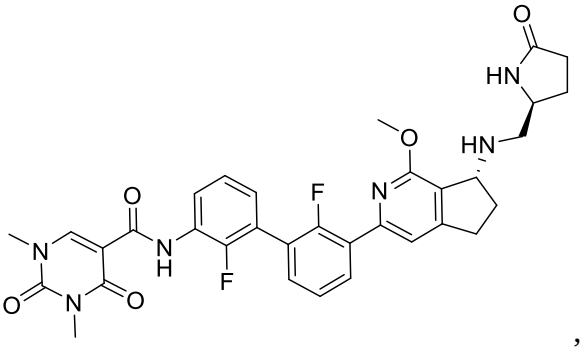
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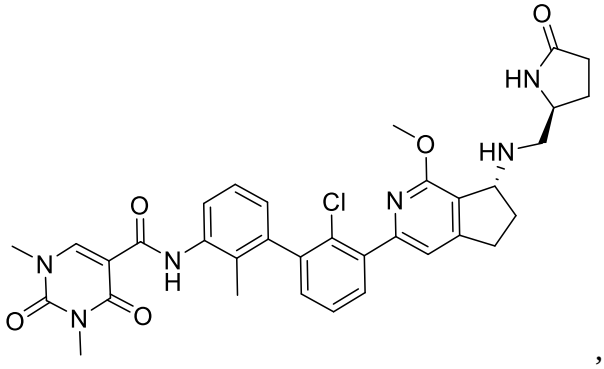
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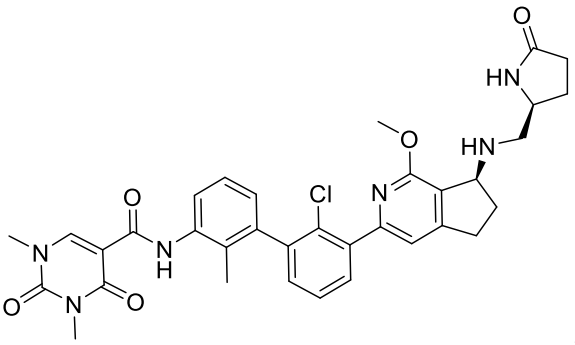
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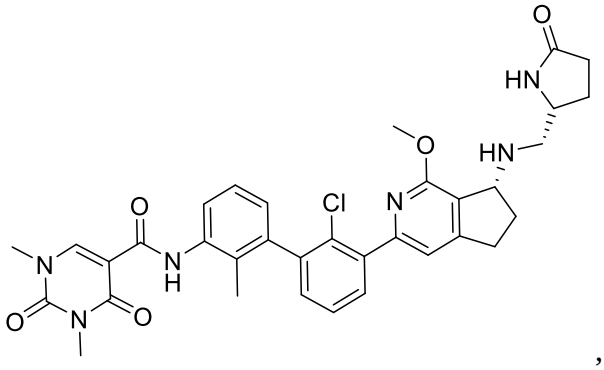
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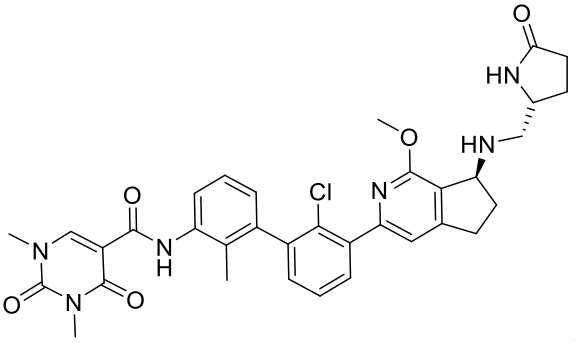
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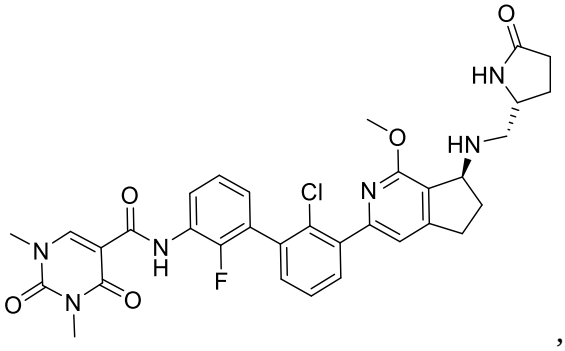
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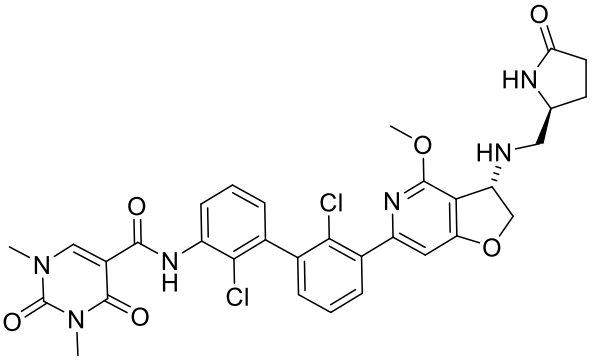
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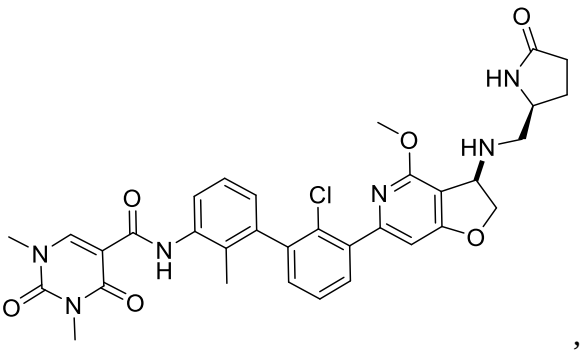
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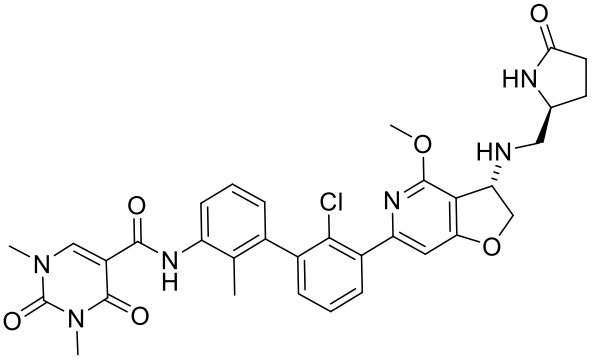
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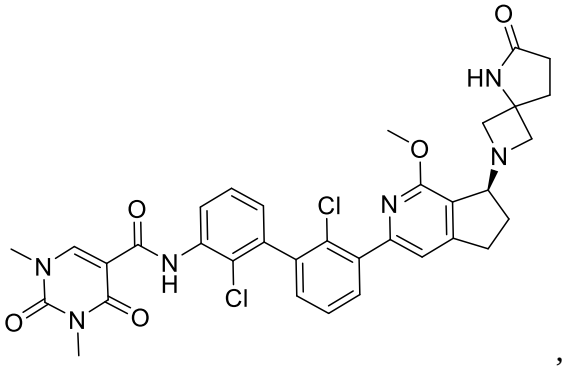
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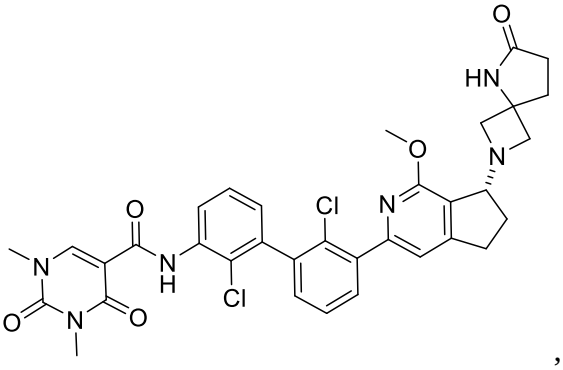
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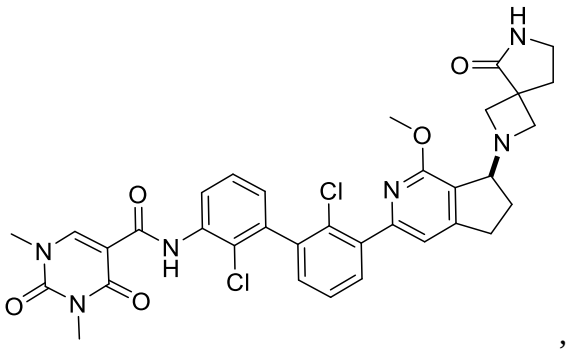
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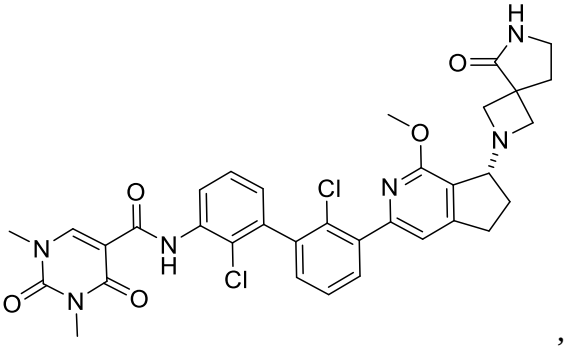
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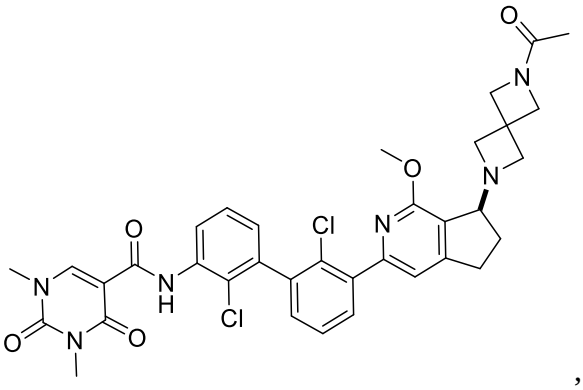
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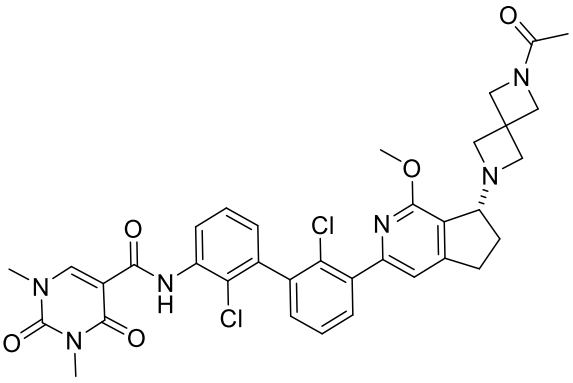
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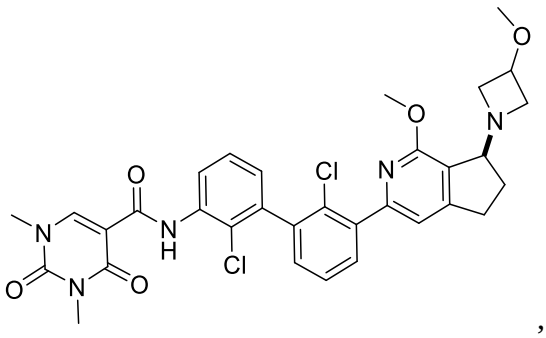
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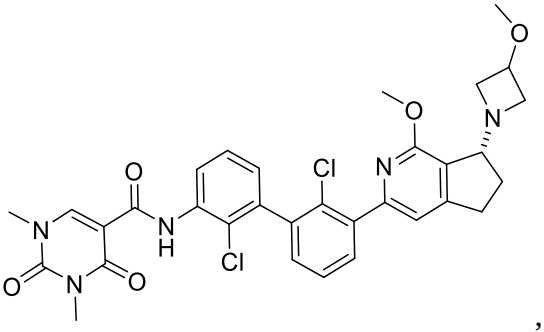
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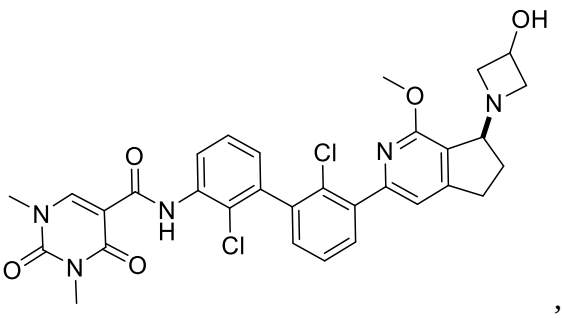
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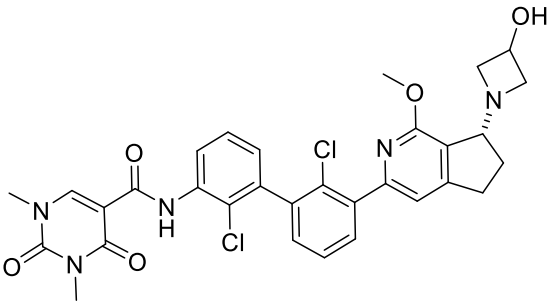
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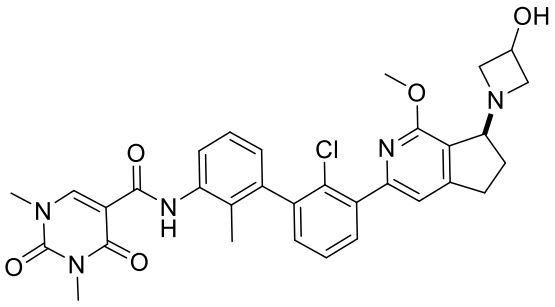
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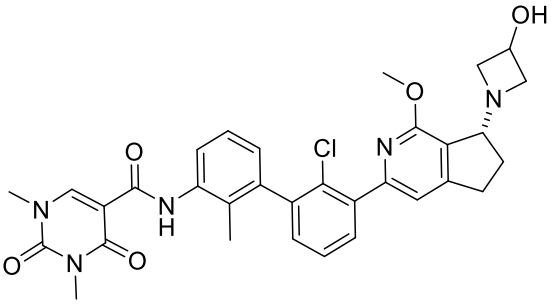
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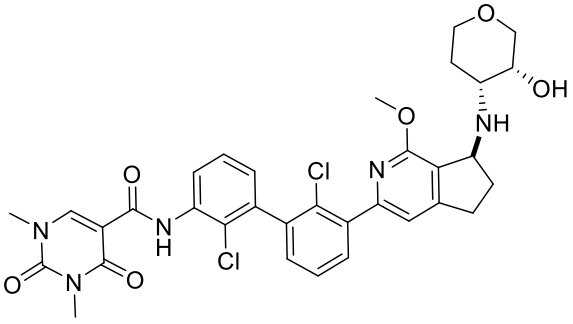
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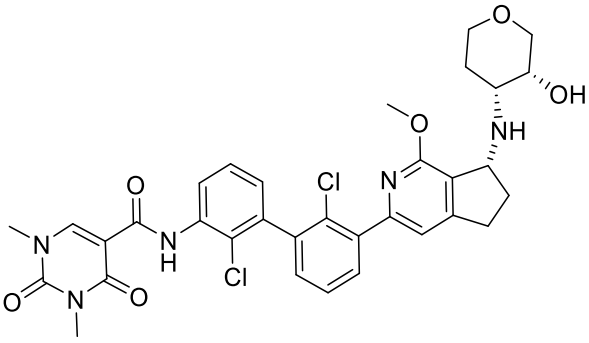
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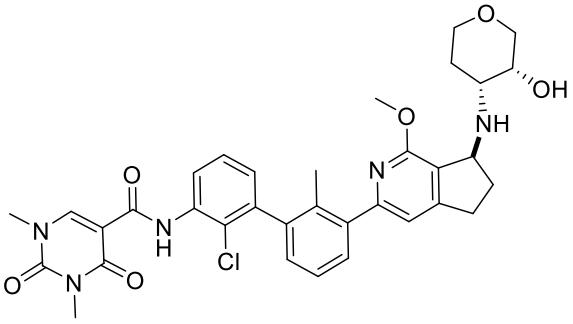
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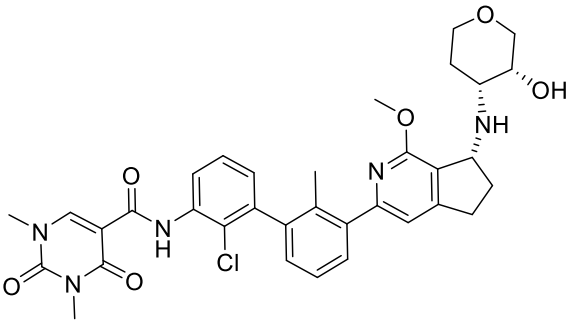
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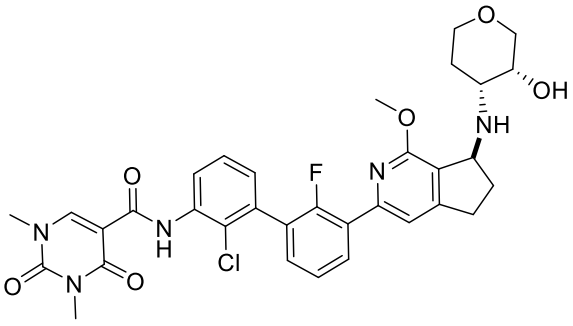
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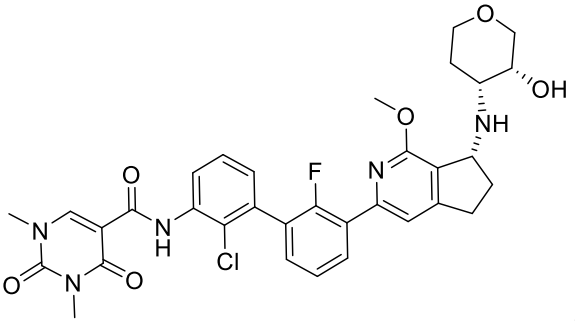
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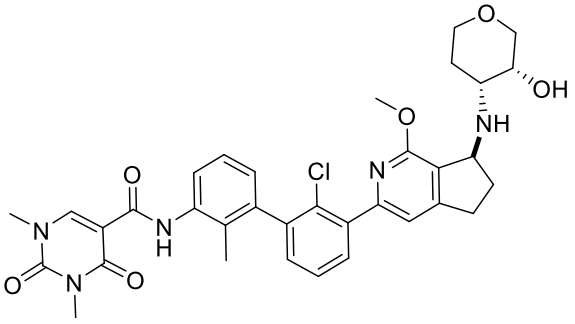
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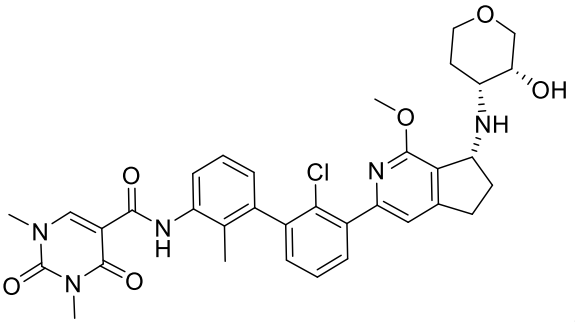
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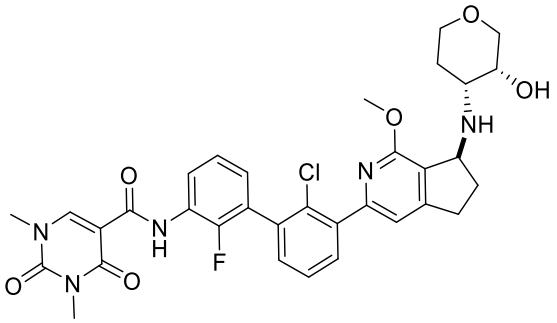
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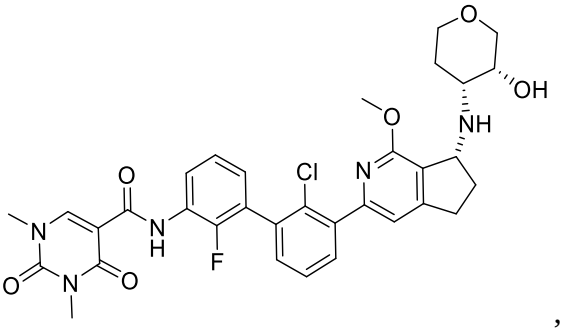
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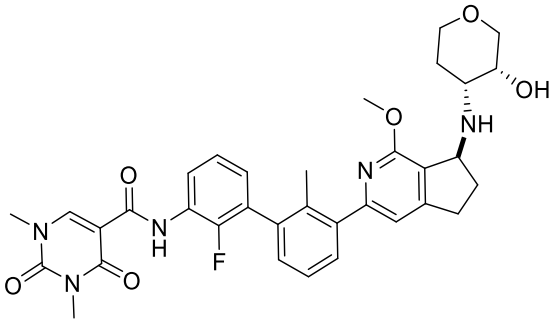
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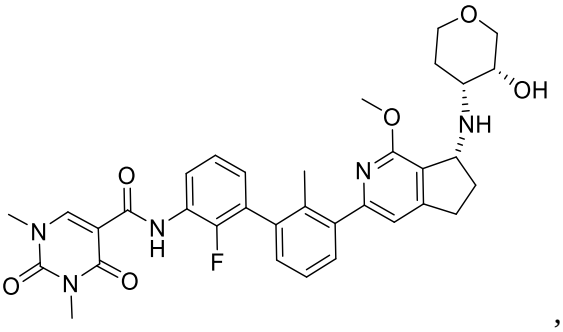
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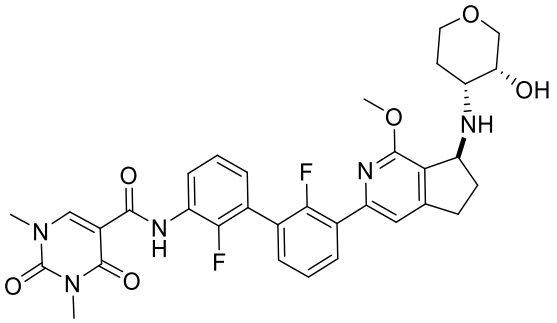
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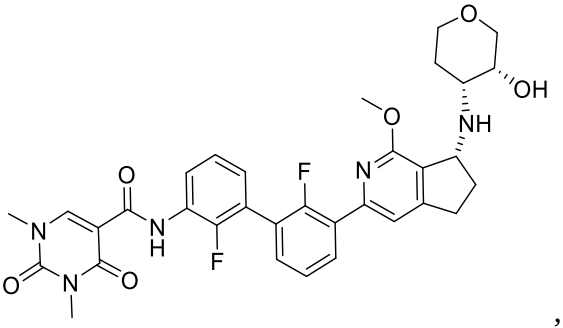
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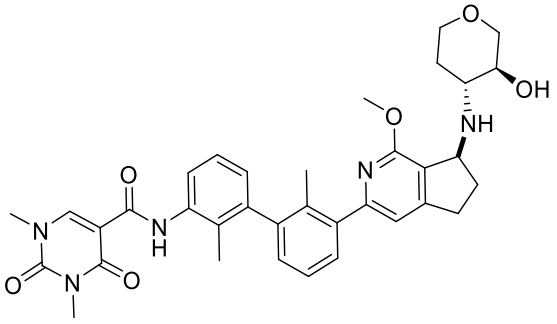
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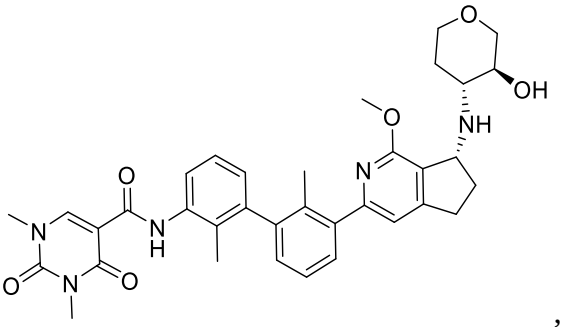
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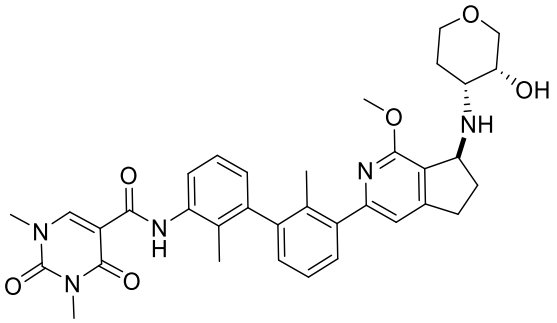
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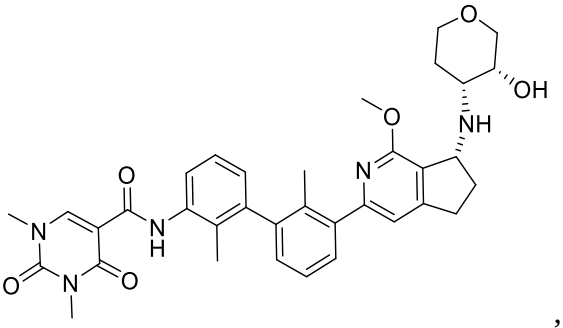
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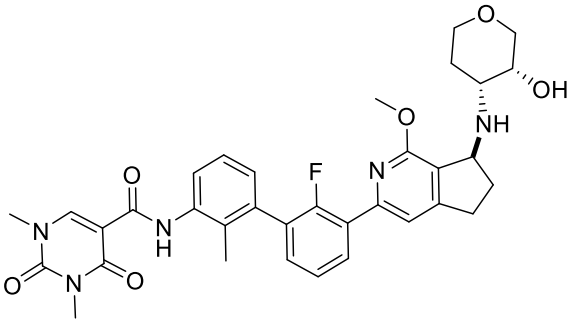
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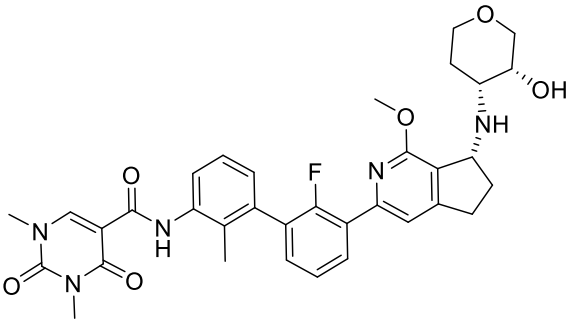
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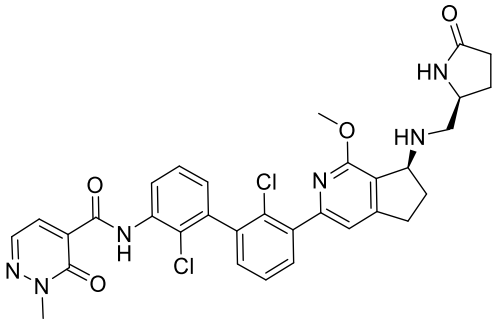
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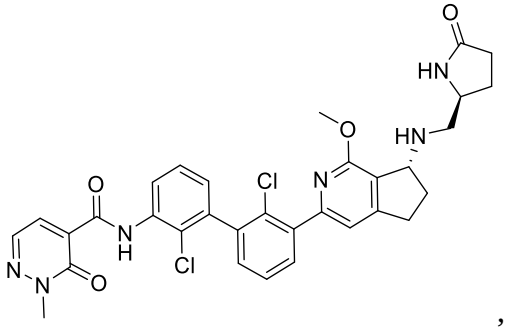
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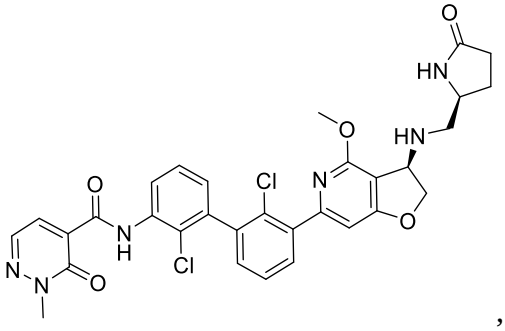
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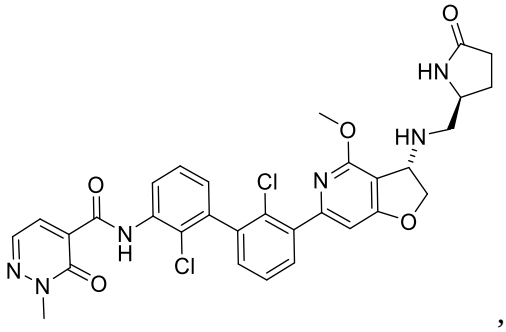
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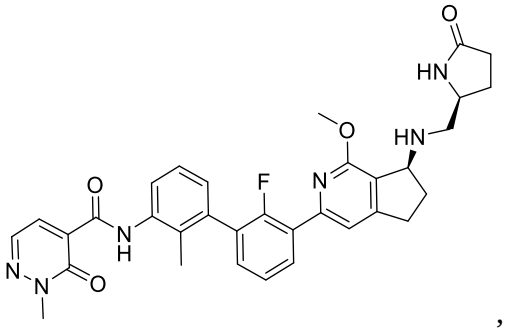
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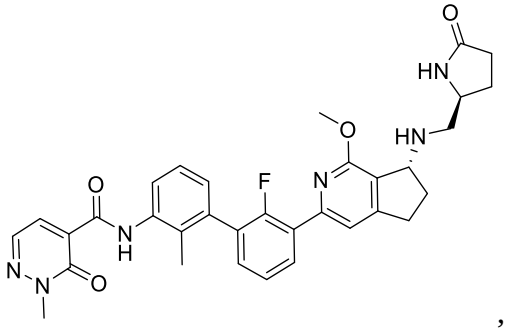
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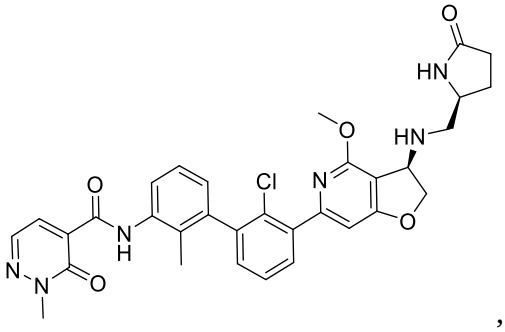
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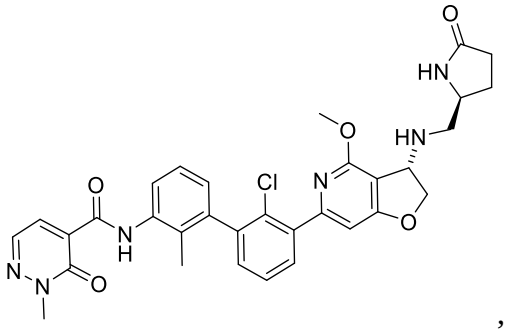
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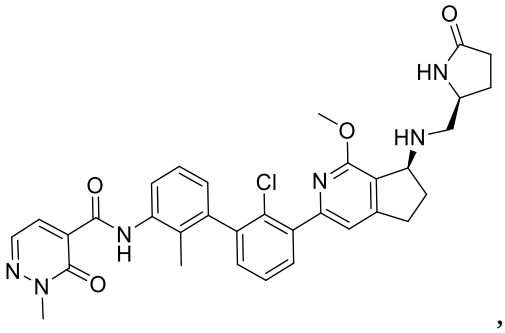
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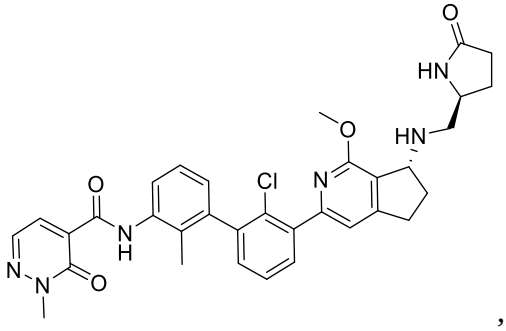
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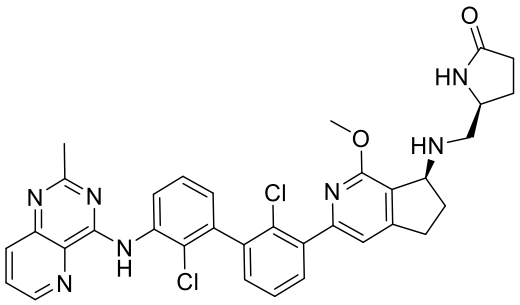
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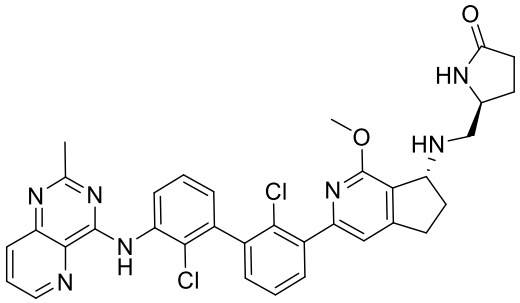
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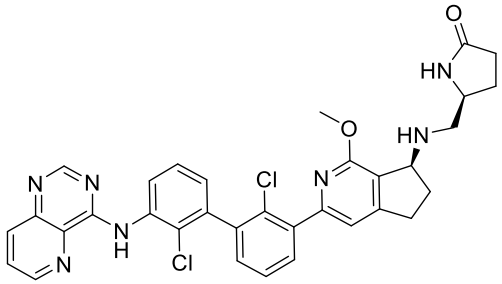
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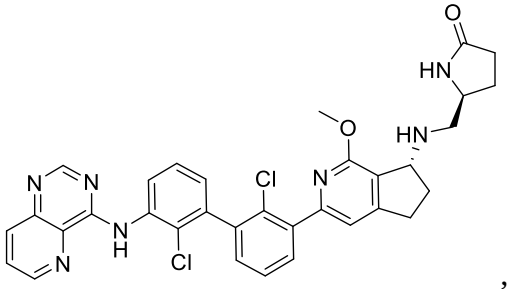
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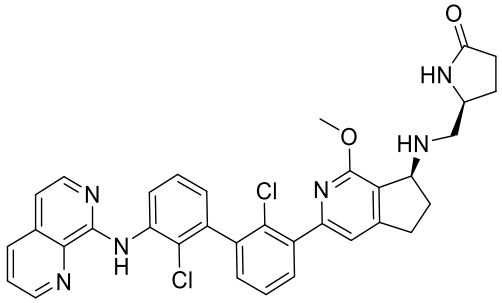
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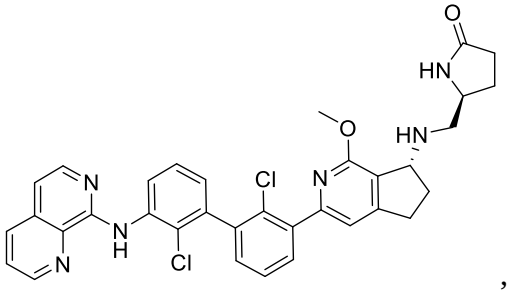
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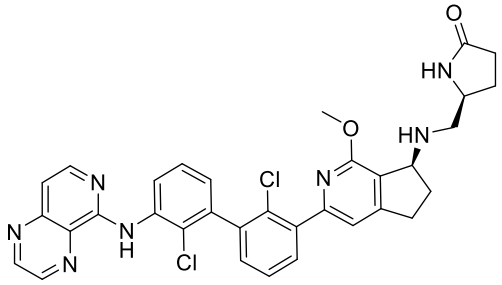
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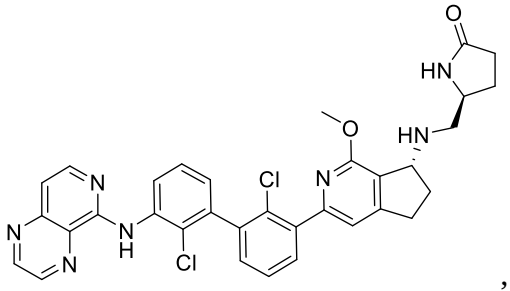
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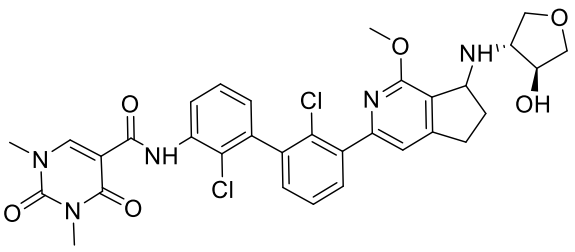
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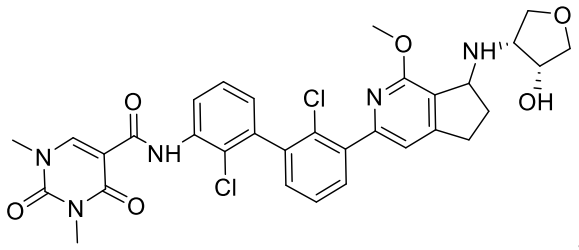
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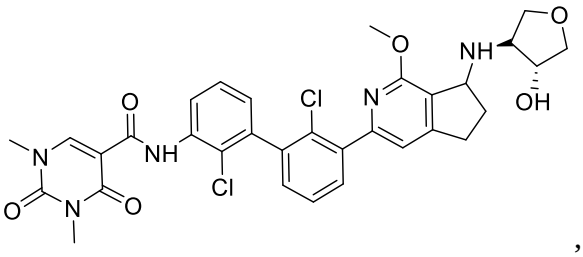
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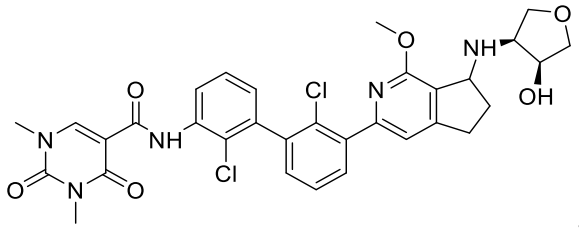
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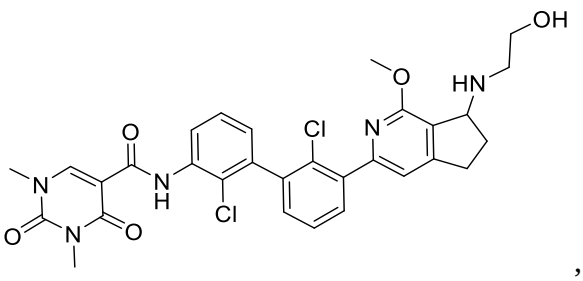
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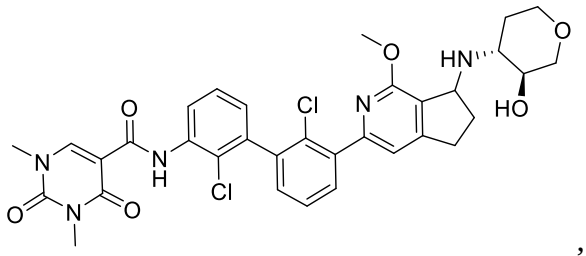
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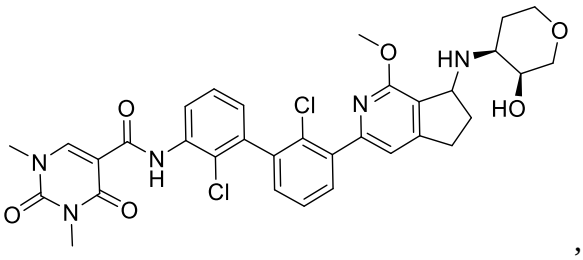
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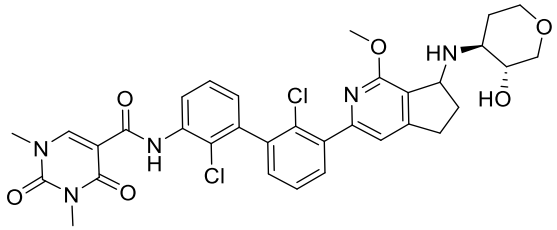
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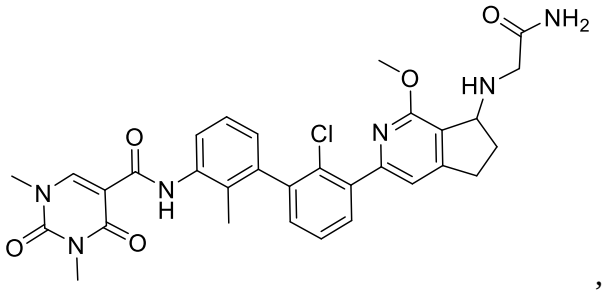
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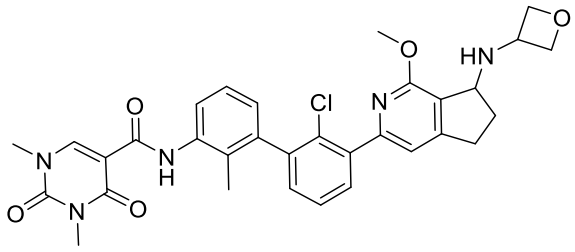
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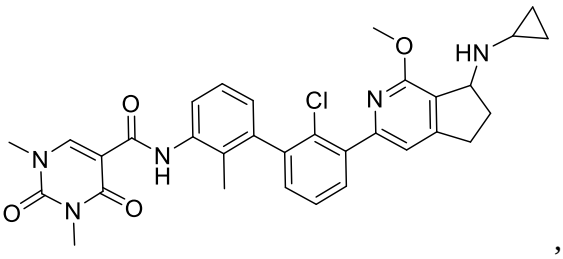
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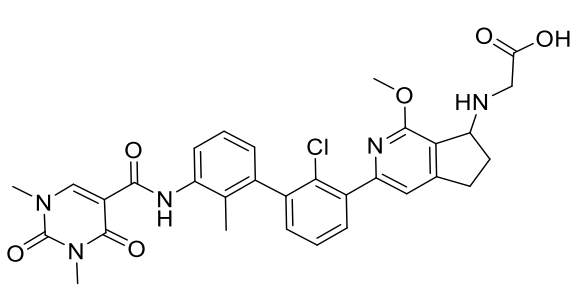
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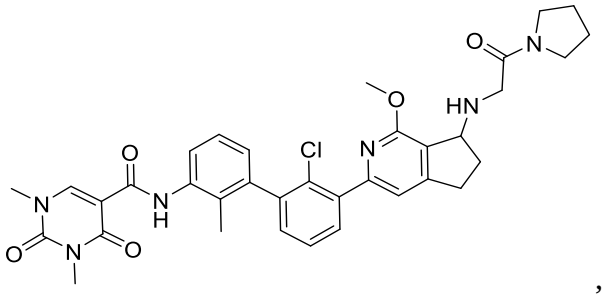
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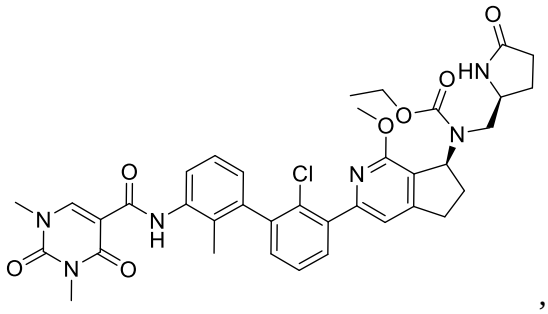
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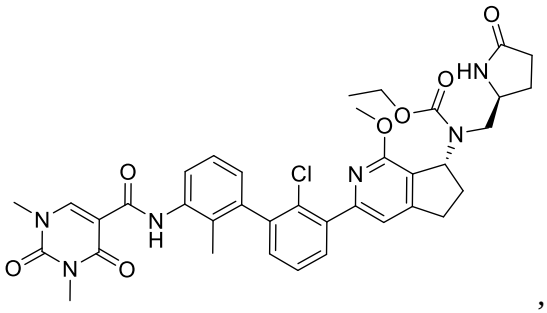
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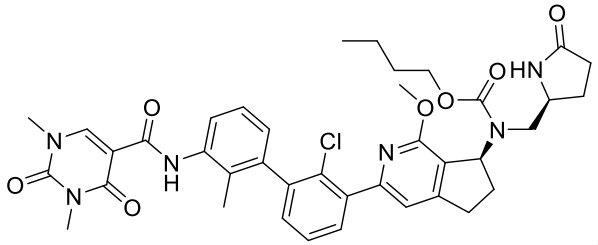
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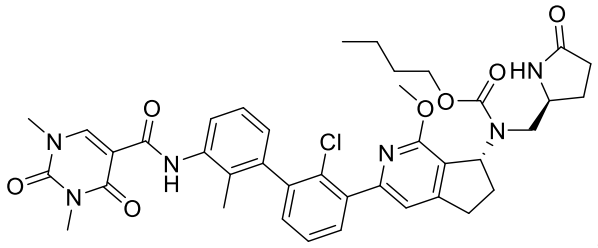
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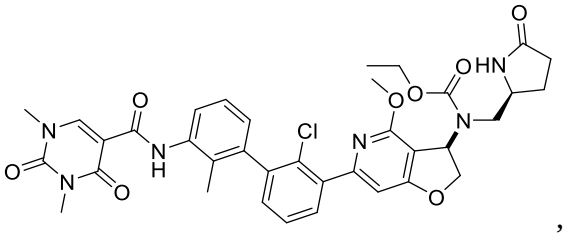
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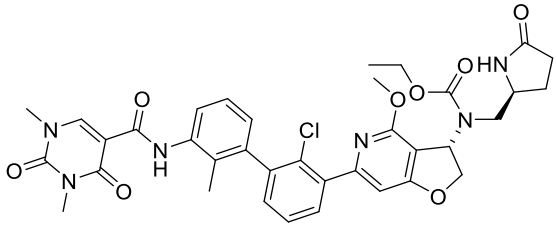
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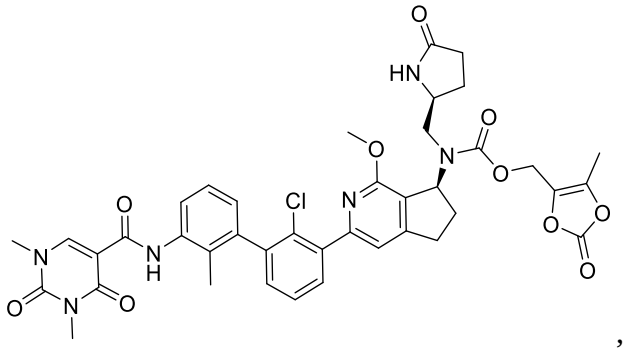
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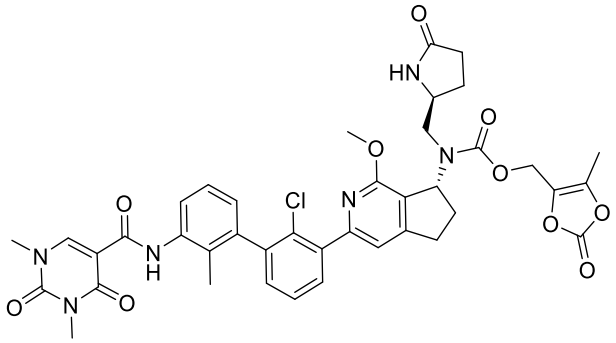
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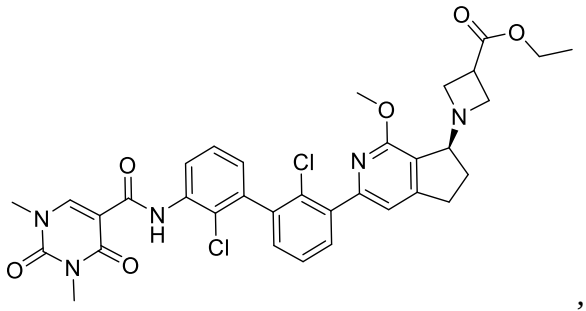
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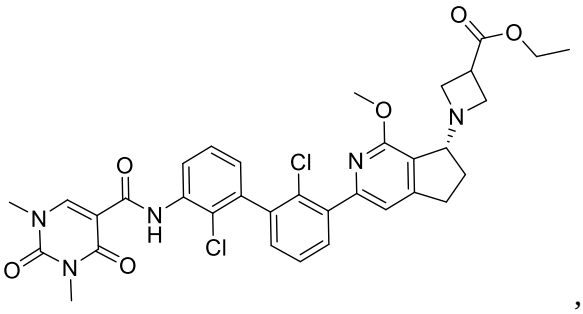
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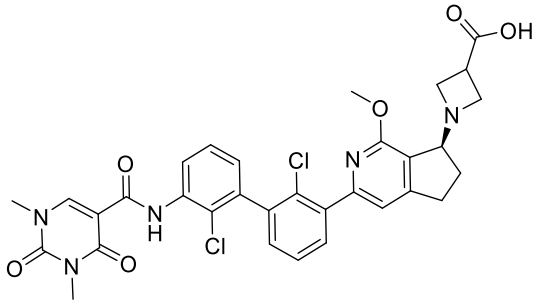
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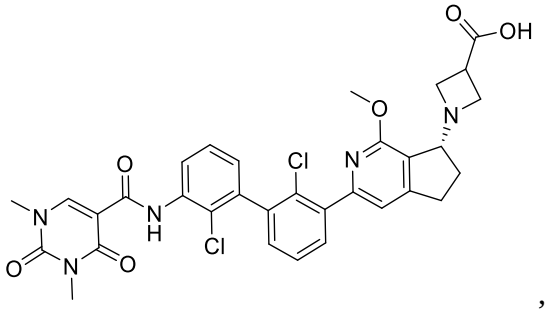
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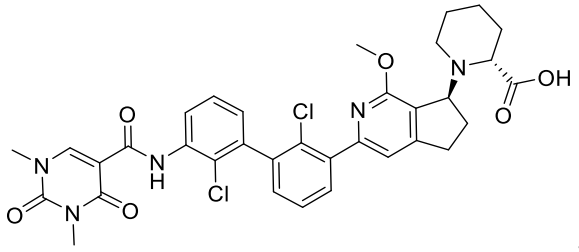
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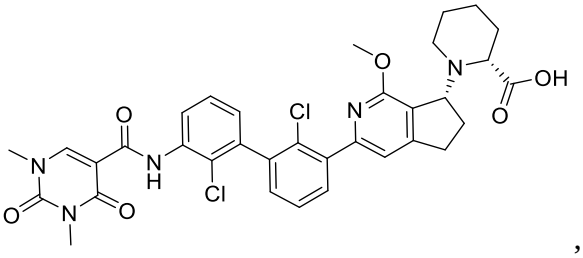
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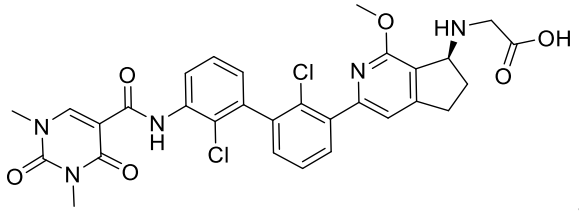
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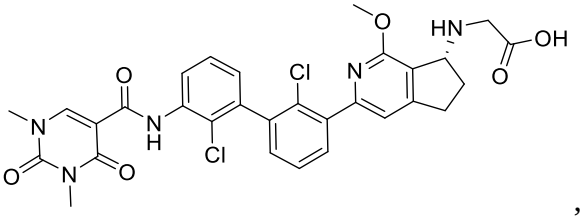
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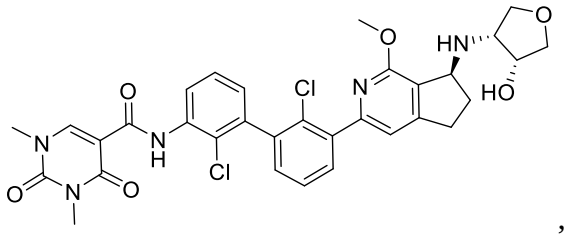
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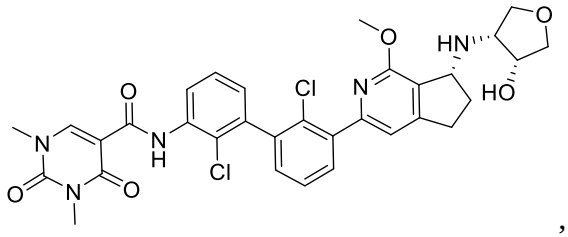
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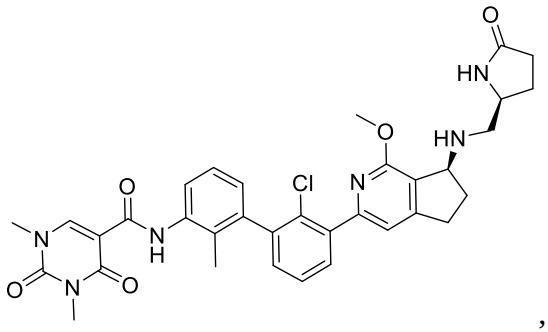
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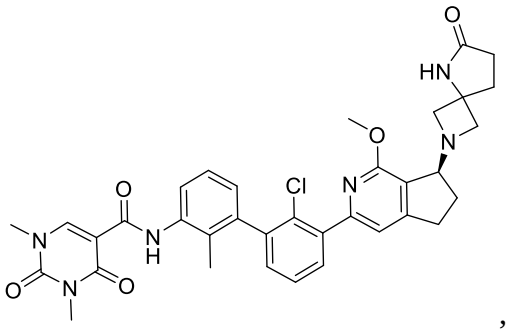
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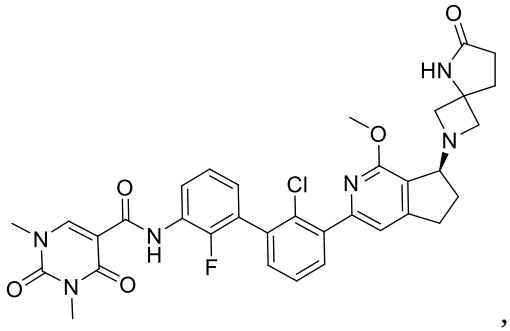
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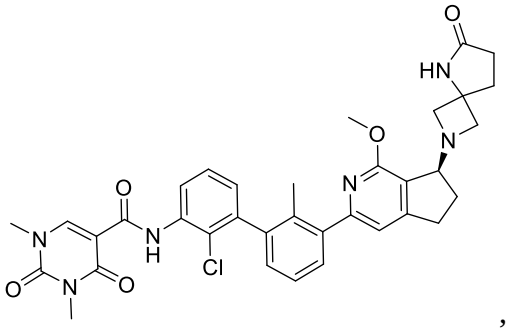
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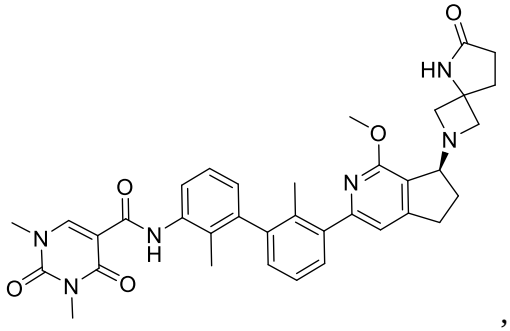
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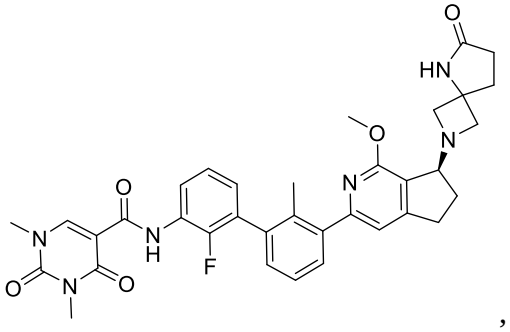
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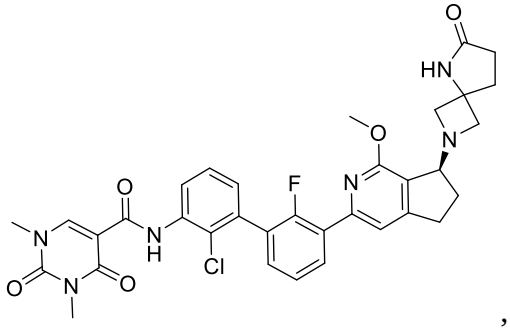
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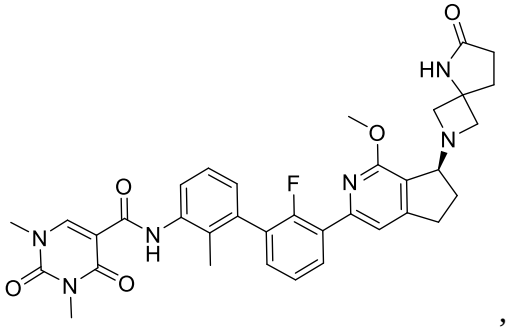
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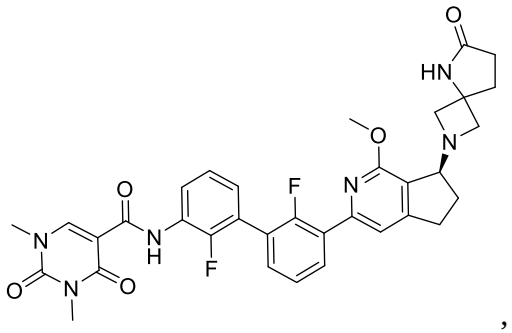
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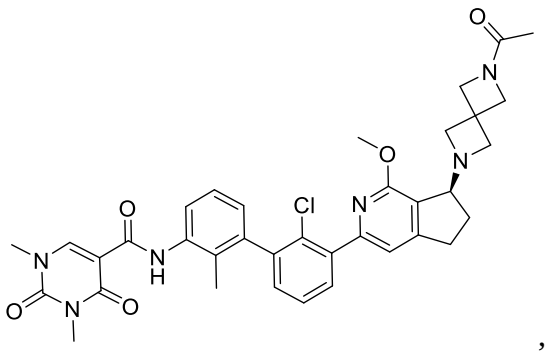
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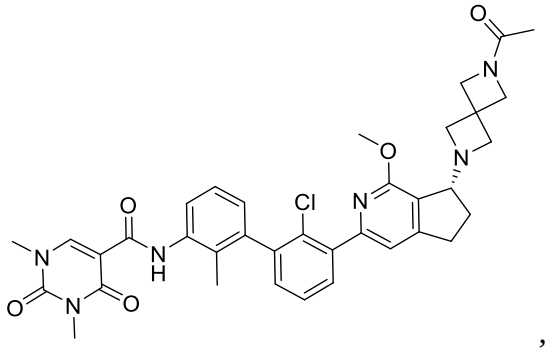
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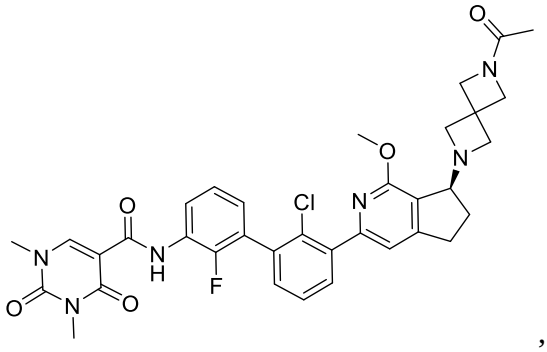
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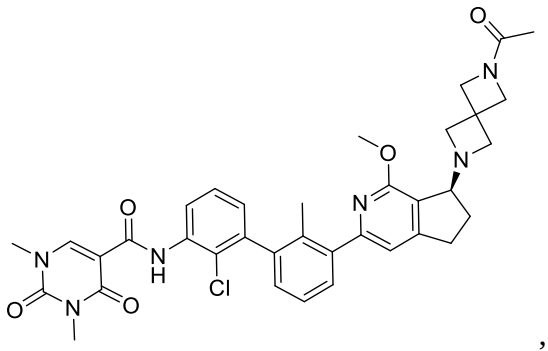
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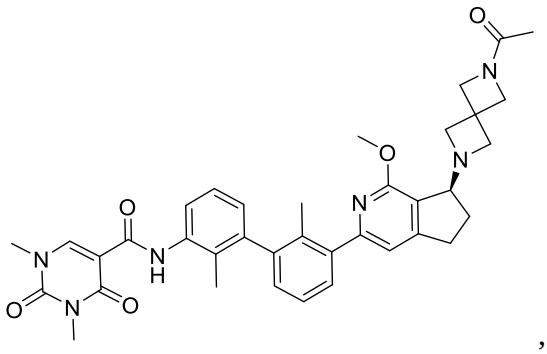
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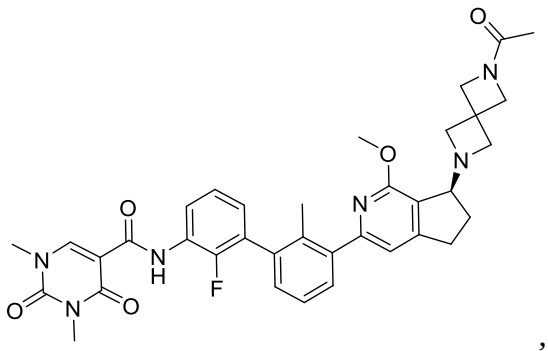
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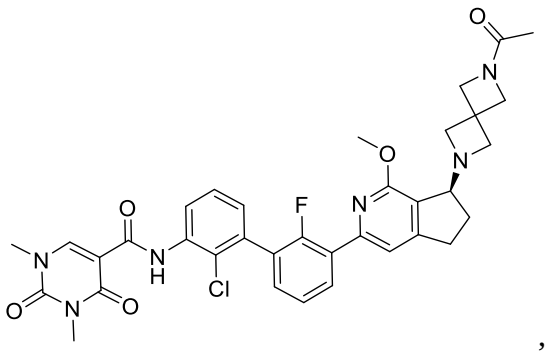
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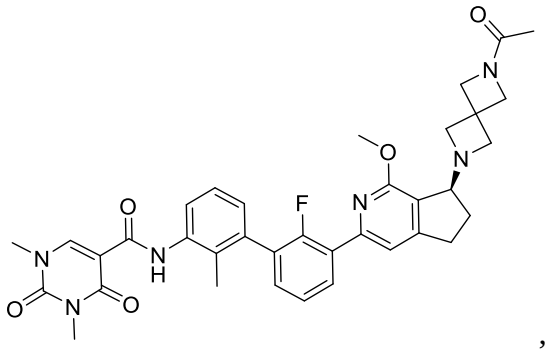
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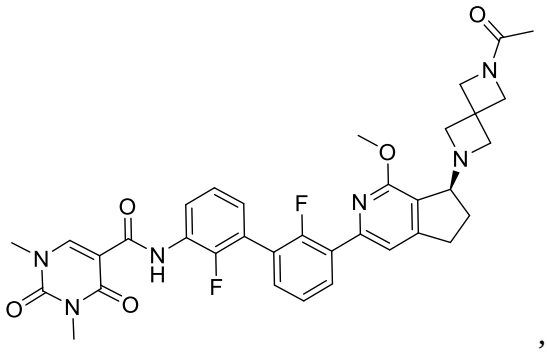
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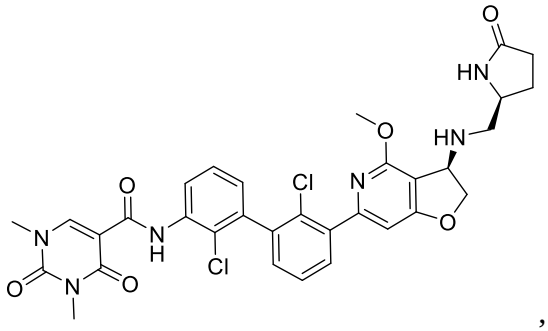
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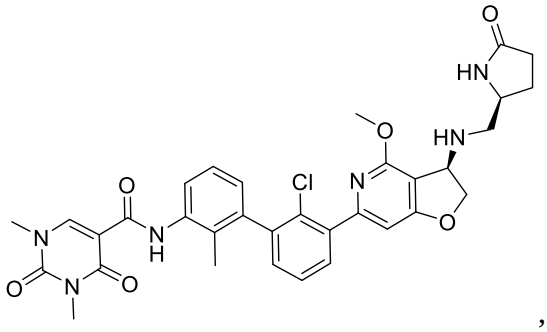
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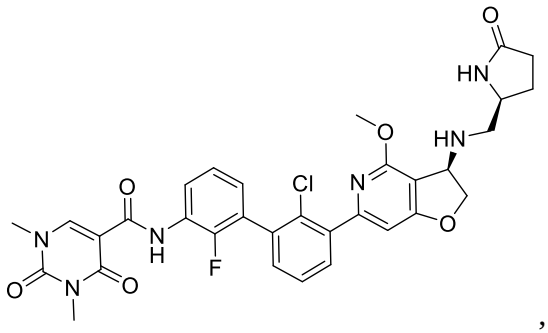
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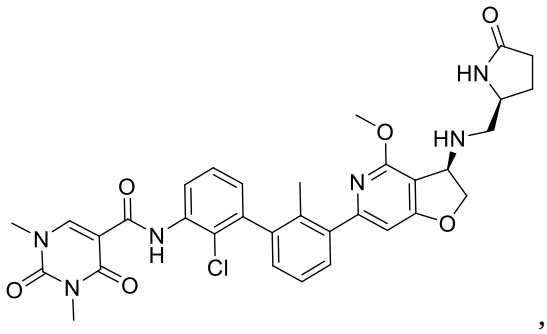
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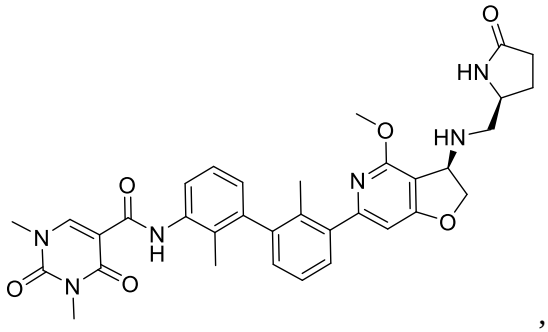
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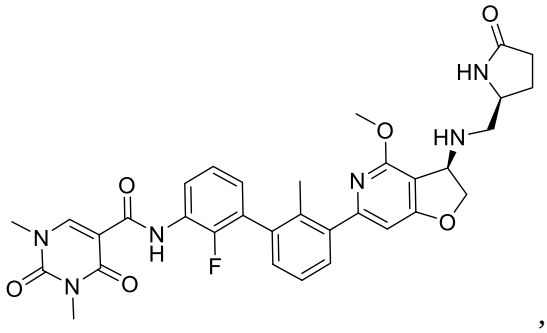
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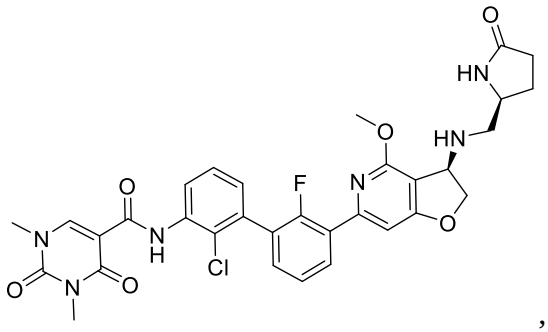
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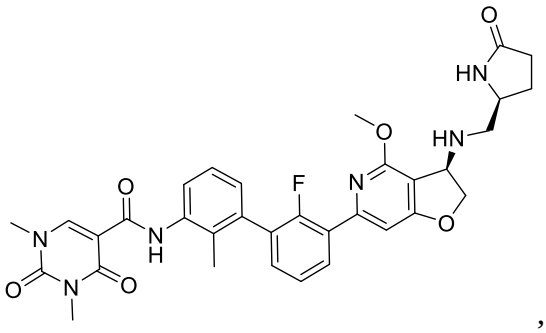
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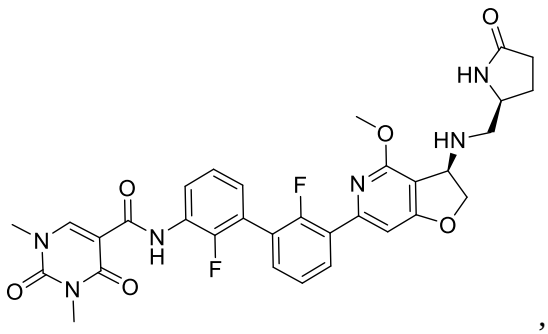
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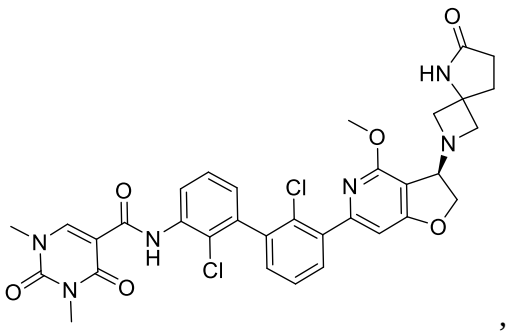
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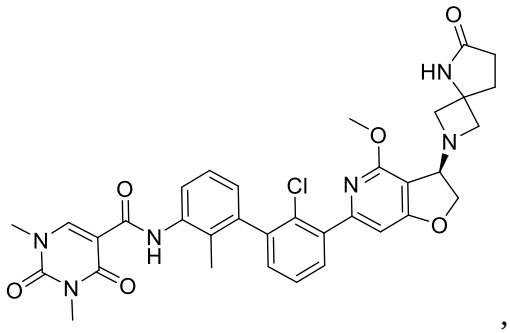
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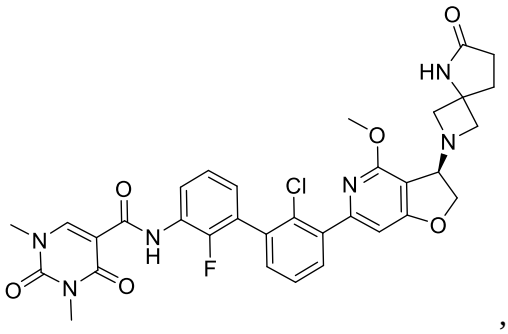
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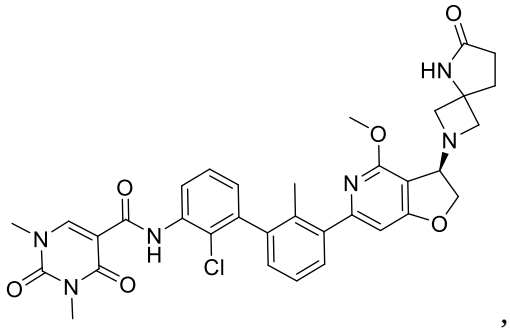
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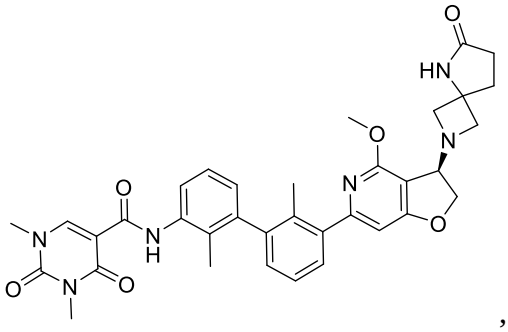
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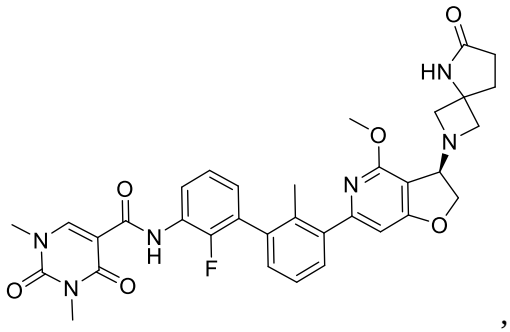
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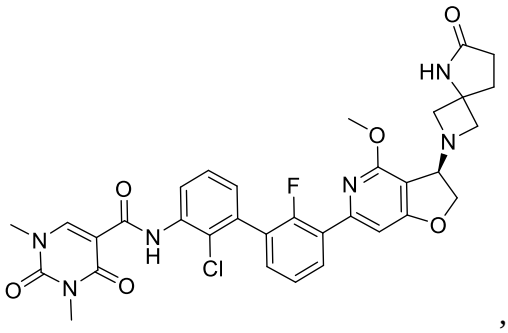
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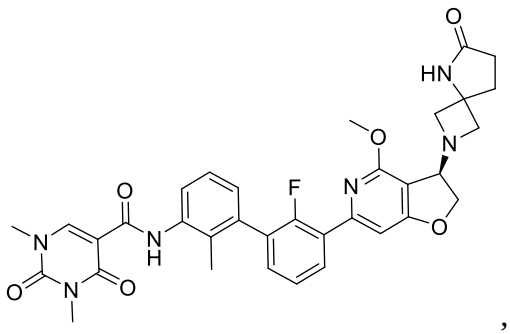
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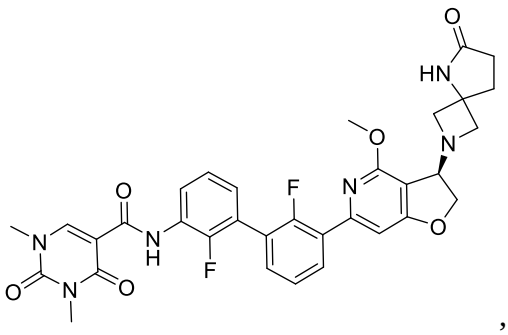
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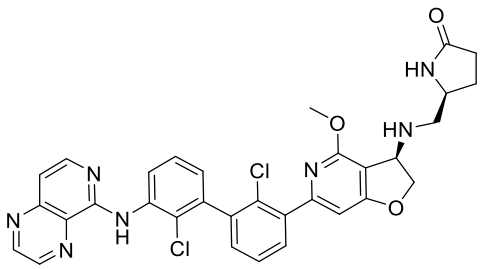
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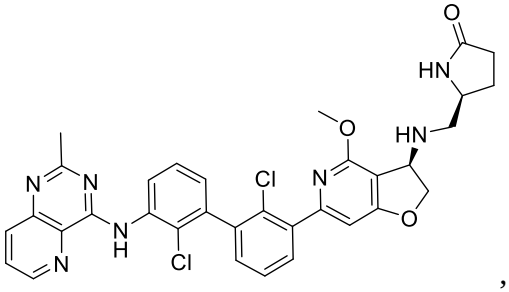
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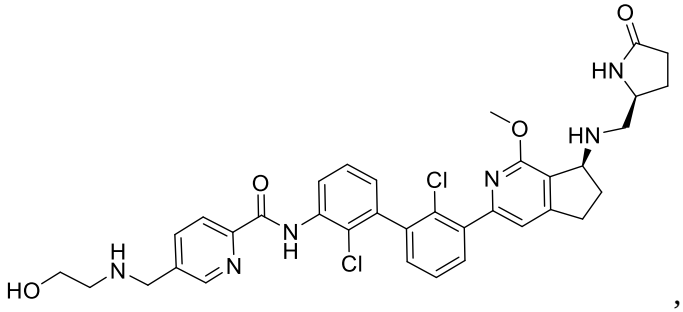
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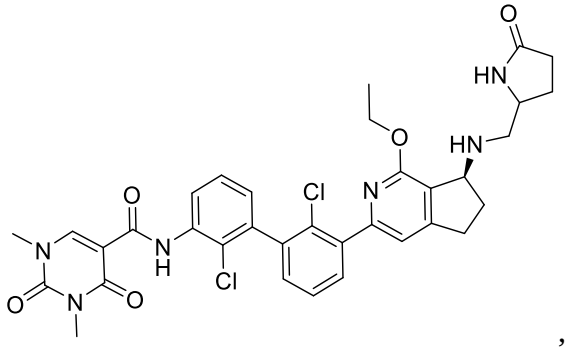
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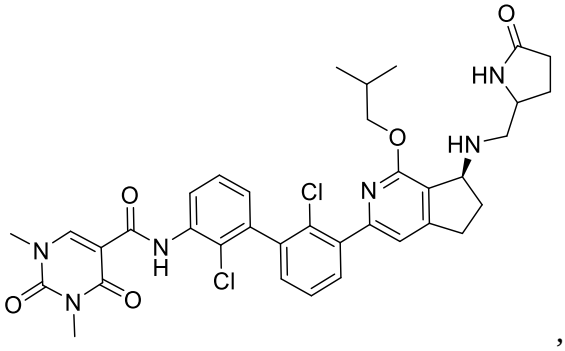
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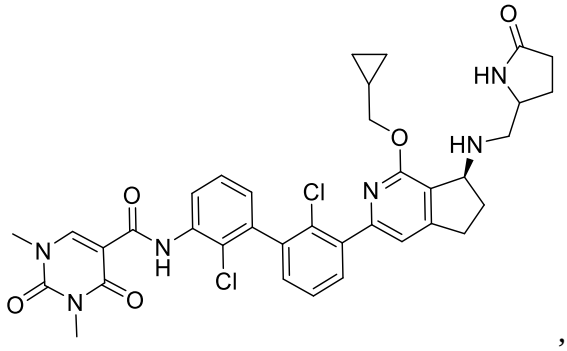
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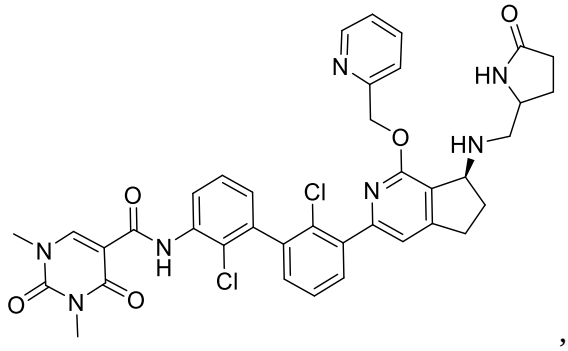
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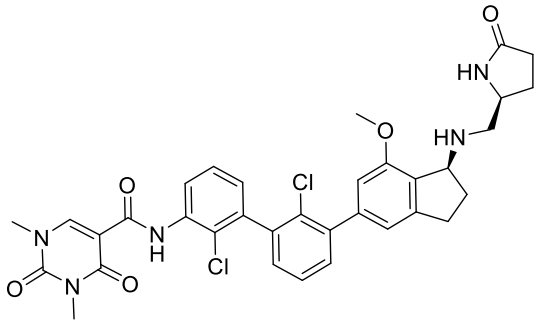
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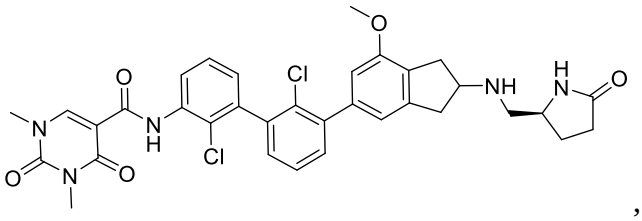
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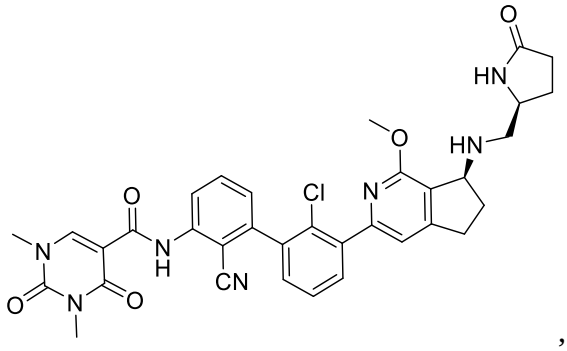
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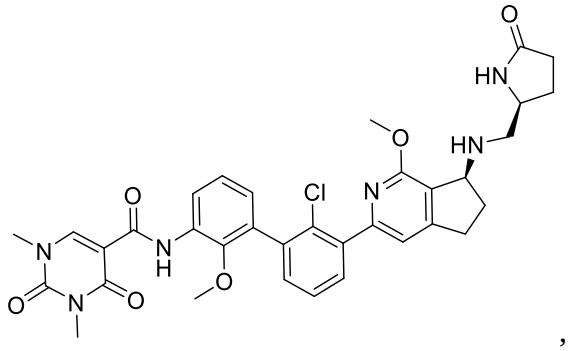
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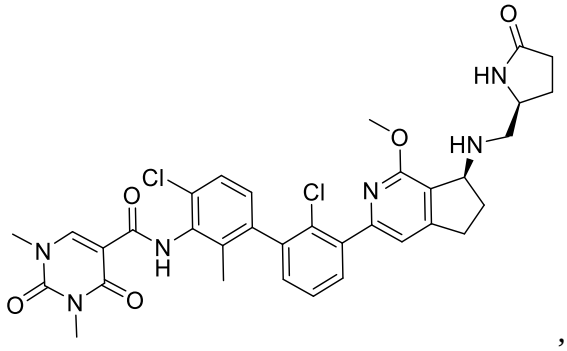
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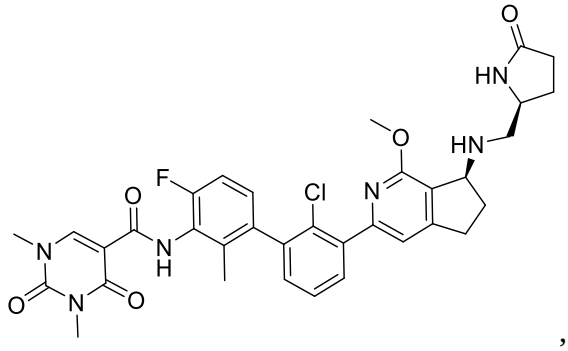
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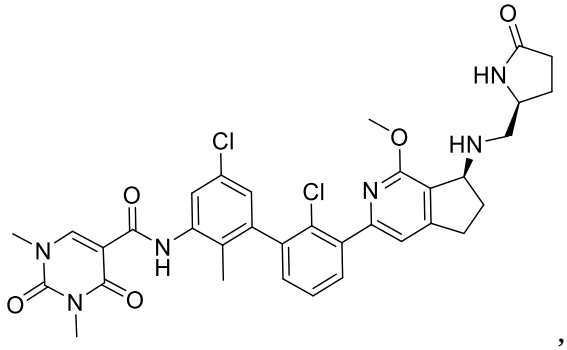
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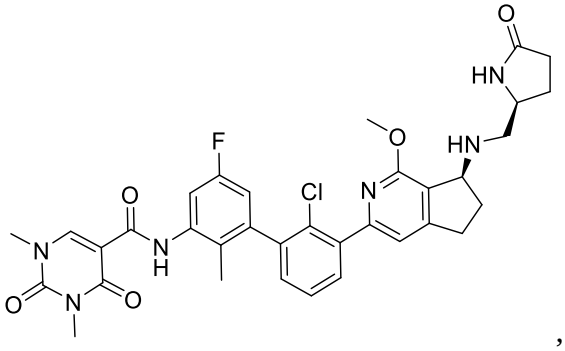
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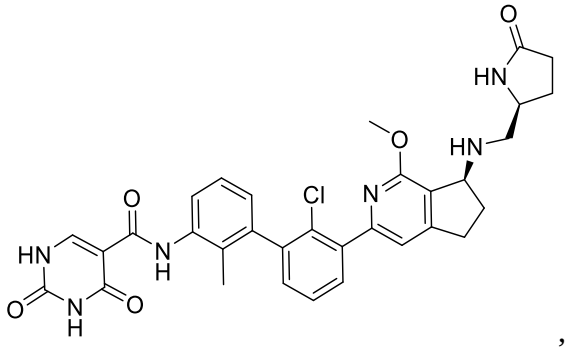
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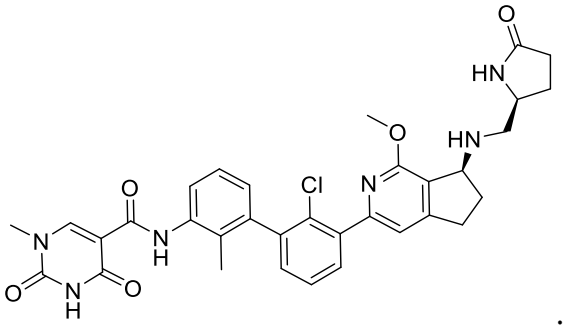
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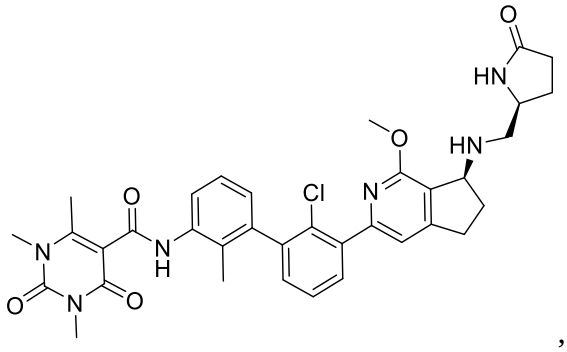
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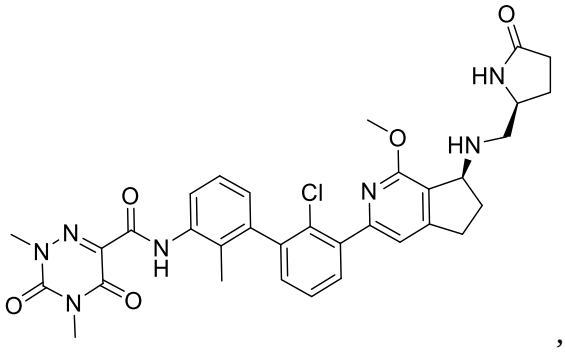
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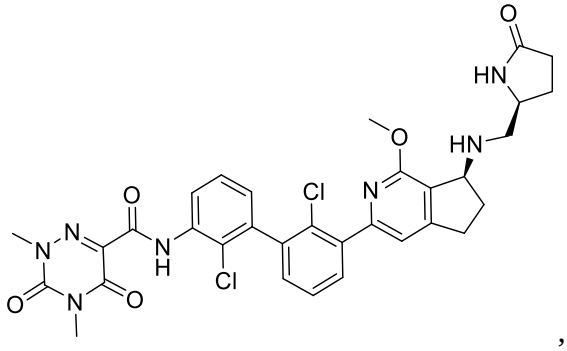
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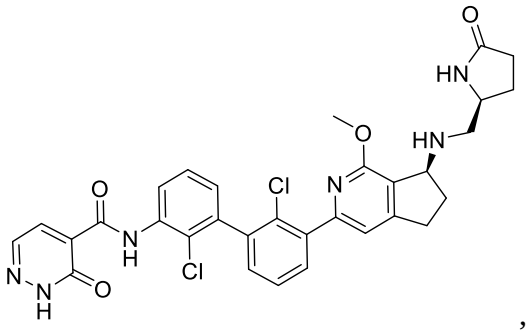
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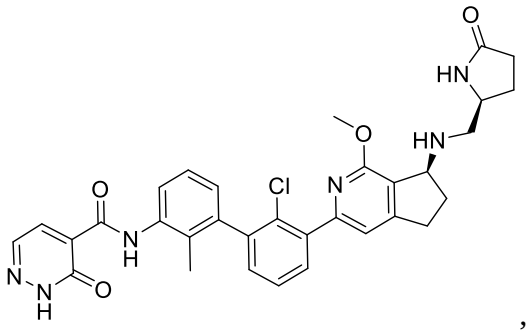
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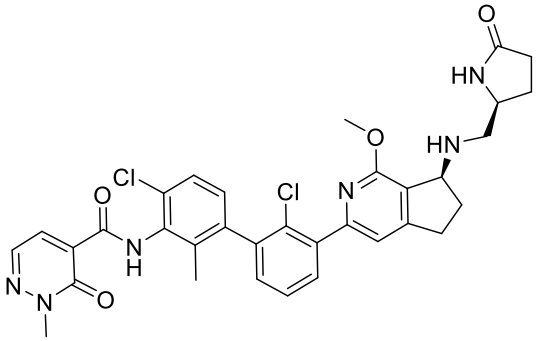
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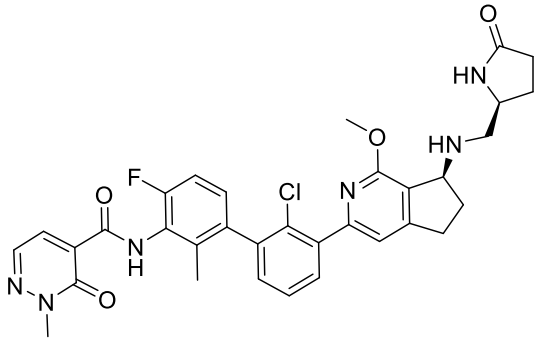
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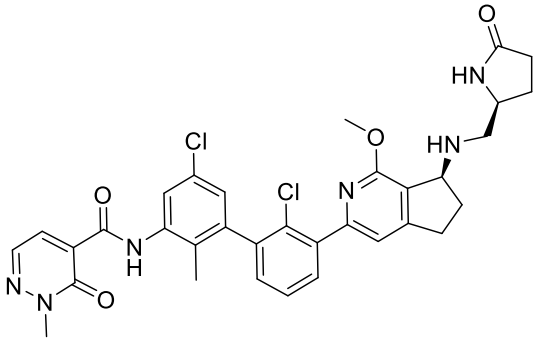
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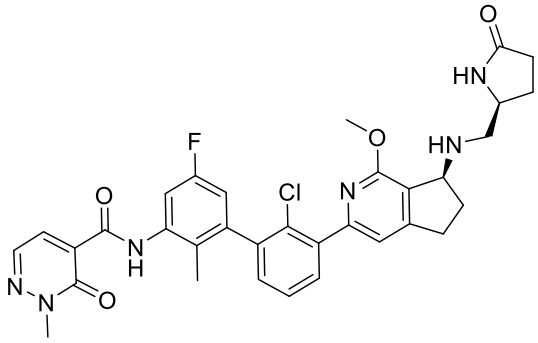
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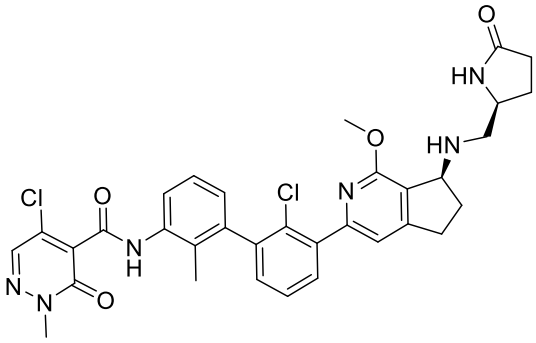
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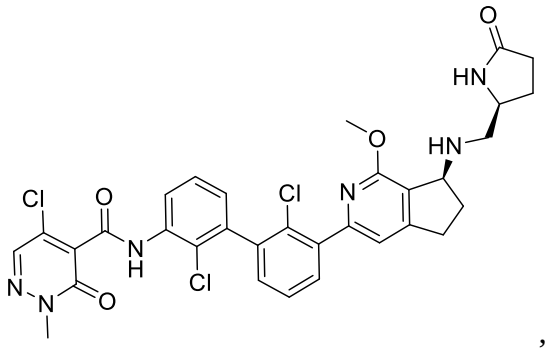
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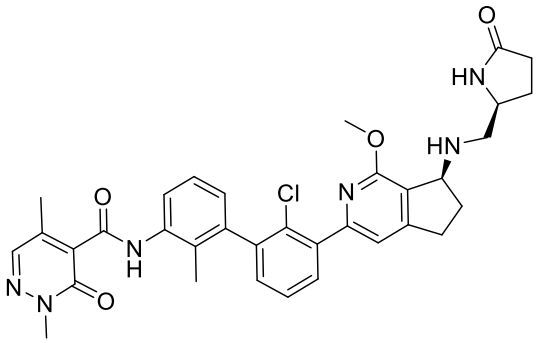
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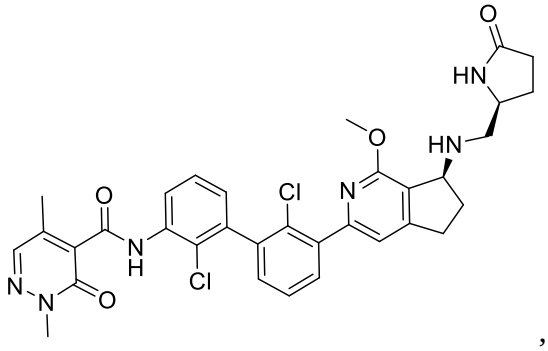
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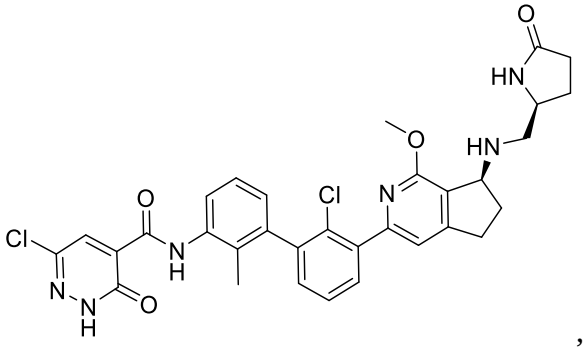
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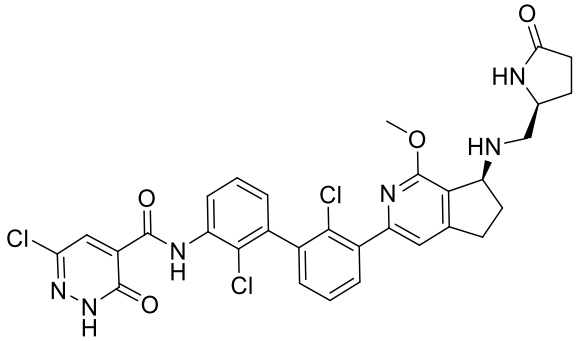
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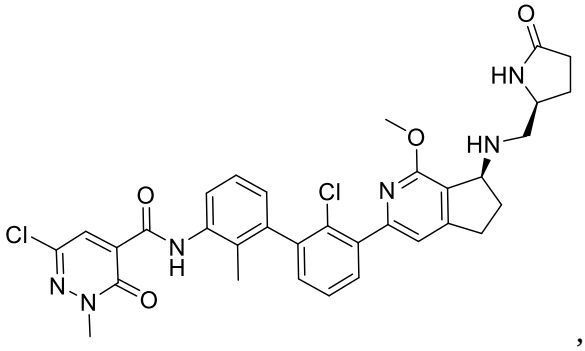
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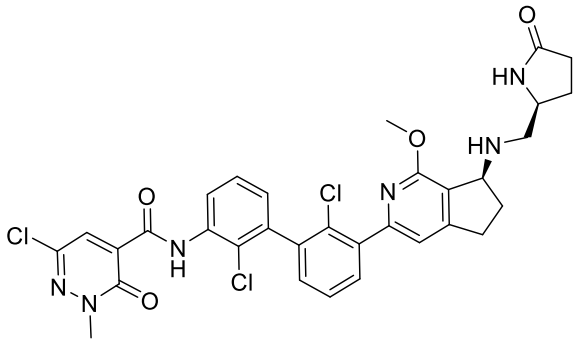
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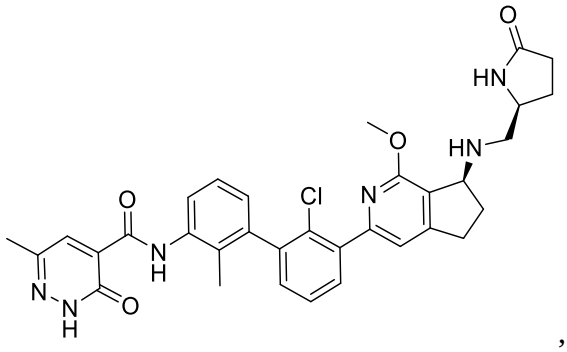
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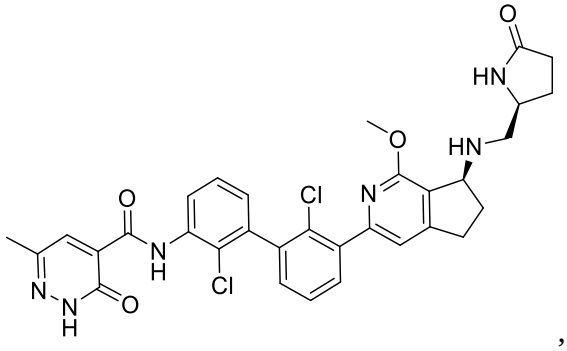
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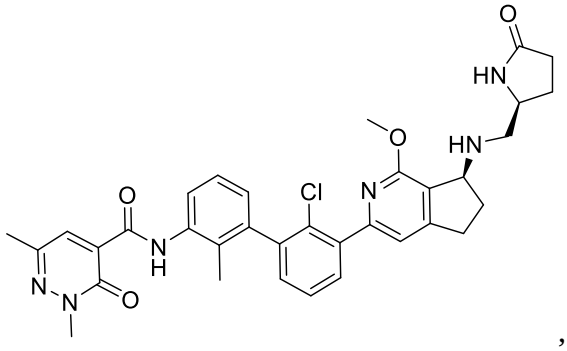
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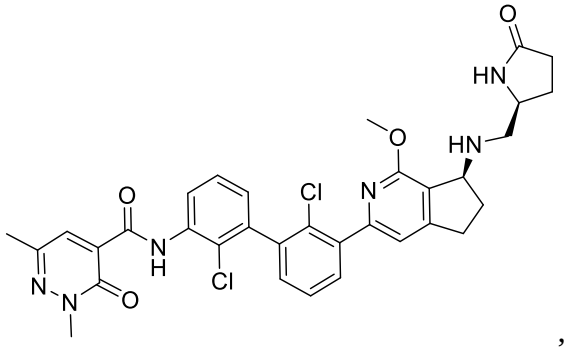
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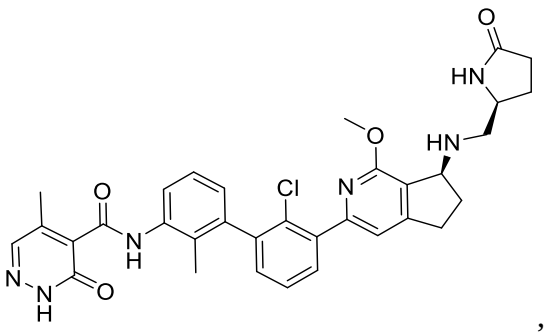
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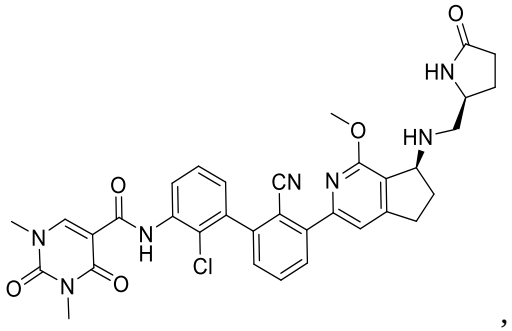
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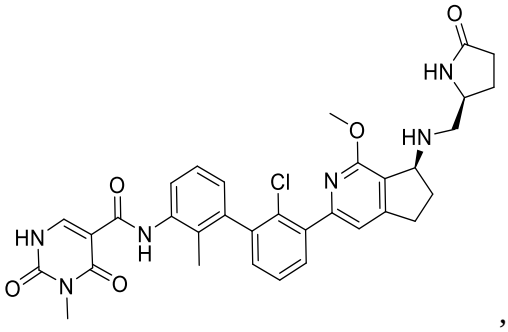
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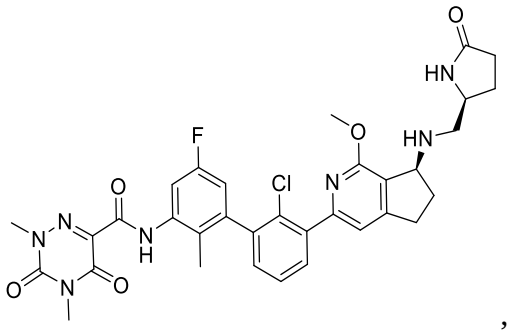
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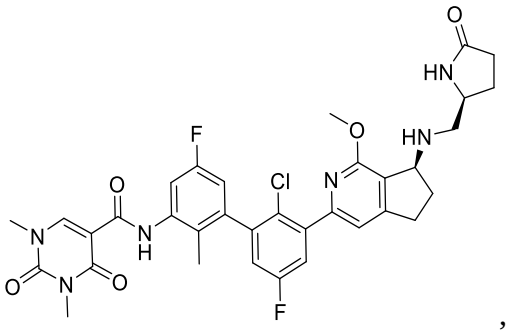
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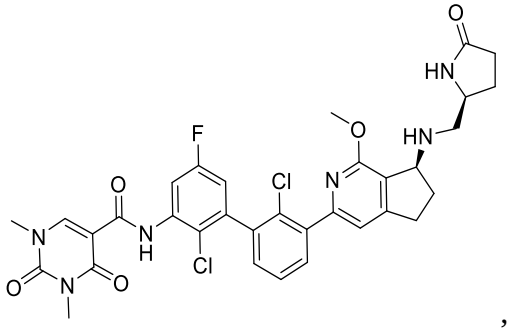
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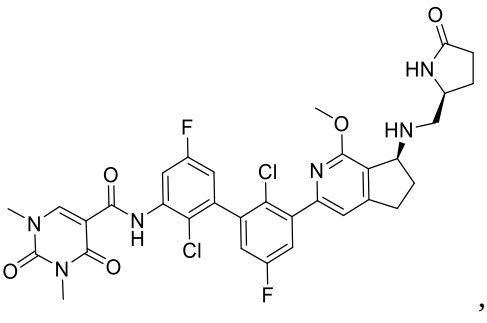
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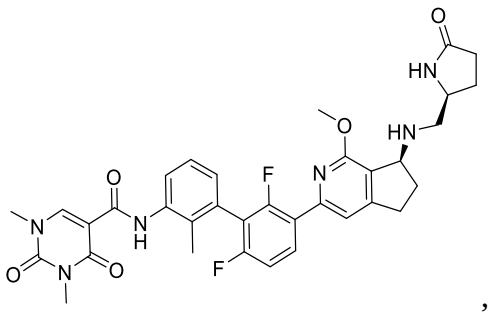
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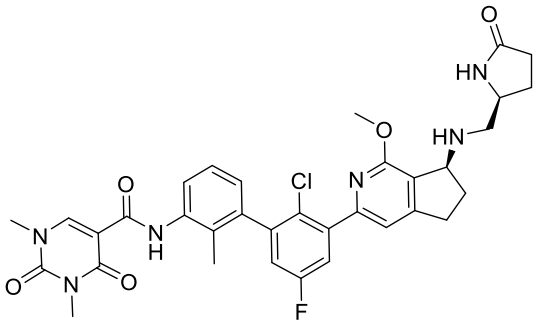
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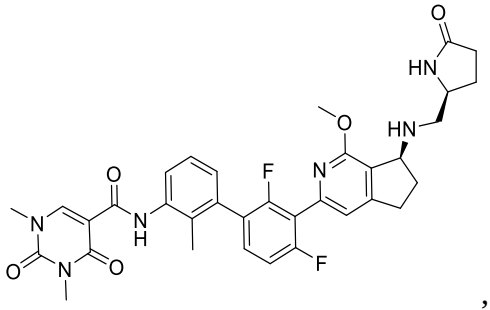
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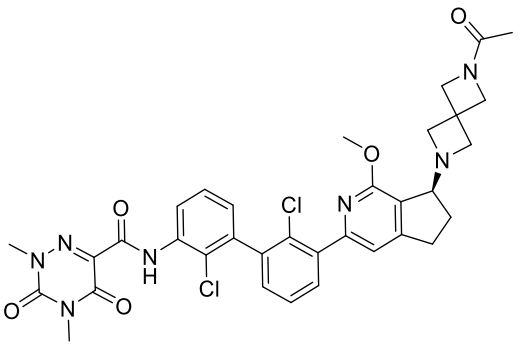
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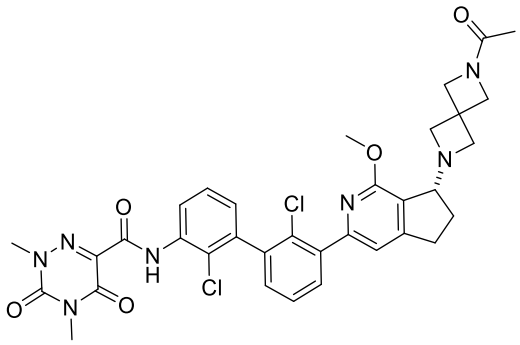
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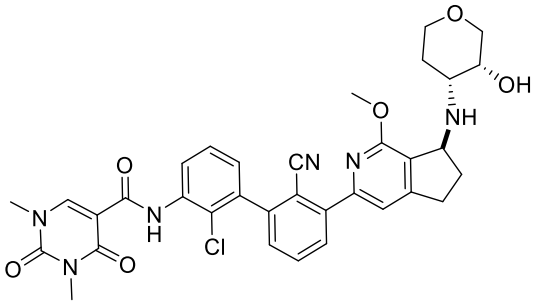
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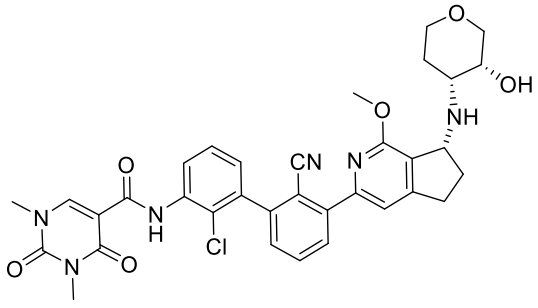
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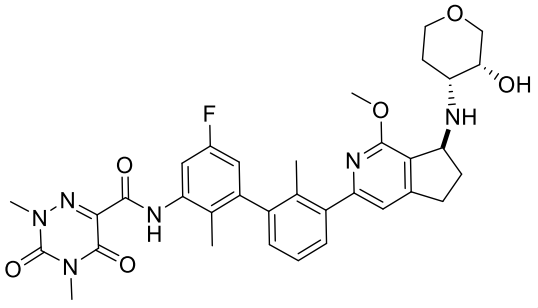
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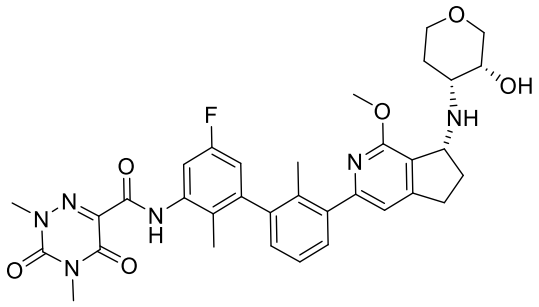
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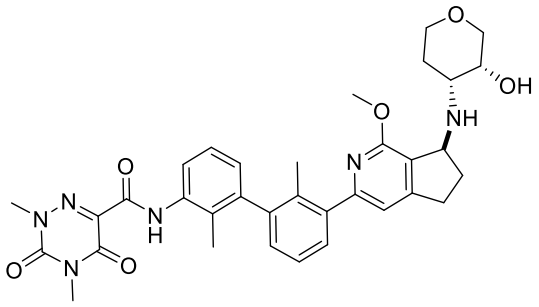
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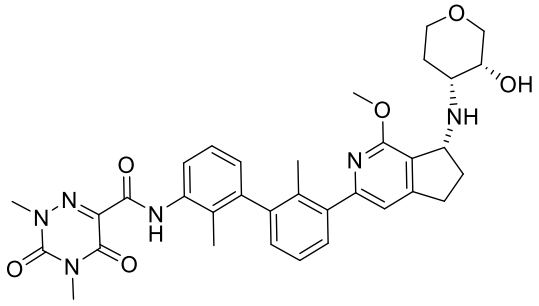
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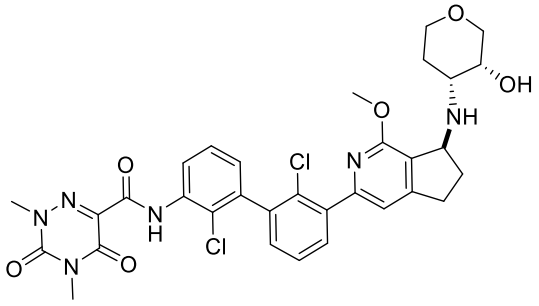
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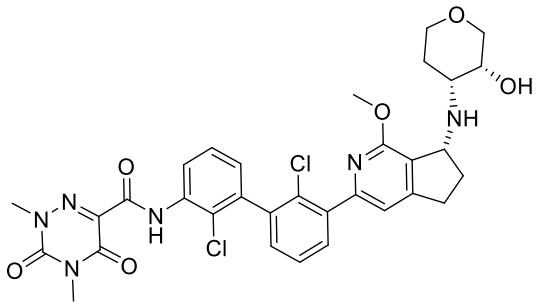
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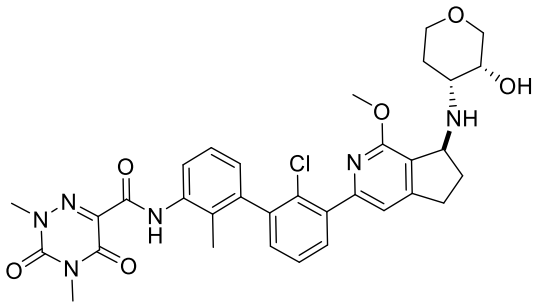
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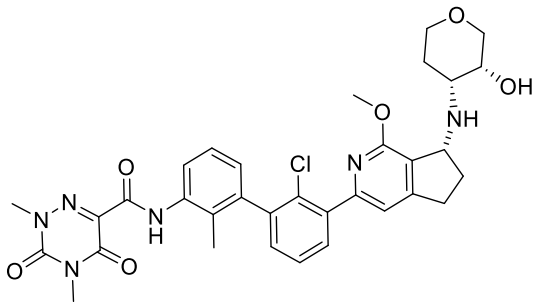
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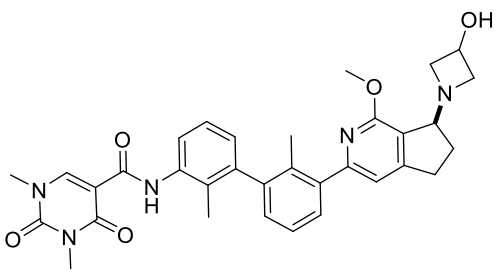
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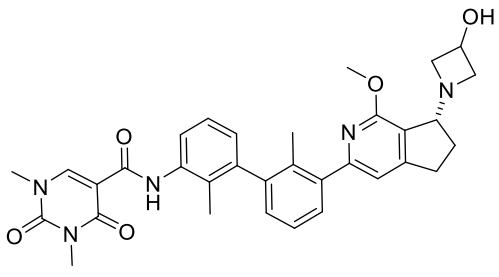
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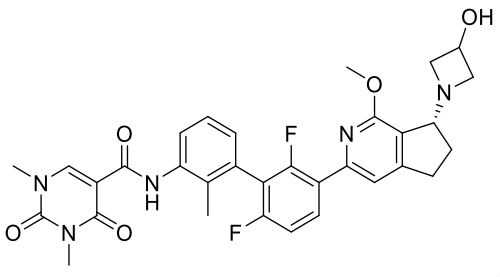
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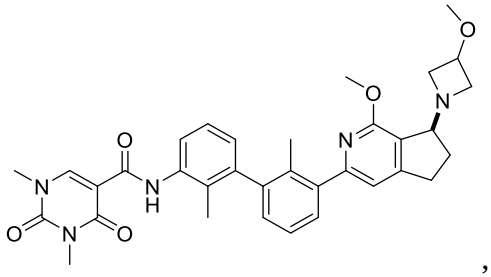
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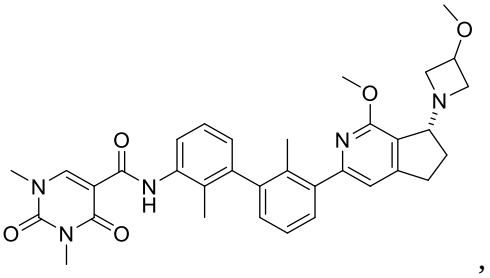
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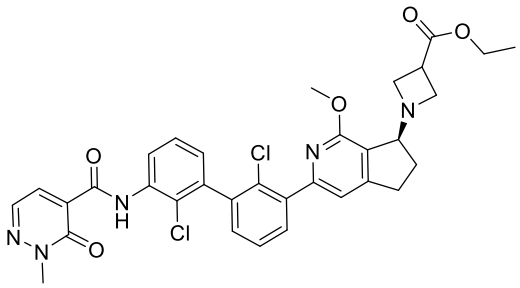
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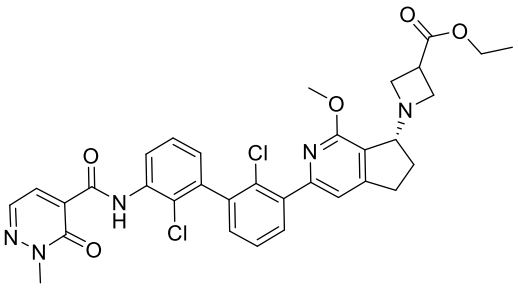
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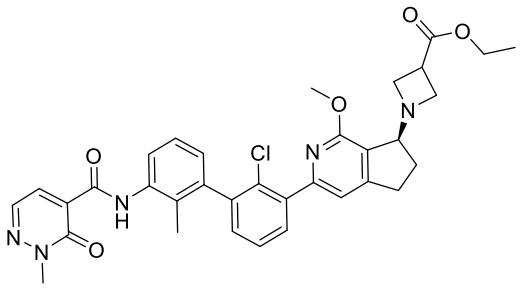
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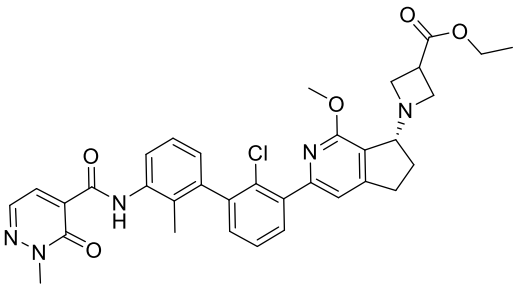
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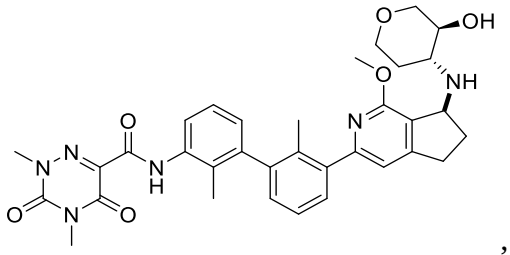
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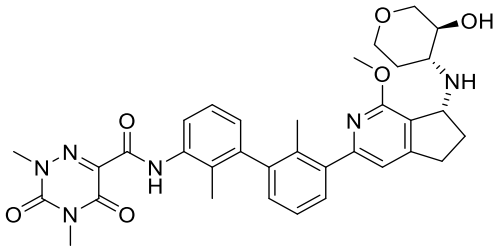
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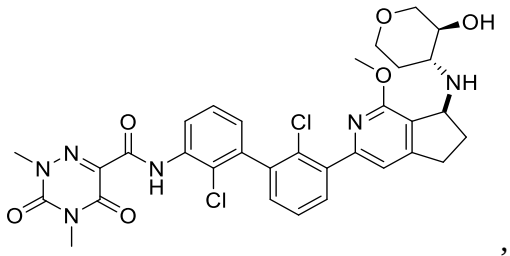
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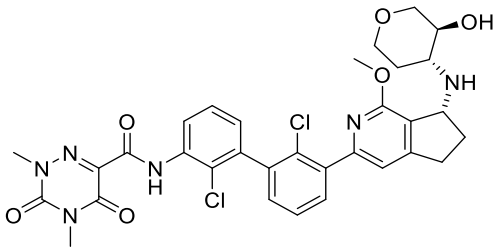
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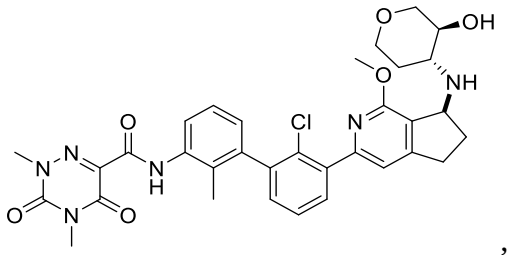
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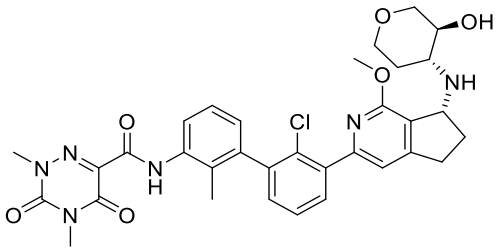
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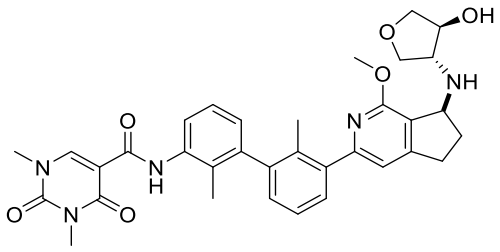
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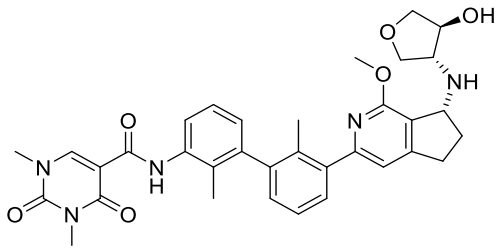
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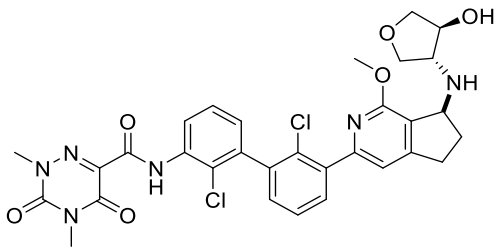
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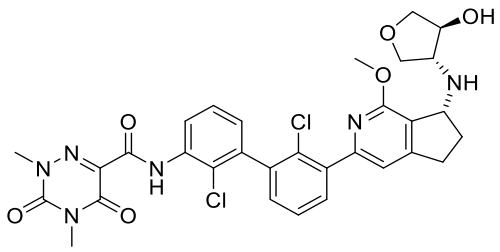
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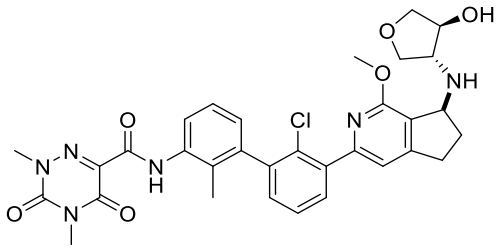
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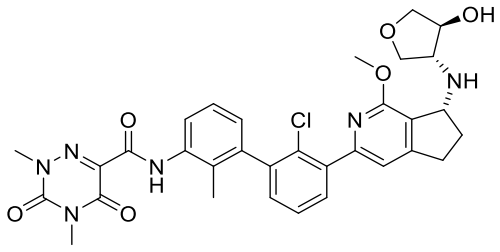
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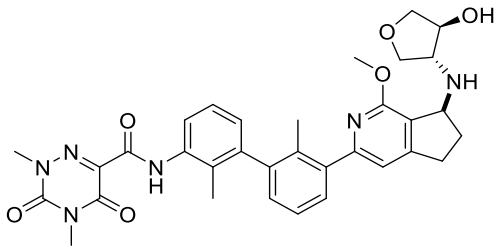
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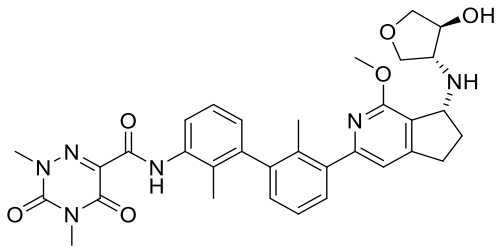
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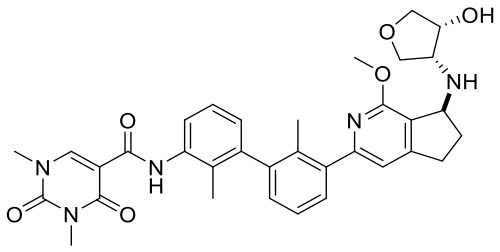
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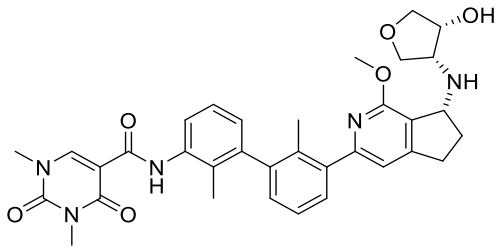
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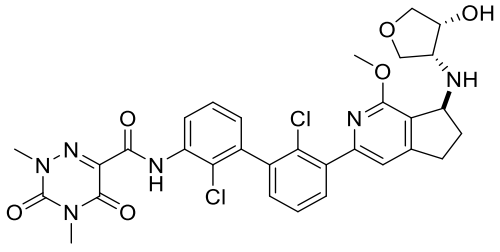
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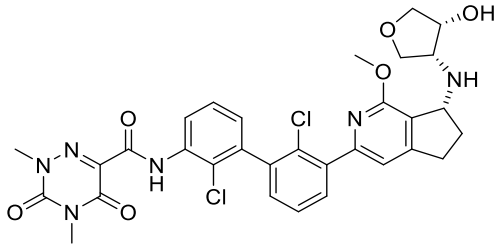
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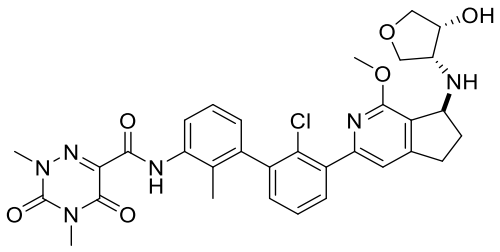
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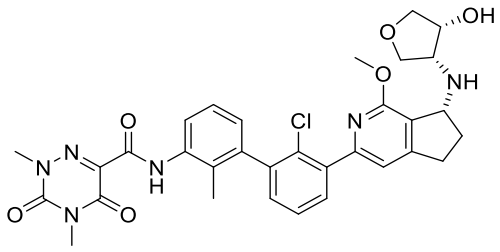
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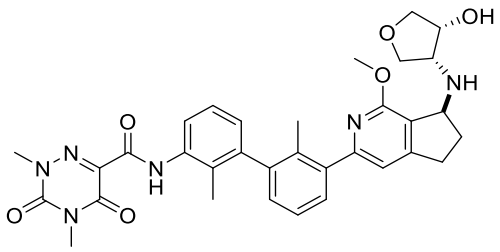
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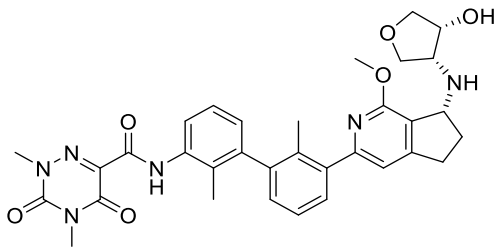
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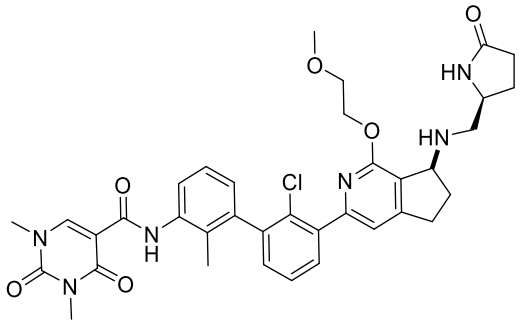
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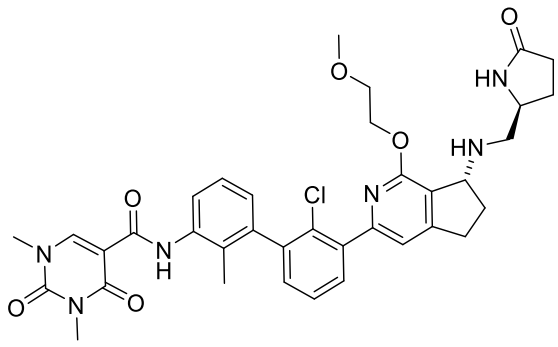
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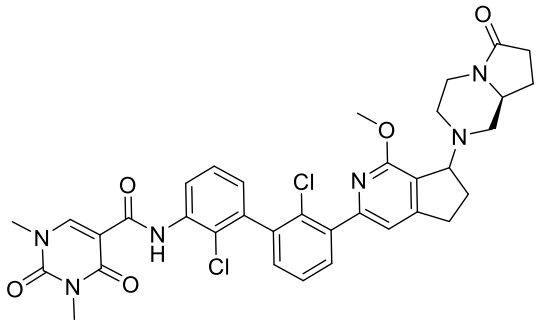
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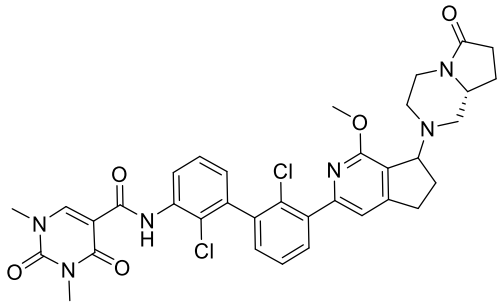
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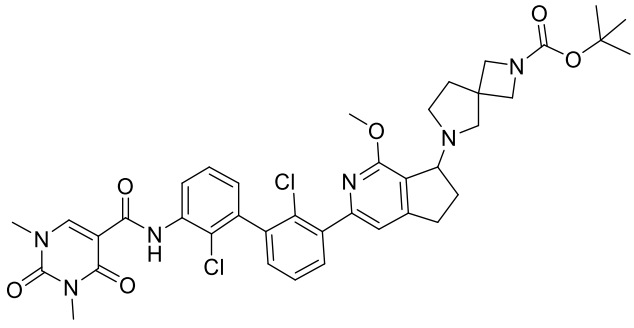
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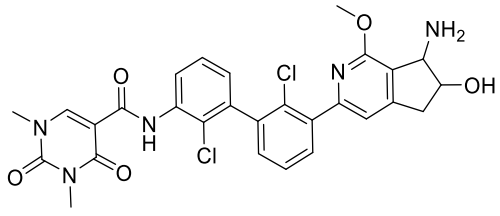
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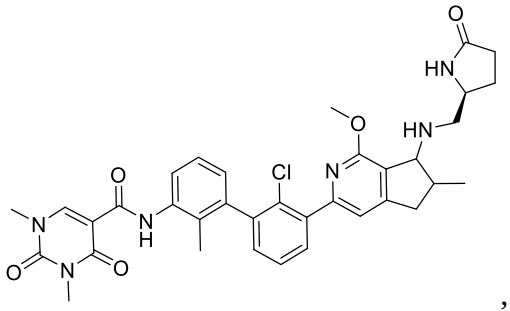
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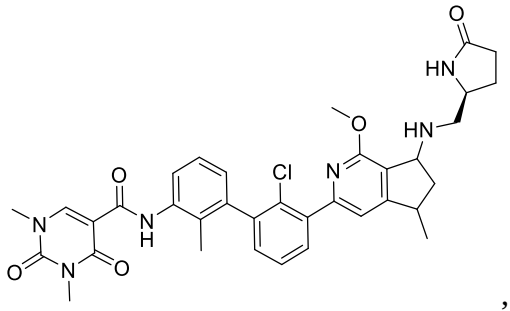
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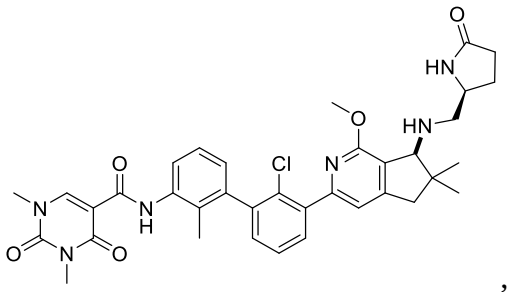
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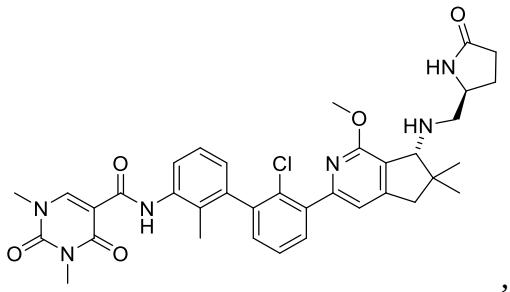
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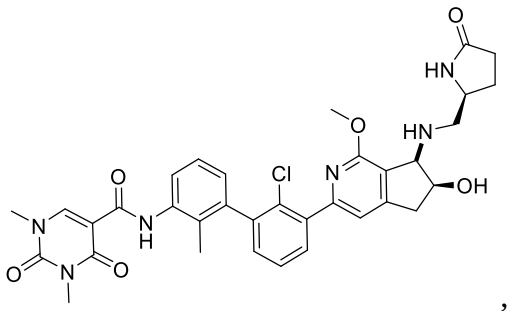
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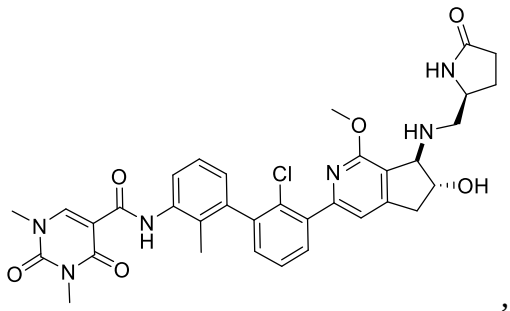
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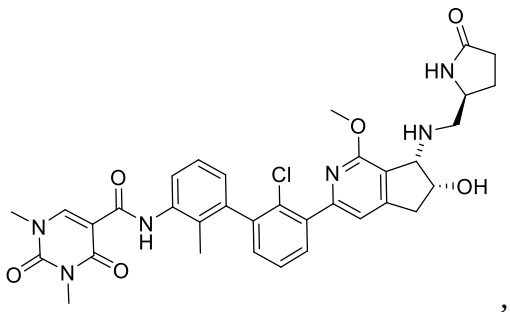
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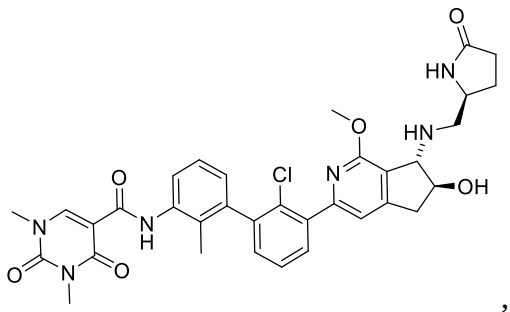
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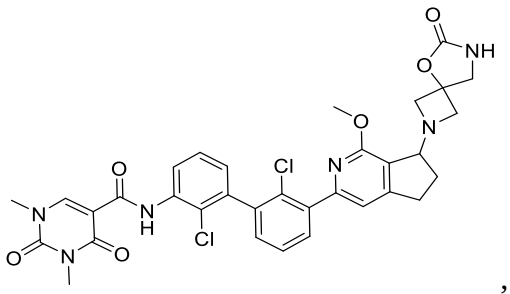
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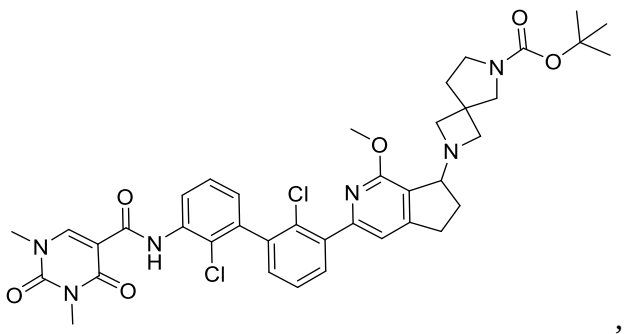
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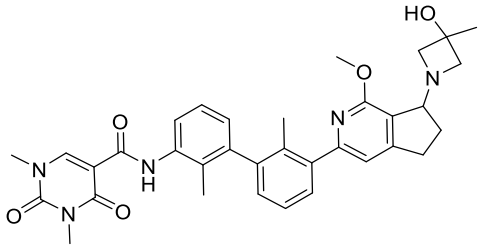
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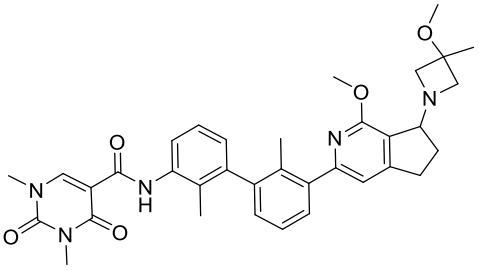
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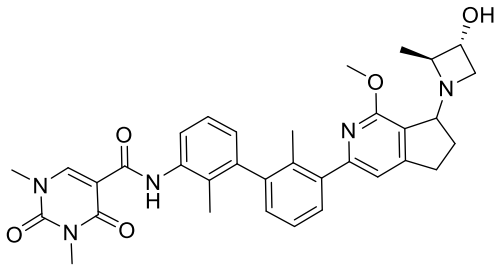
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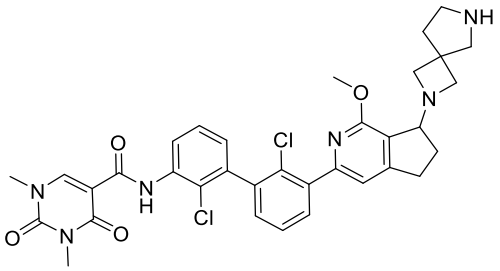
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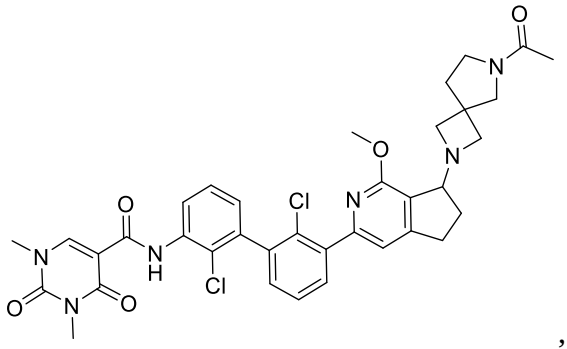
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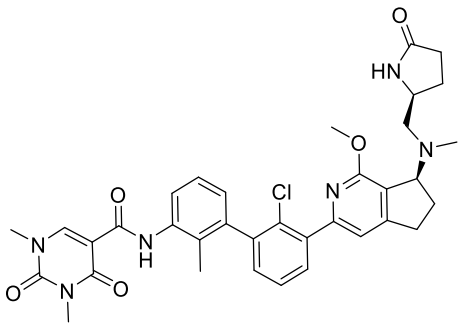
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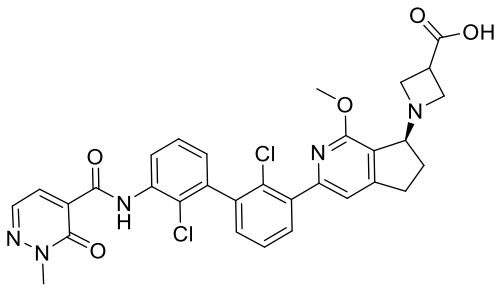
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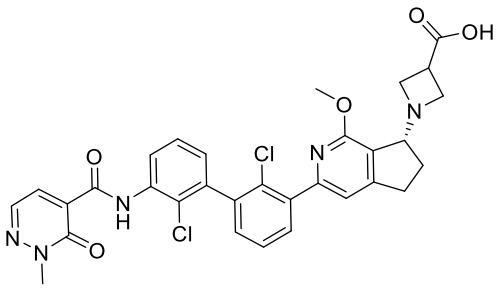
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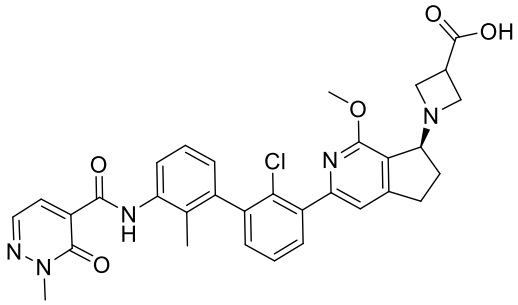
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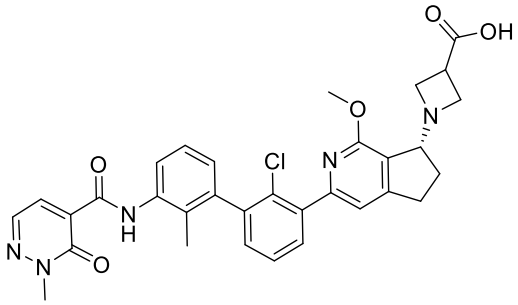
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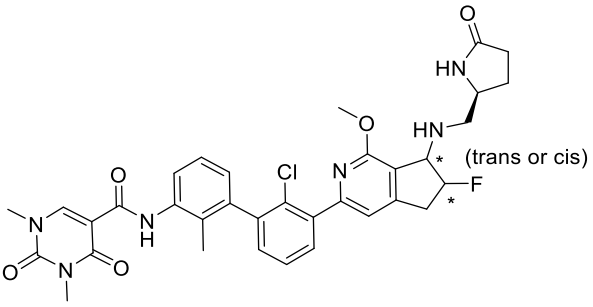
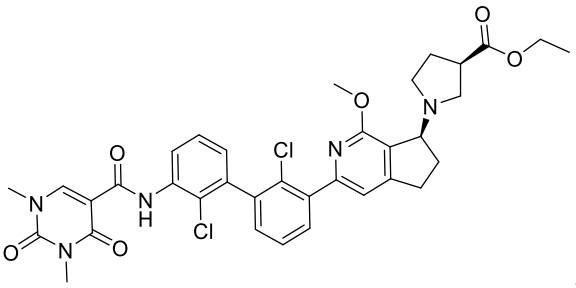


, or a pharmaceutically acceptable salt of any of the foregoing.

145. The compound of Claim 1 selected from the group consisting of:



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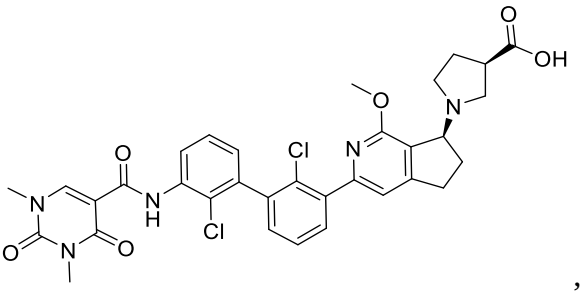

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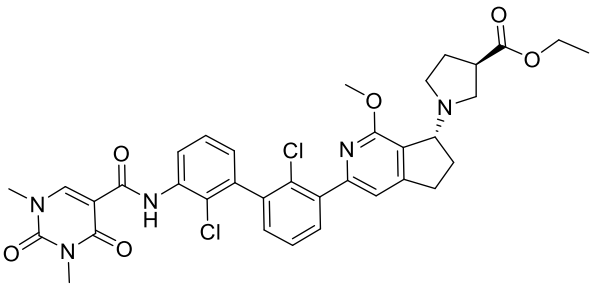

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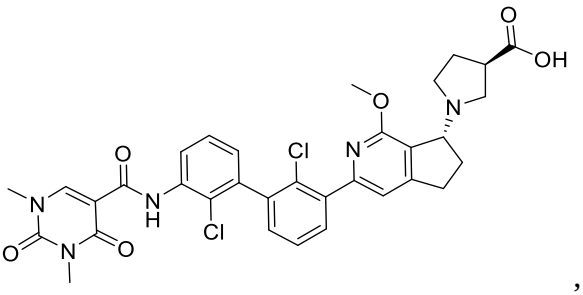

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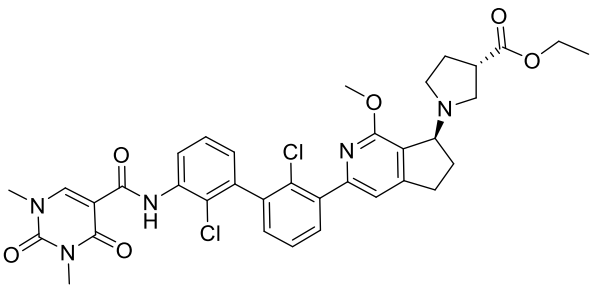

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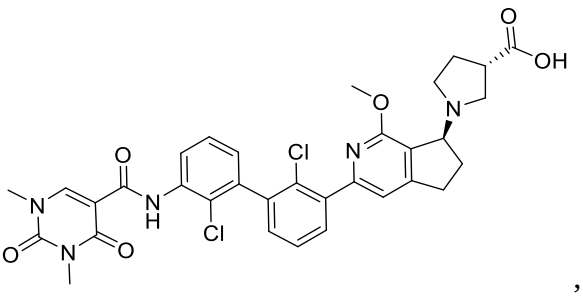

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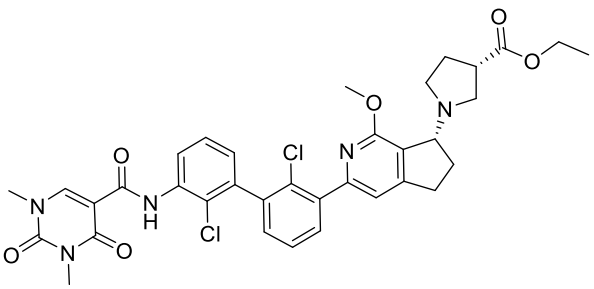

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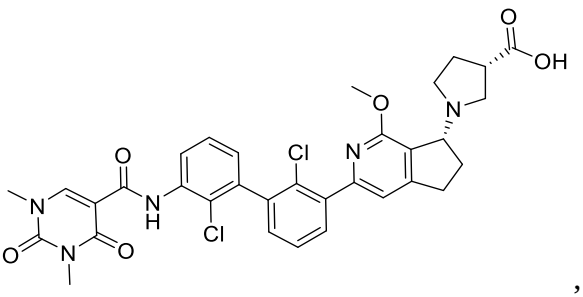

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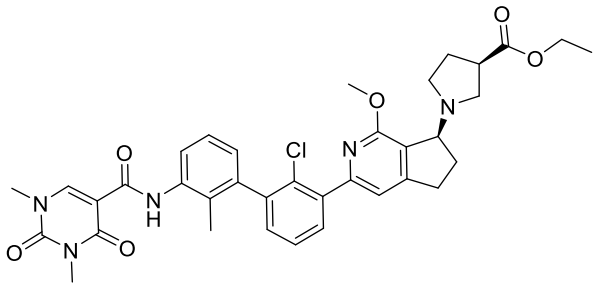
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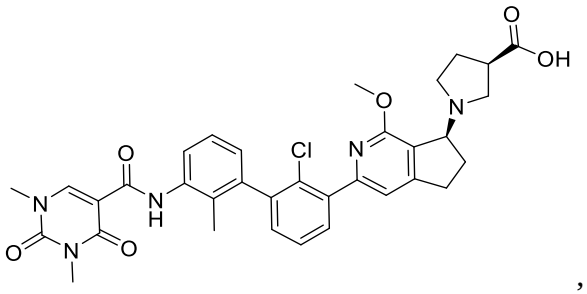
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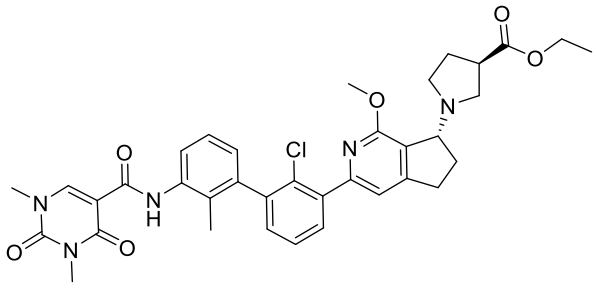
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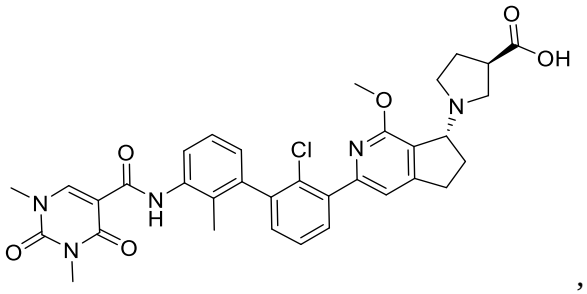
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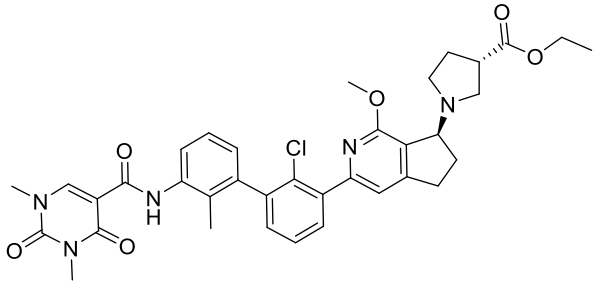
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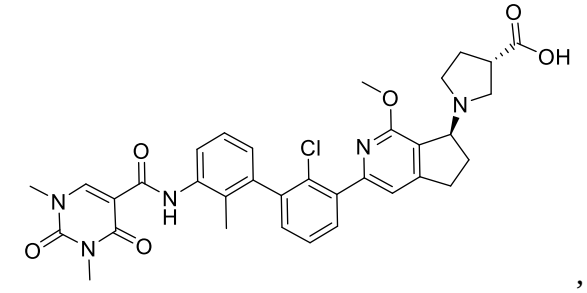
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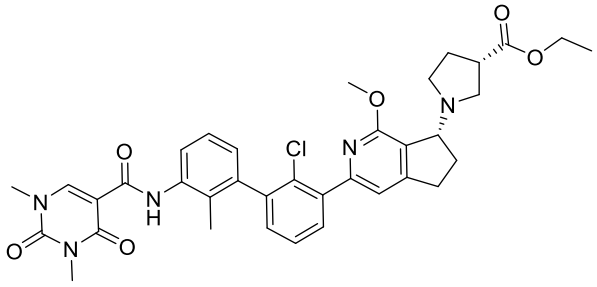
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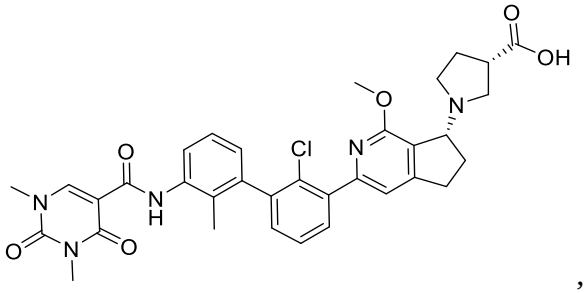
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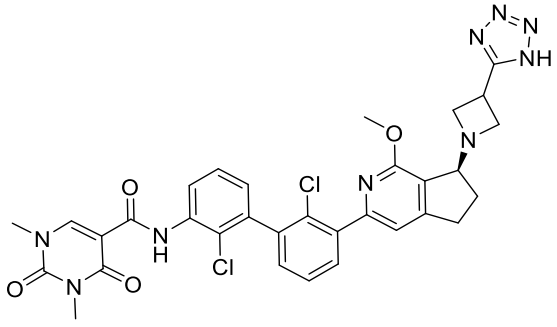
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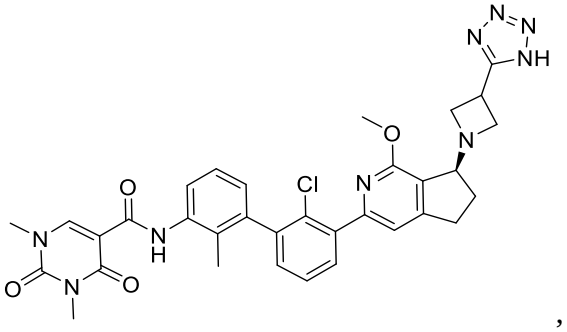
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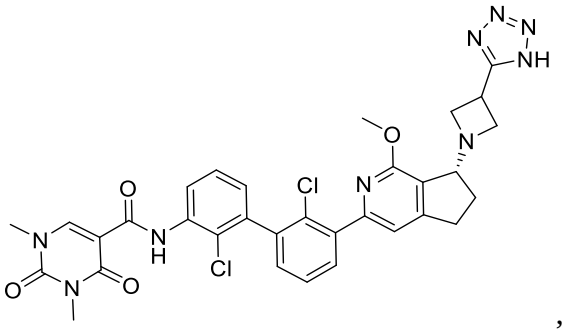
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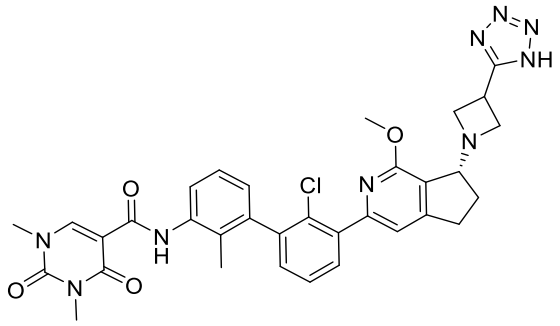
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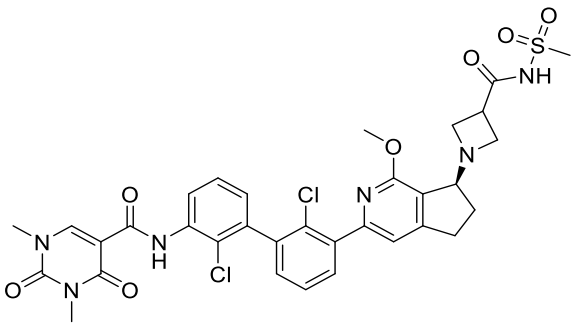
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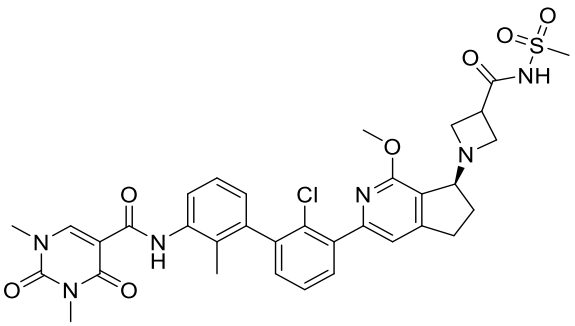
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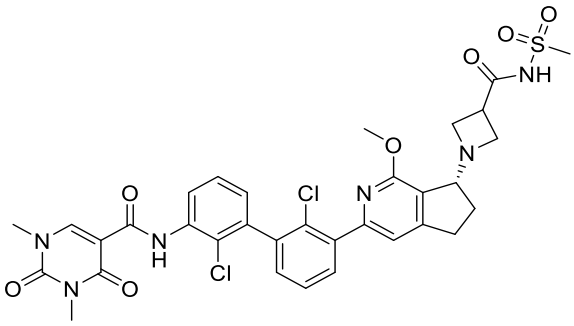
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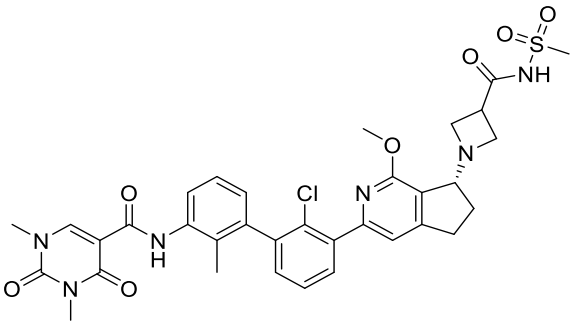
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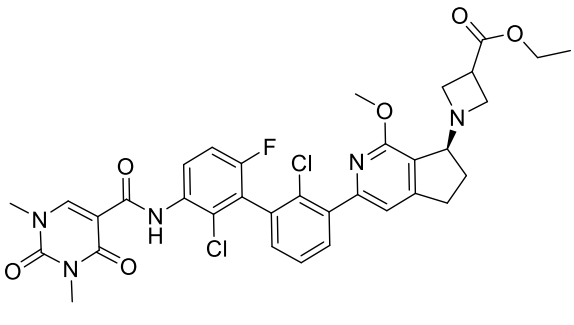
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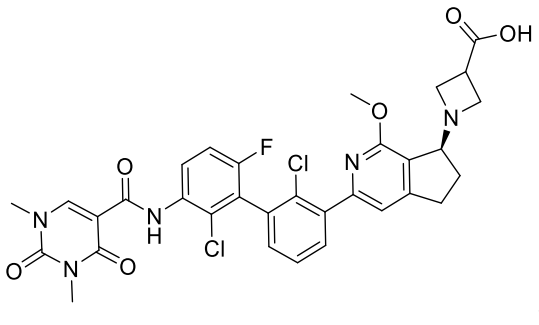
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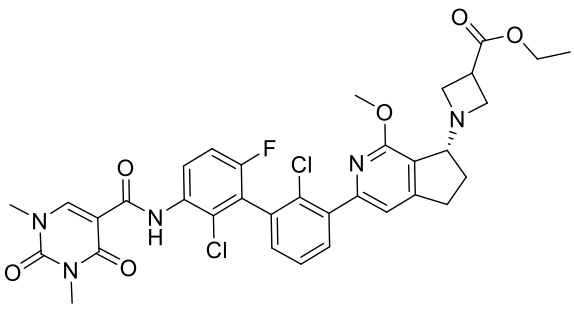
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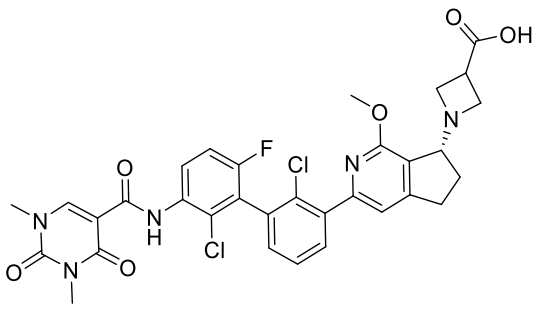
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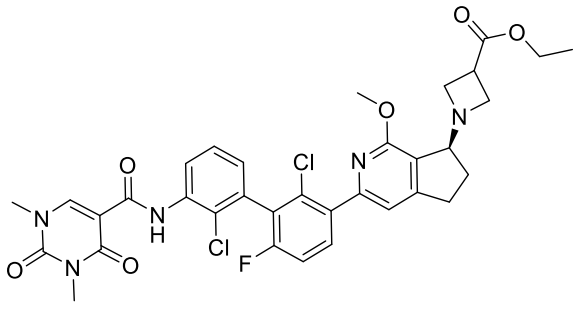
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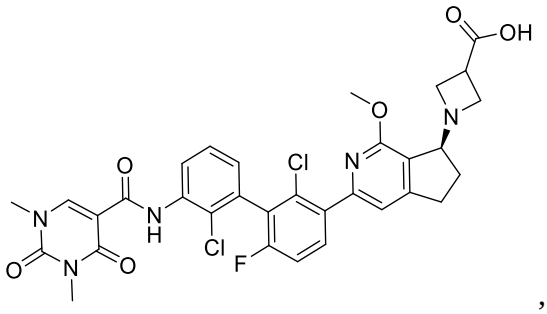
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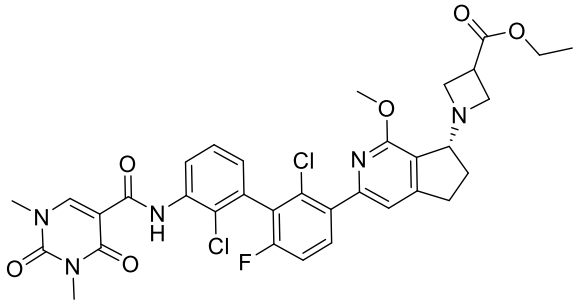
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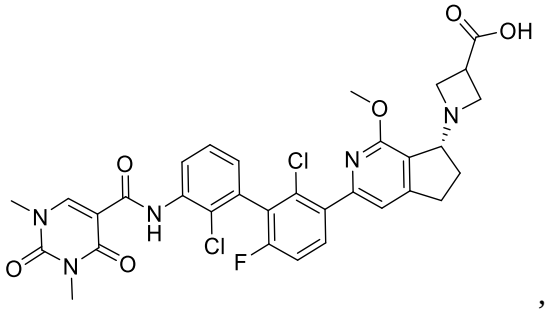
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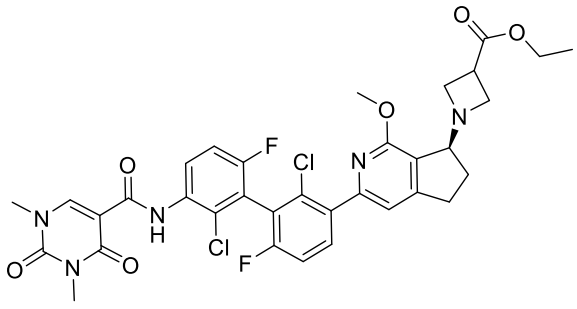
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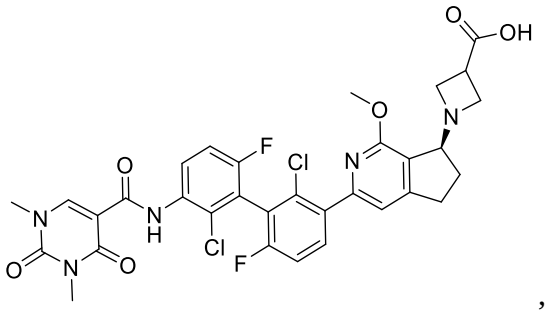
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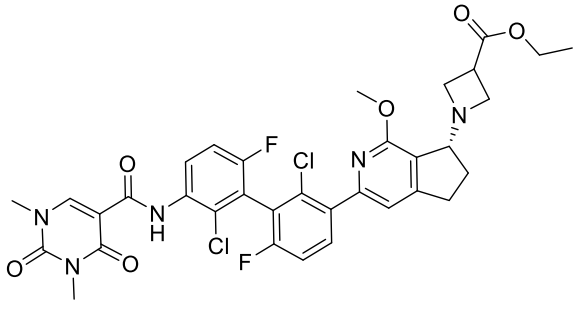
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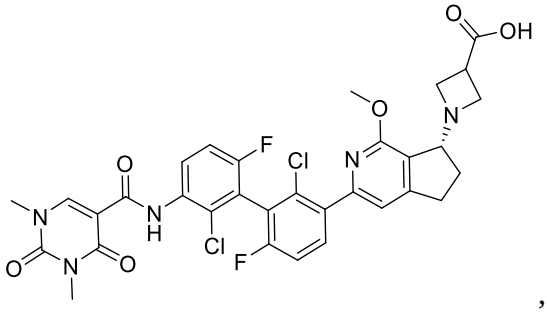
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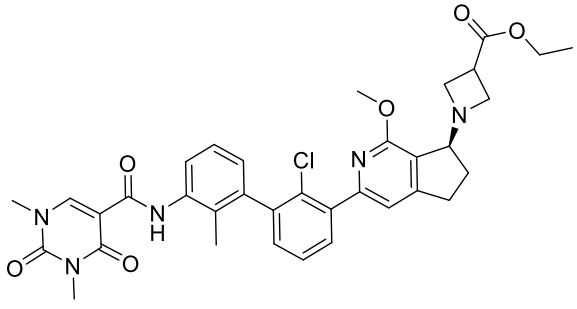
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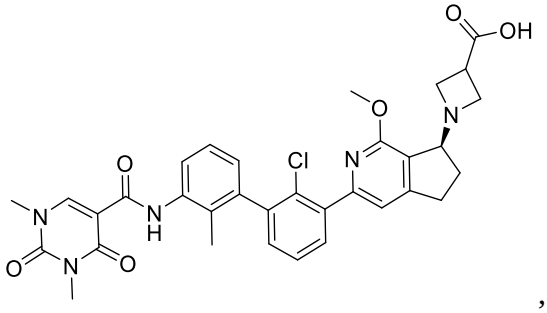
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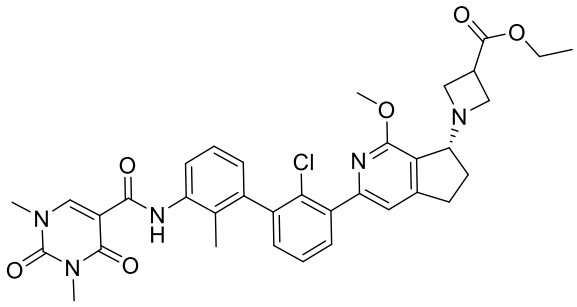
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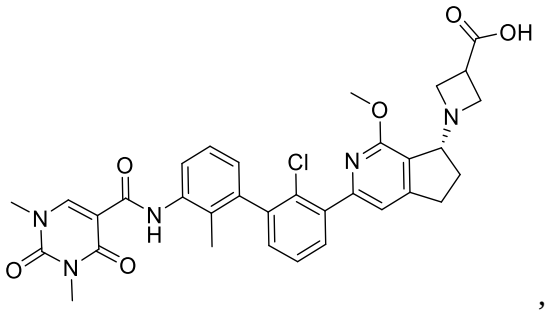
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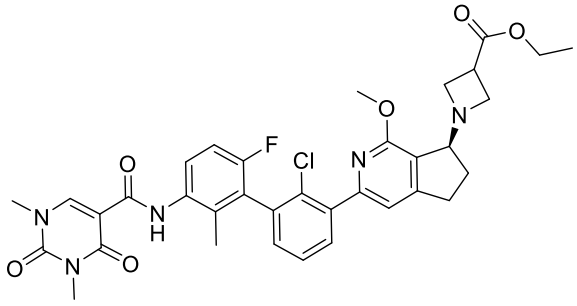
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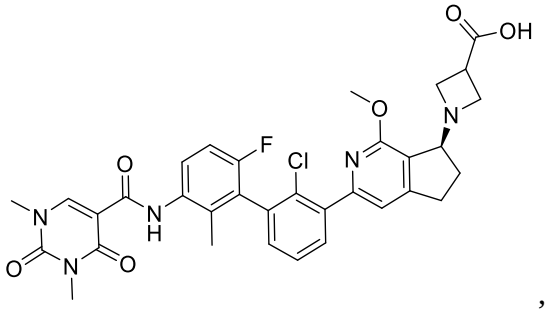
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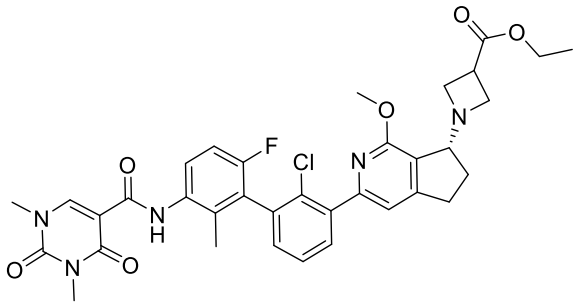
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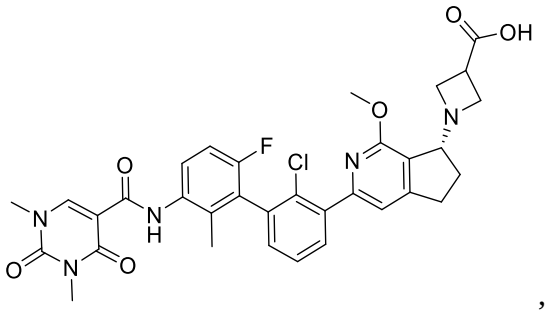
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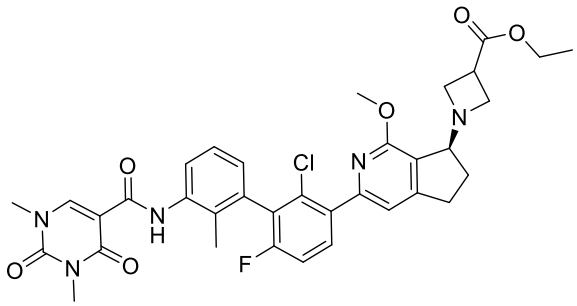
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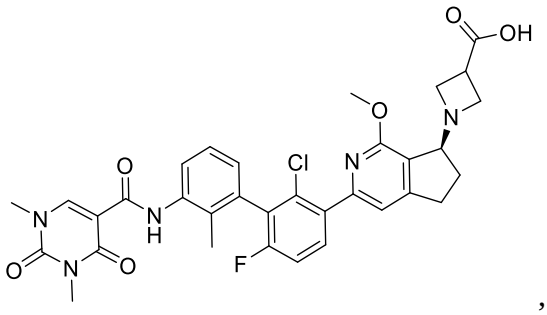
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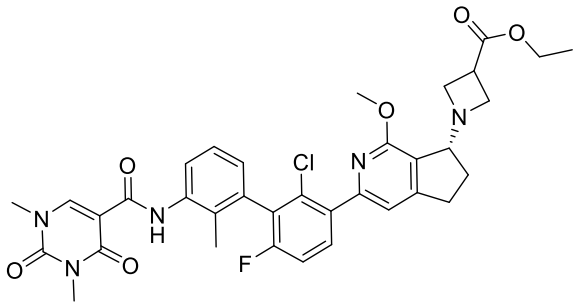
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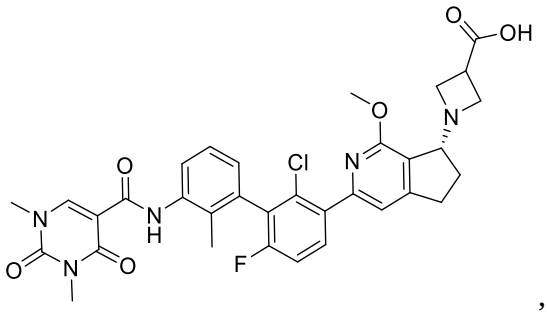
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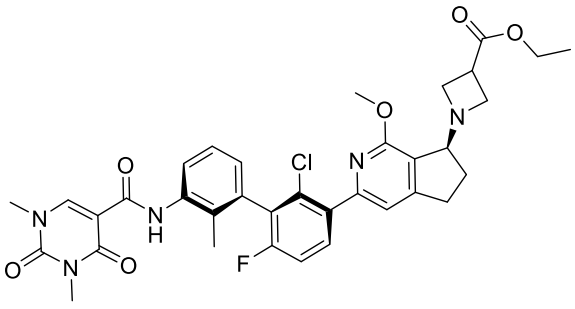
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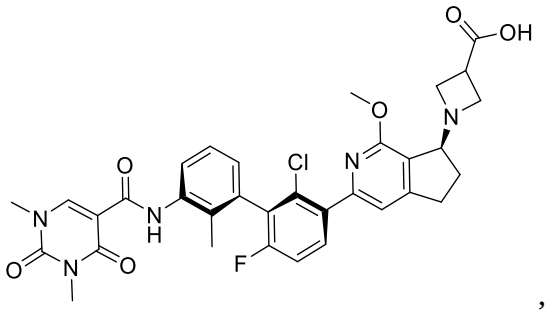
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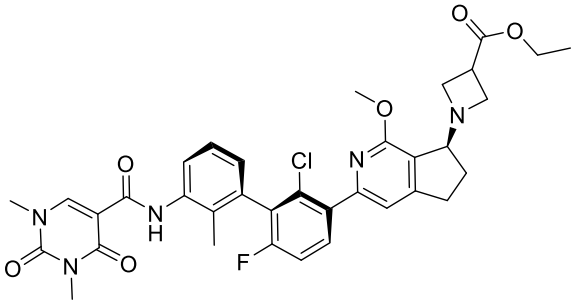
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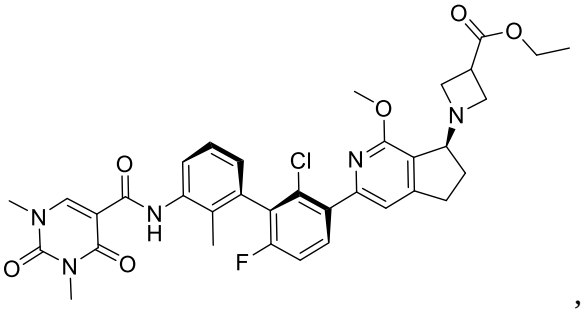
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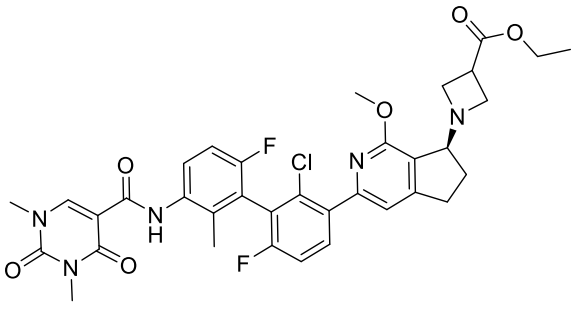
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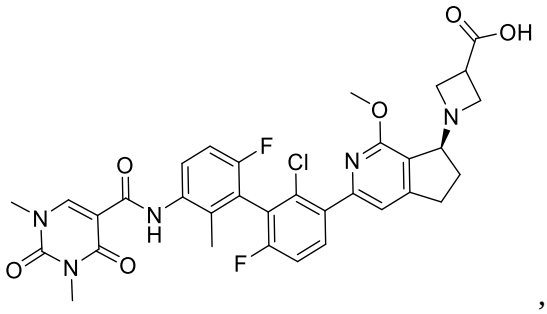
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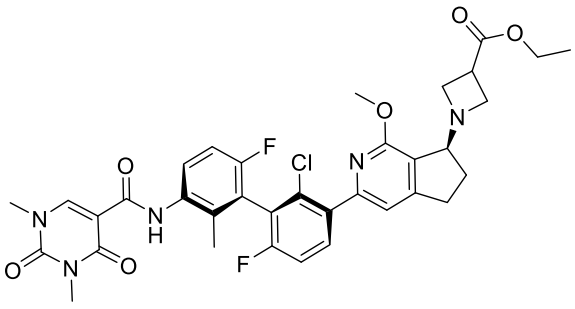
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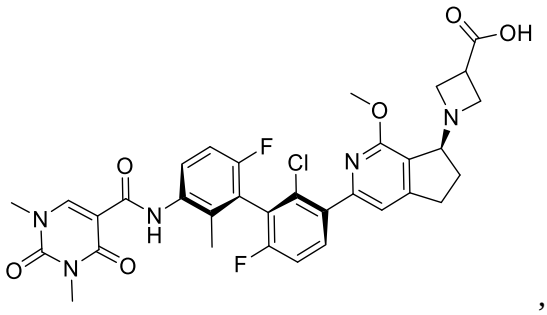
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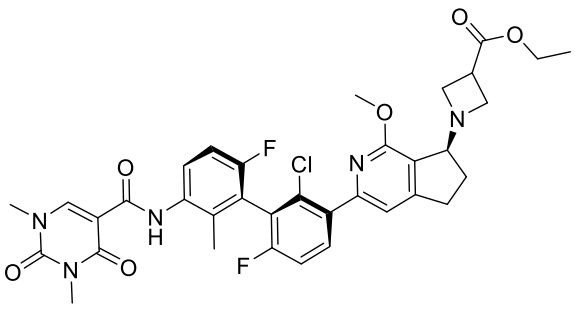
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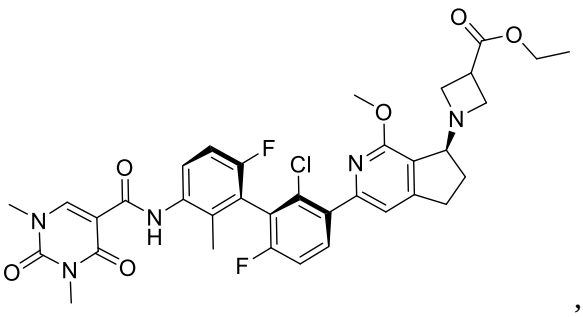
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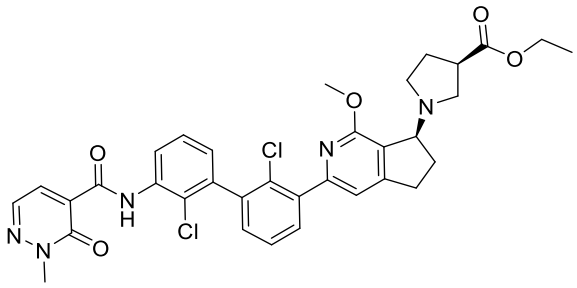
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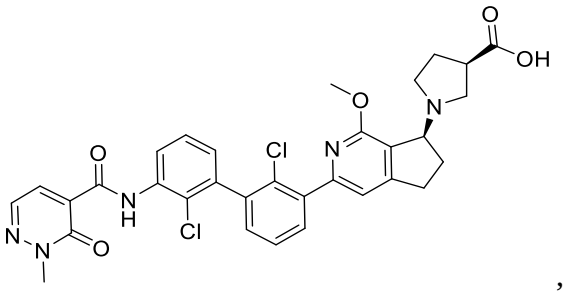
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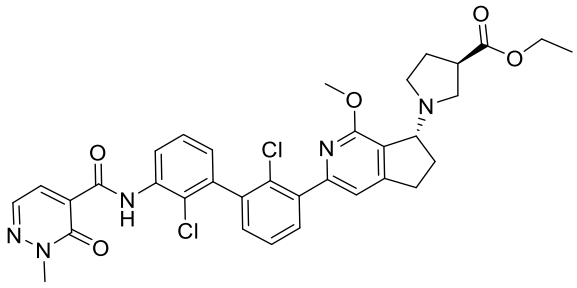
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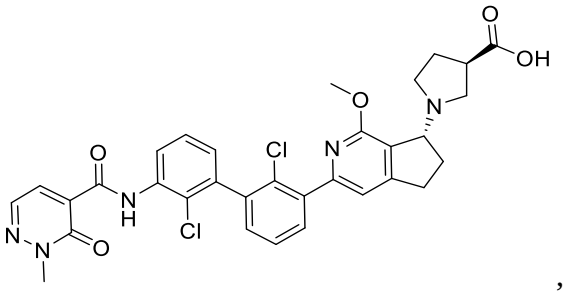
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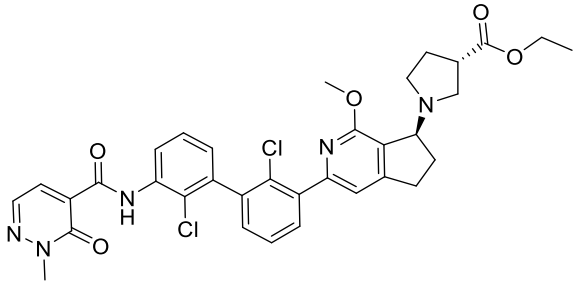
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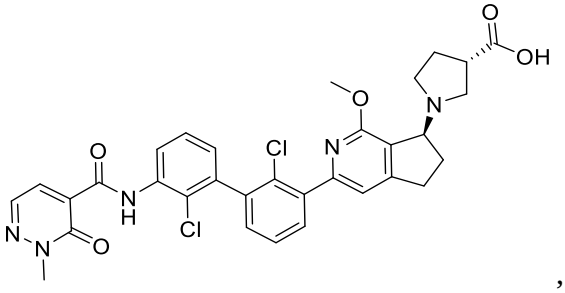
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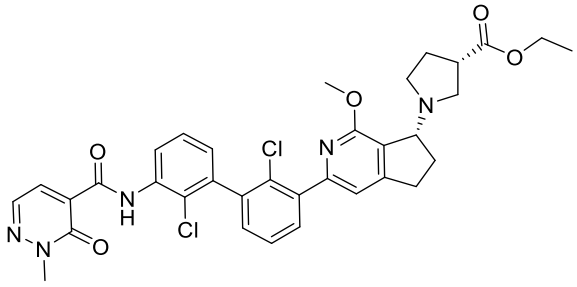
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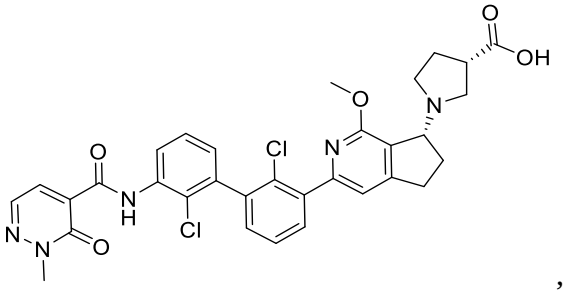
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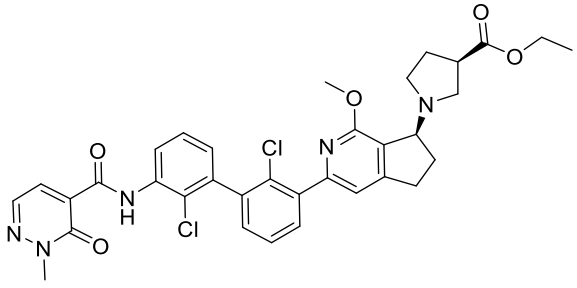
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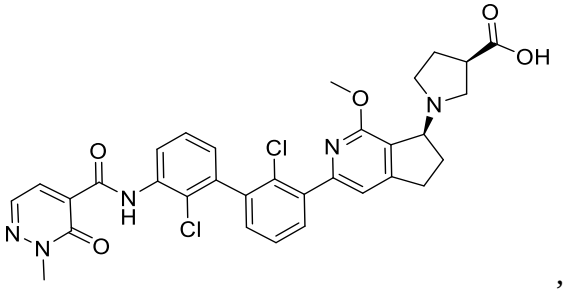
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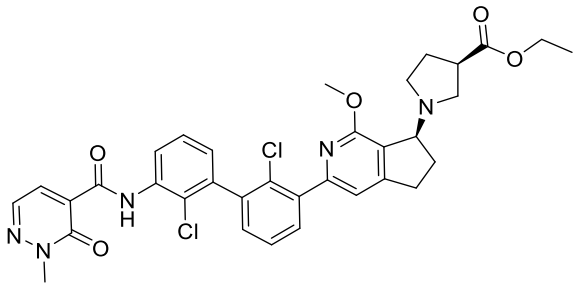
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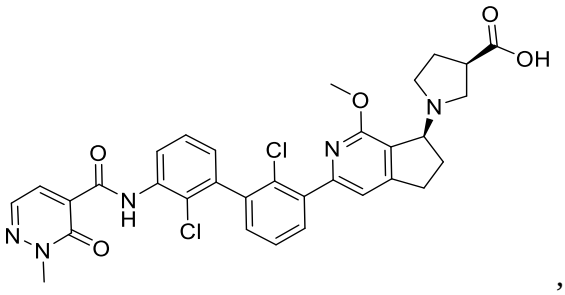
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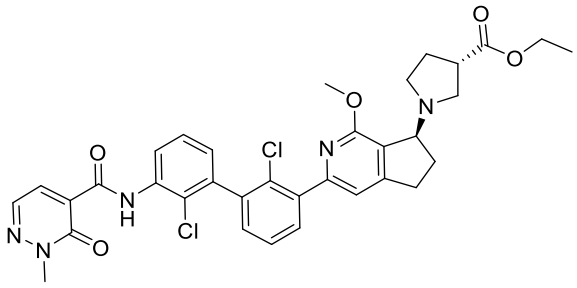
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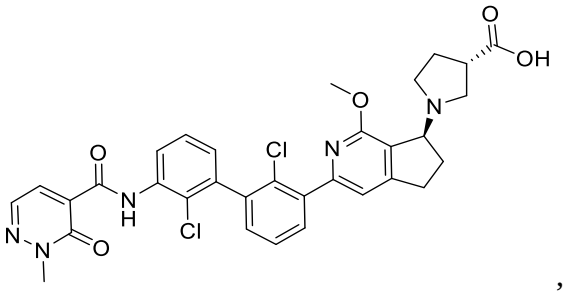
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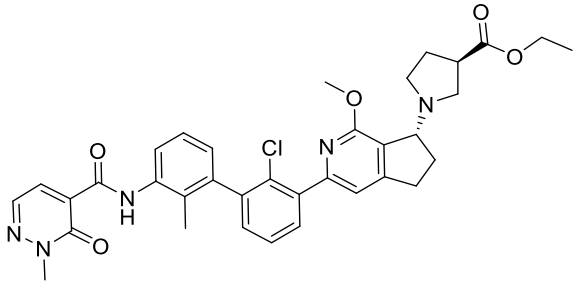
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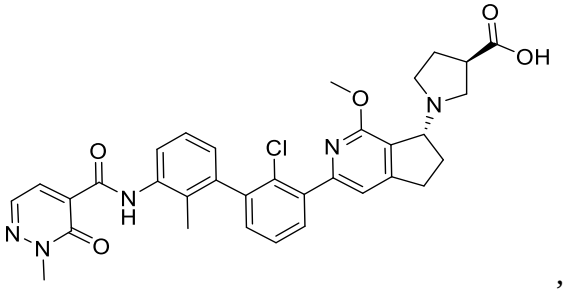
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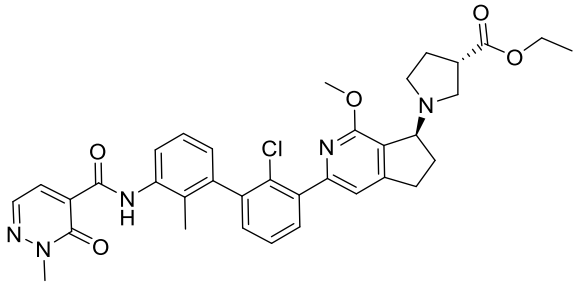
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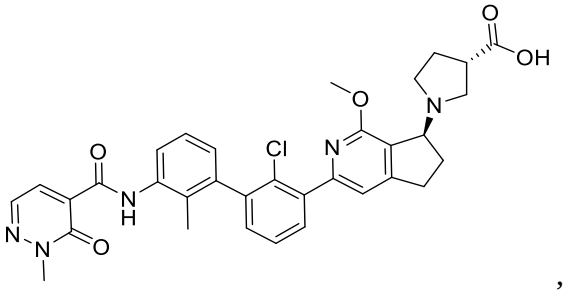
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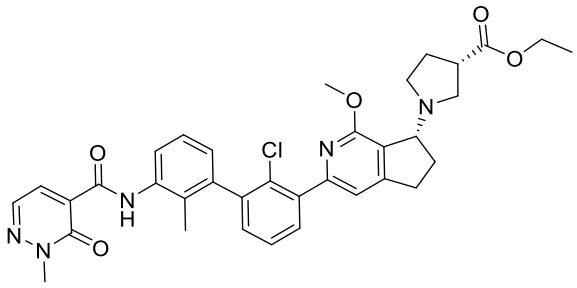
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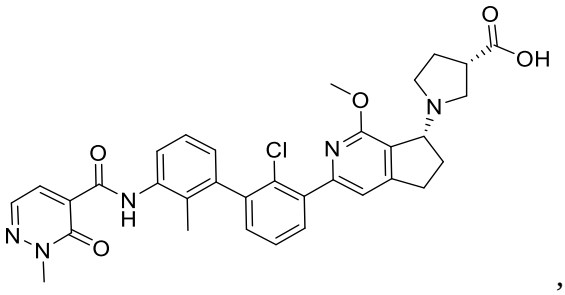
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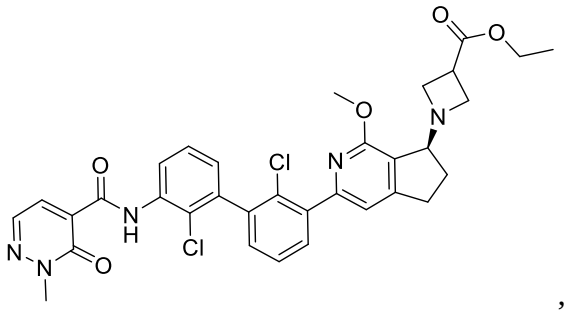
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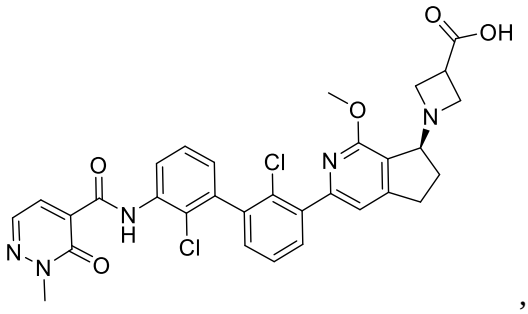
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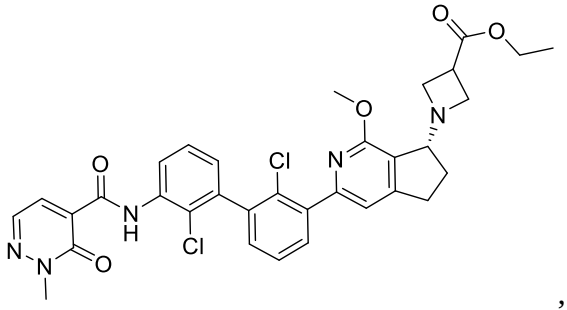
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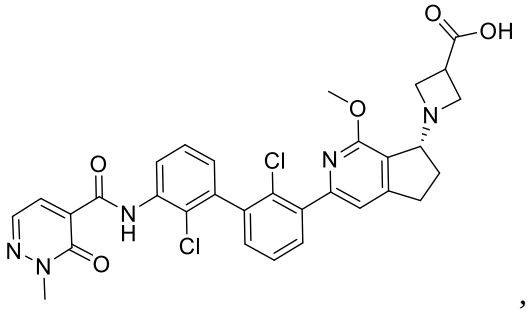
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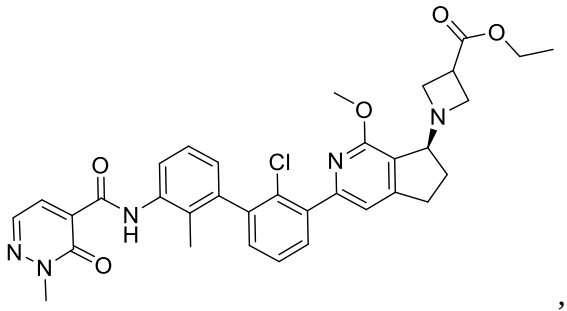
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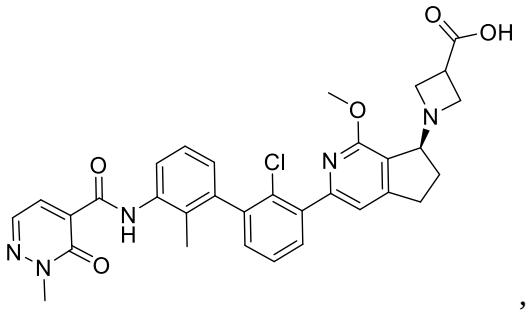
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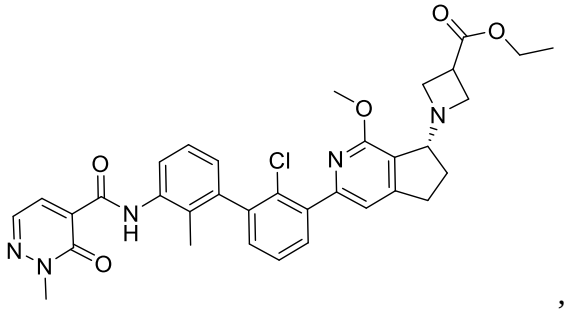
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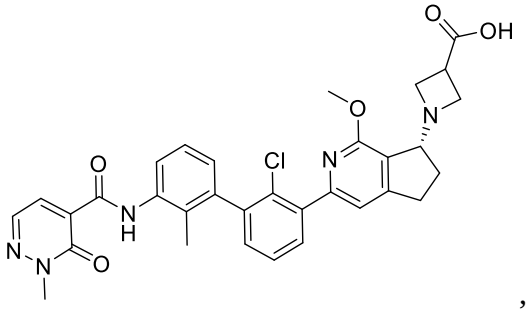
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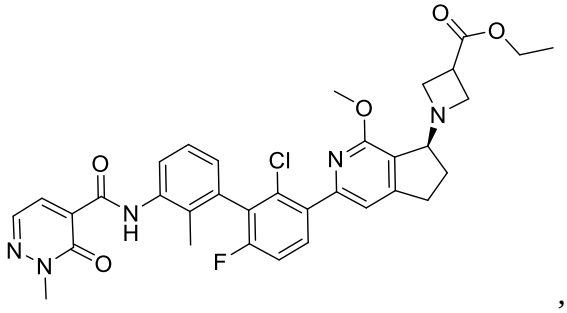
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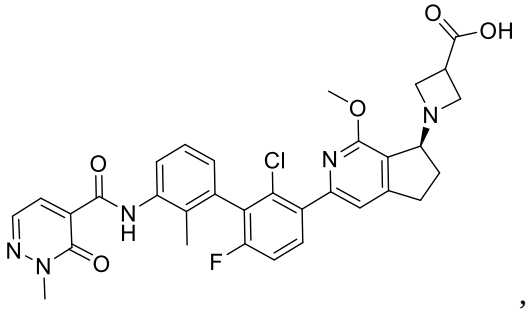
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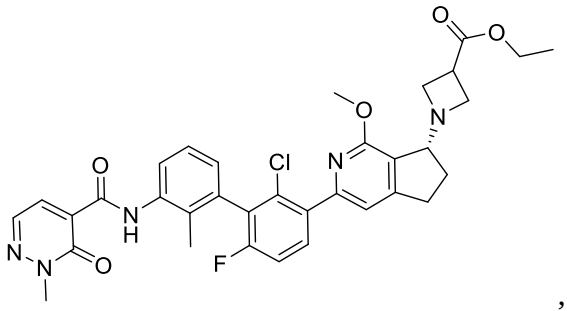
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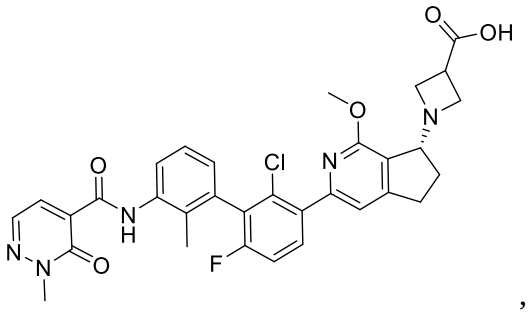
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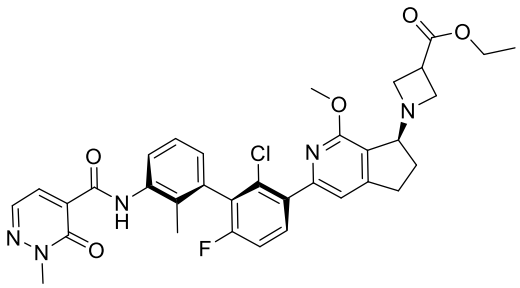
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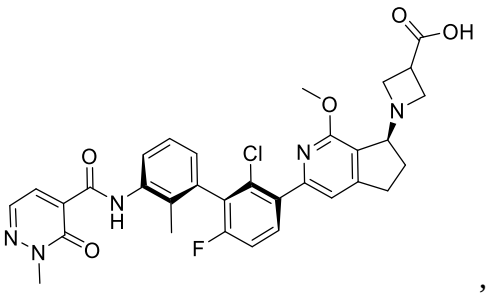
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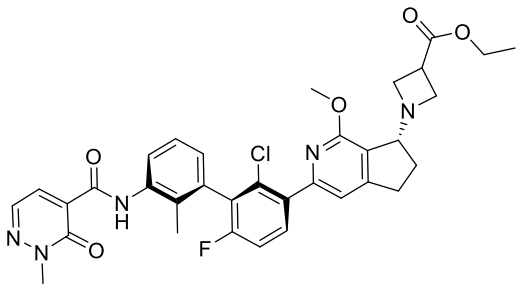
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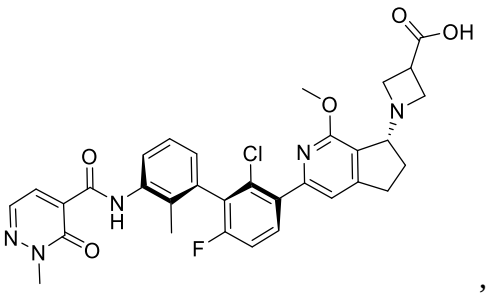
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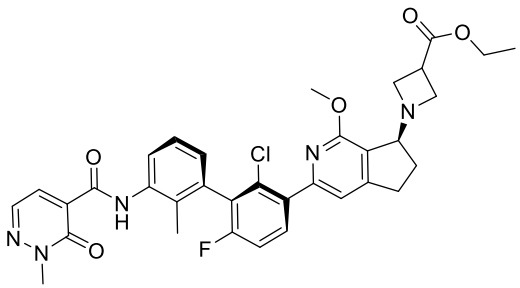
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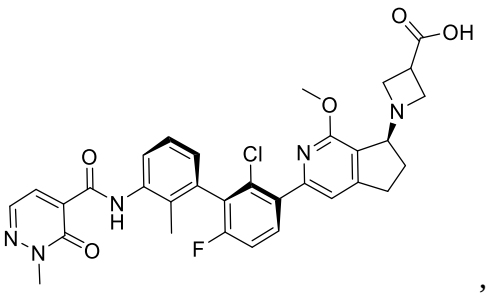
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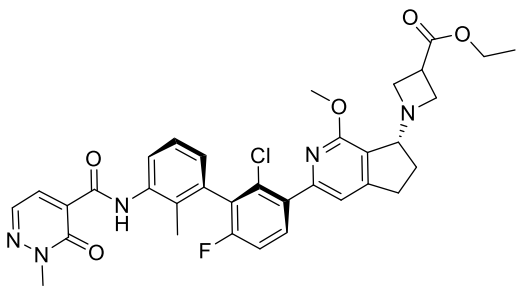
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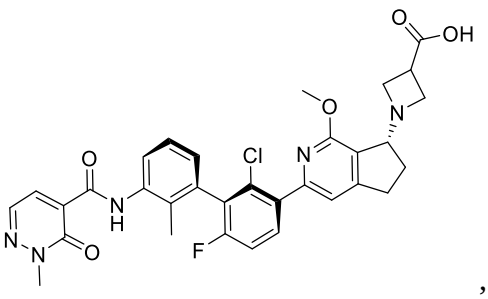
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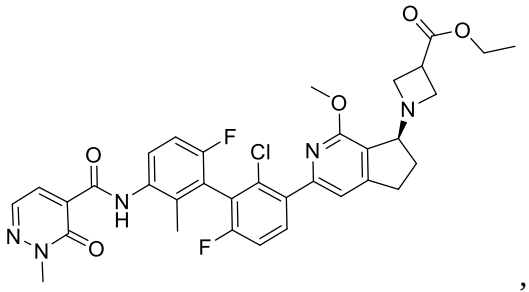
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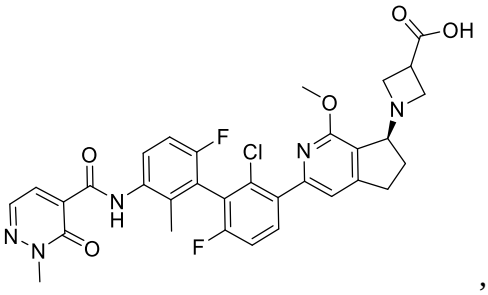
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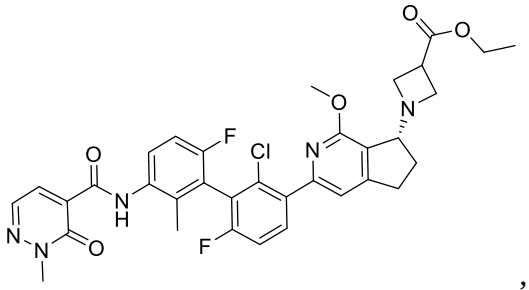
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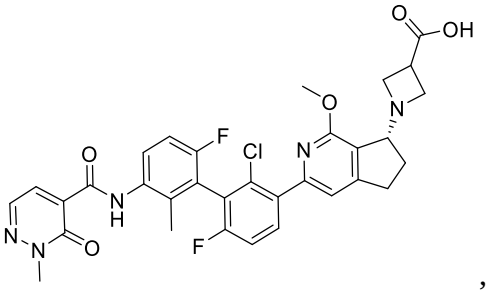
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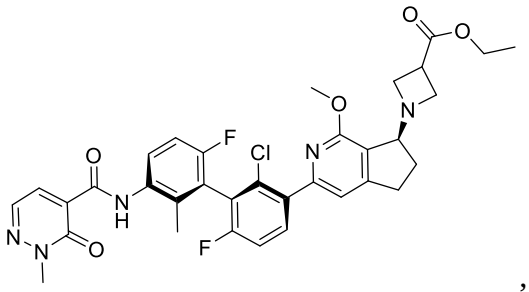
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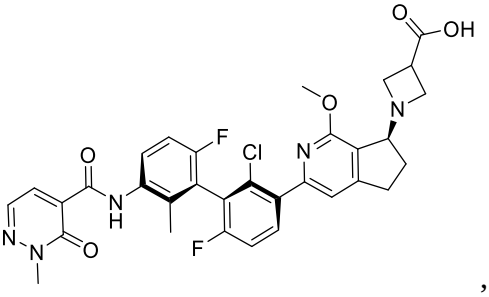
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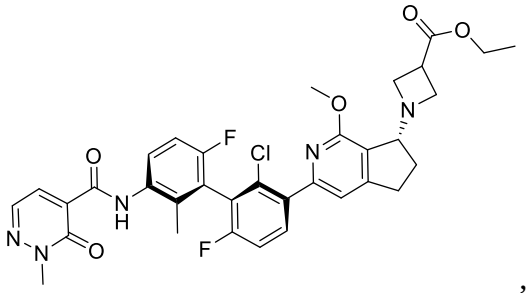
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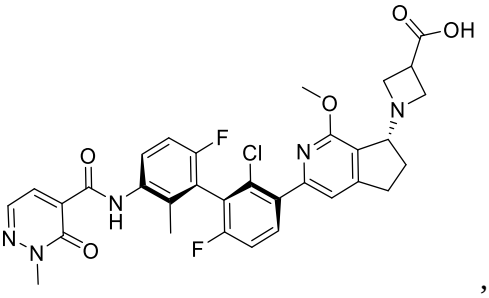
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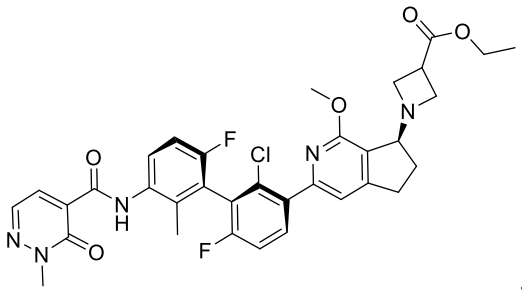
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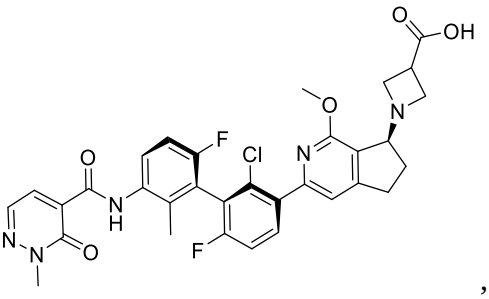
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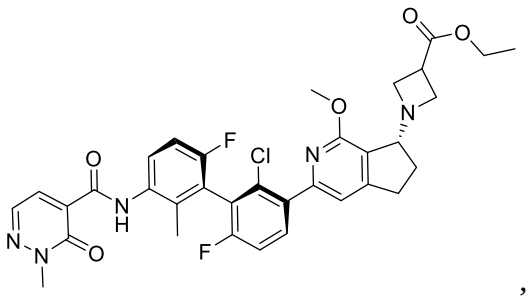
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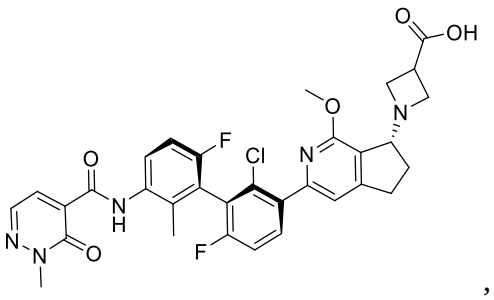
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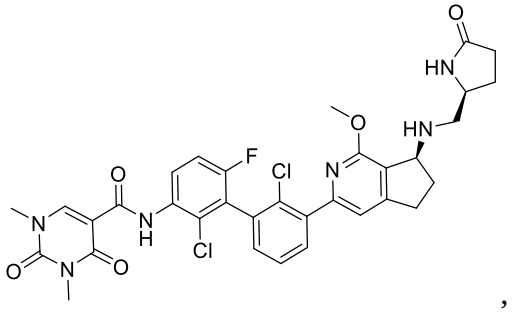
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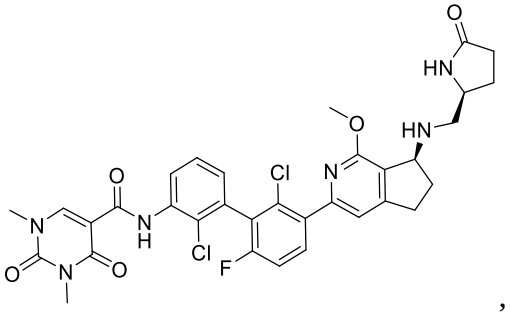
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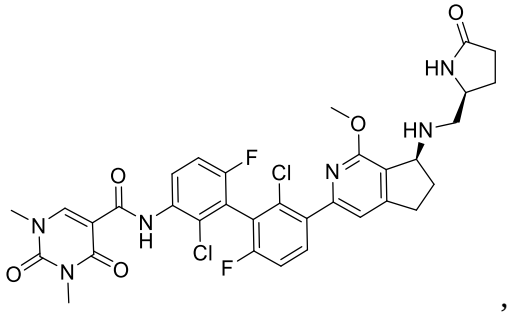
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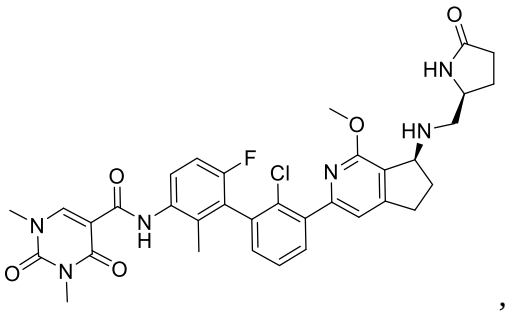
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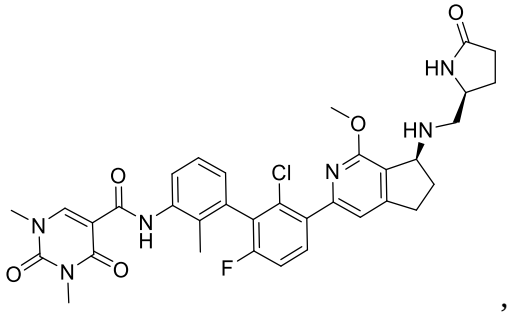
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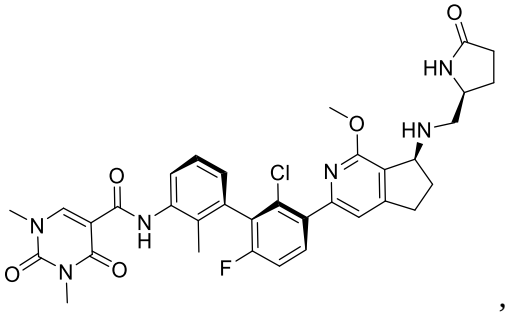
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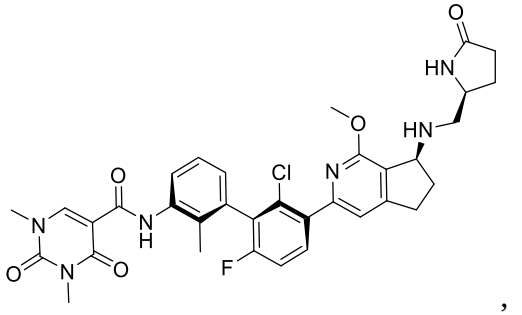
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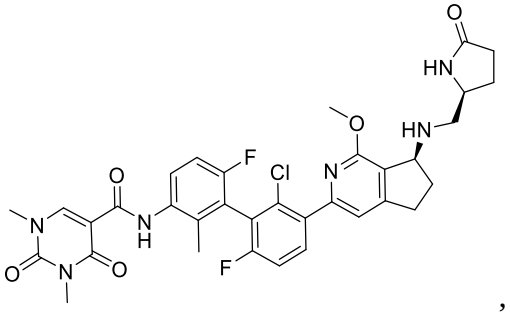
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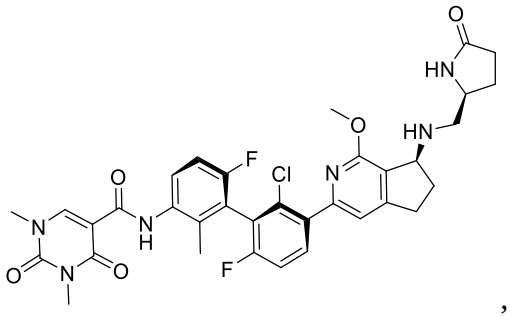
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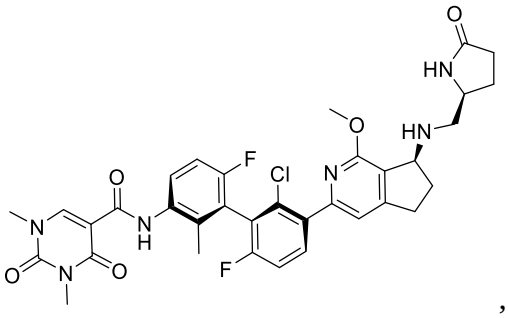
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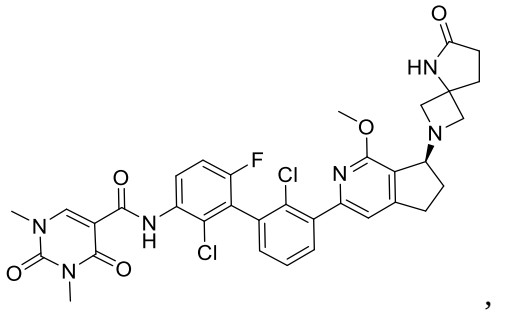
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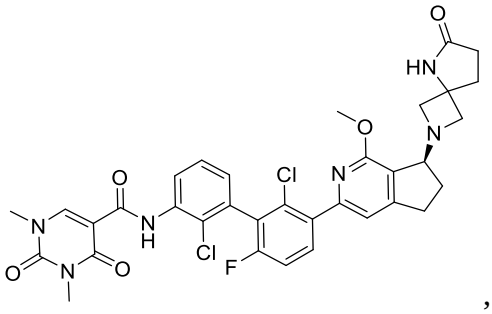
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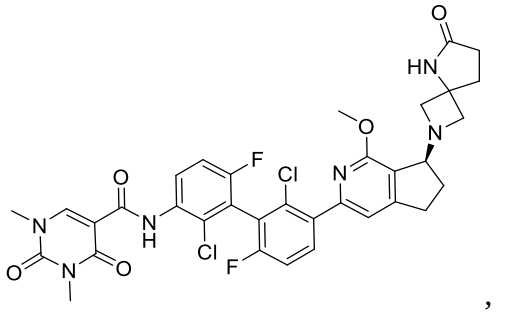
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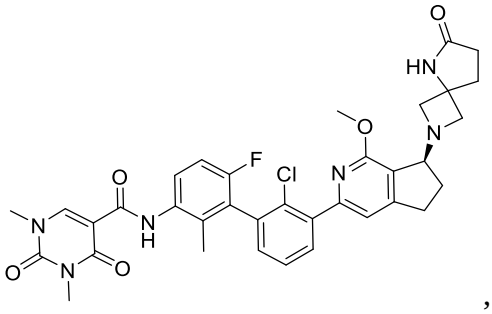
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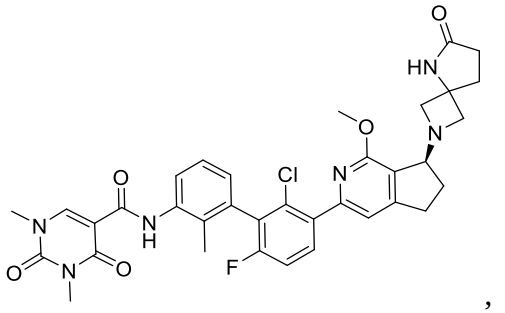
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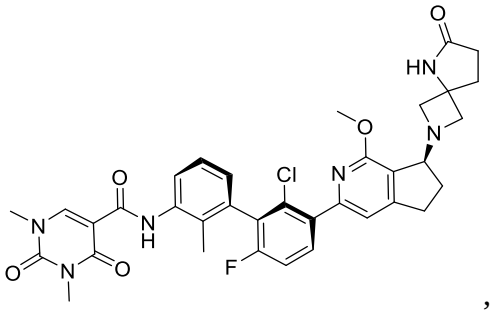
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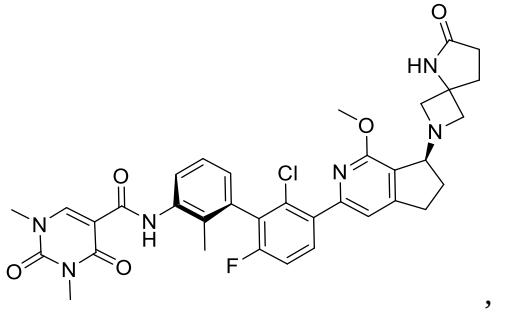
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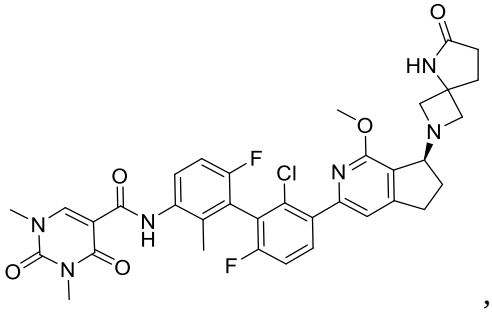
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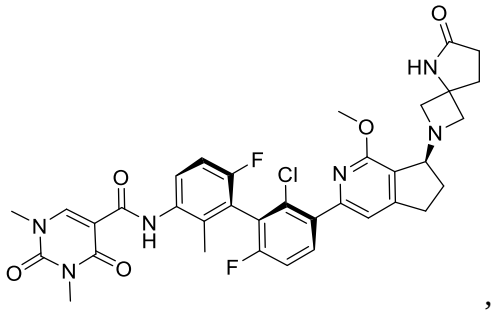
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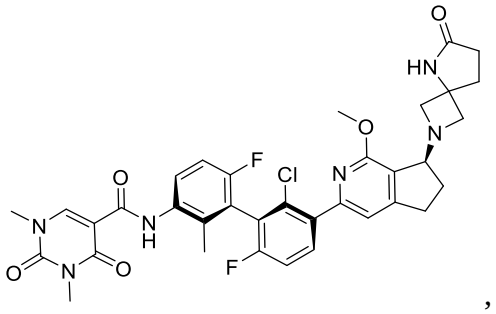
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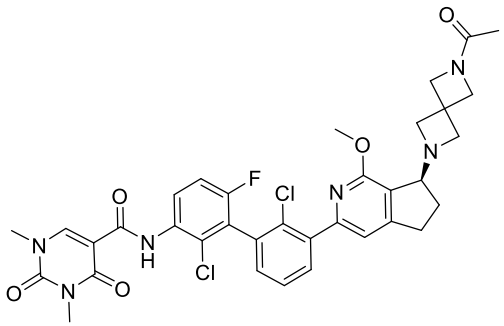
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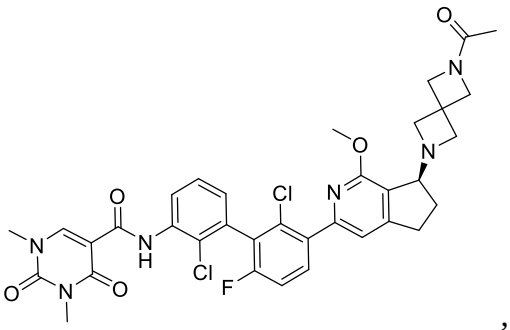
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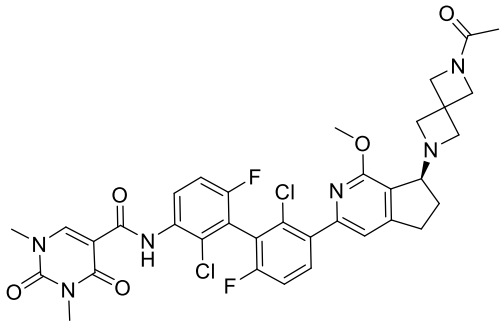
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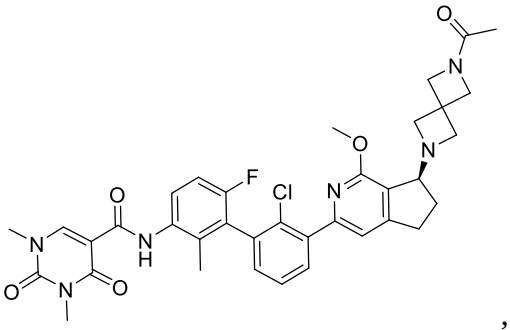
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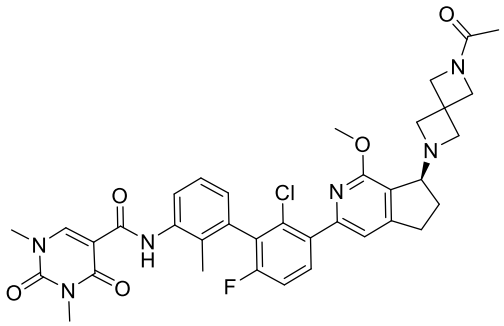
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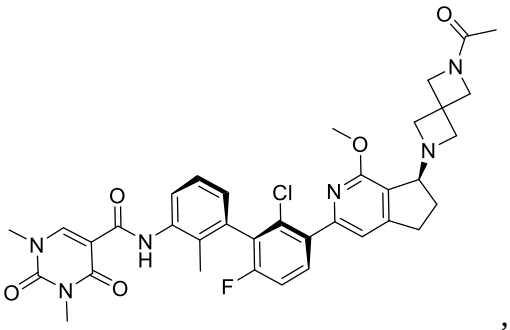
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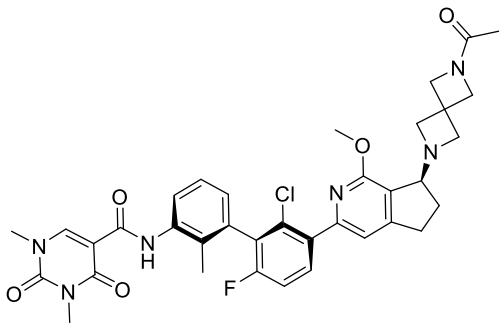
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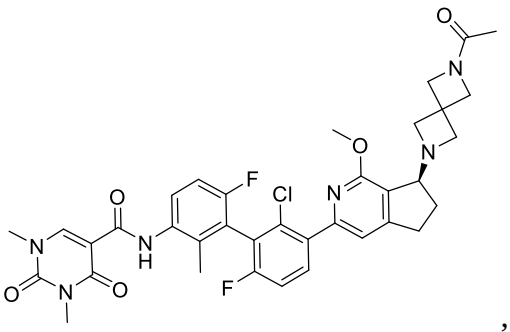
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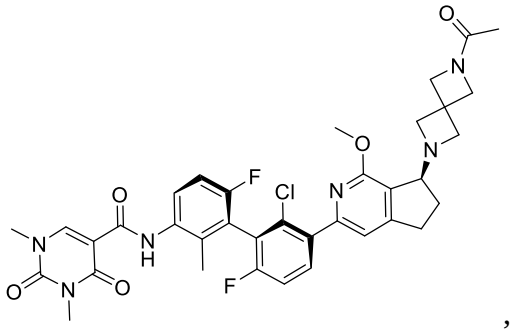
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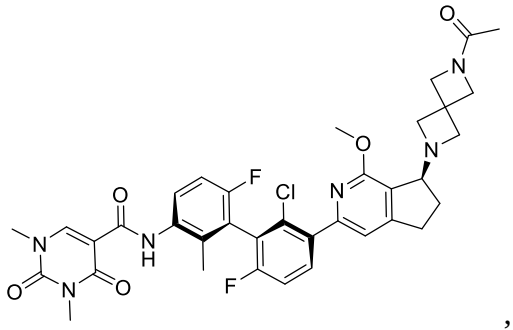
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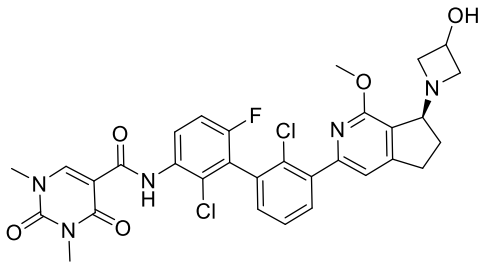
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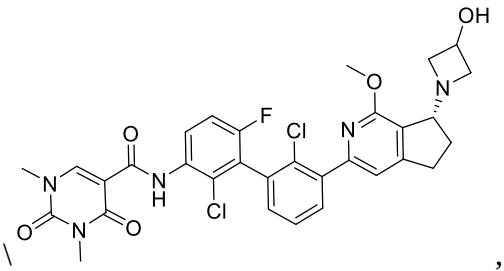
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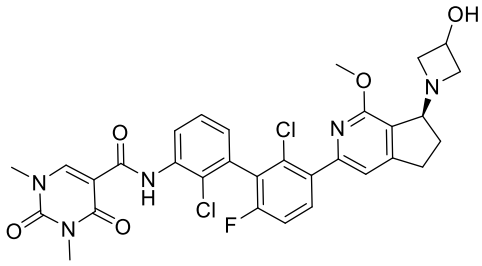
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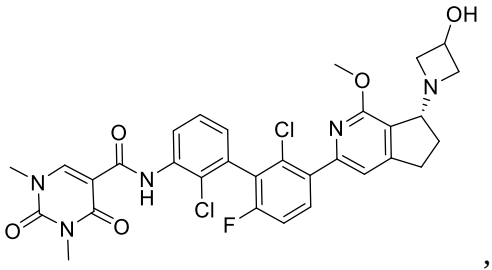
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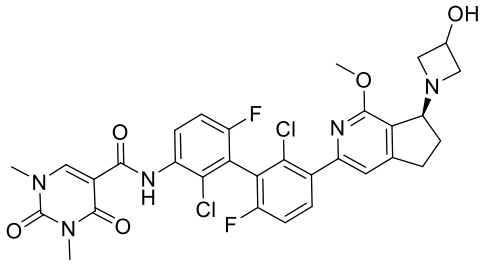
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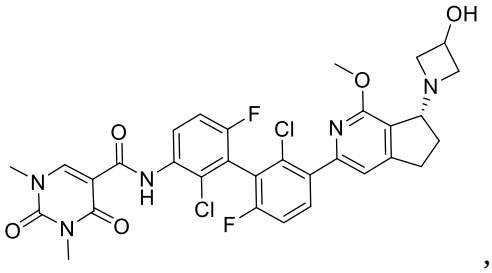
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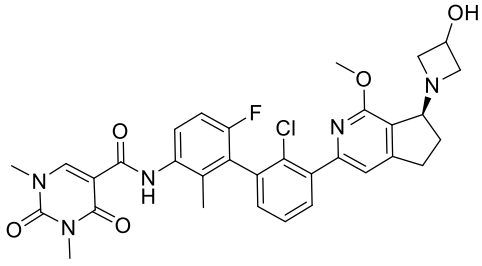
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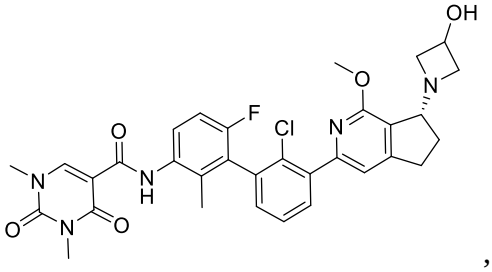
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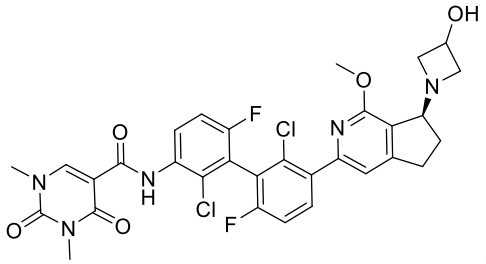
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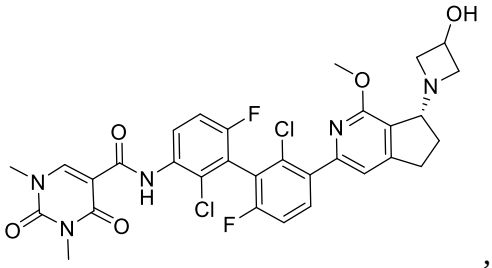
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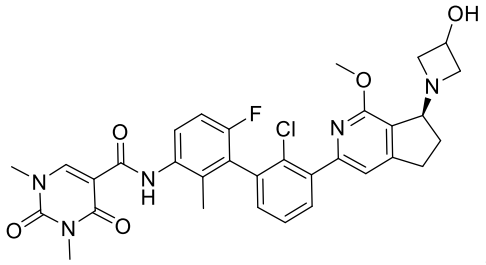
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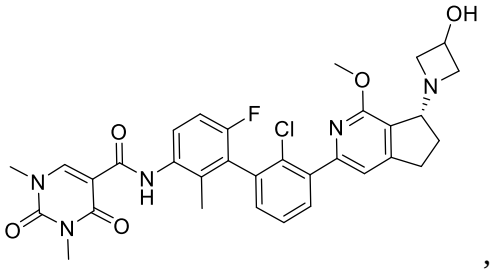
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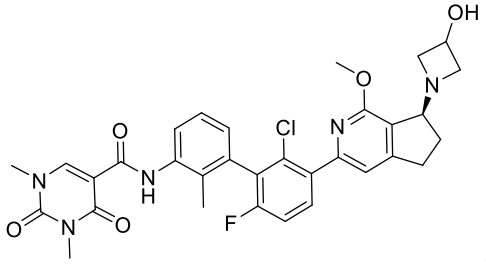
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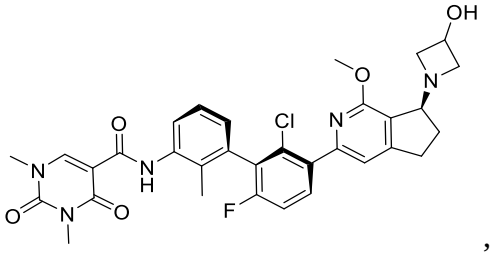
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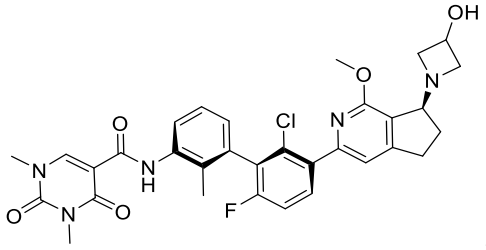
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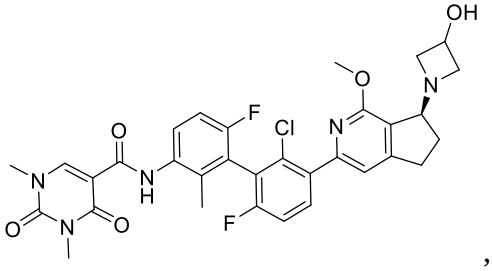
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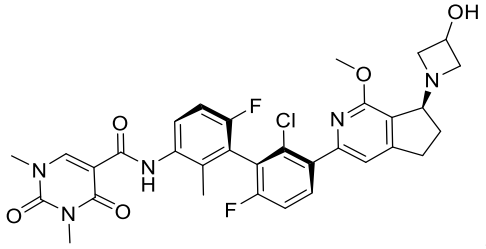
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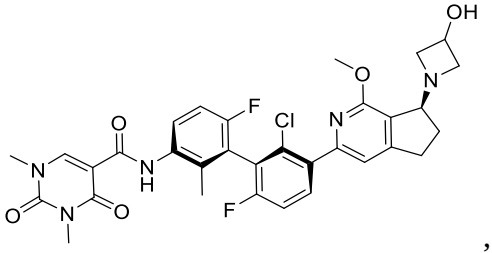
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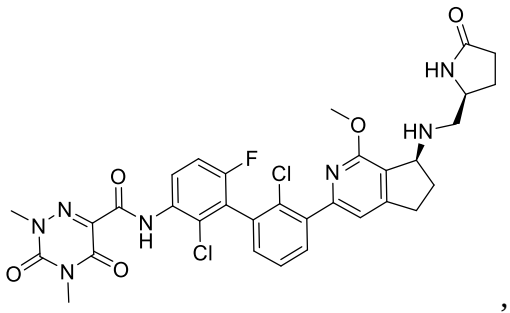
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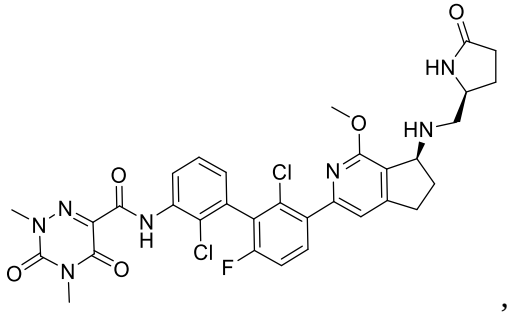
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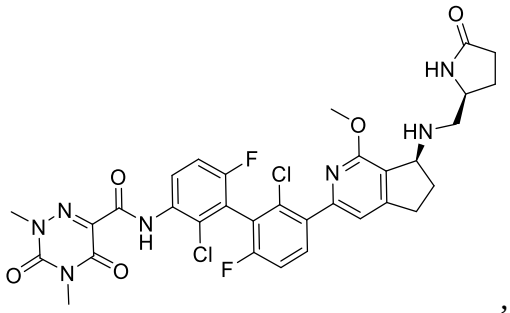
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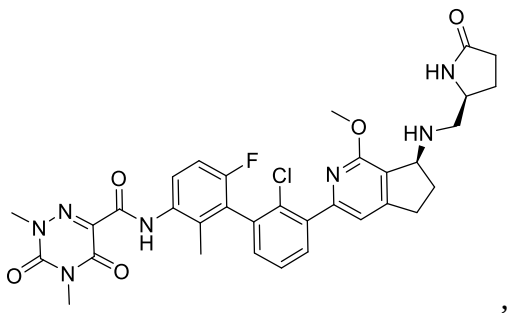
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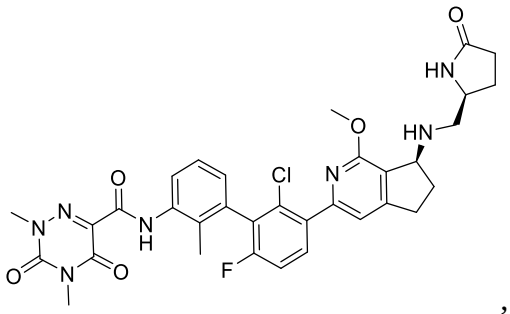
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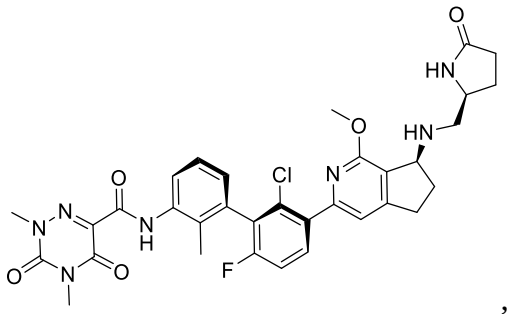
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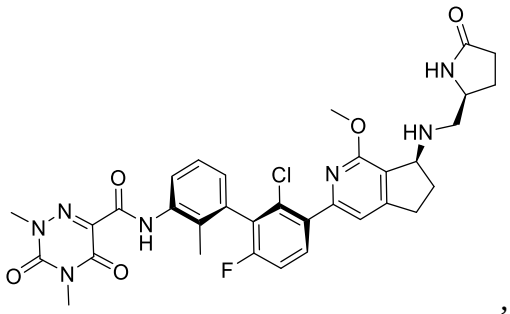
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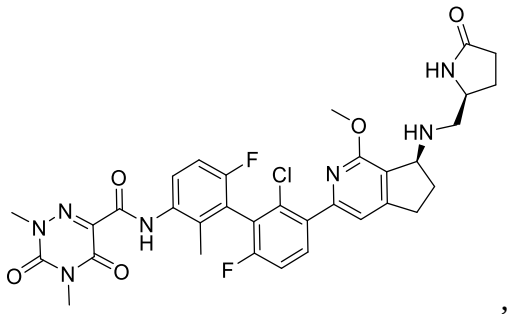
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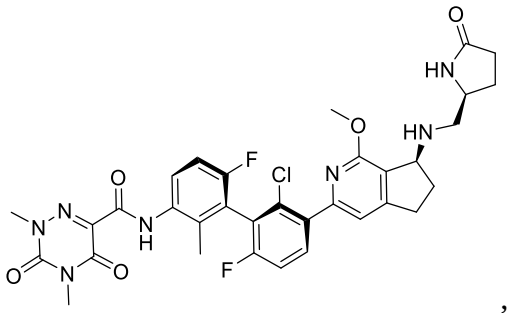
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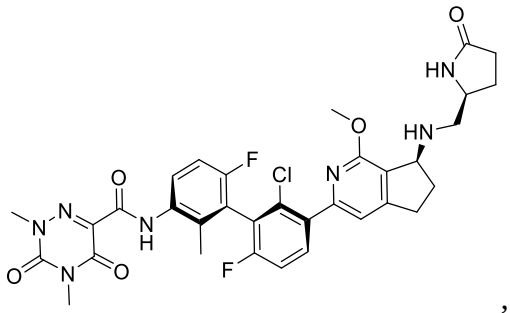
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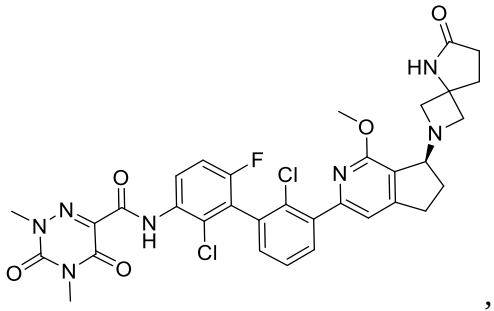
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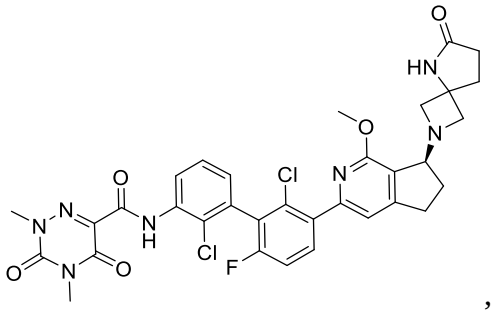
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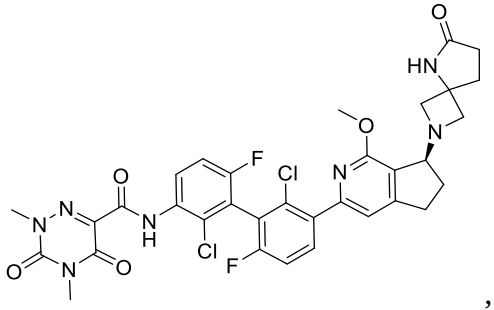
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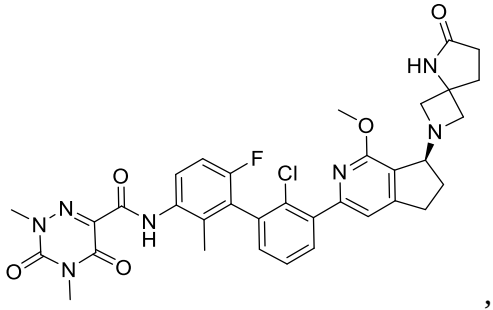
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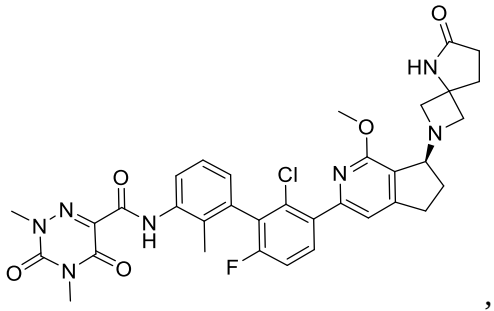
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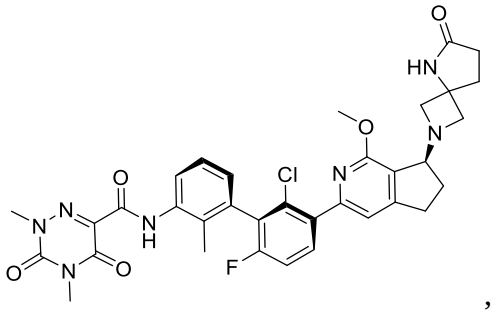
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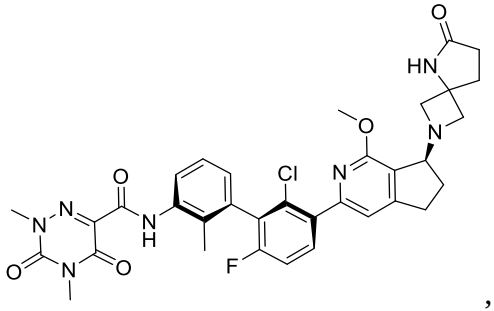
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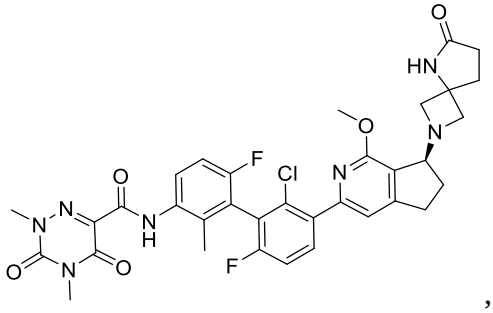
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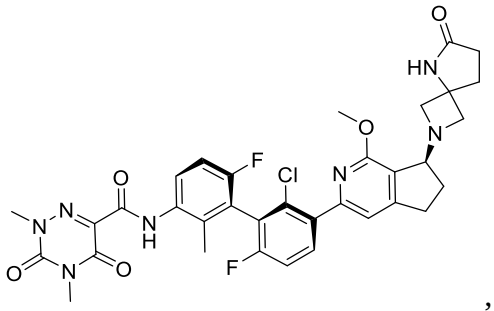
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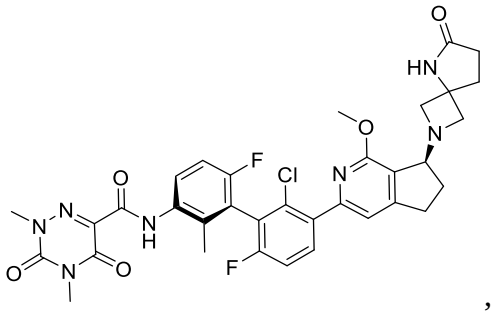
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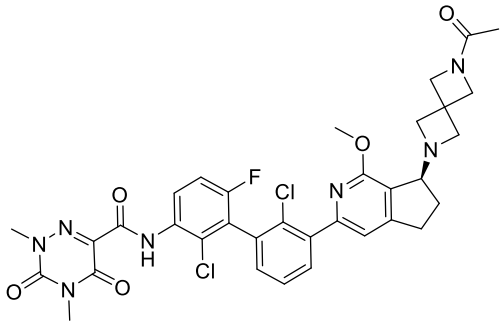
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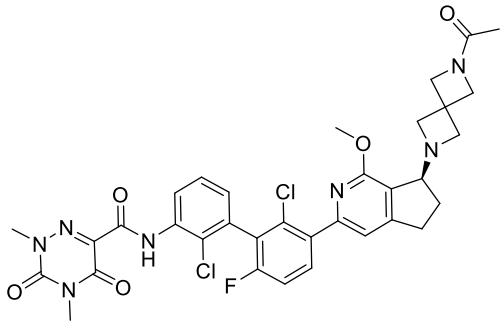
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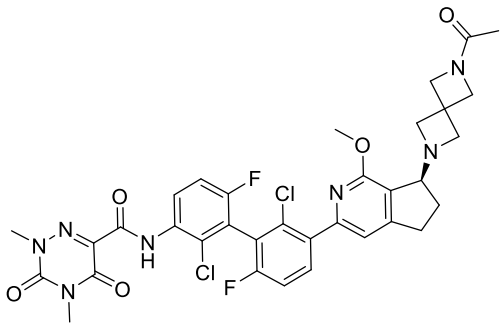
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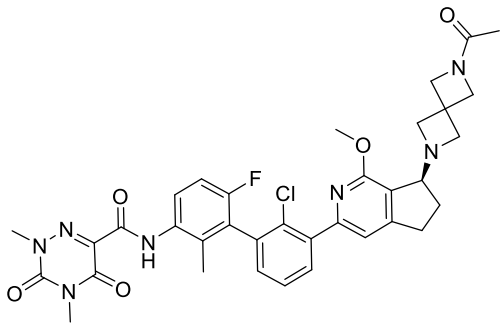
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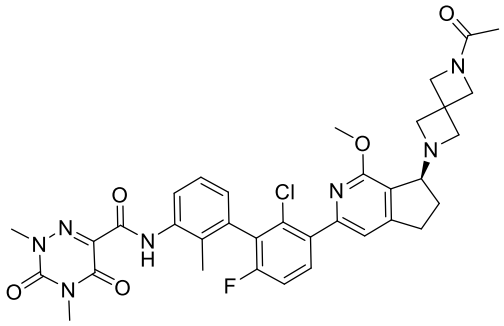
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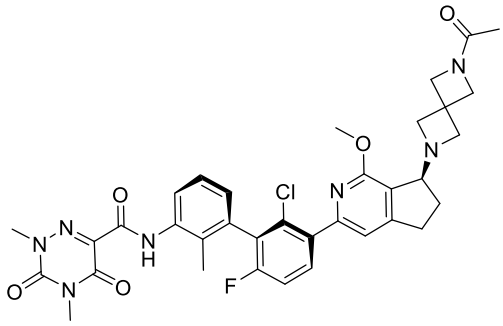
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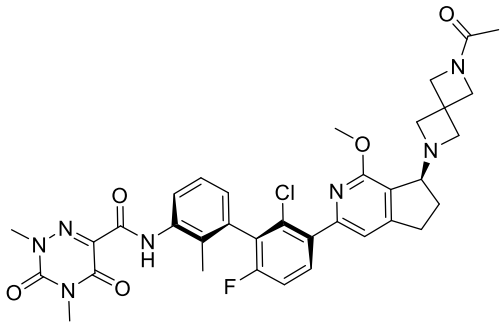
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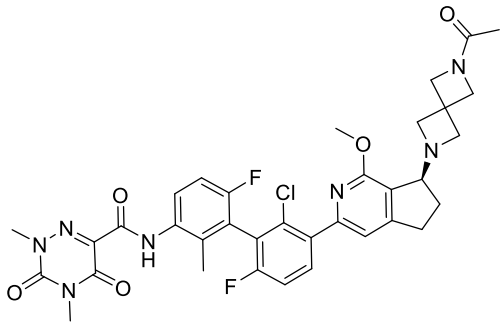
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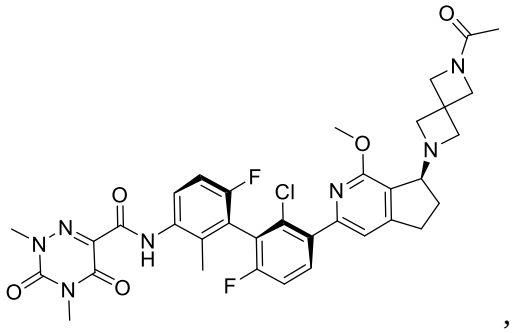
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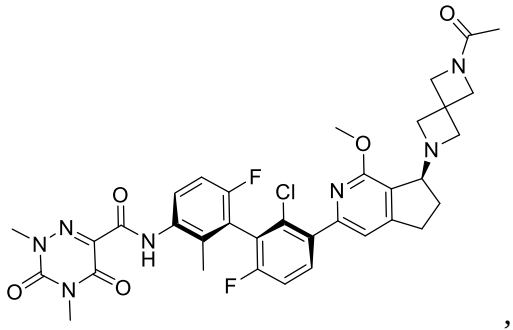
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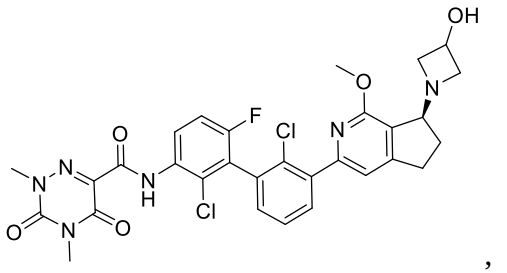
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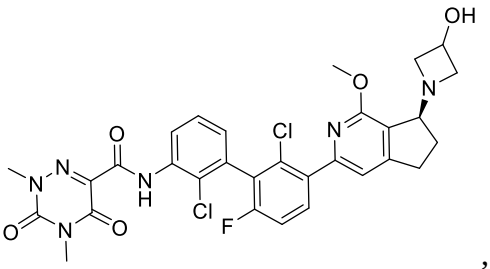
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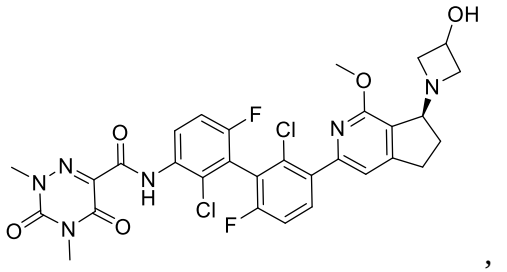
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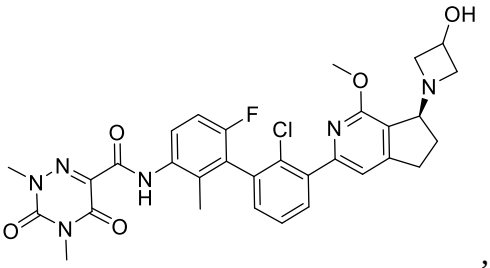
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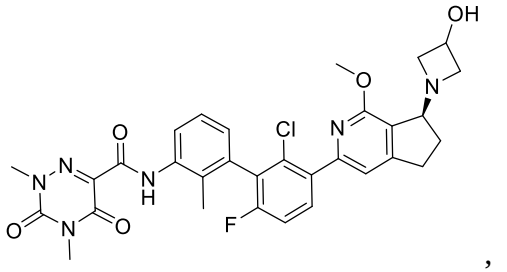
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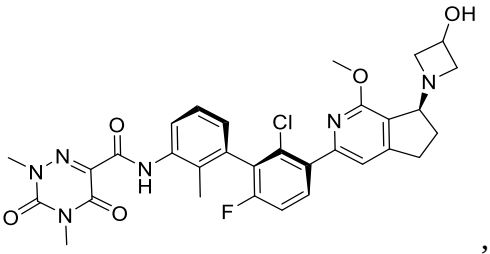
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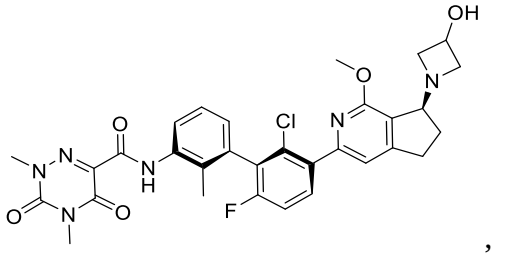
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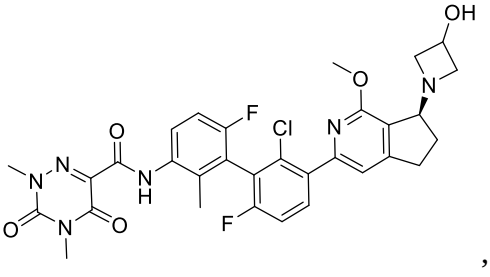
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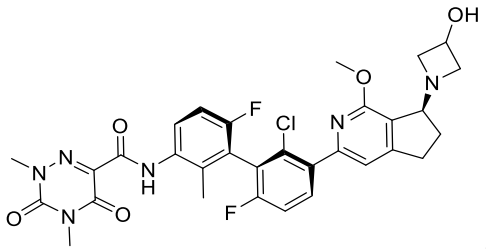
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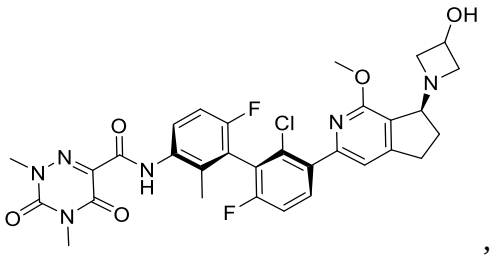
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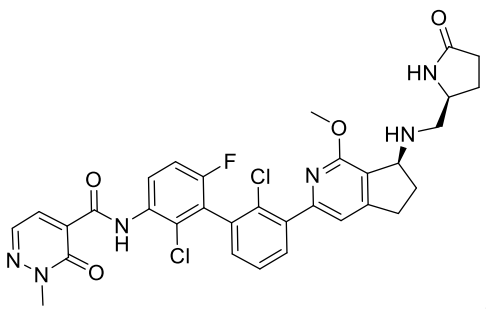
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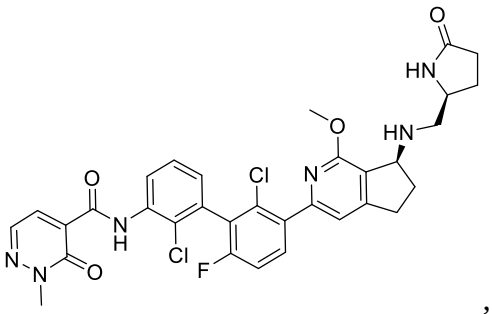
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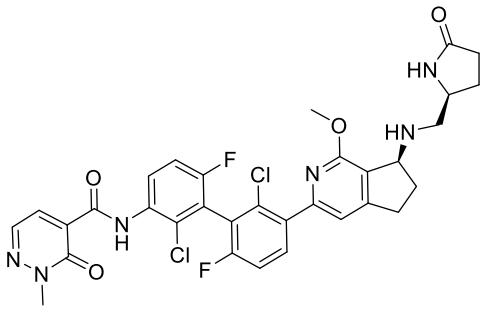
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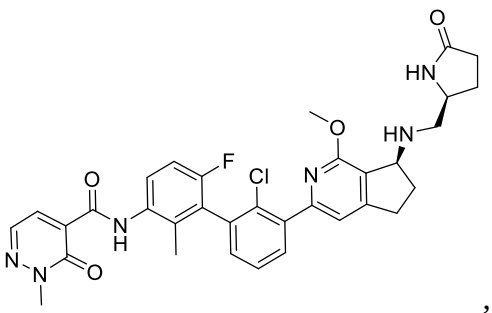
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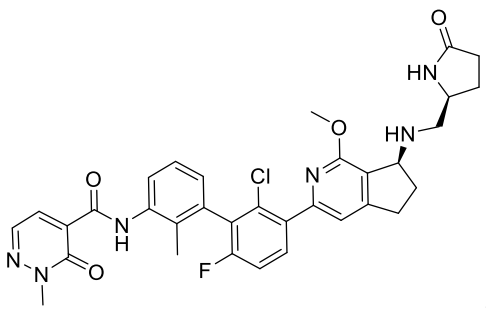
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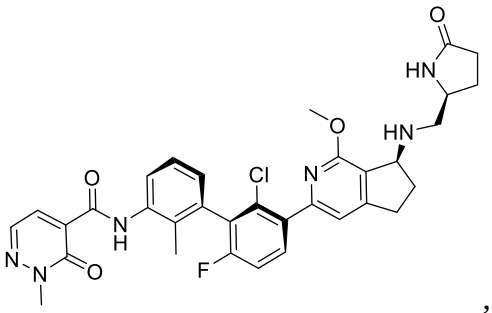
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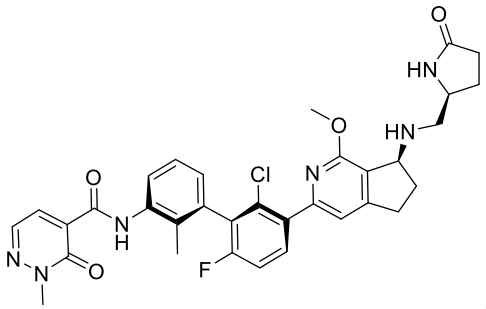
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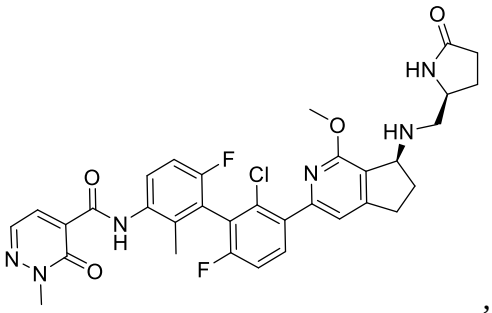
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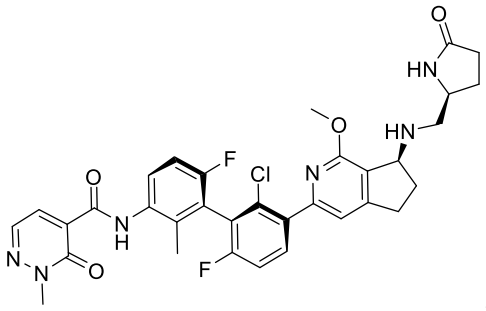
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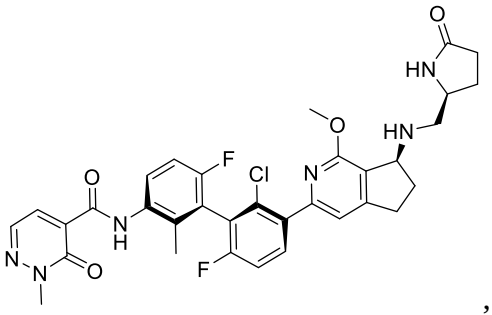
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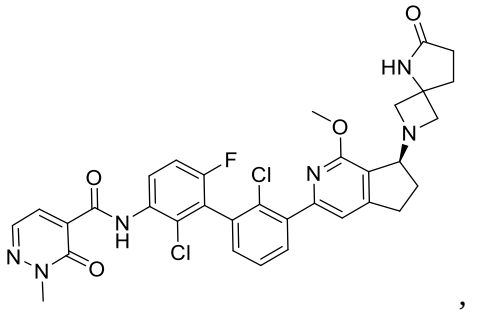
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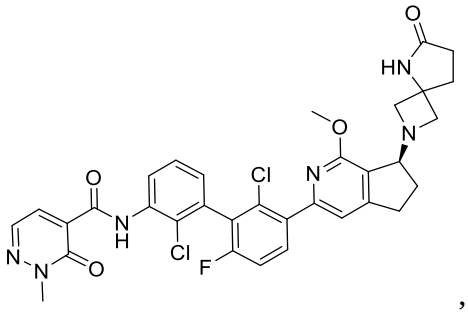
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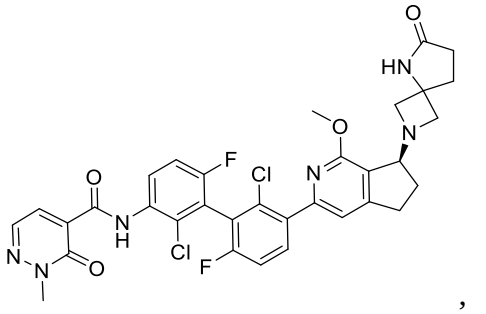
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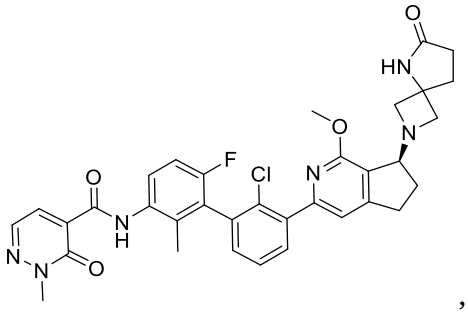
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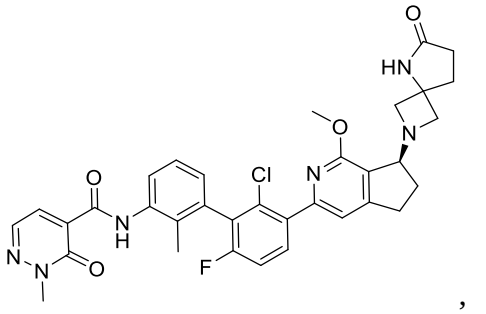
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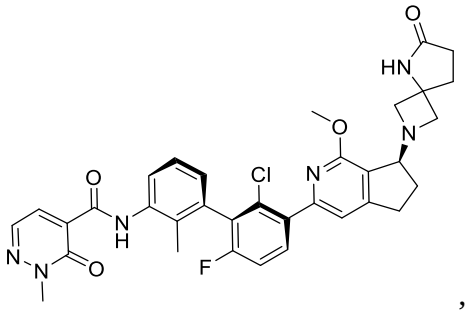
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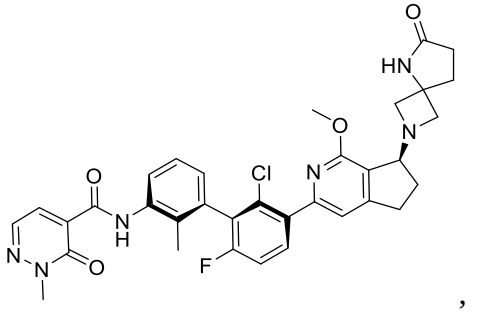
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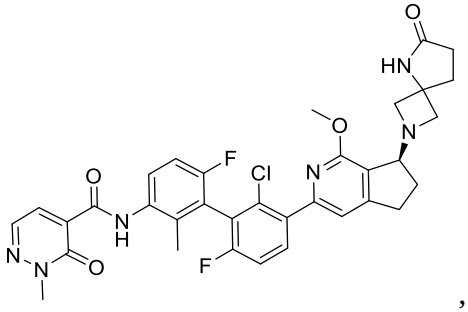
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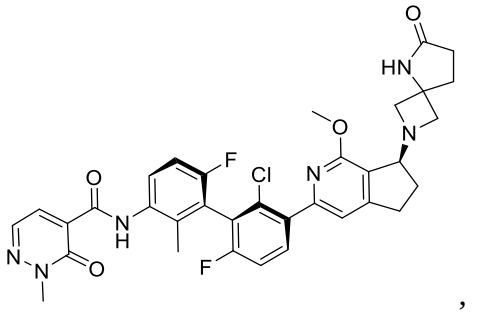
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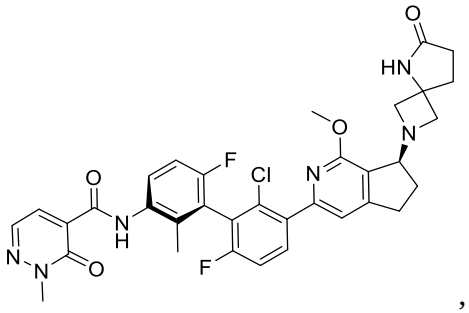
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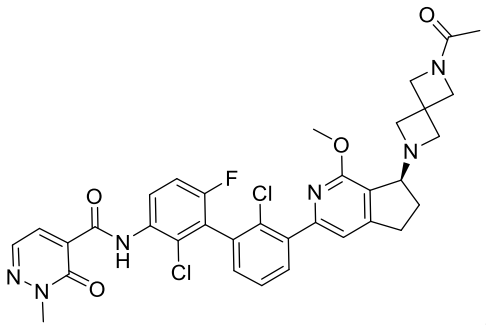
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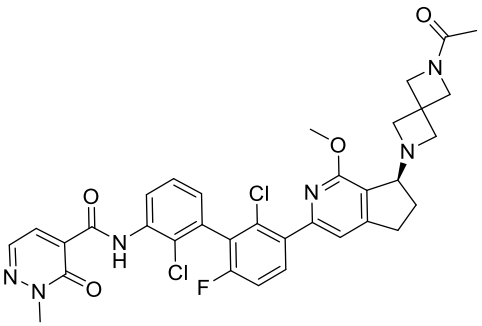
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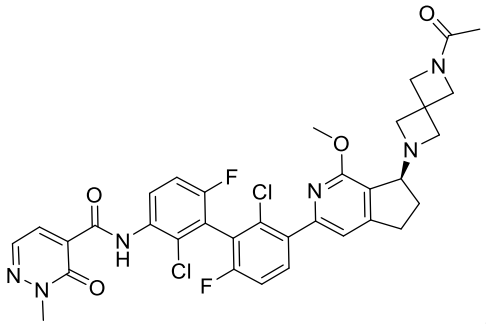
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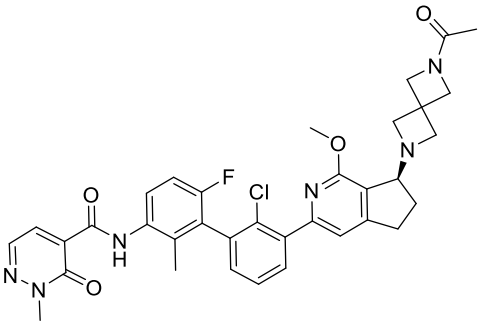
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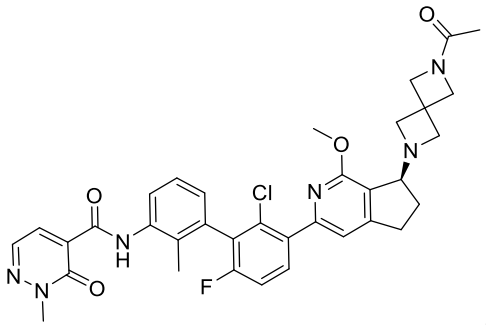
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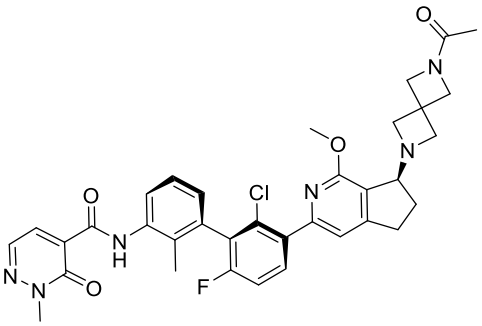
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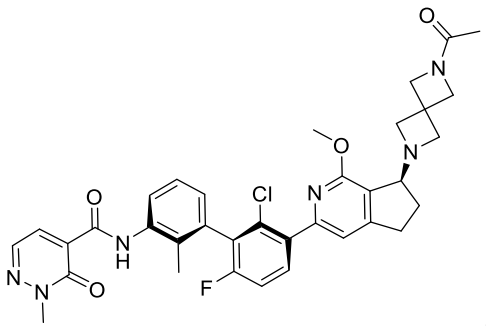
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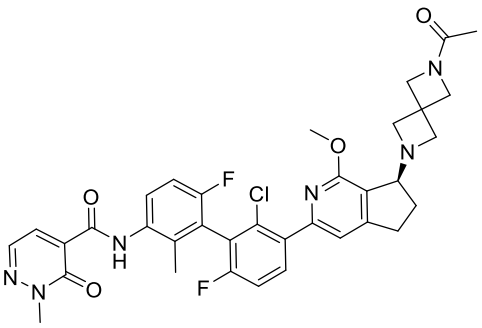
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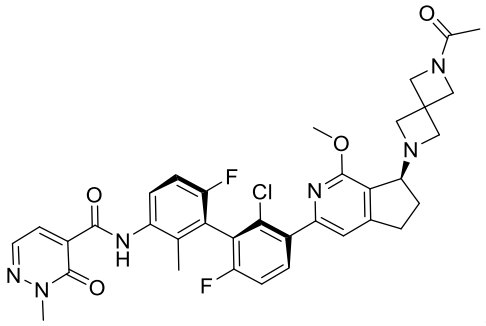
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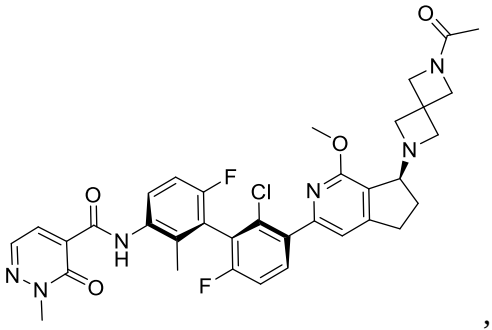
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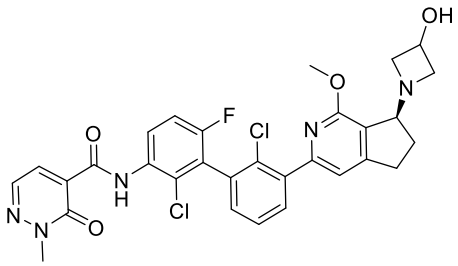
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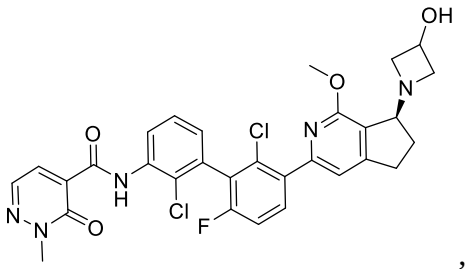
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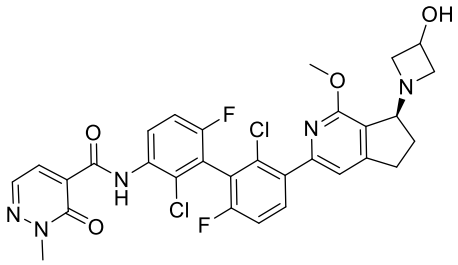
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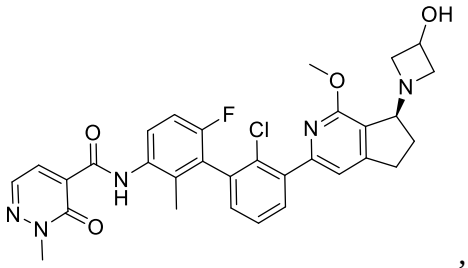
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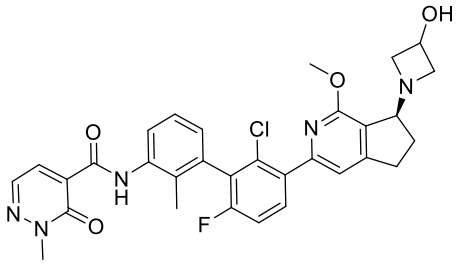
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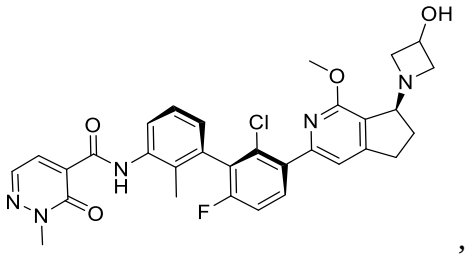
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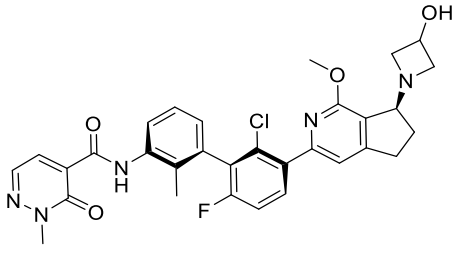
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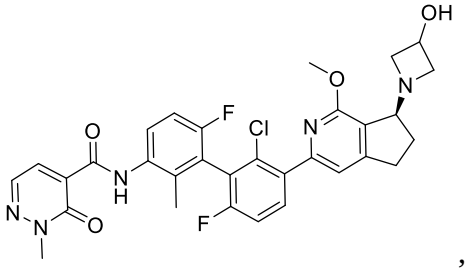
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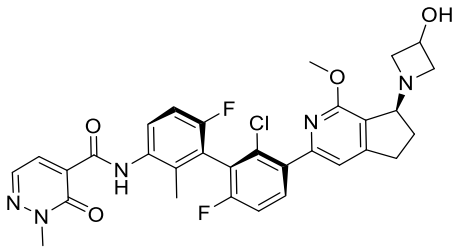
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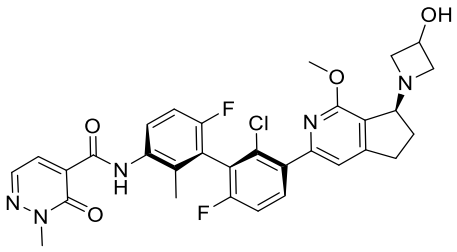
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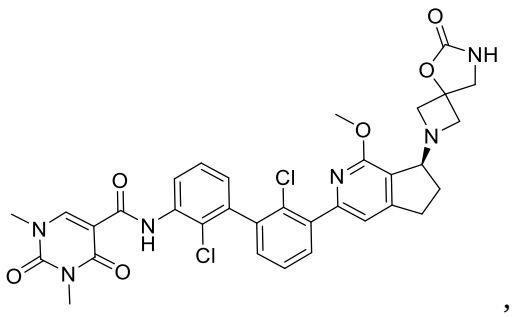
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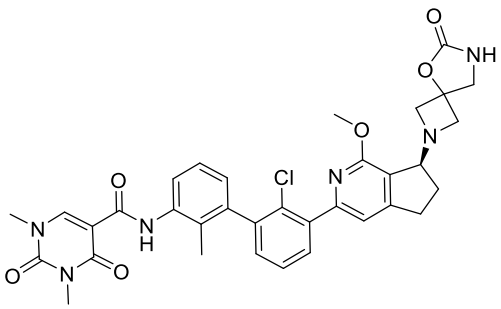
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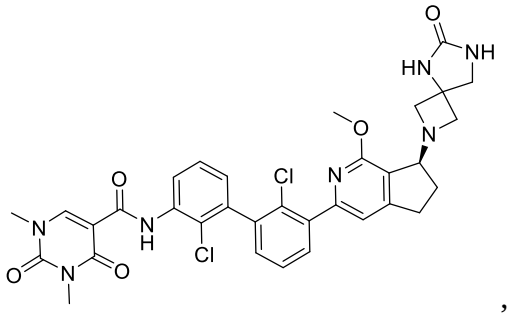
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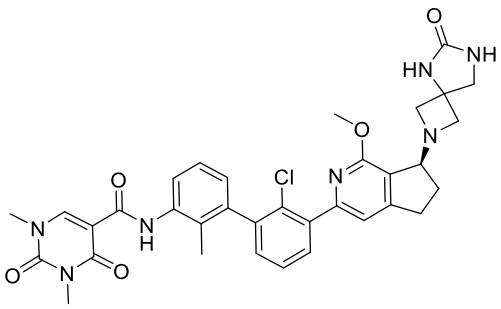
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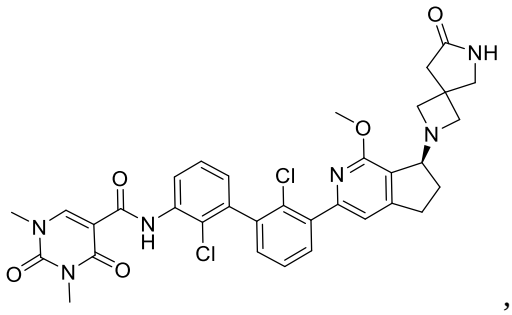
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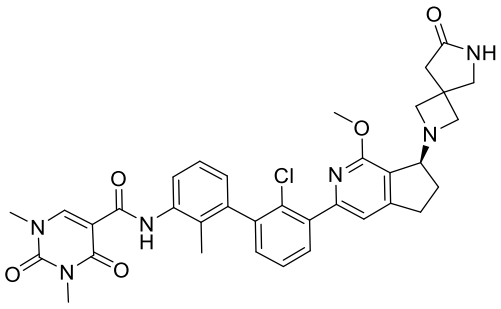
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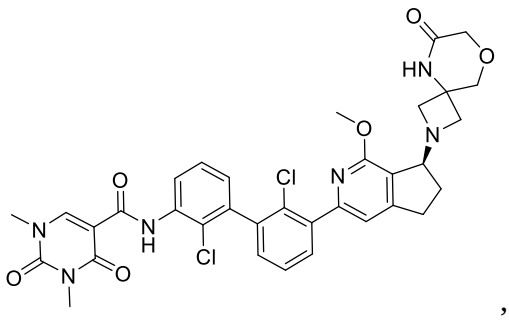
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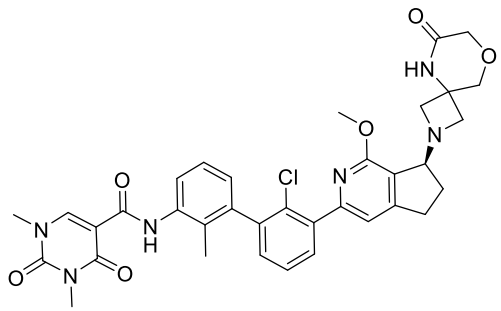
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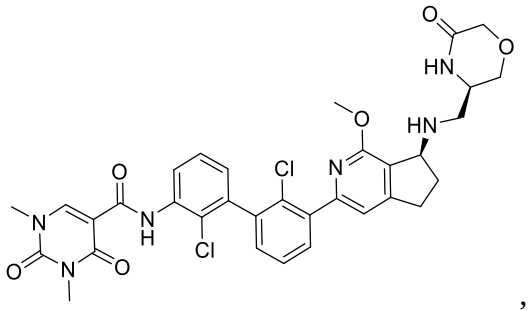
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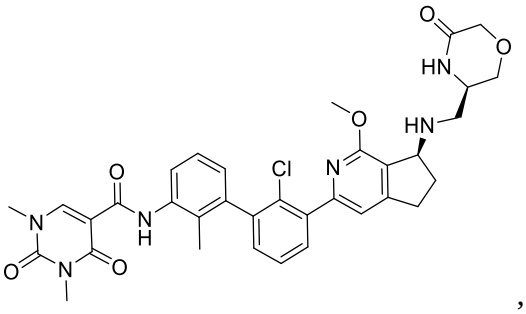
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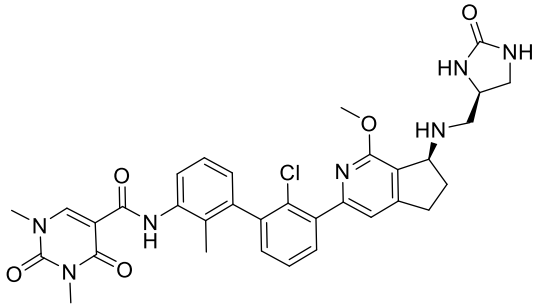
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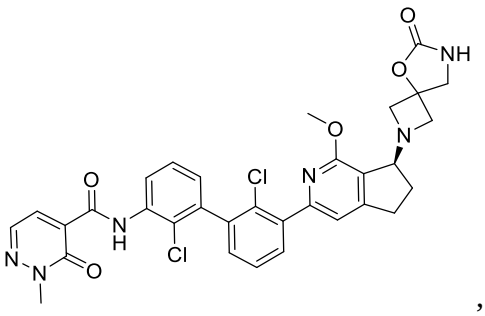
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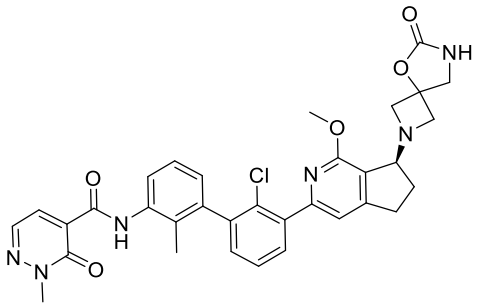
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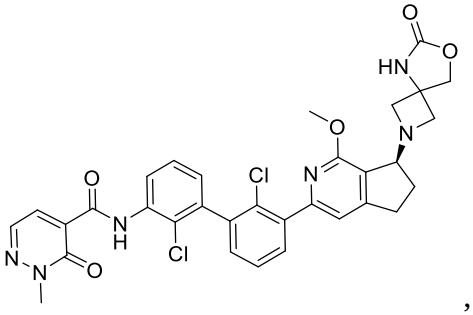
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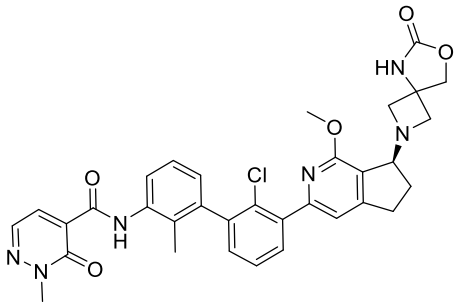
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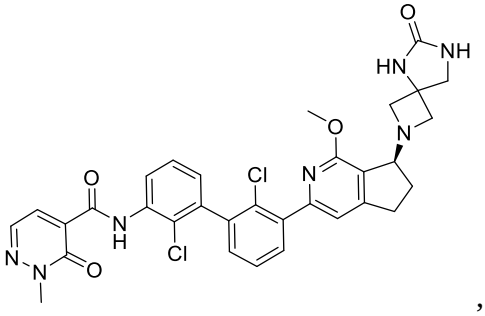
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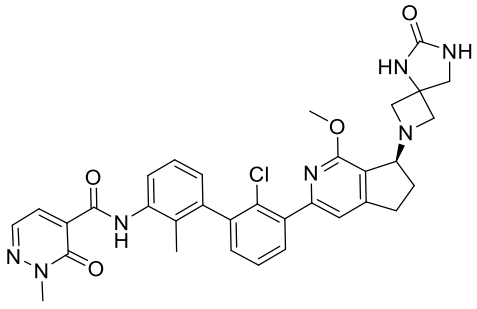
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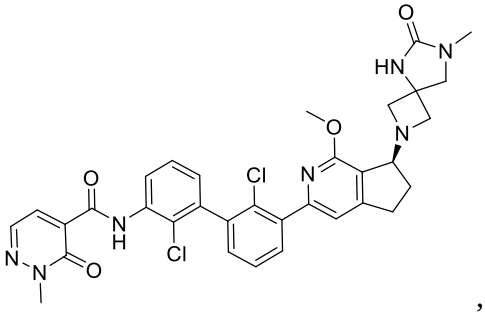
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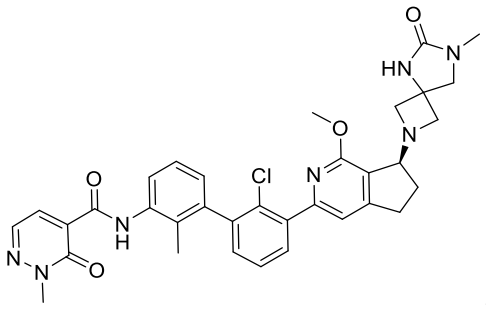
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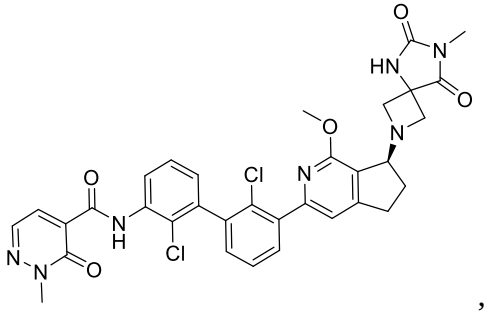
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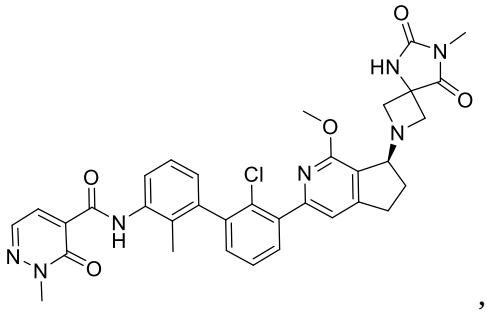
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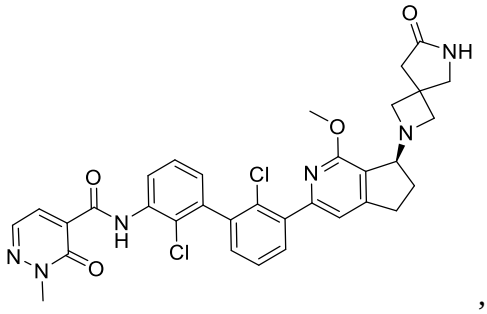
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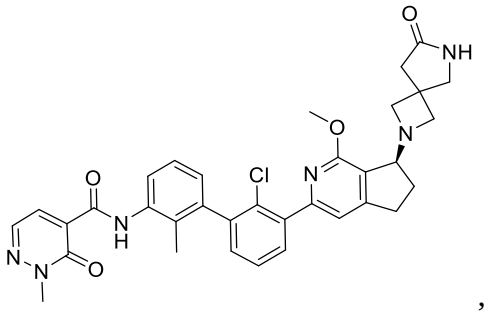
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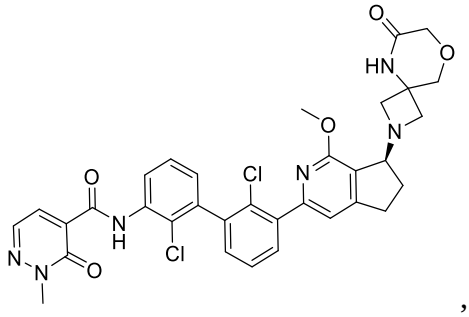
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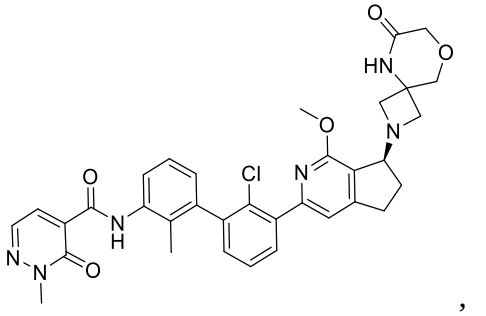
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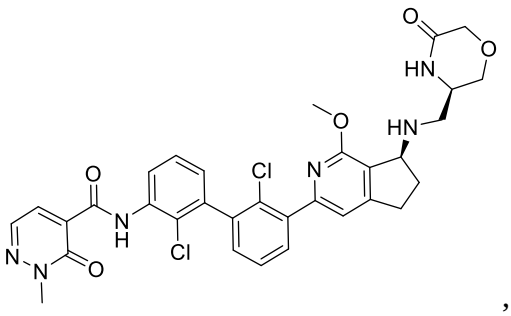
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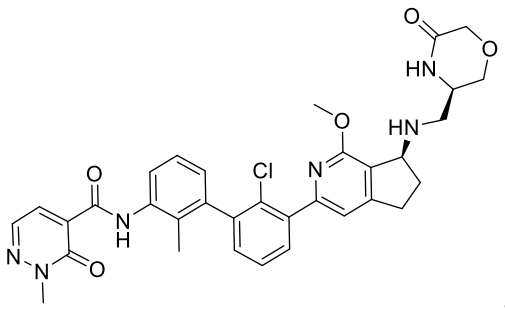
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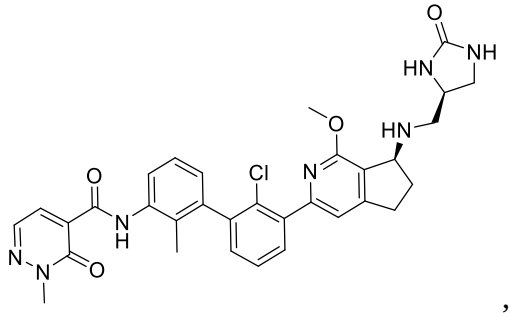
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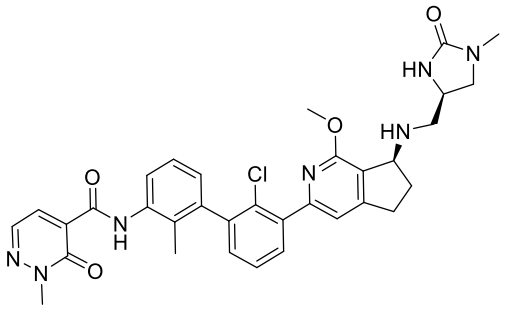
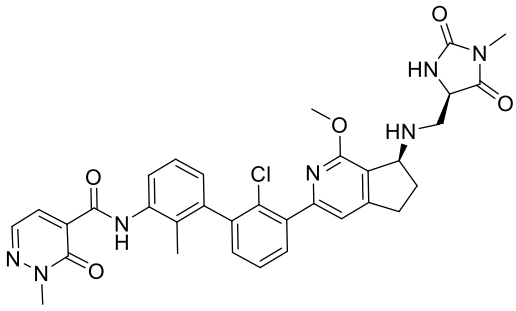
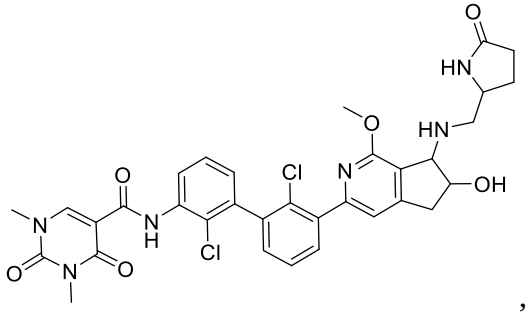
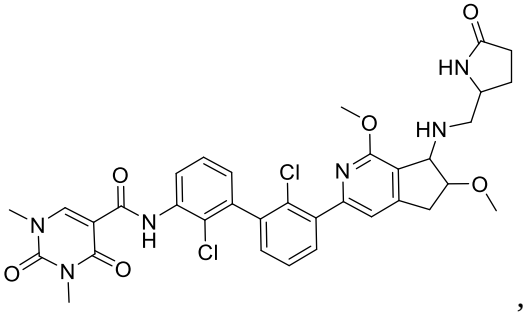
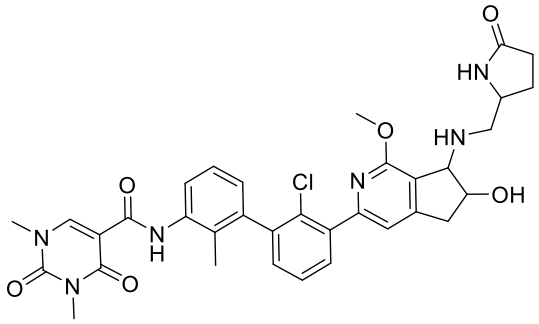
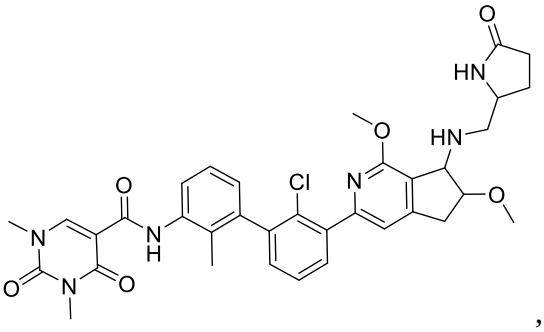
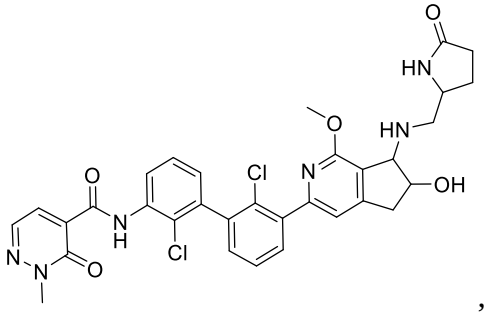
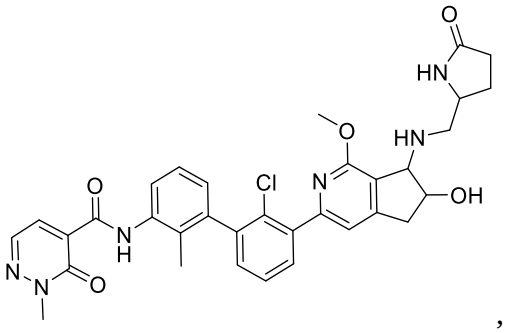
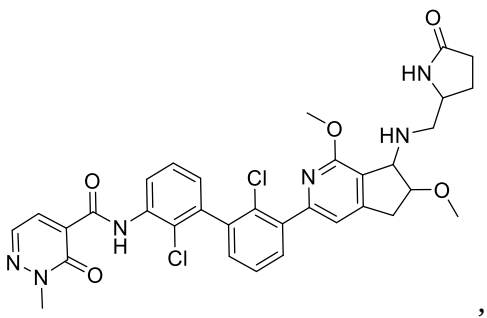
 and  , or a pharmaceutically acceptable salt of any of the foregoing.

146. The compound of Claim 1 selected from the group consisting of:

 ,  ,

 ,  ,

 ,  ,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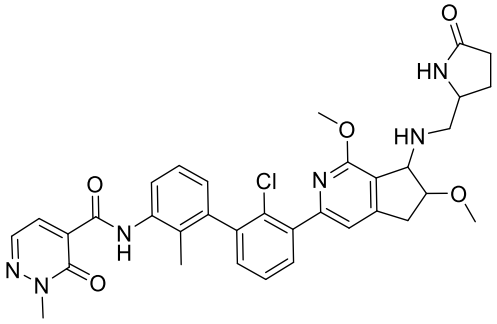
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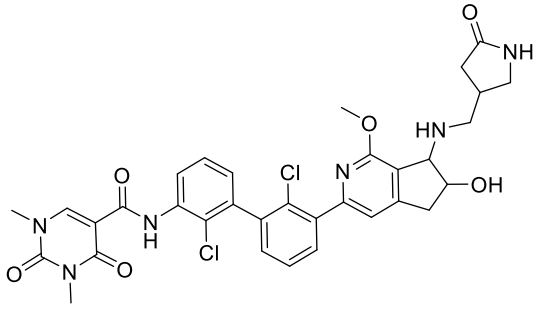
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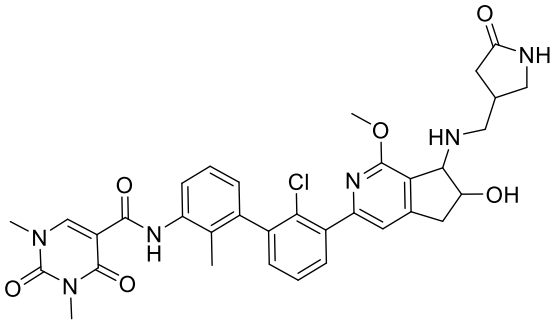
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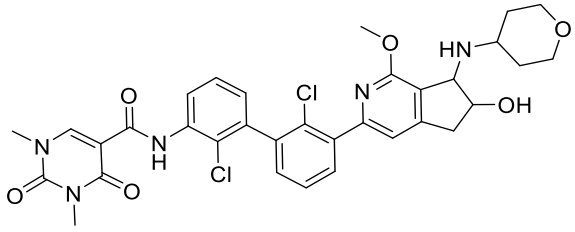
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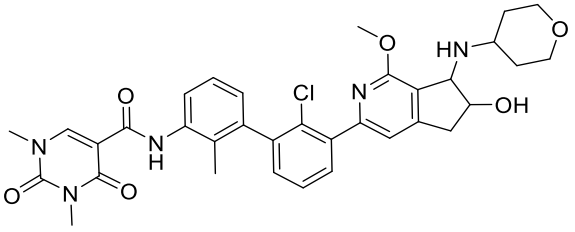
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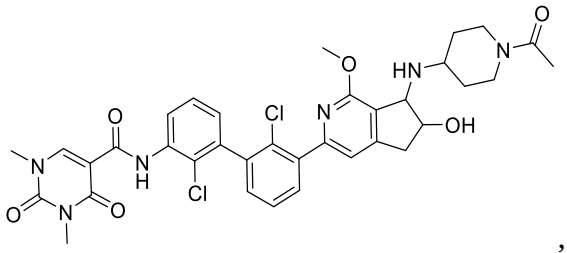
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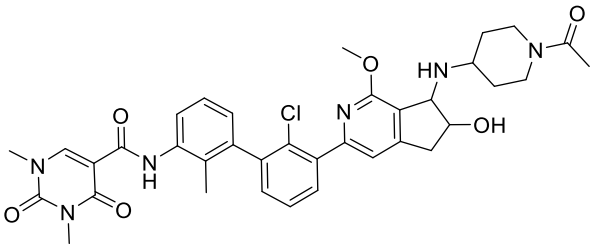
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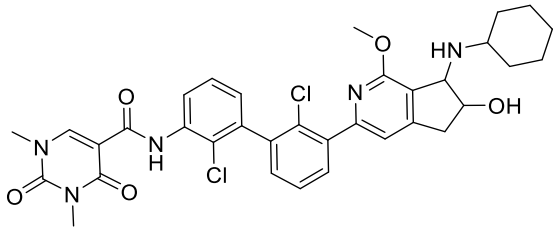
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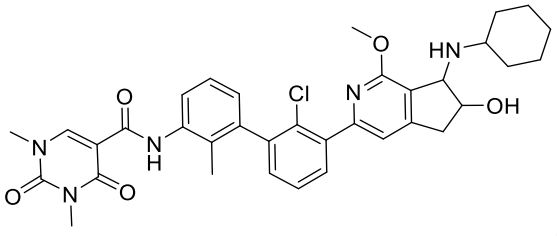
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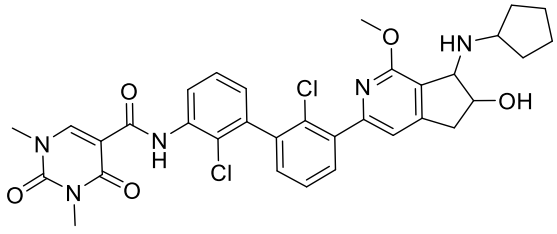
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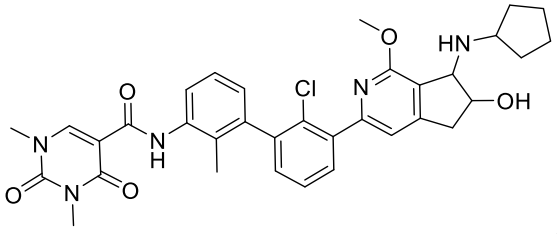
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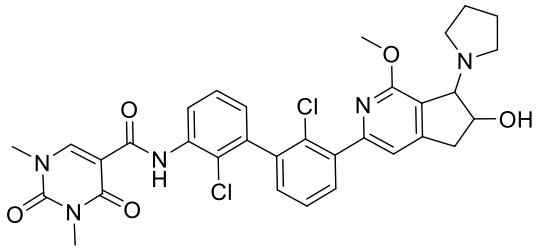
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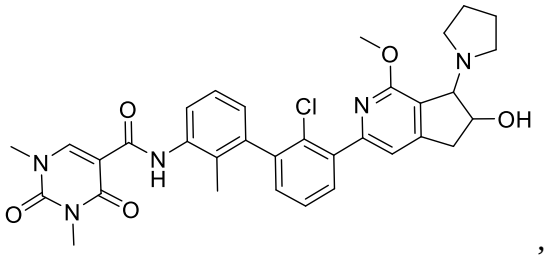
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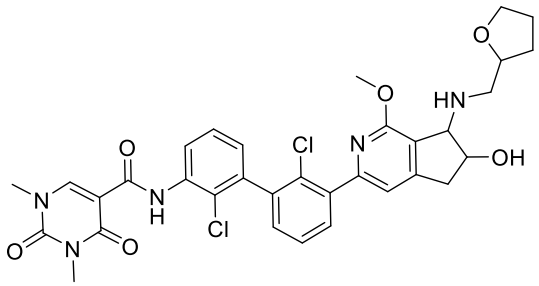
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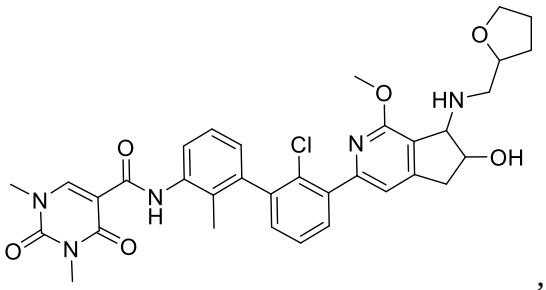
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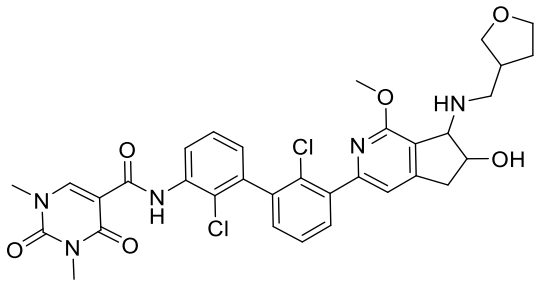
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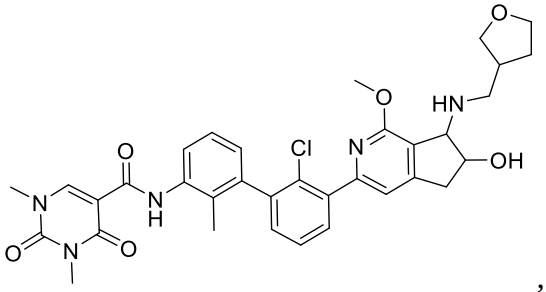
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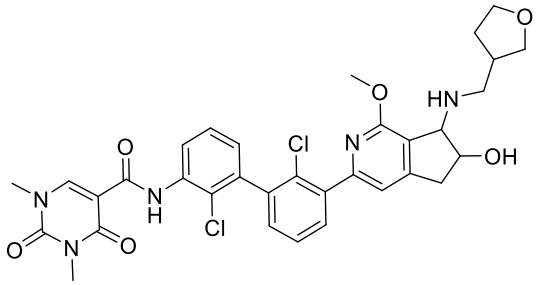
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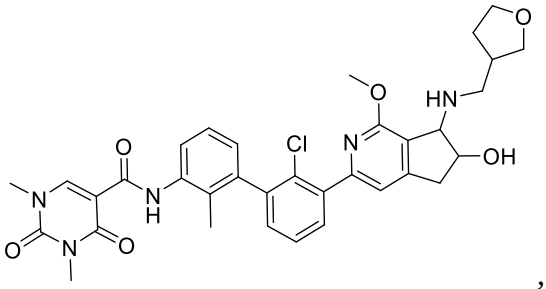
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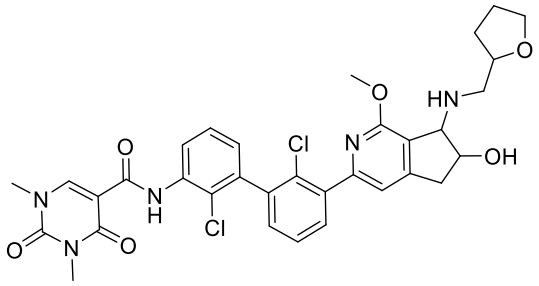
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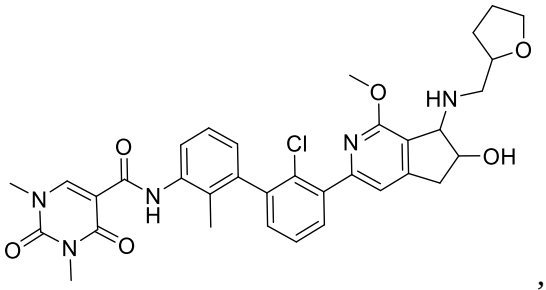
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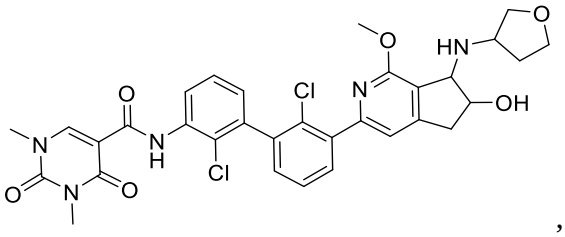
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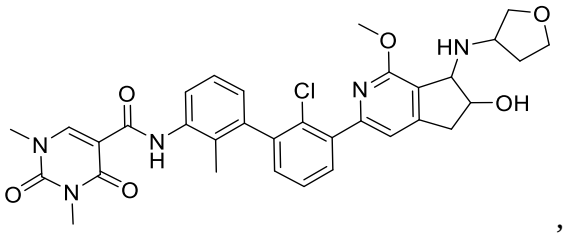
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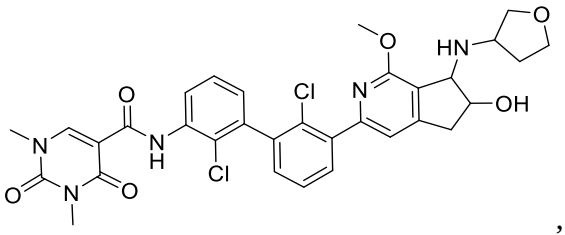
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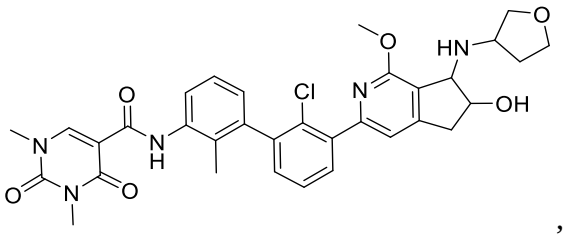
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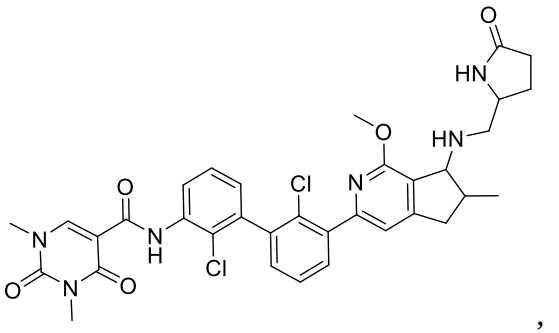
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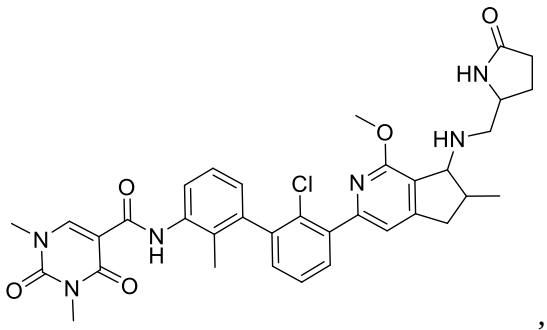
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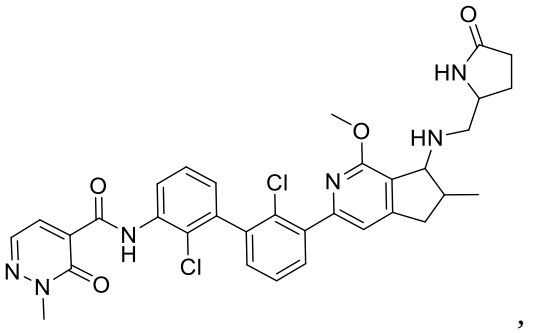
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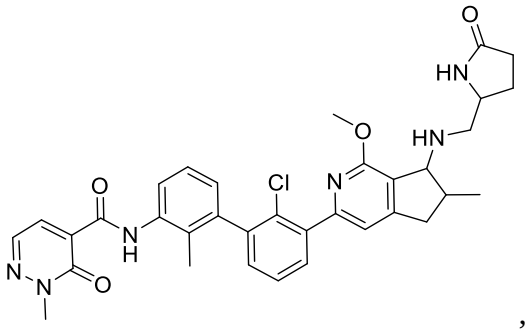
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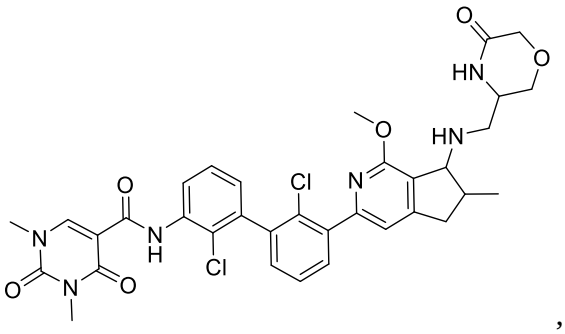
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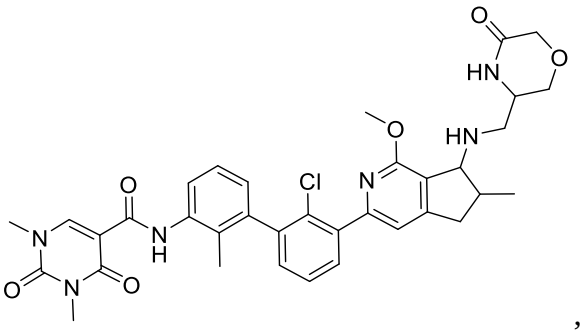
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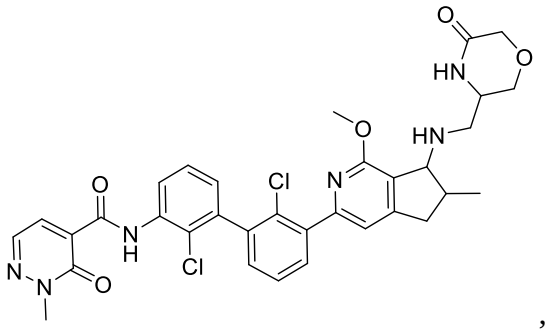
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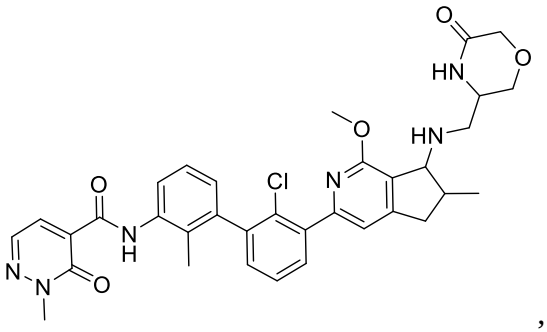
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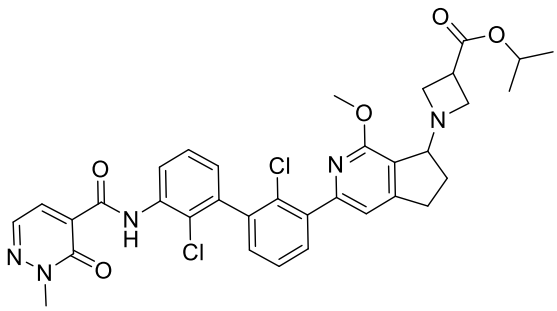
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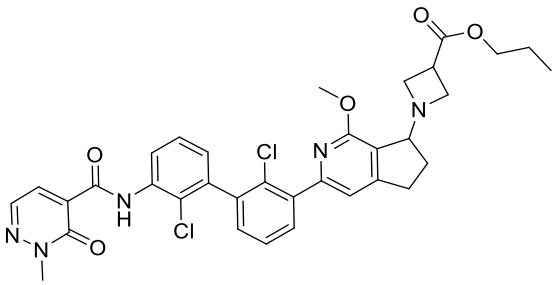
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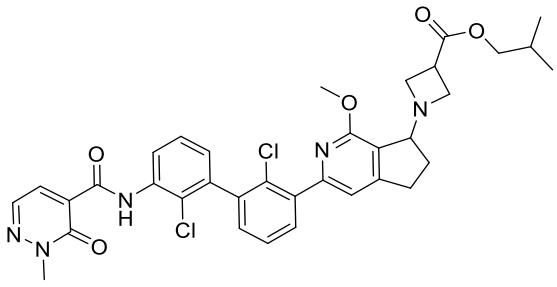
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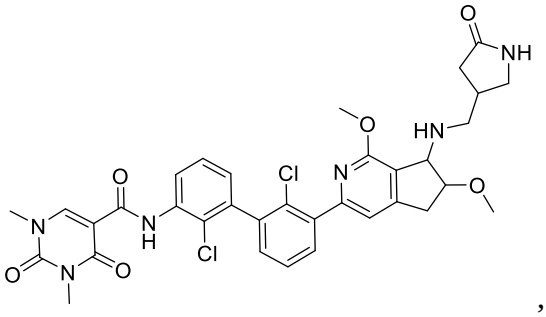
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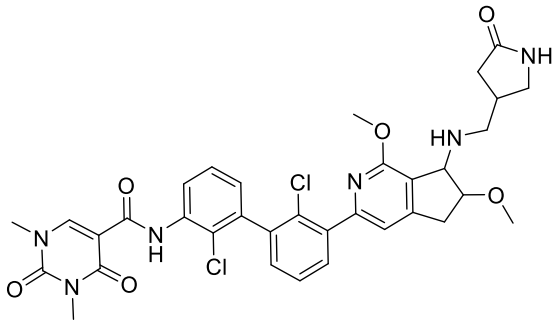
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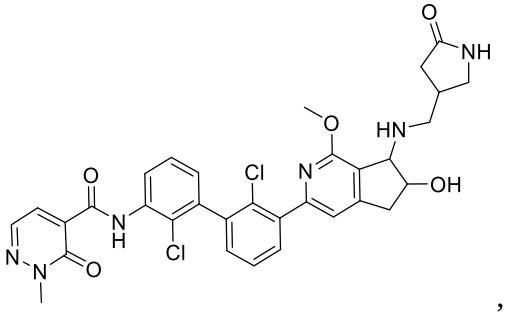
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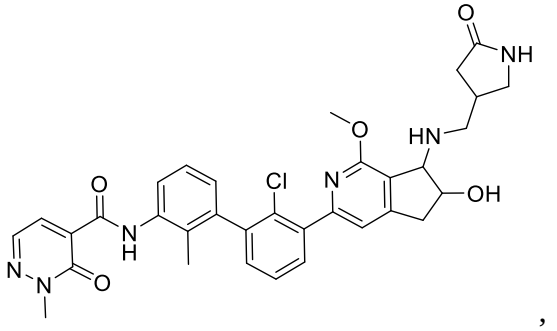
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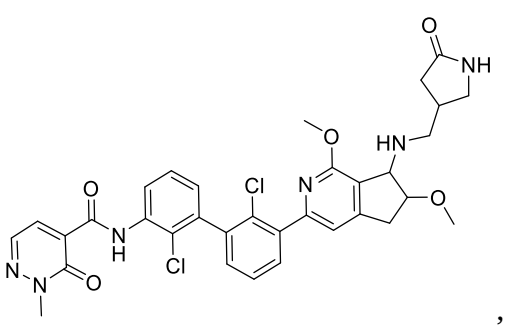
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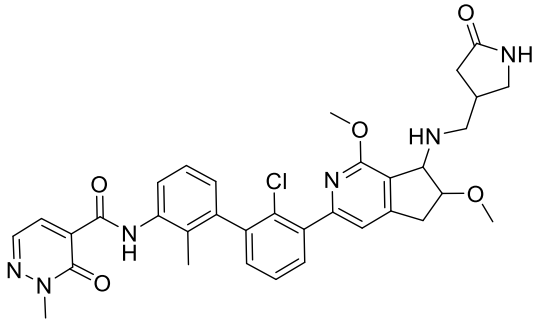
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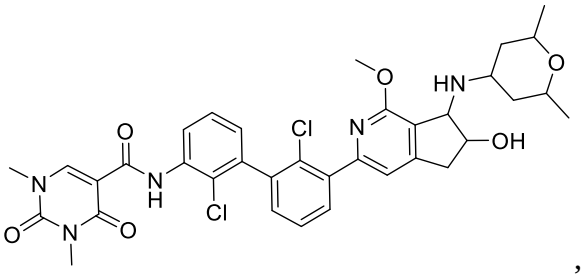
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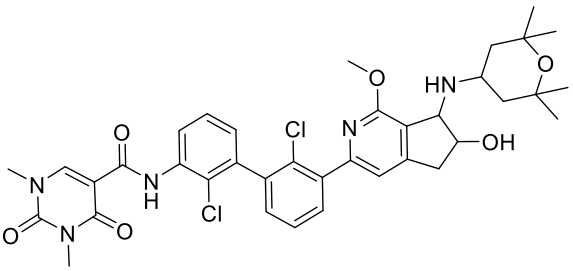
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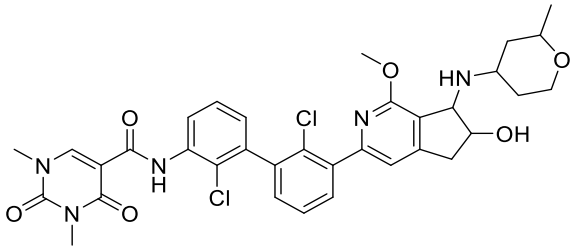
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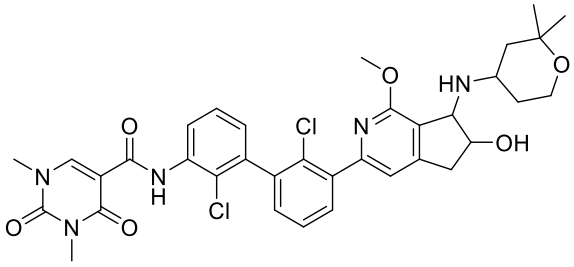
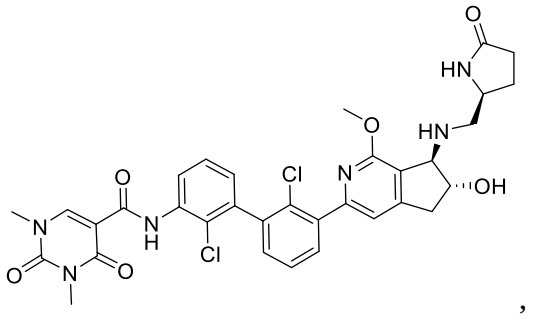

, or a pharmaceutically acceptable salt of any of the foregoing.

147. The compound of Claim 1 selected from the group consisting of: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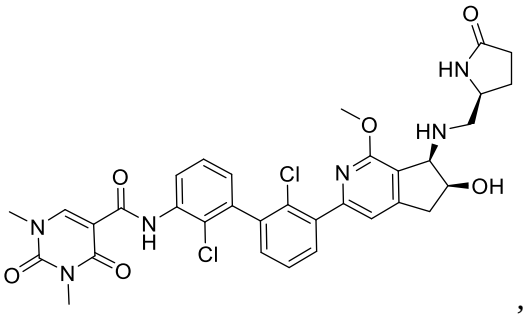
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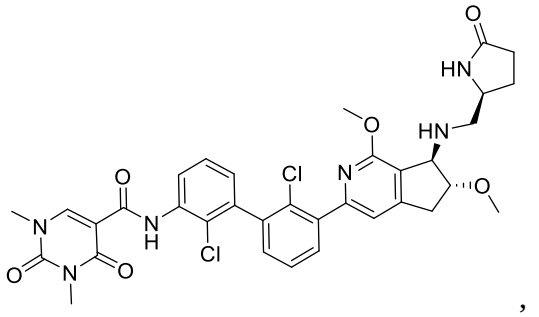
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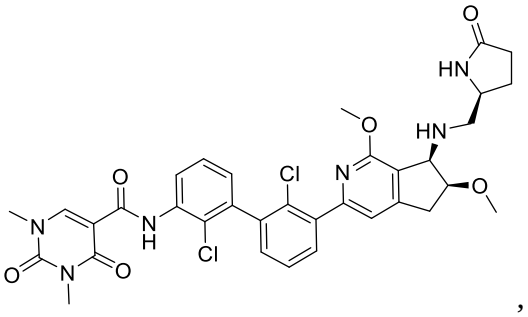
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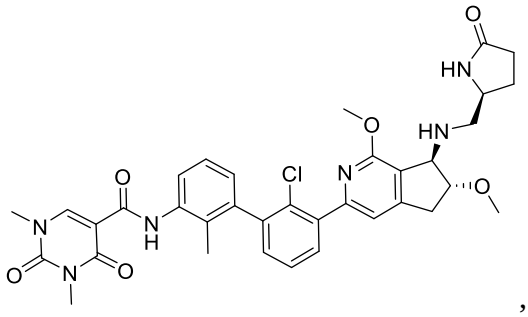
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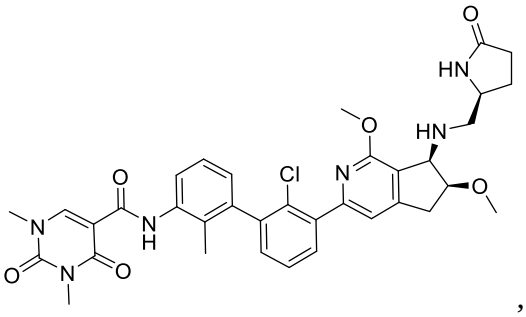
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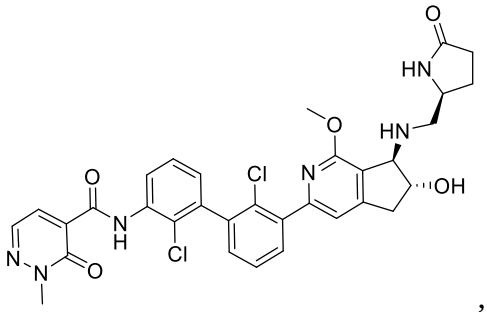
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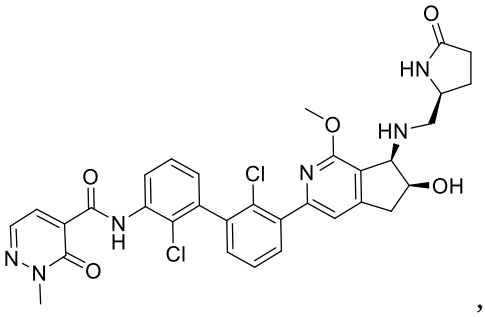
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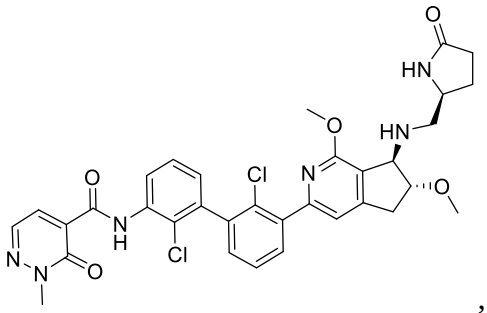
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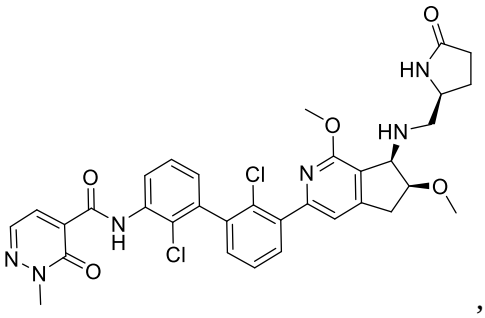
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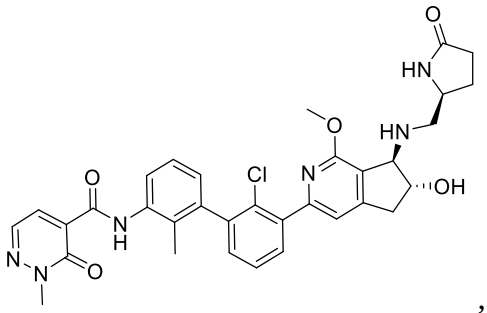
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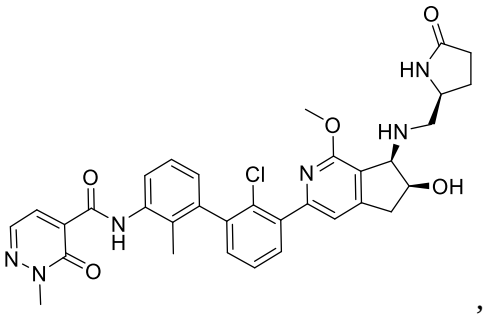
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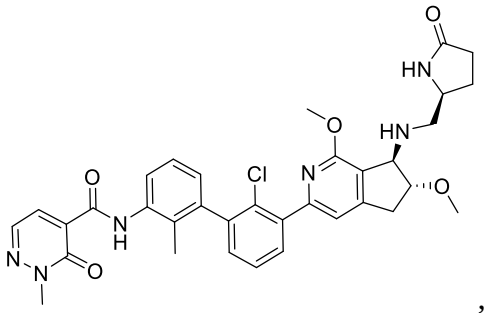
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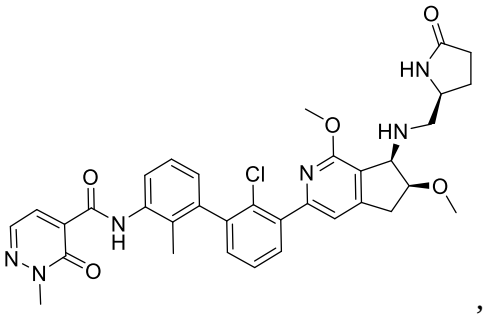
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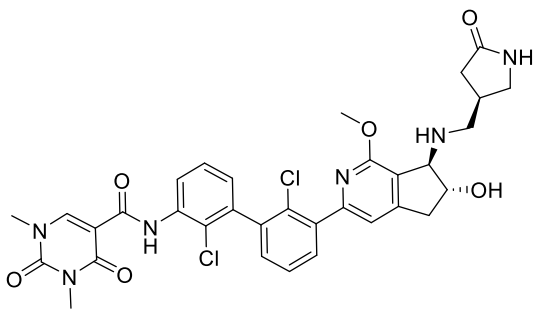
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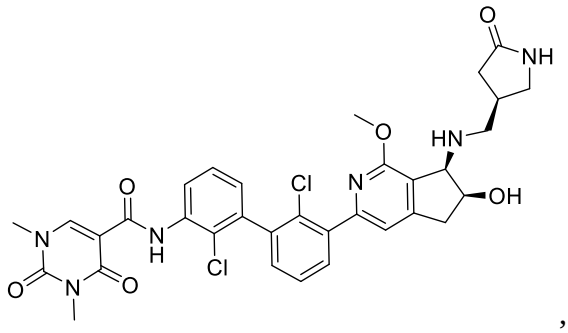
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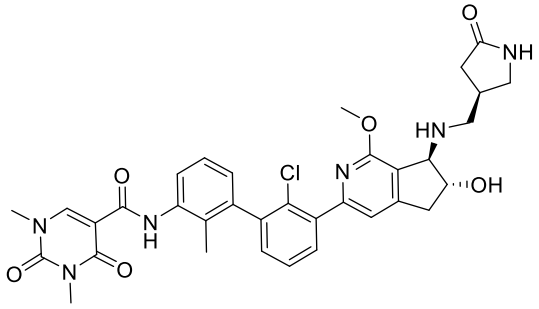
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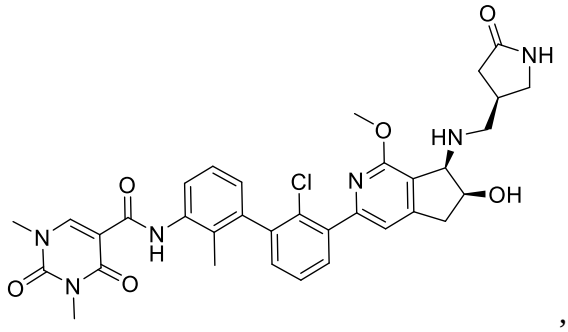
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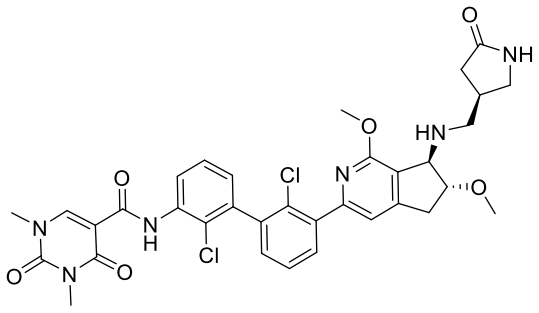
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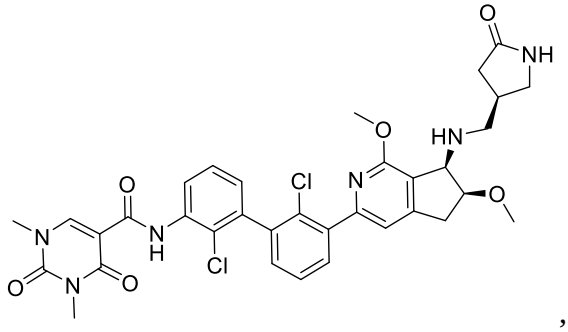
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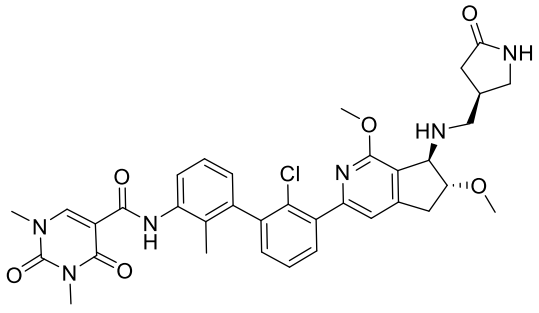
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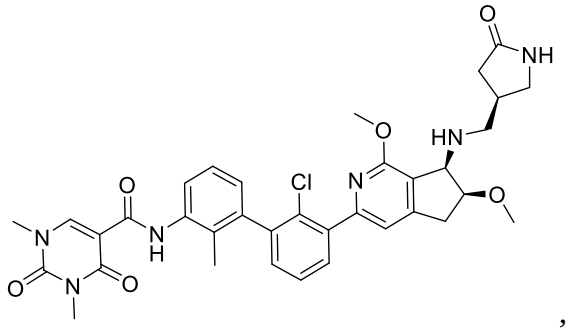
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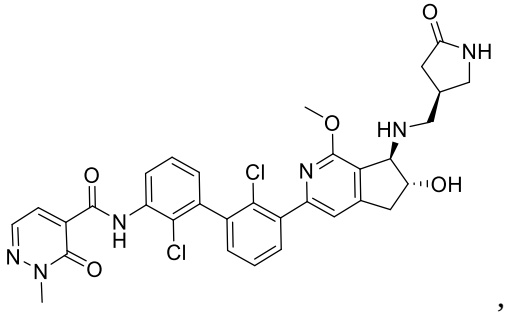
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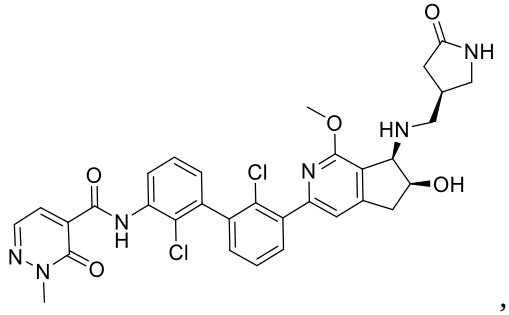
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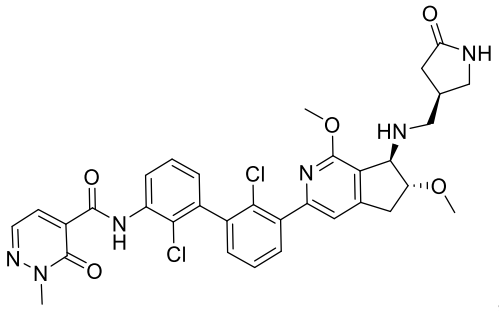
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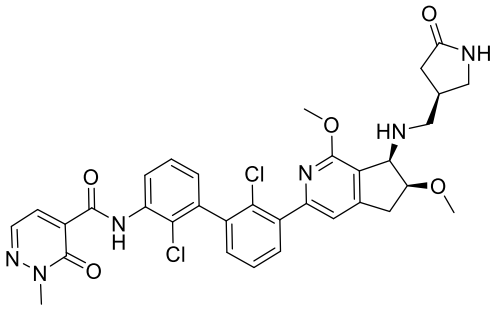
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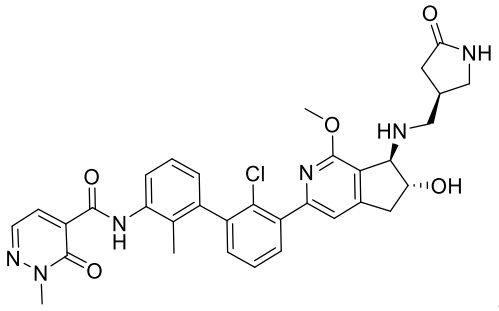
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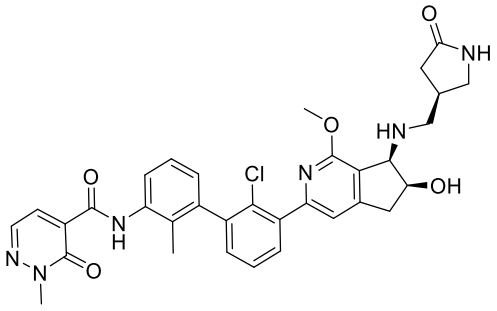
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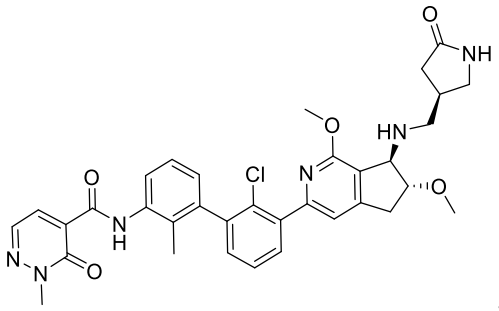
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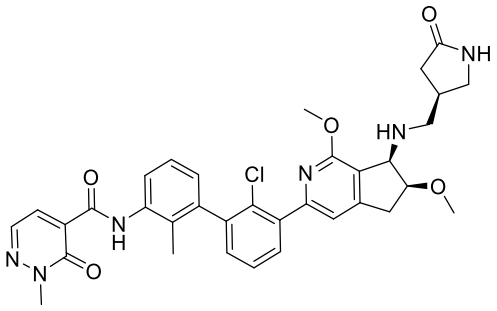
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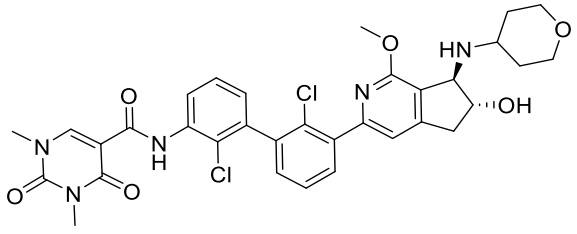
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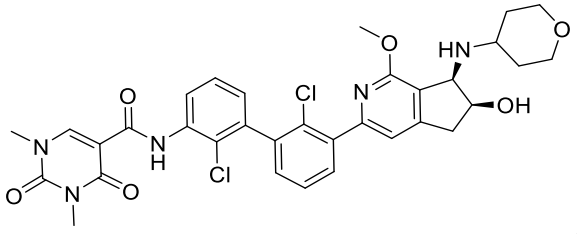
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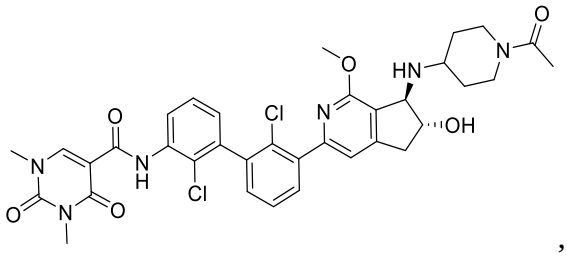
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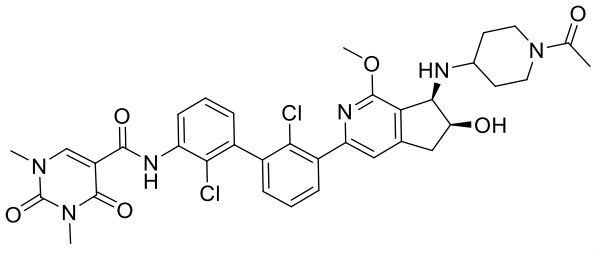
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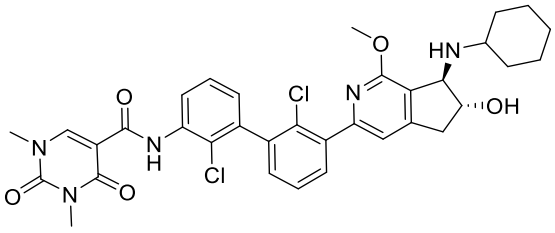
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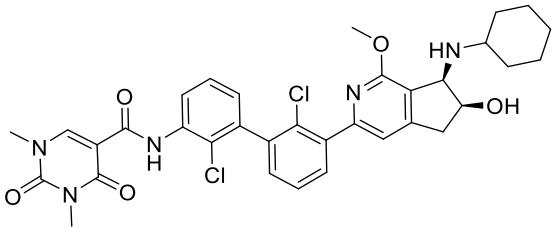
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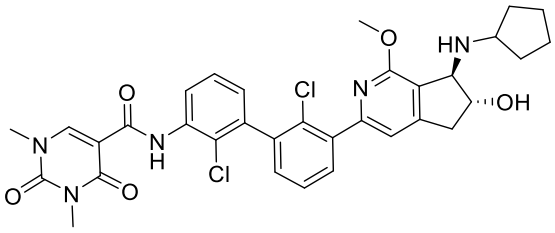
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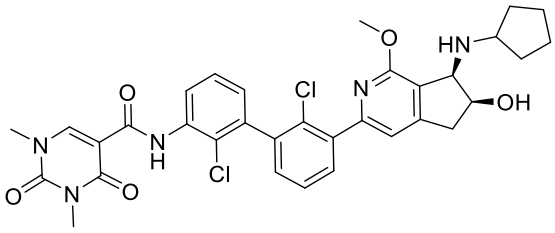
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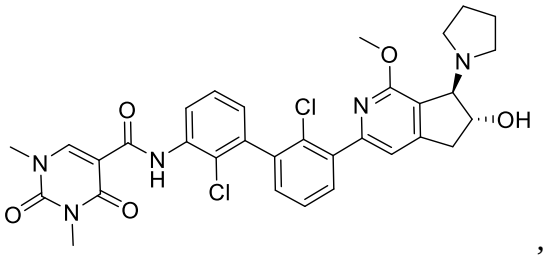
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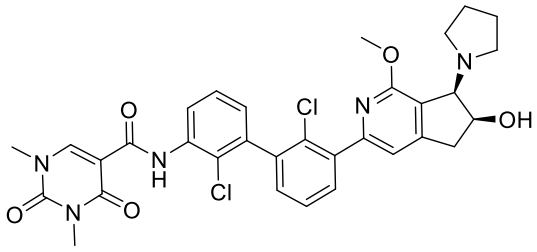
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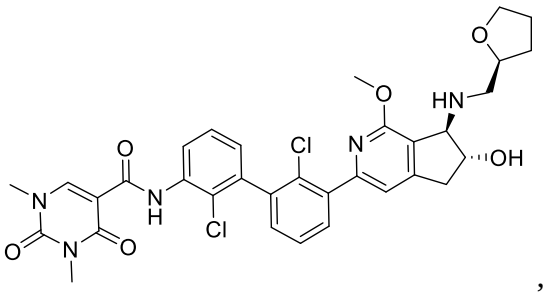
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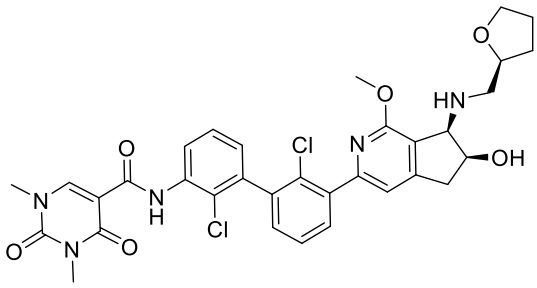
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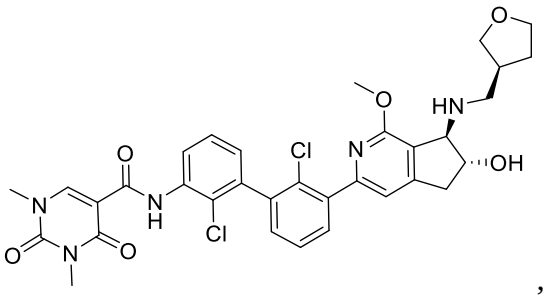
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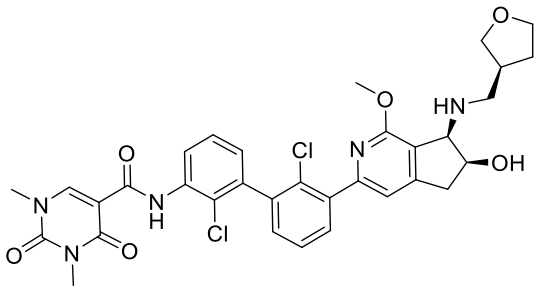
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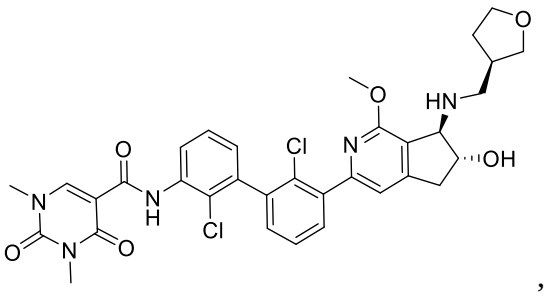
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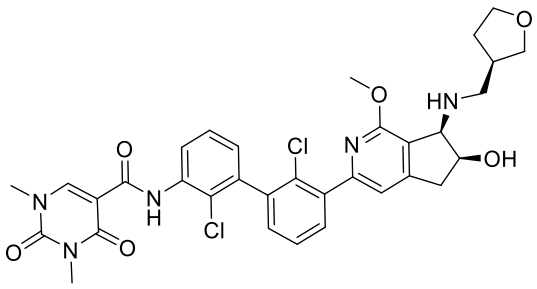
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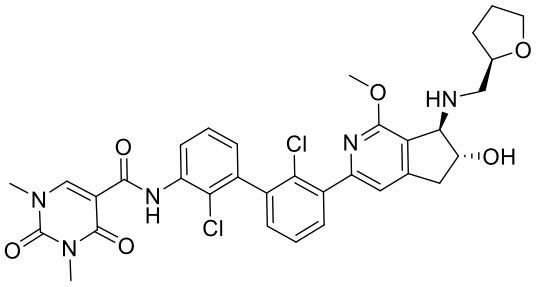
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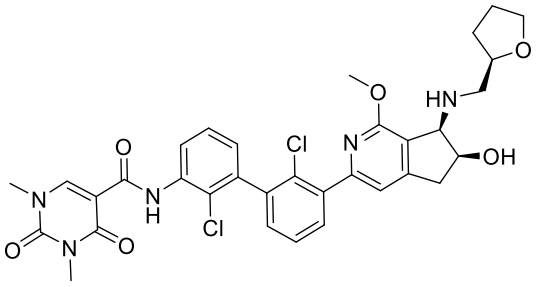
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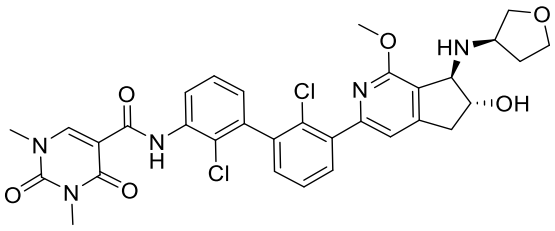
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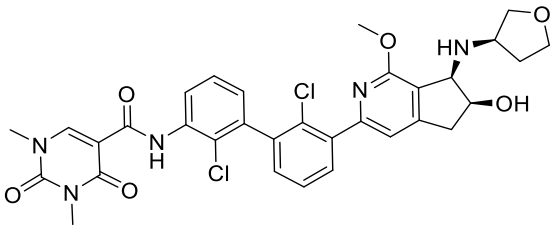
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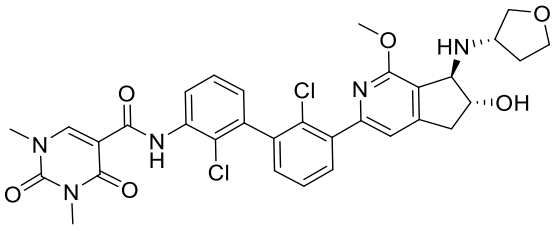
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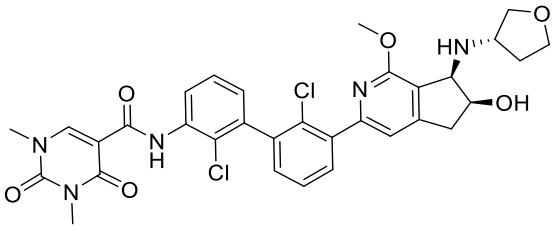
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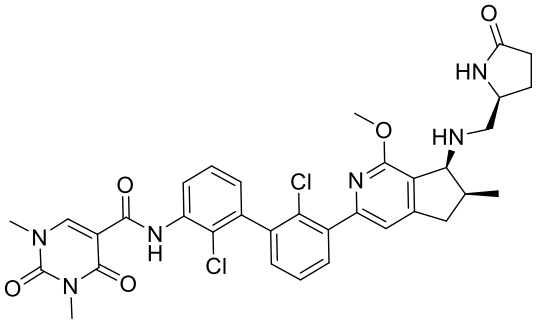
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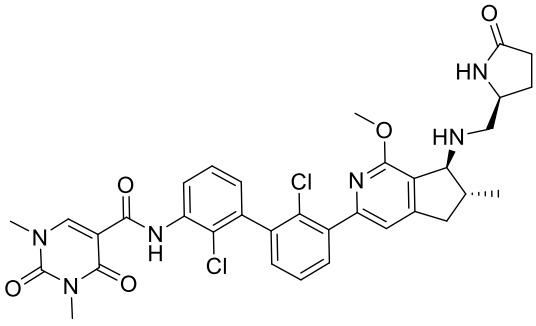
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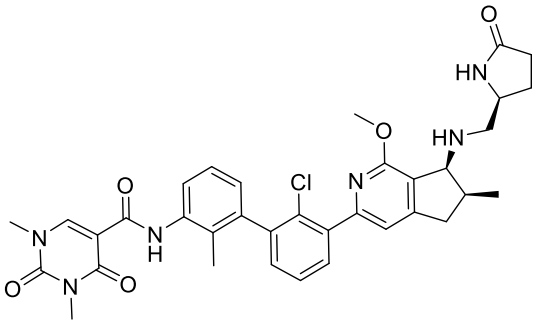
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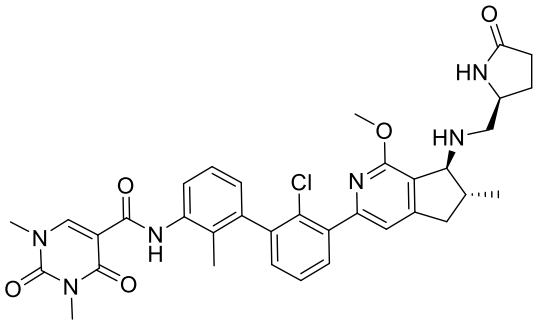
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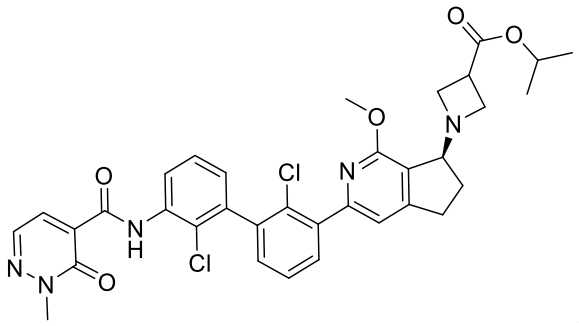
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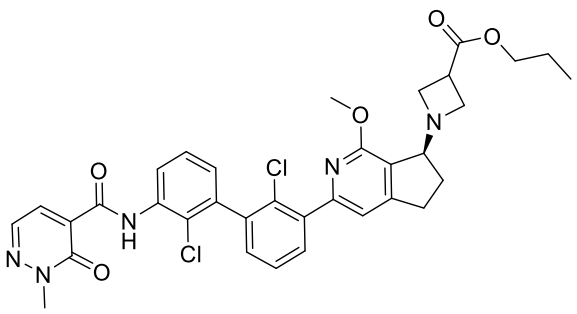
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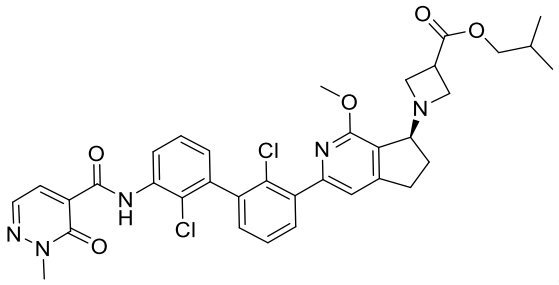
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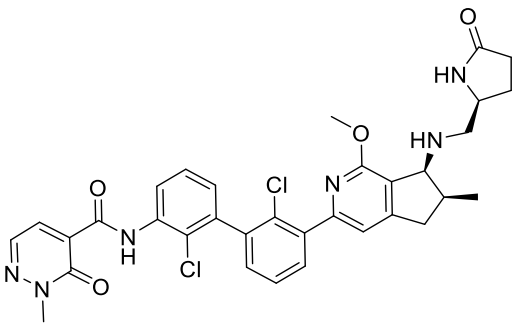
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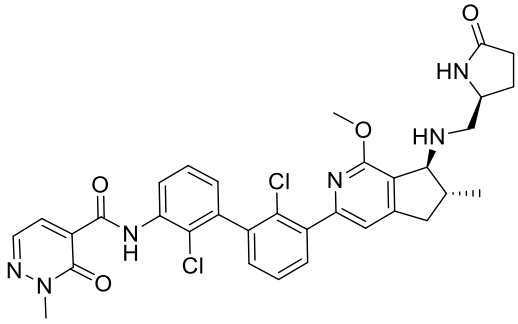
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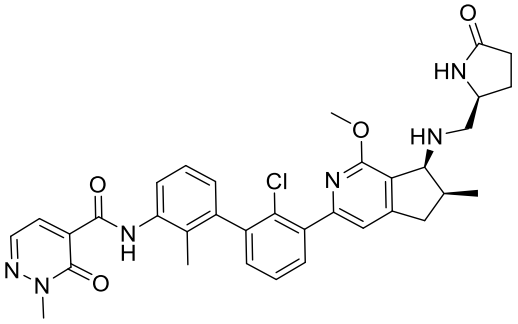
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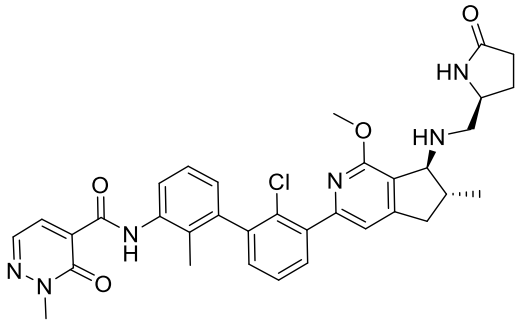
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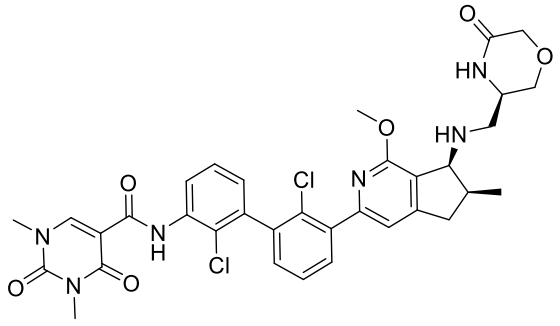
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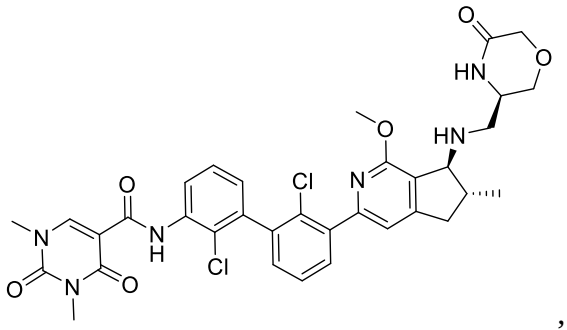
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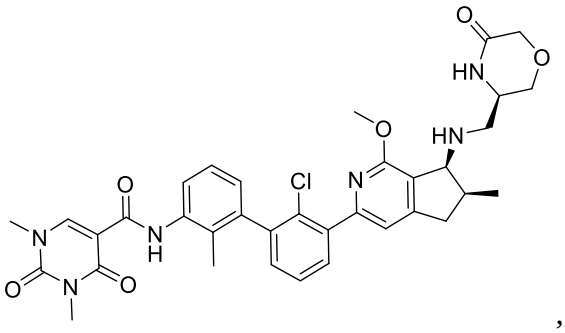
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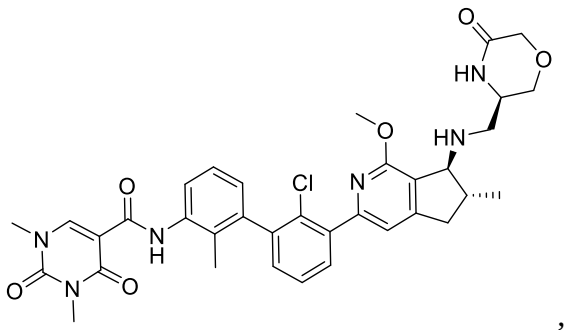
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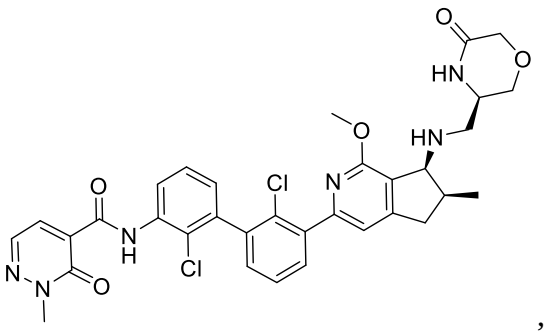
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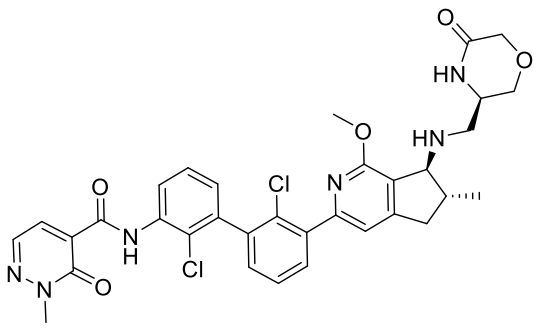
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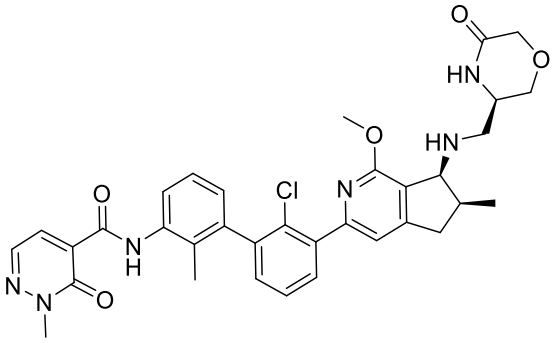
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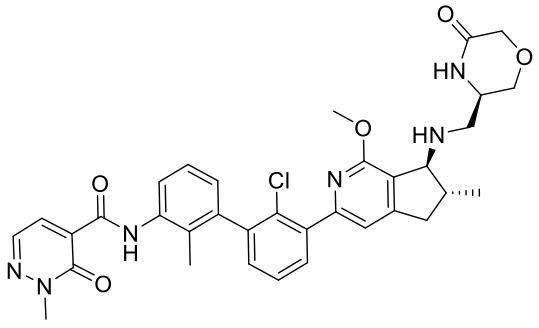
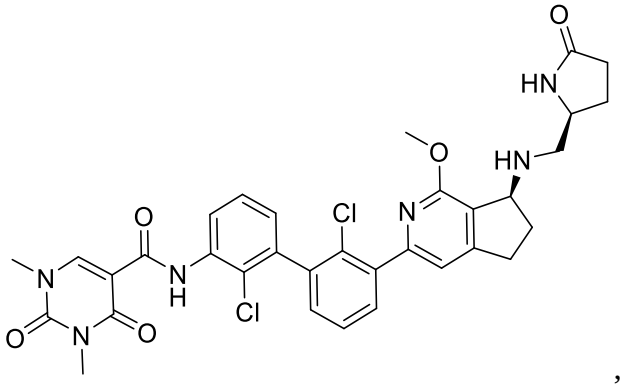
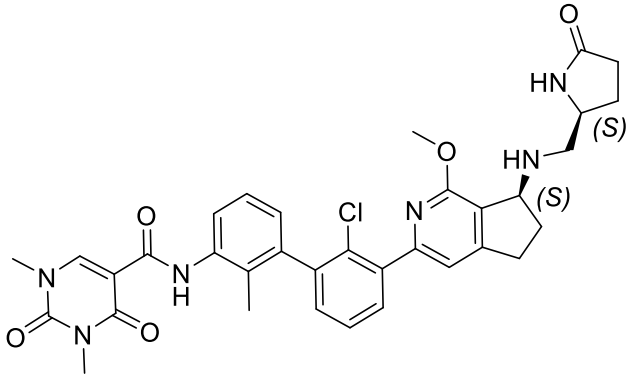
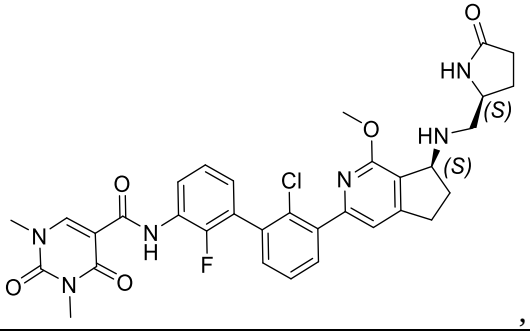
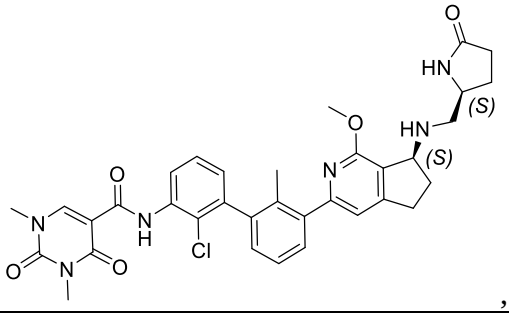
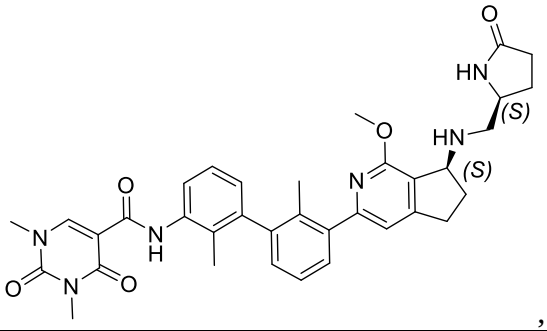
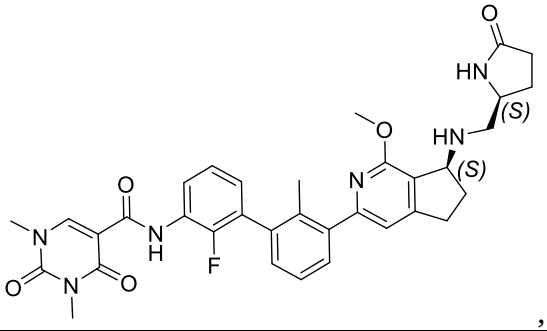
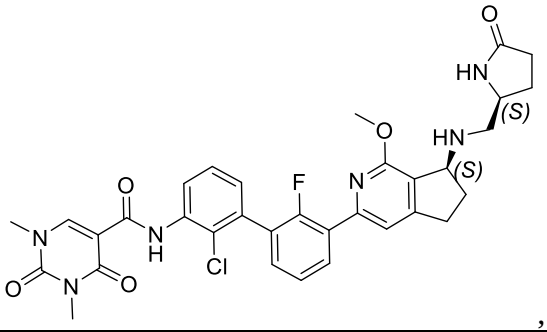
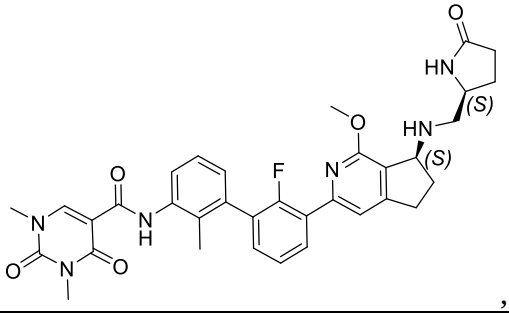
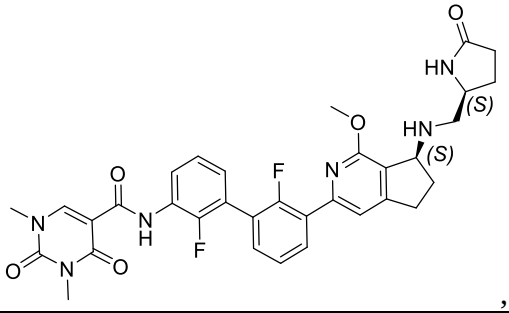
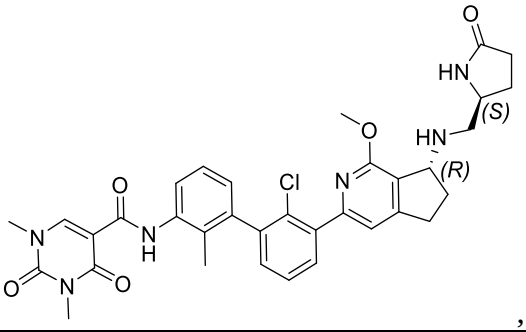
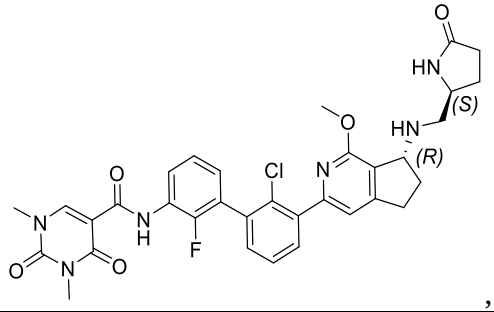
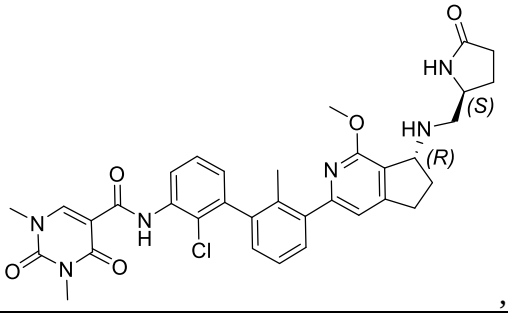
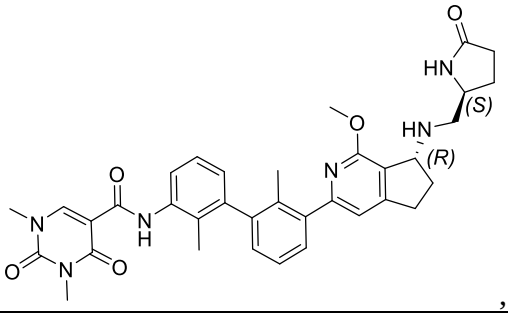
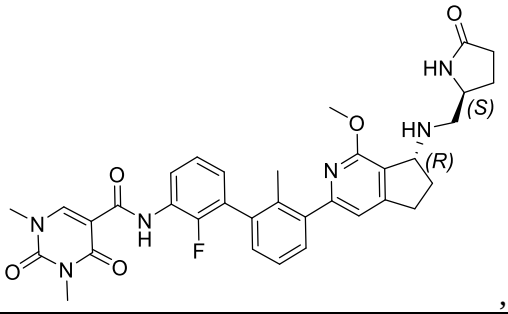
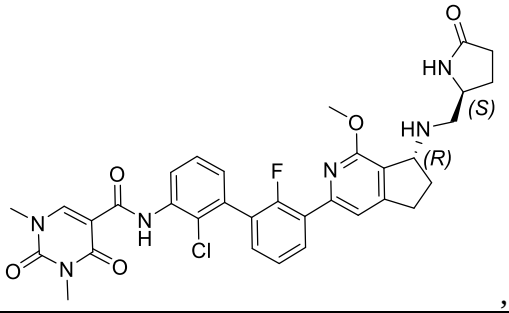
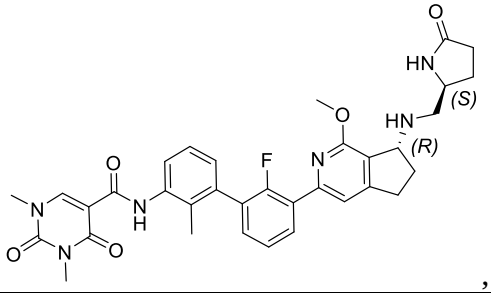
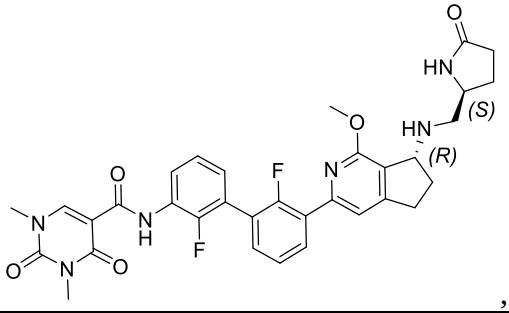
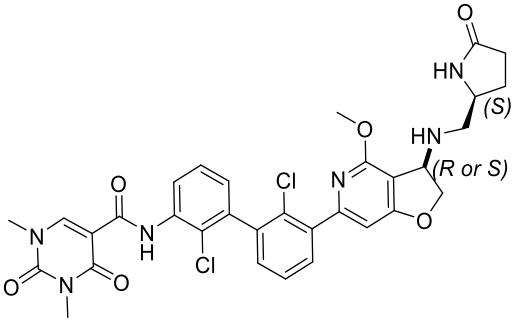
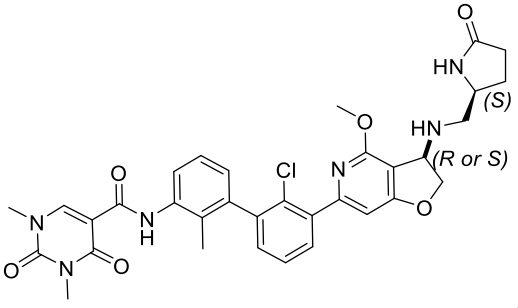

, or a pharmaceutically acceptable salt of any of the foregoing.

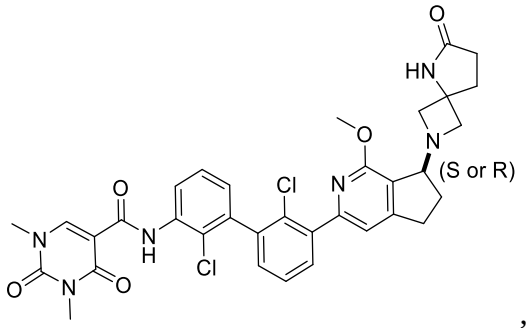
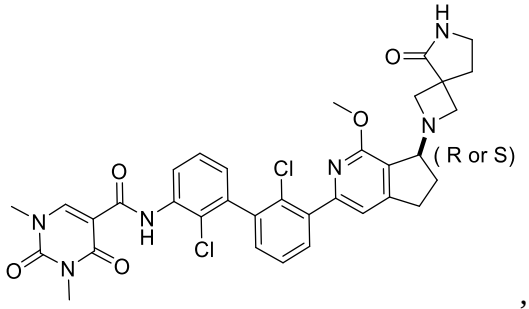
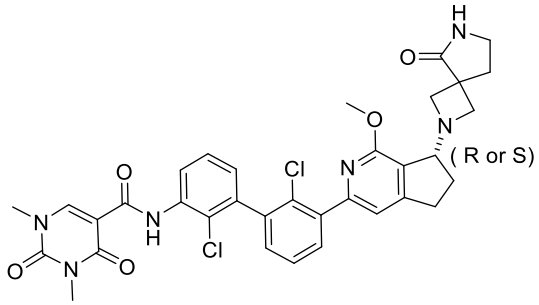
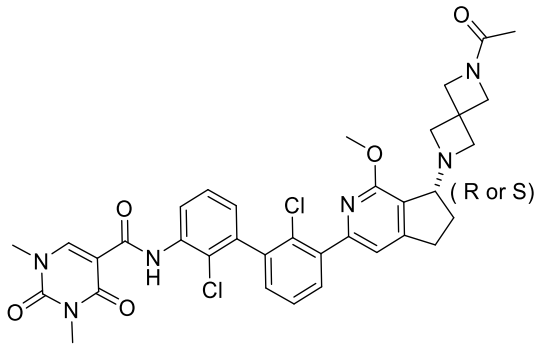
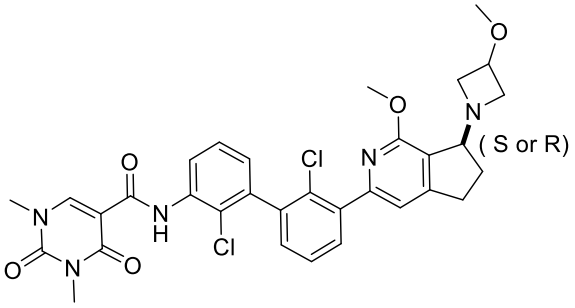
148. The compound of Claim 1 selected from the group consisting of:

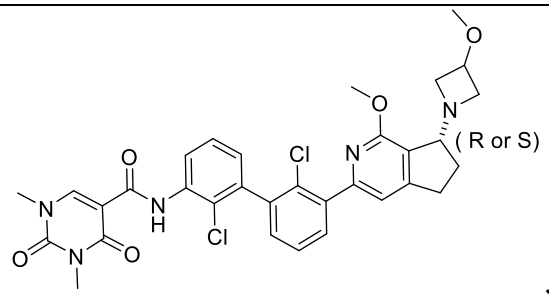
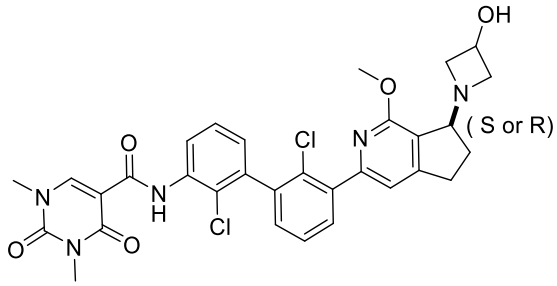
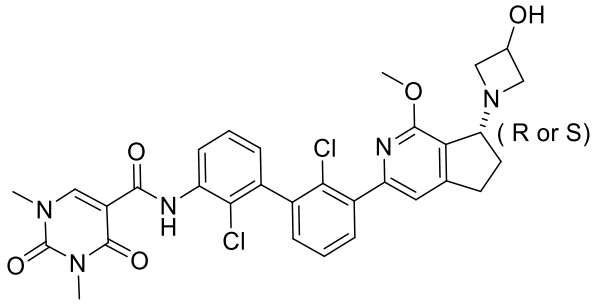
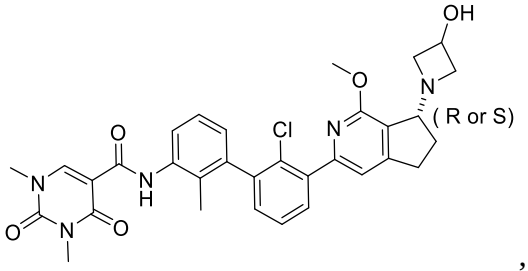
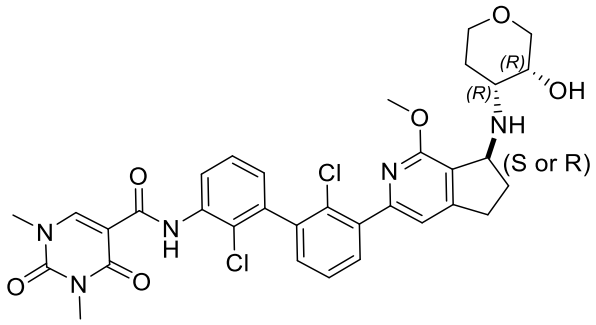
A-1	 ,
A-2	 ,
A-3	 ,
A-4	 ,

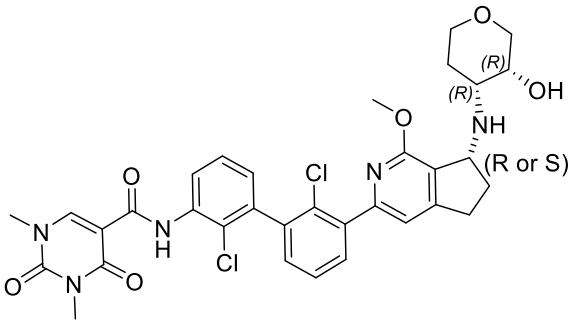
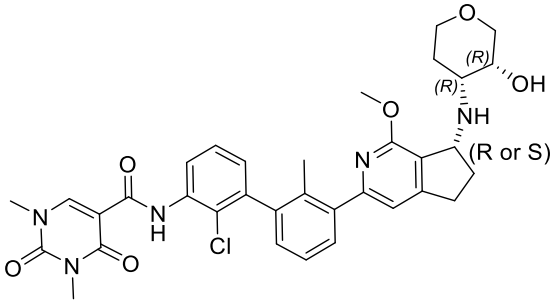
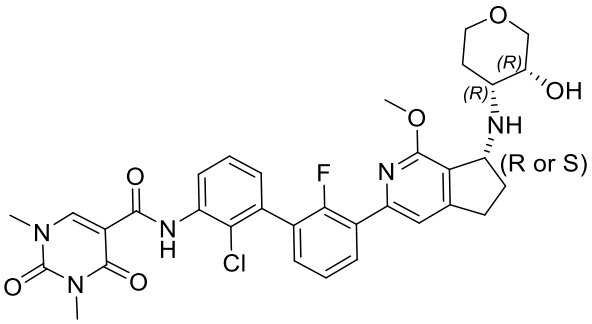
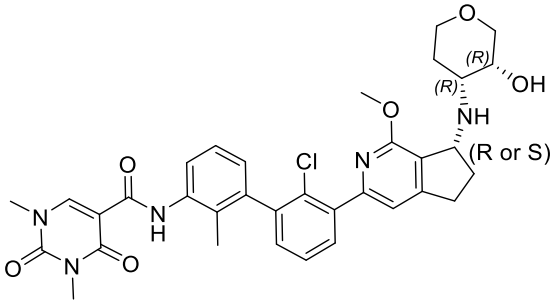
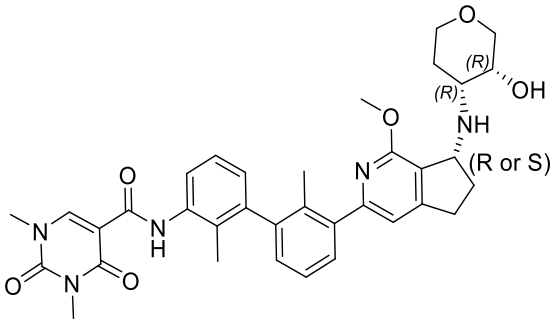
A-5	 ,
A-6	 ,
A-7	 ,
A-8	 ,
A-9	 ,

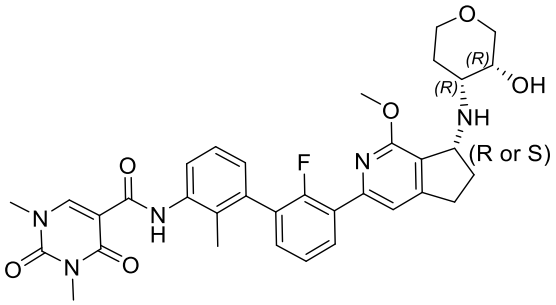
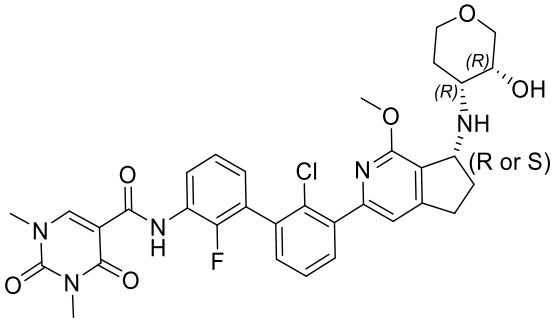
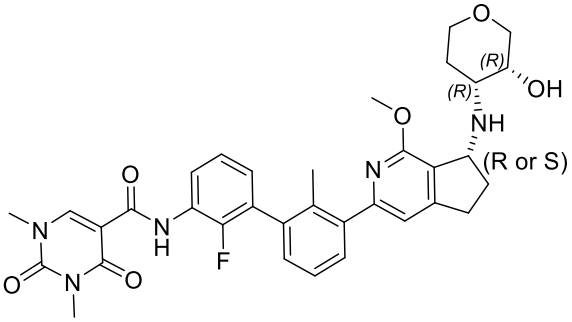
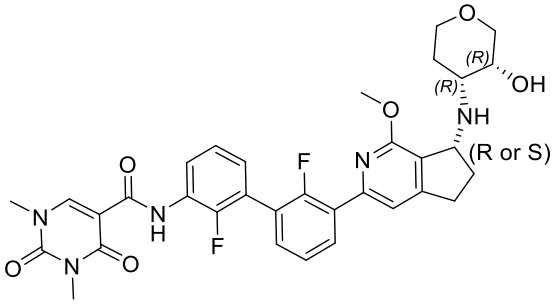
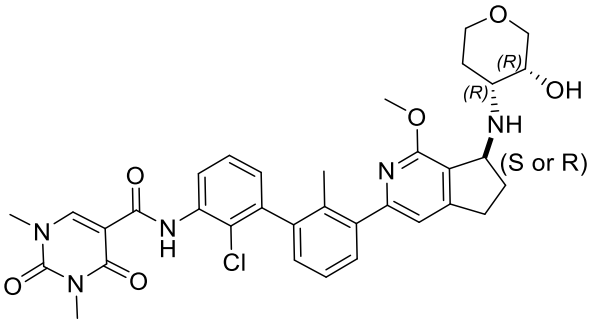
A-10	 ,
A-11	 ,
A-12	 ,
A-13	 ,
A-14	 ,

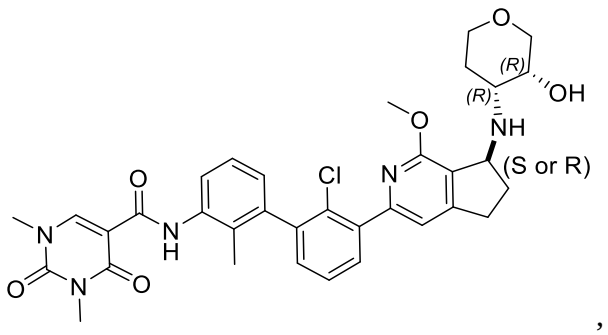
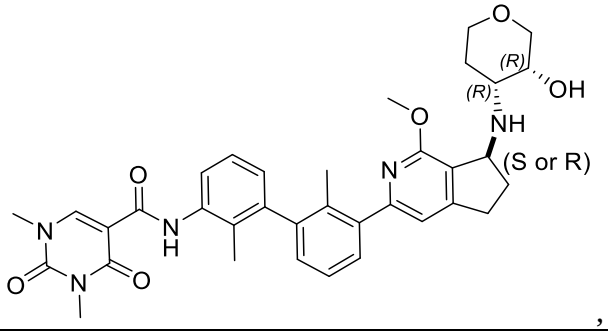
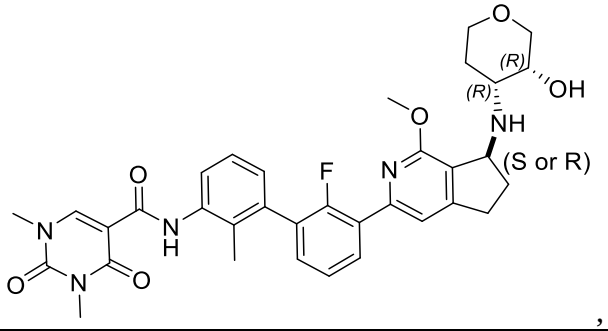
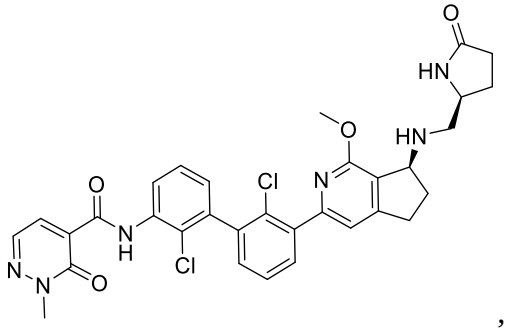
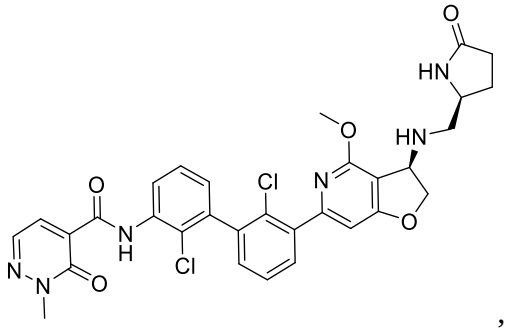
A-15	 ,
A-16	 ,
A-17	 ,
A-18	 ,
A-19	 ,

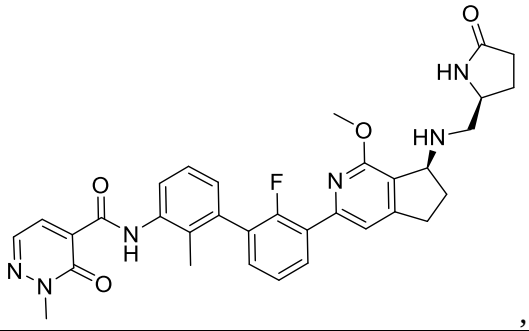
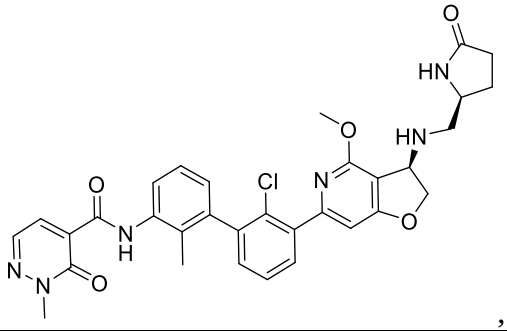
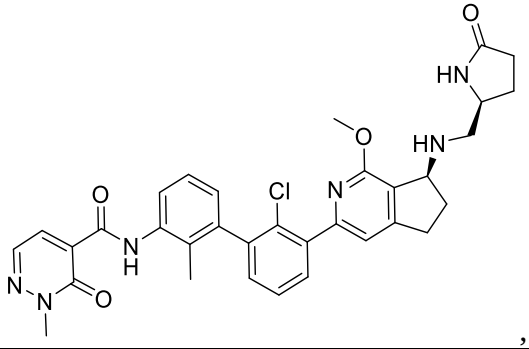
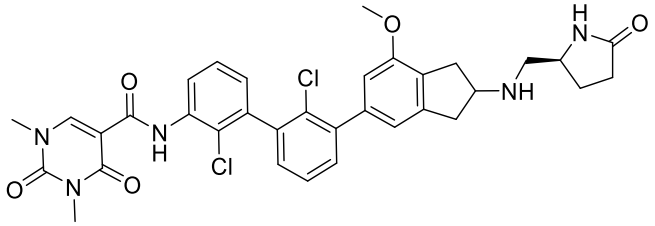
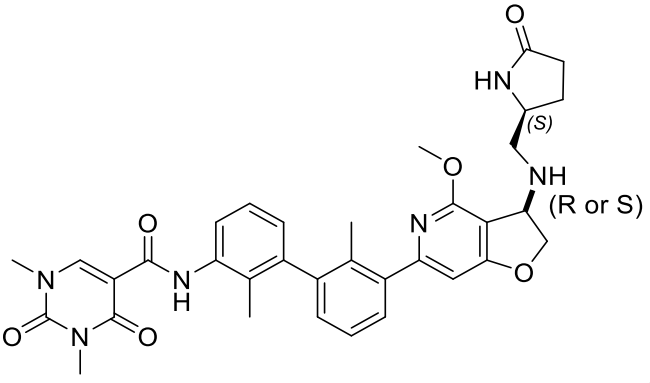
A-20	 ,
A-21	 ,
A-22	 ,
A-23	 ,
A-24	 ,

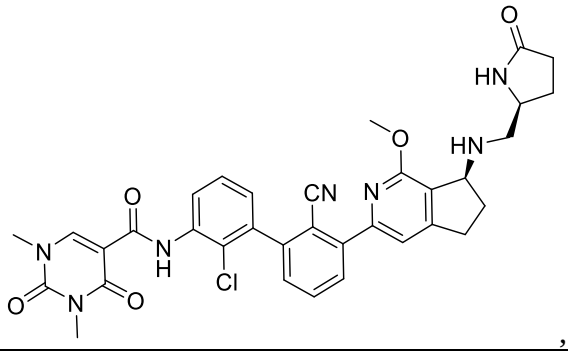
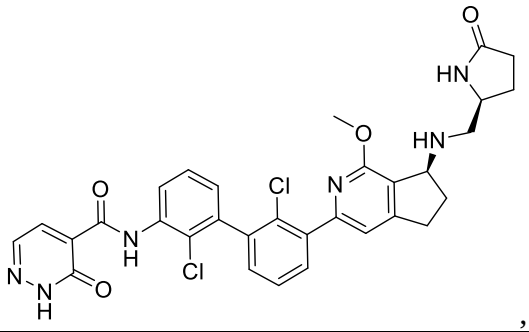
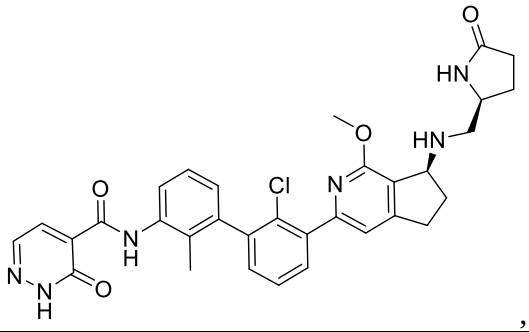
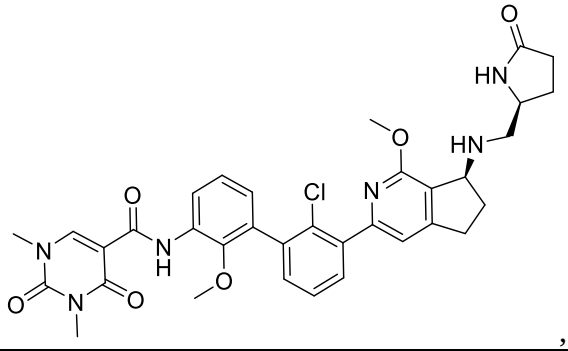
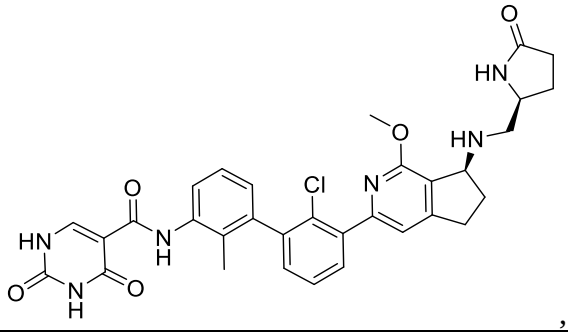
A-25	 ,
A-26	 ,
A-27	 ,
A-28	 ,
A-29	 ,

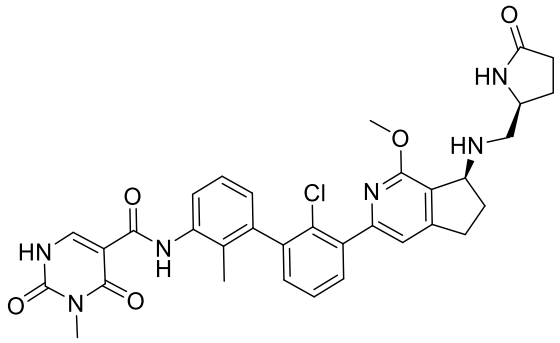
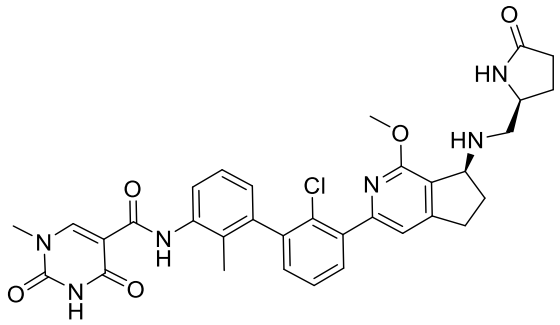
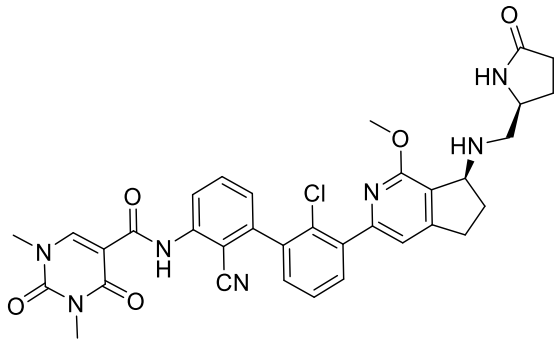
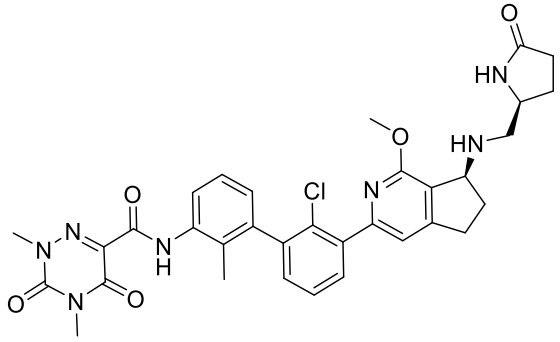
A-30	 ,
A-31	 ,
A-32	 ,
A-33	 ,
A-34	 ,

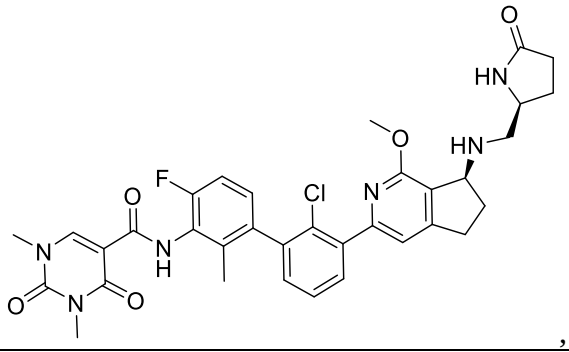
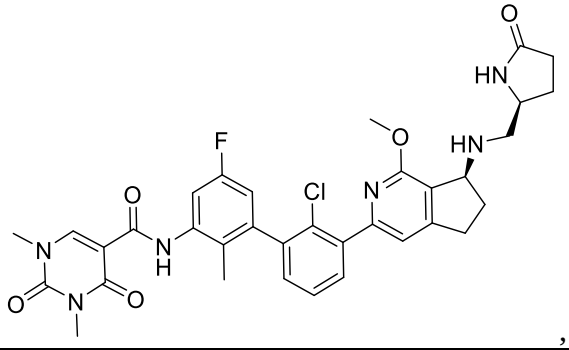
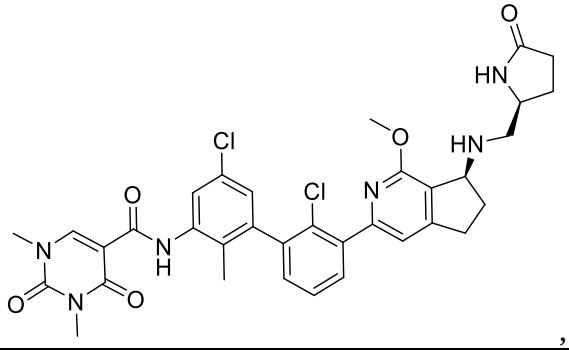
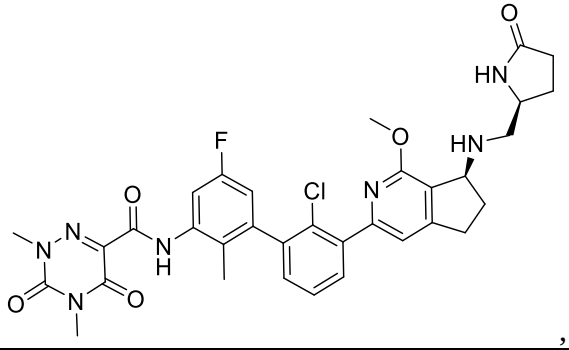
A-35	 ,
A-36	 ,
A-37	 ,
A-38	 ,
A-39	 ,

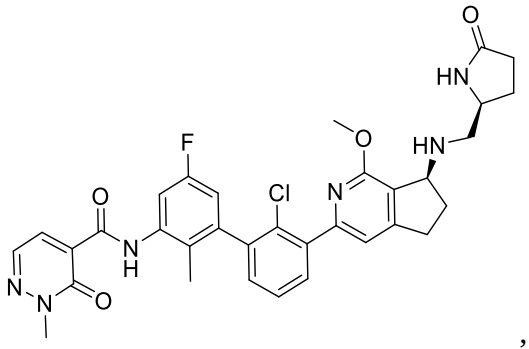
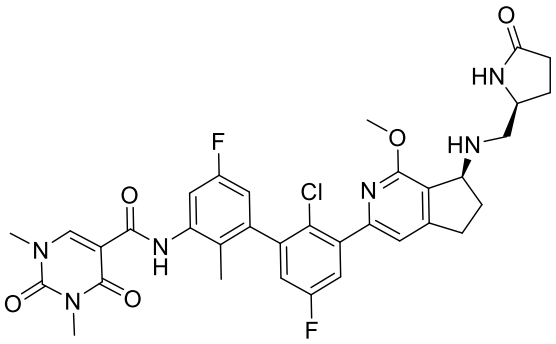
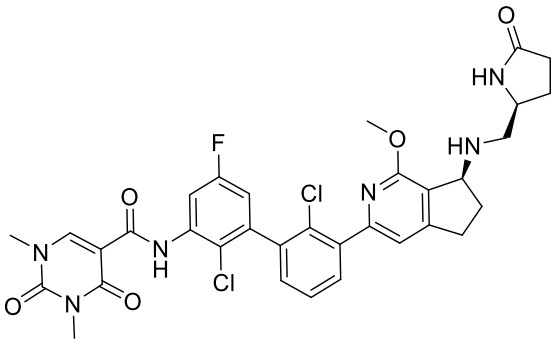
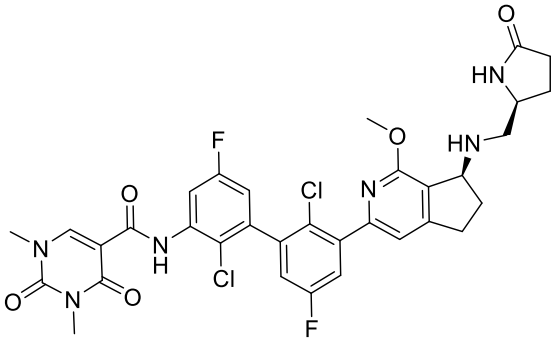
A-40	 ,
A-41	 ,
A-42	 ,
A-43	 ,
A-44	 ,

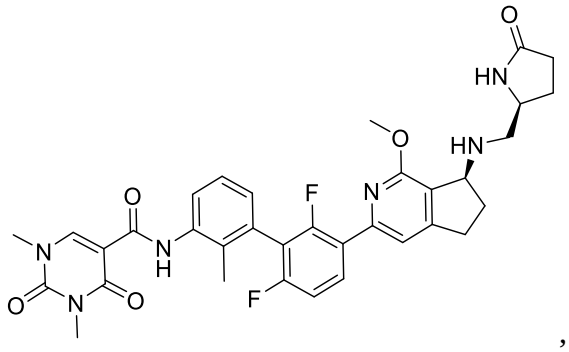
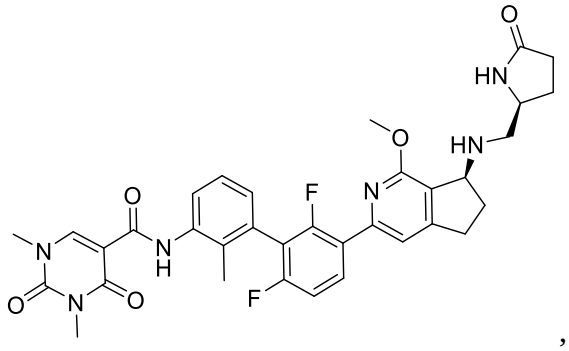
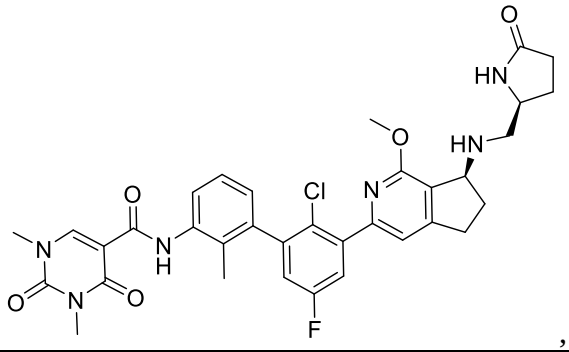
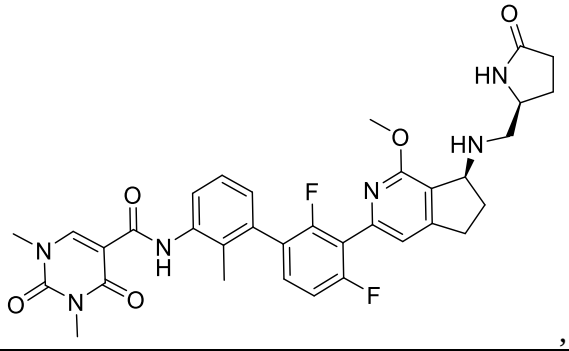
A-45	 ,
A-46	 ,
A-47	 ,
A-48	 ,
A-49	 ,

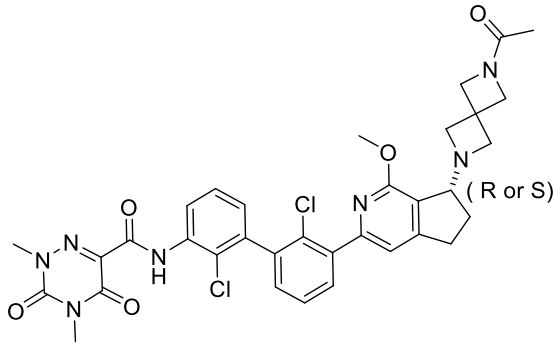
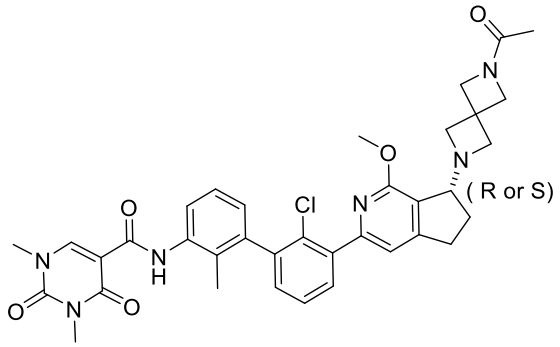
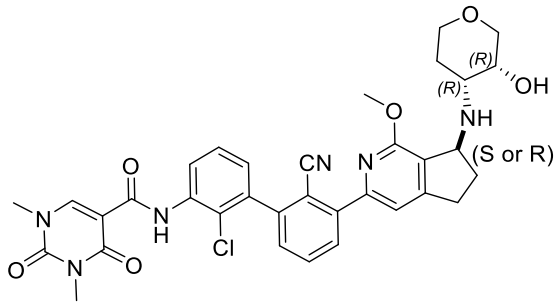
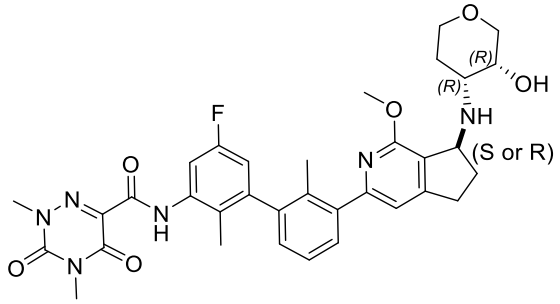
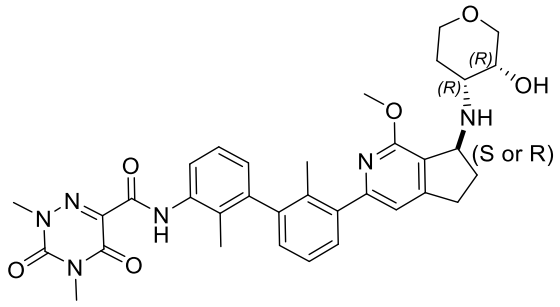
A-50	 ,
A-51	 ,
A-52	 ,
A-53	 ,
A-54	 ,

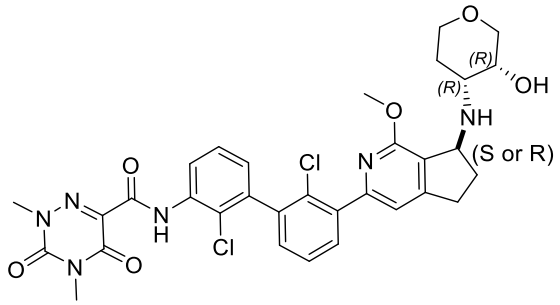
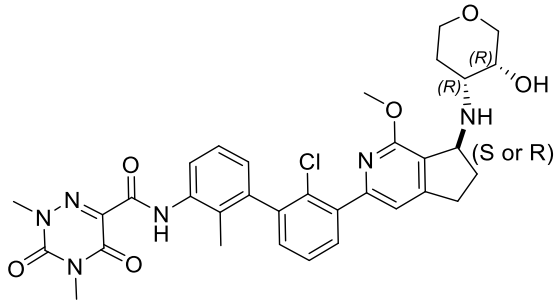
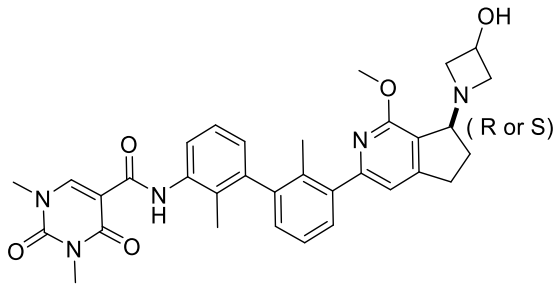
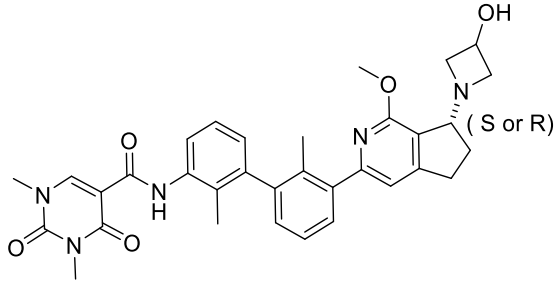
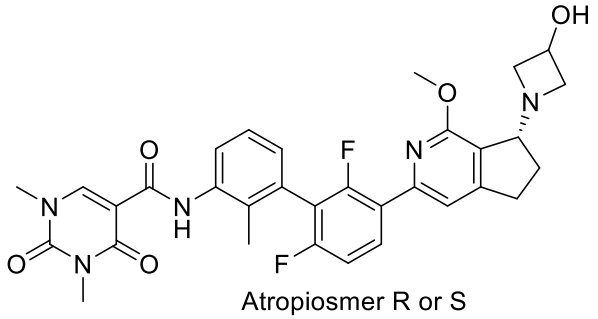
A-55	 ,
A-56	 ,
A-57	 ,
A-58	 ,

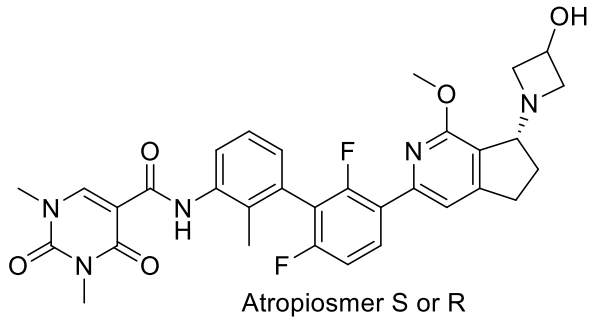
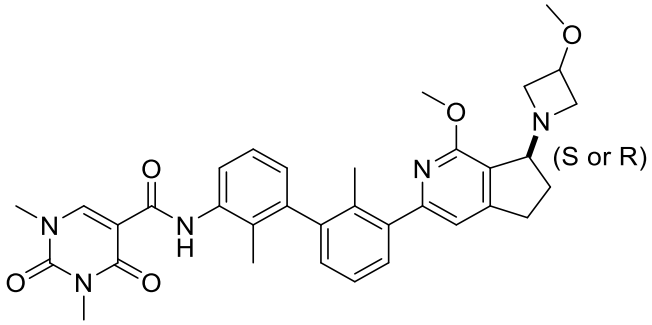
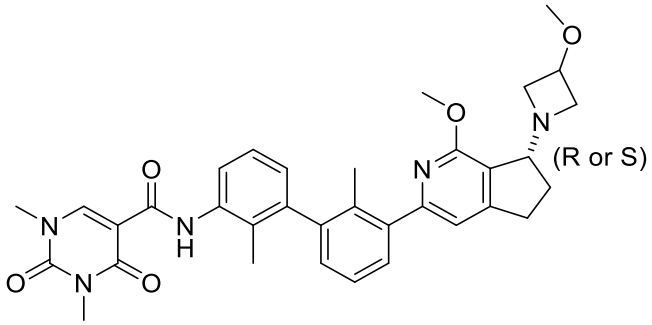
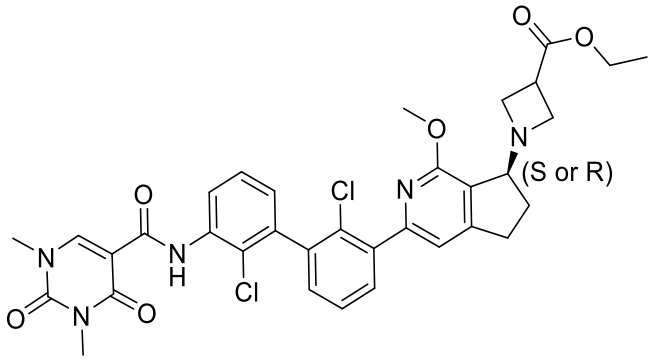
A-59	 ,
A-60	 ,
A-61	 ,
A-62	 ,

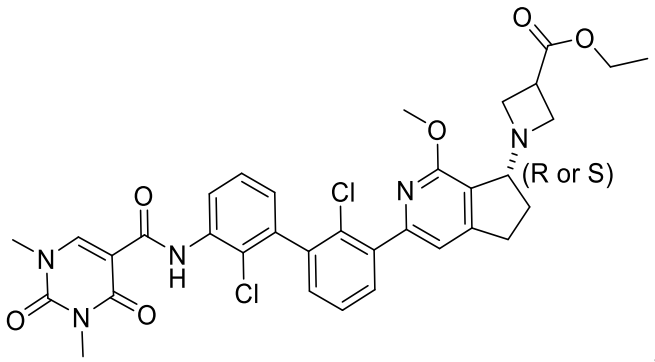
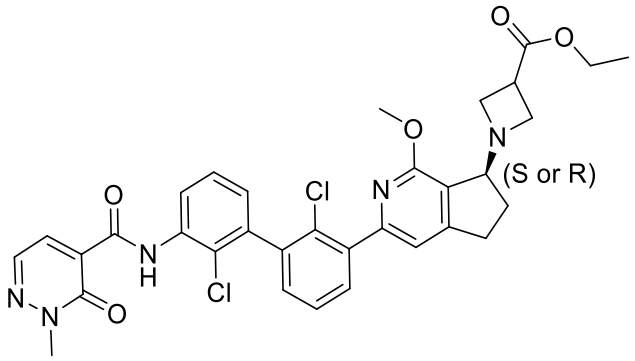
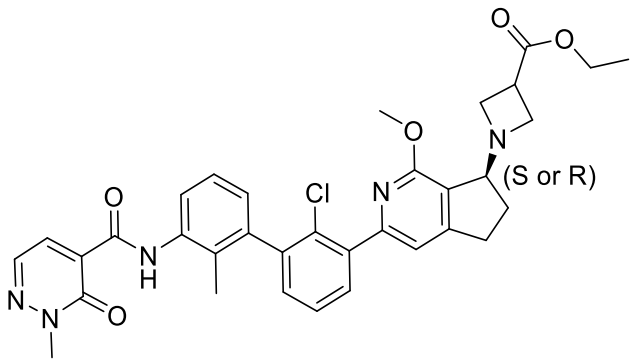
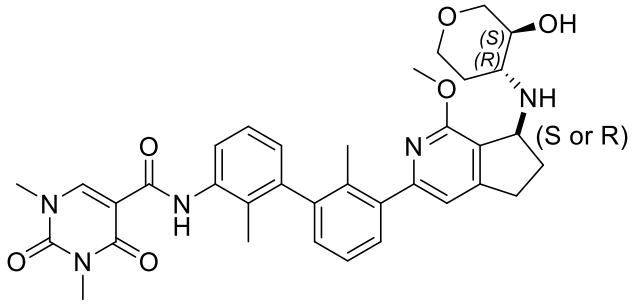
A-63	 ,
A-64	 ,
A-65	 ,
A-66	 ,

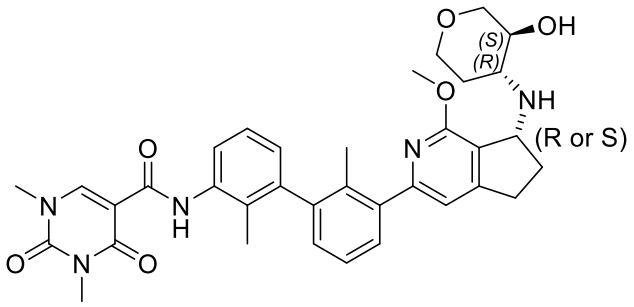
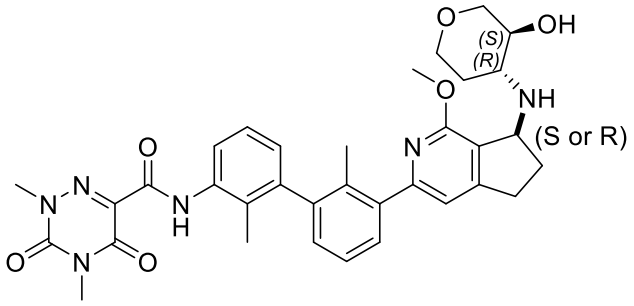
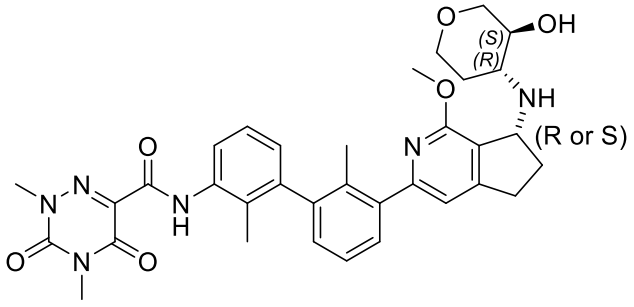
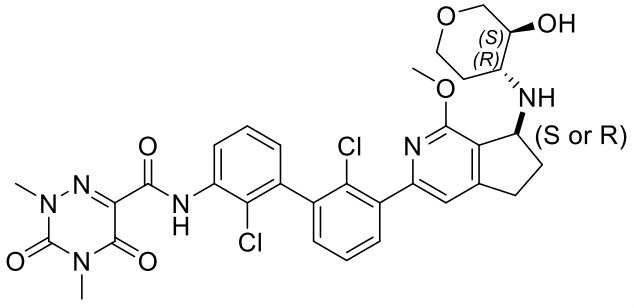
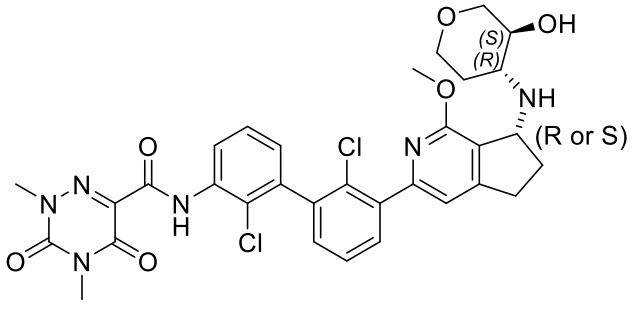
A-67	 , atropoisomer R or S
A-68	 , atropoisomer S or R
A-69	 ,
A-70	 ,

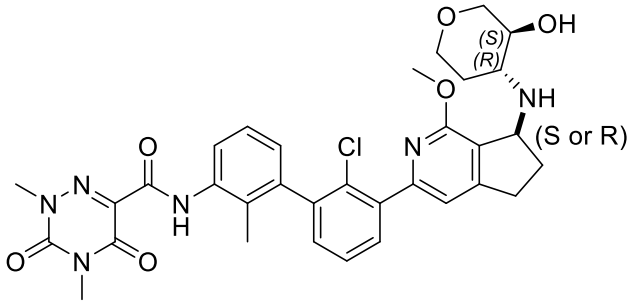
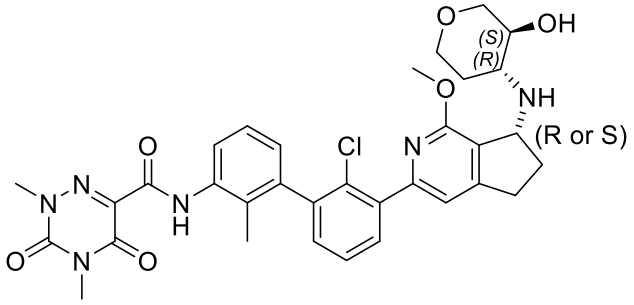
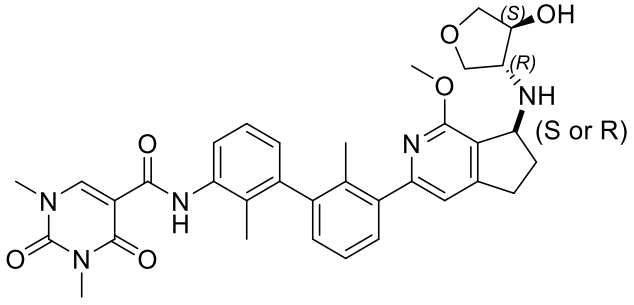
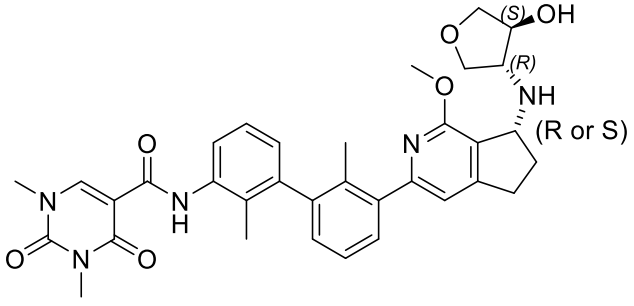
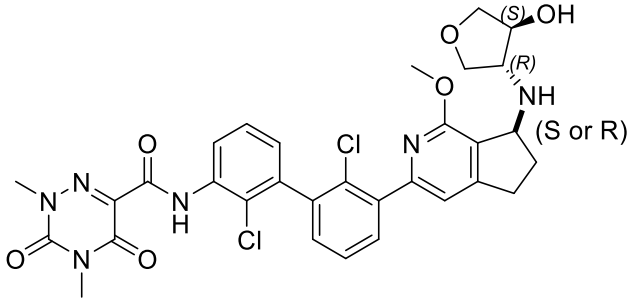
A-71	 ,
A-72	 ,
A-73	 ,
A-74	 ,
A-75	 ,

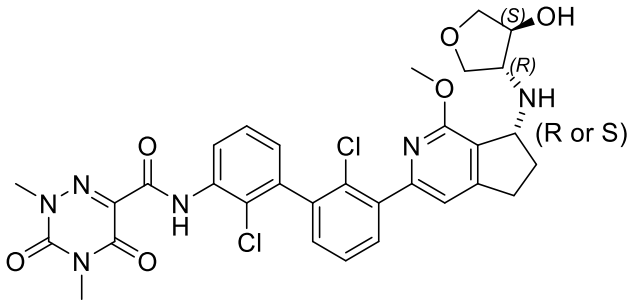
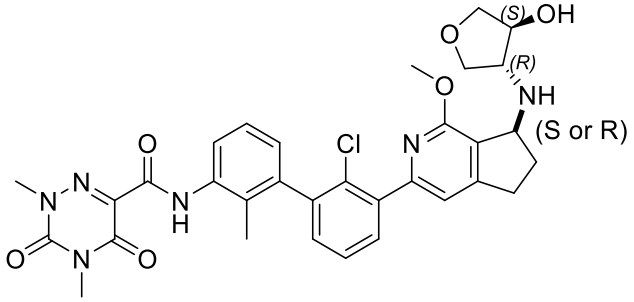
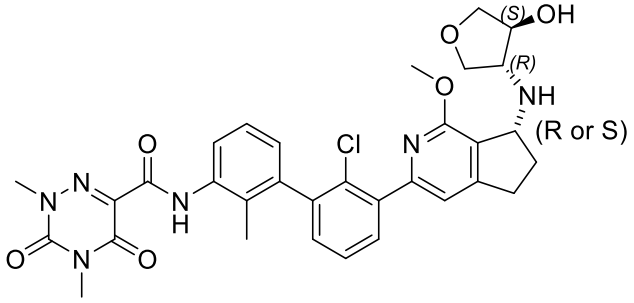
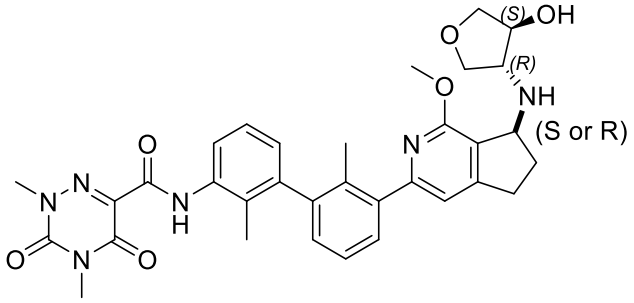
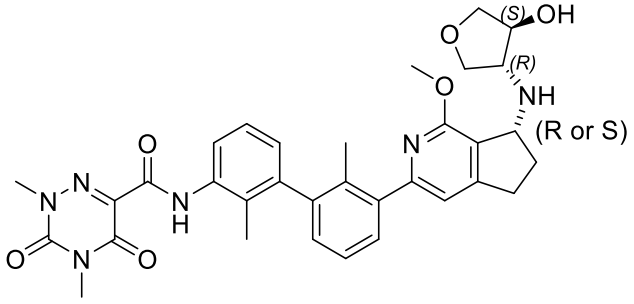
A-76	 ,
A-77	 ,
A-79	 ,
A-80	 ,
A-81	 Atropiosmer R or S ,

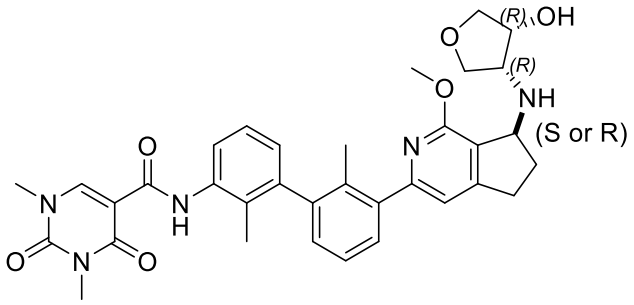
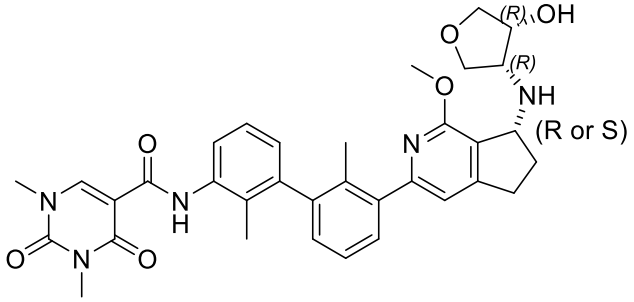
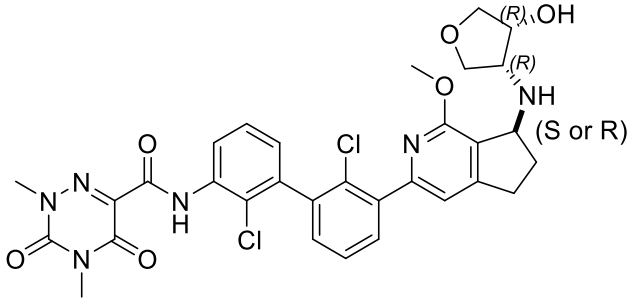
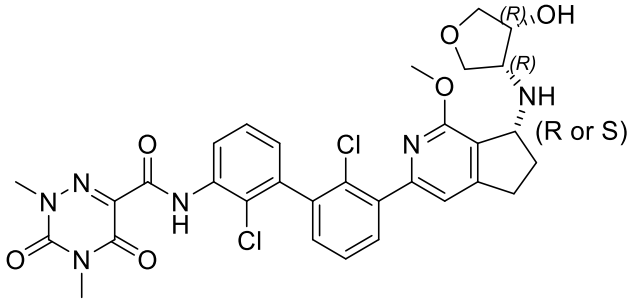
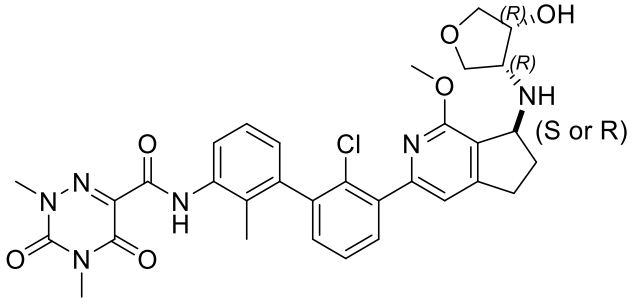
A-82	 Atropiosmer S or R ,
A-83	 ,
A-84	 ,
A-85	 ,

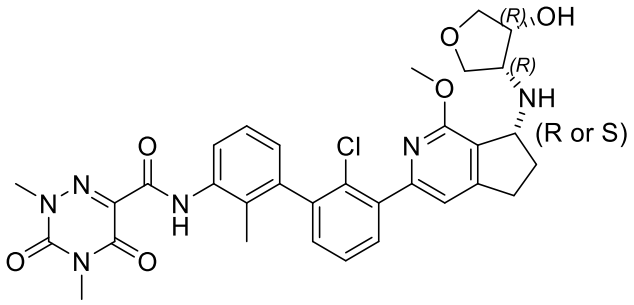
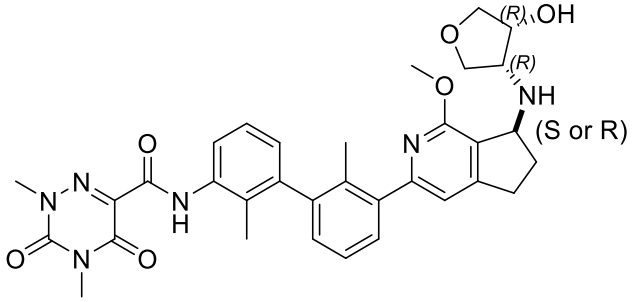
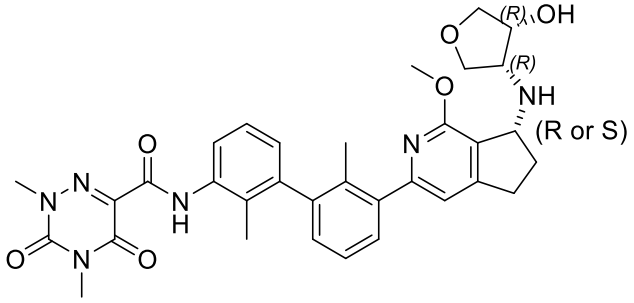
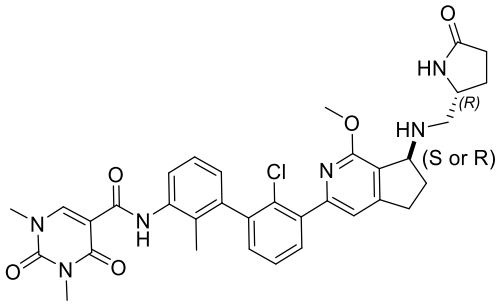
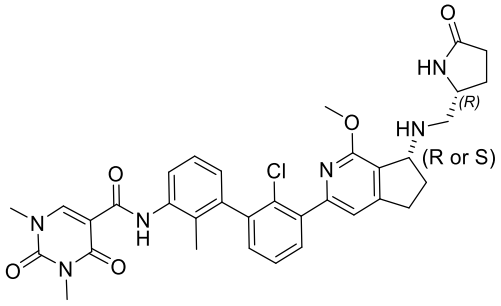
A-86	 ,
A-87	 ,
A-88	 ,
A-89	 ,

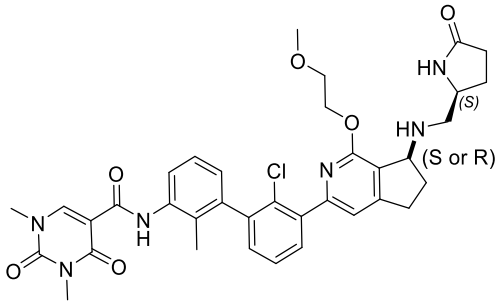
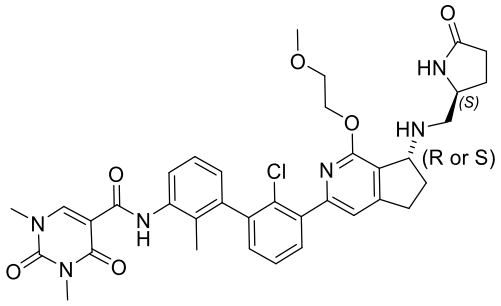
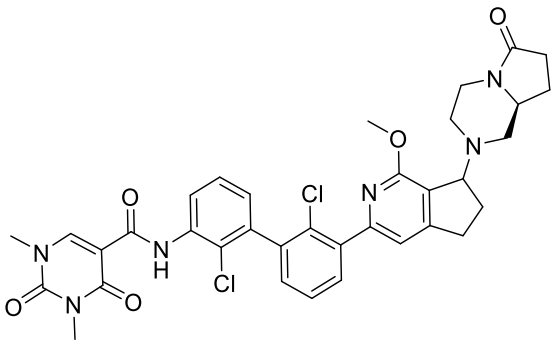
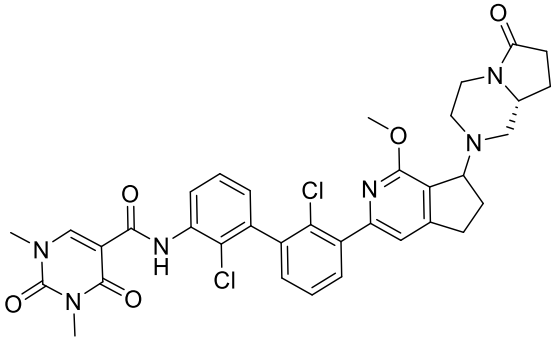
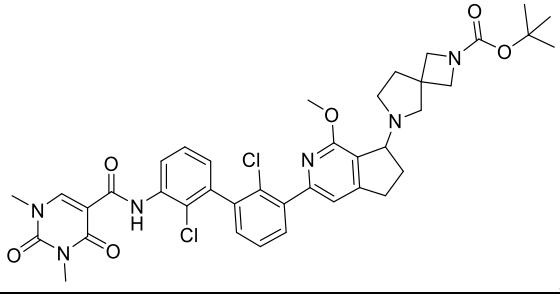
A-90	 ,
A-91	 ,
A-92	 ,
A-93	 ,
A-94	 ,

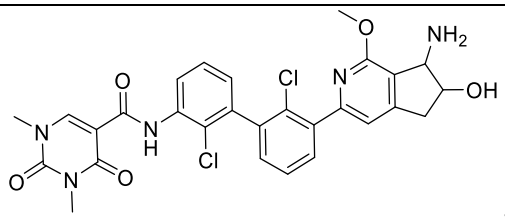
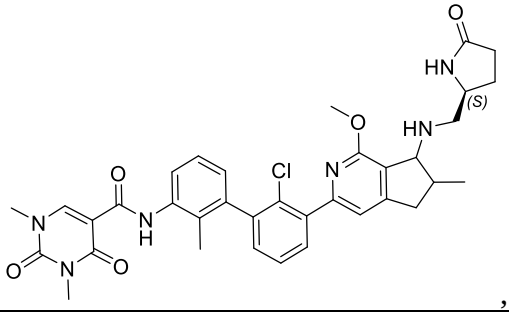
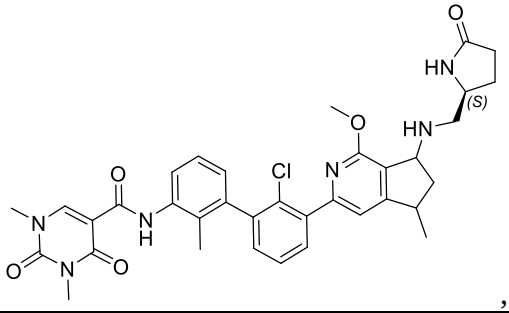
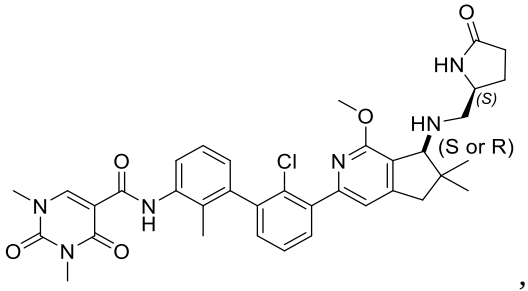
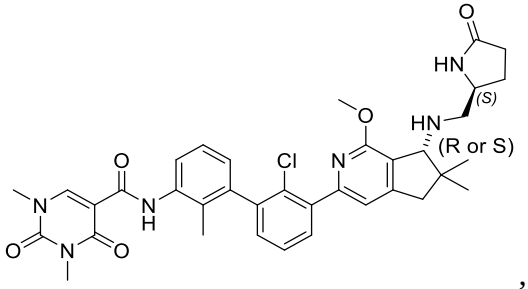
A-95	 ,
A-96	 ,
A-97	 ,
A-98	 ,
A-99	 ,

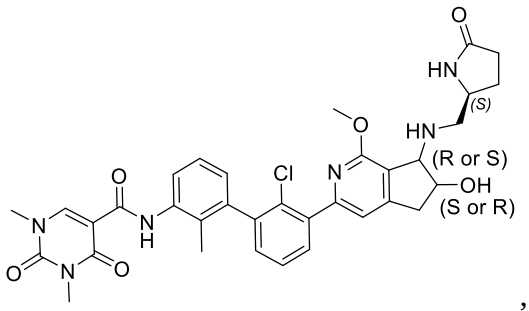
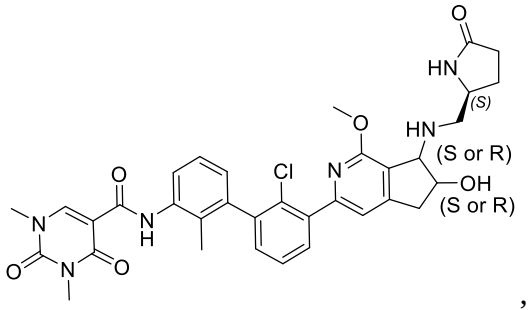
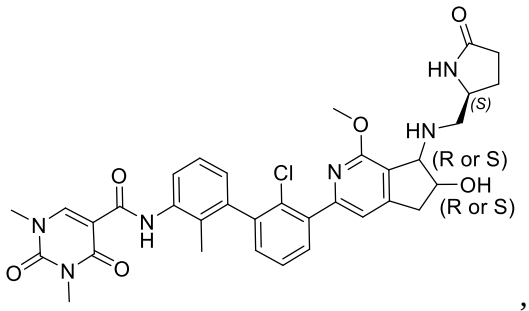
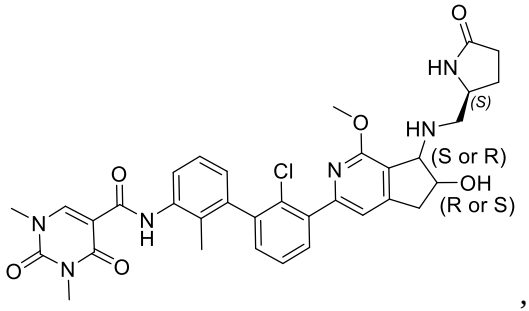
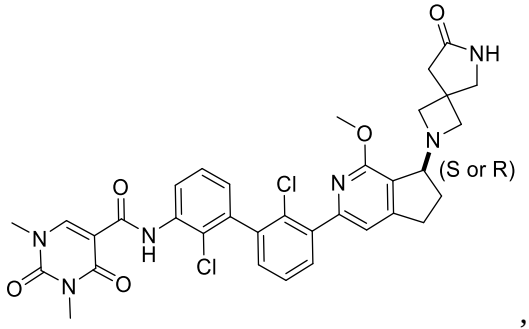
A-100	 ,
A-101	 ,
A-102	 ,
A-103	 ,
A-104	 ,

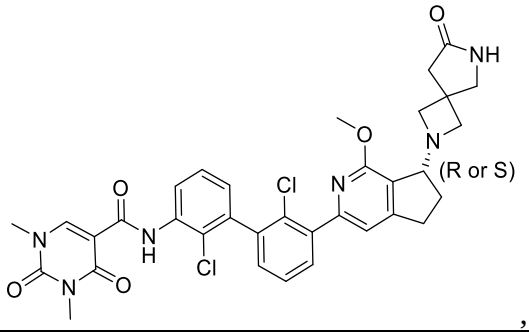
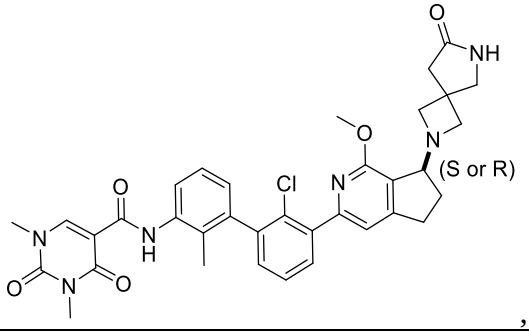
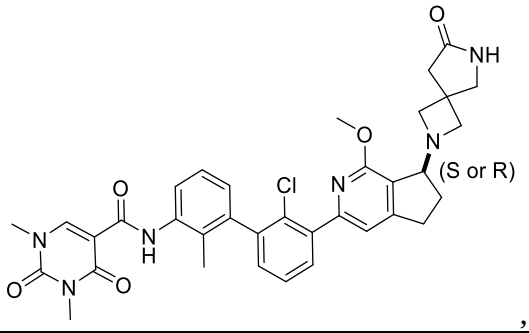
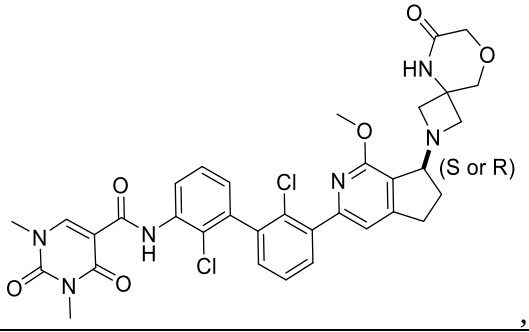
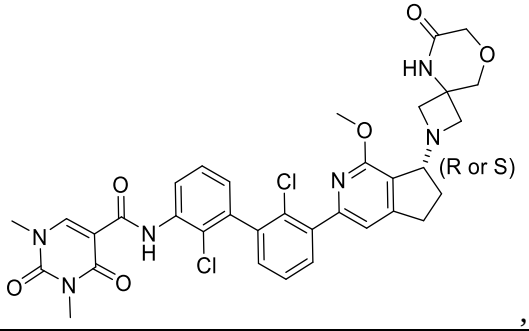
A-105	 ,
A-106	 ,
A-107	 ,
A-108	 ,
A-109	 ,

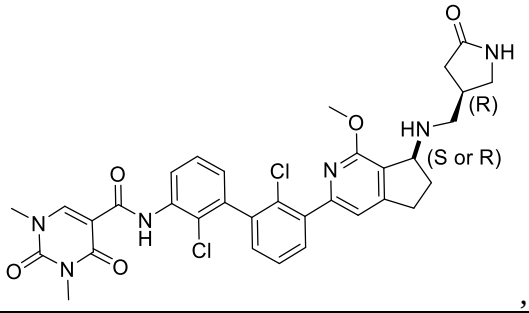
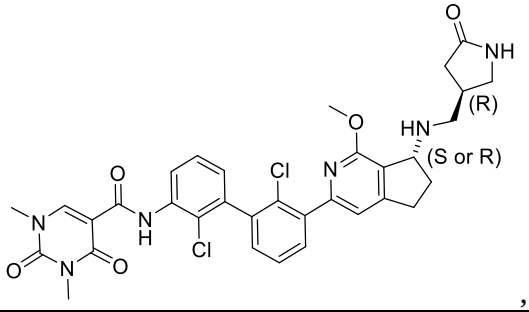
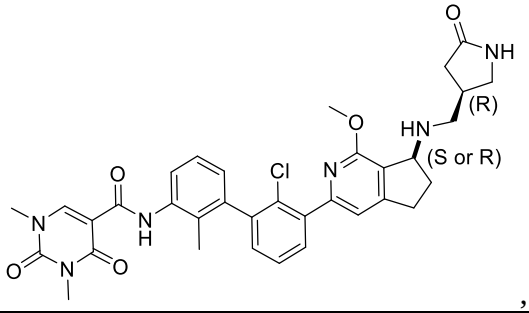
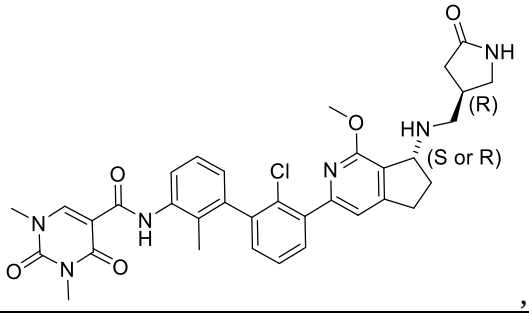
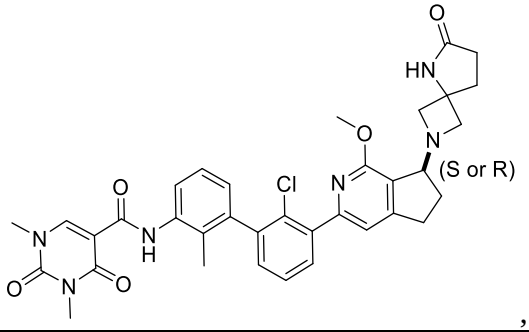
A-110	 ,
A-111	 ,
A-112	 ,
A-113	 ,
A-114	 ,

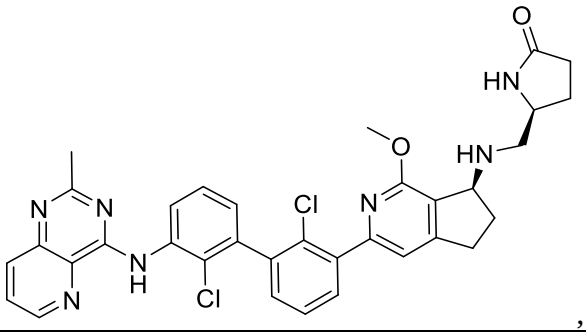
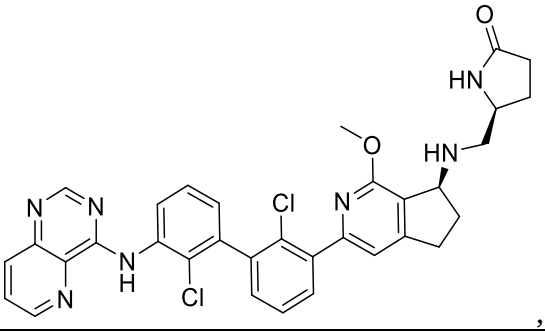
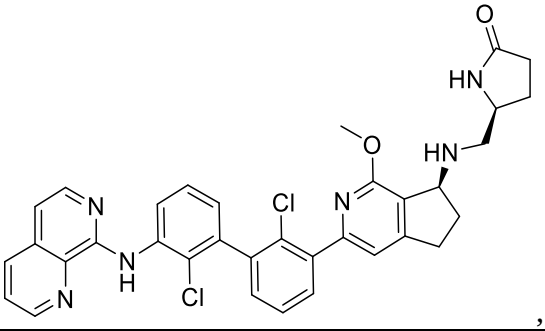
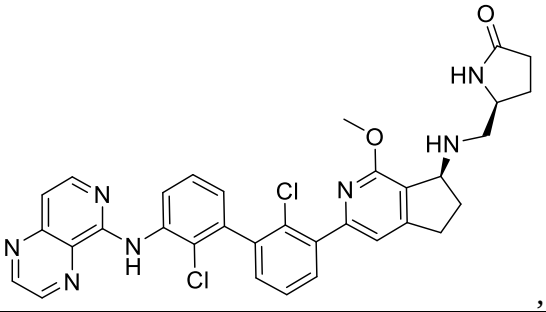
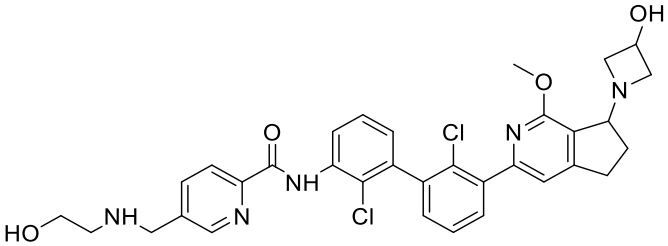
A-115	 ,
A-116	 ,
A-117	 ,
A-118	 ,
A-119	 ,

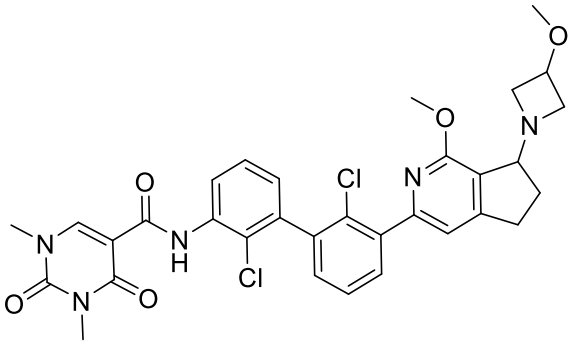
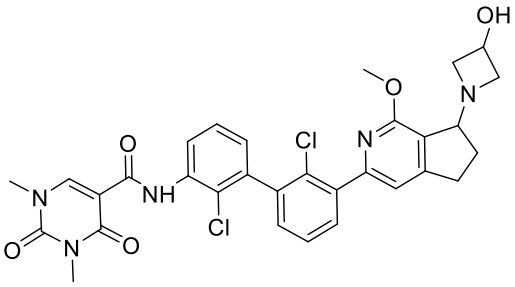
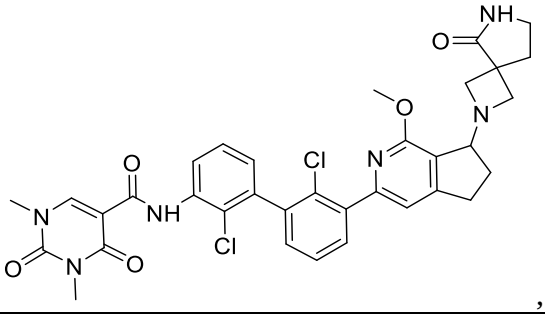
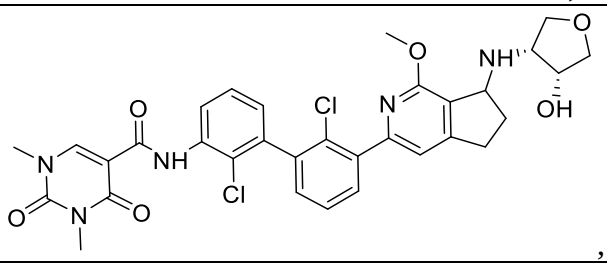
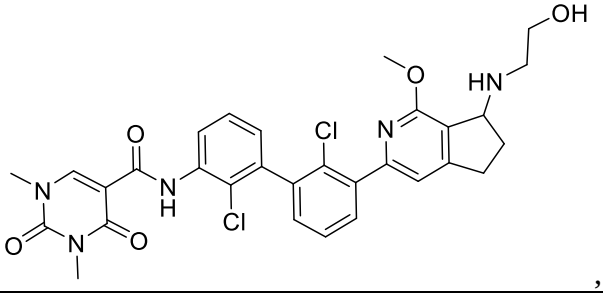
A-120	 ,
A-121	 ,
A-122	 ,
A-123	 ,
A-124	 ,

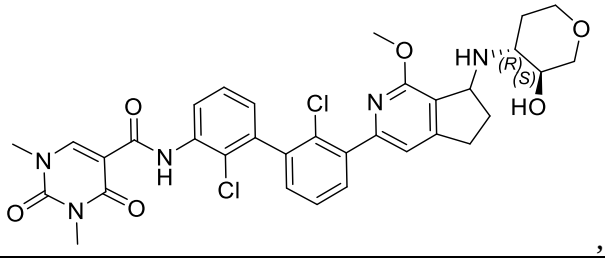
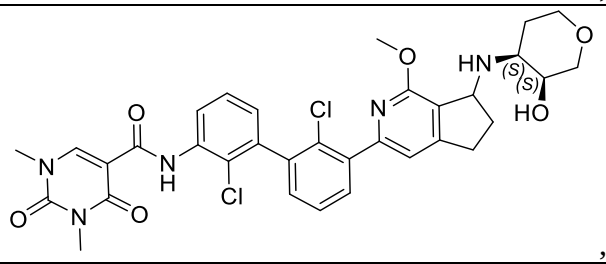
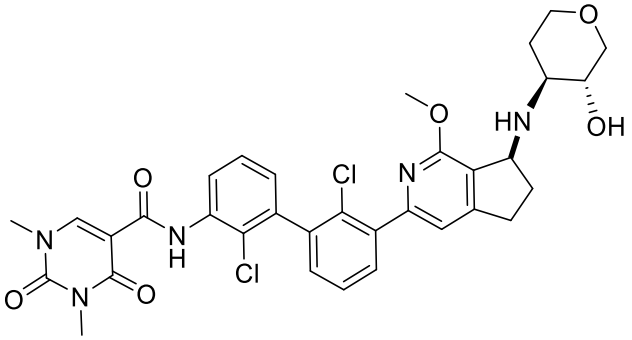
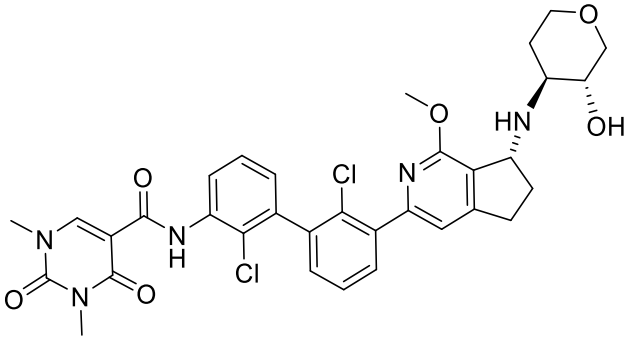
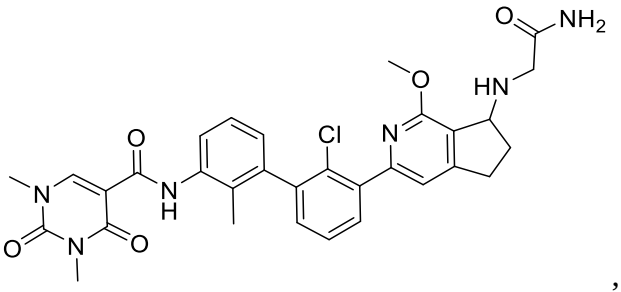
A-125	 ,
A-126	 ,
A-127	 ,
A-128	 ,
A-129	 ,

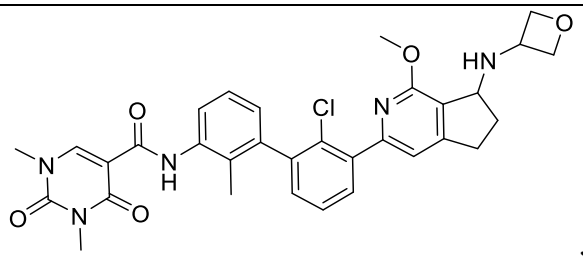
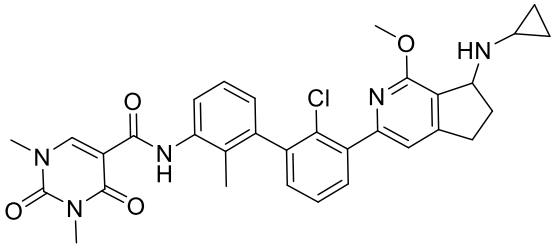
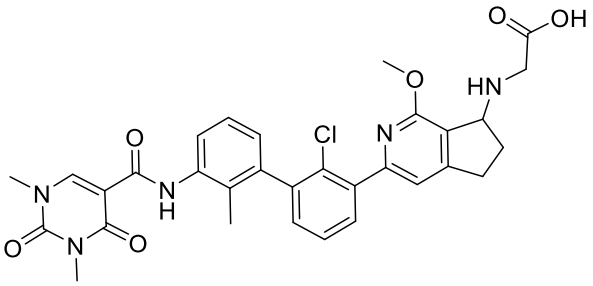
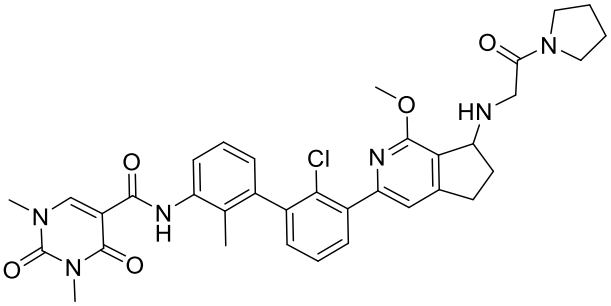
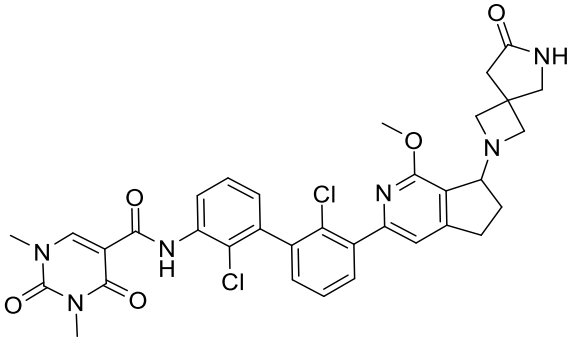
A-130	 (R or S) ,
A-131	 (S or R) ,
A-132	 (S or R) ,
A-133	 (S or R) ,
A-134	 (R or S) ,

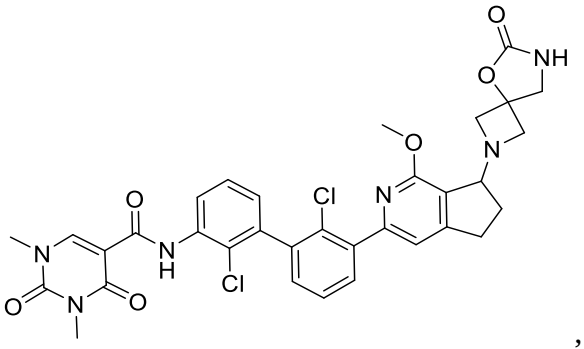
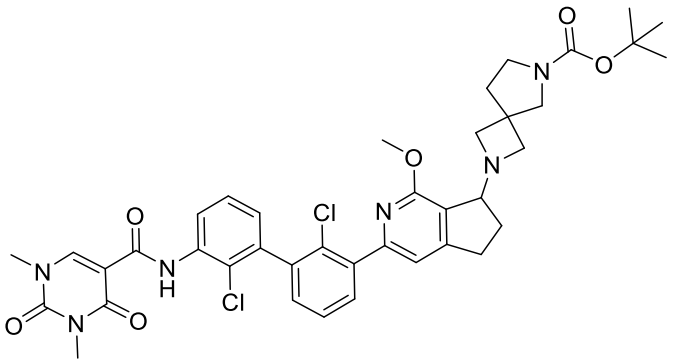
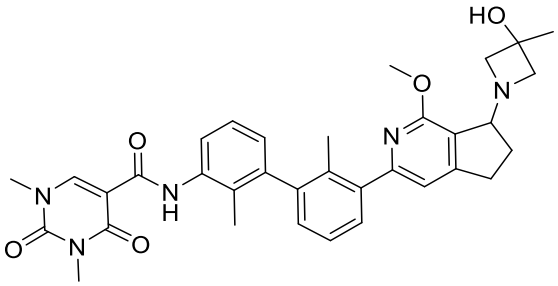
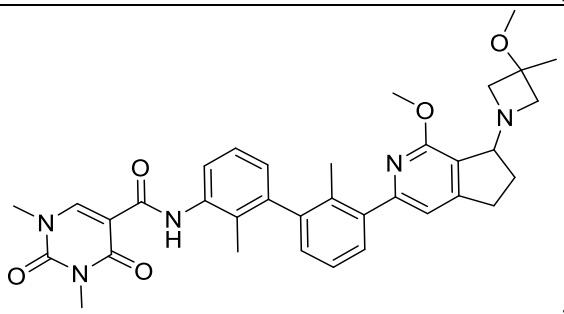
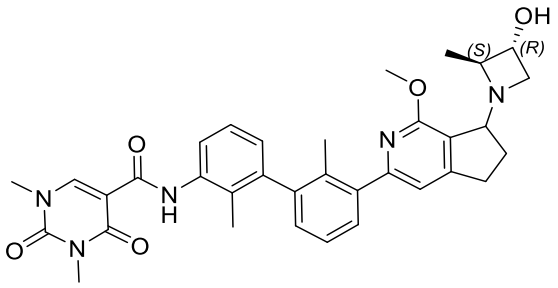
A-135	 ,
A-136	 ,
A-137	 ,
A-138	 ,
A-139	 ,

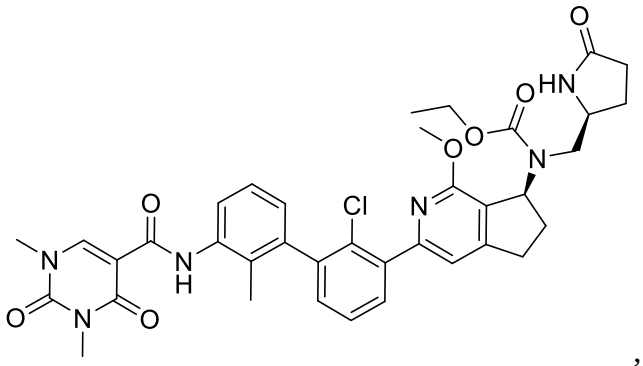
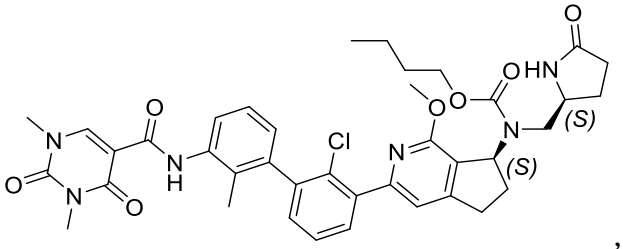
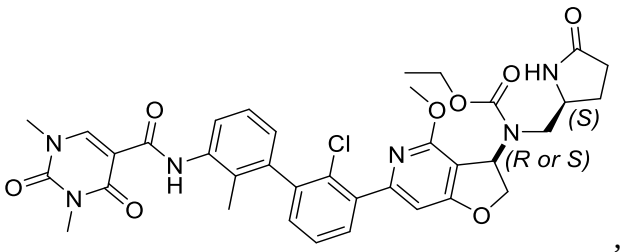
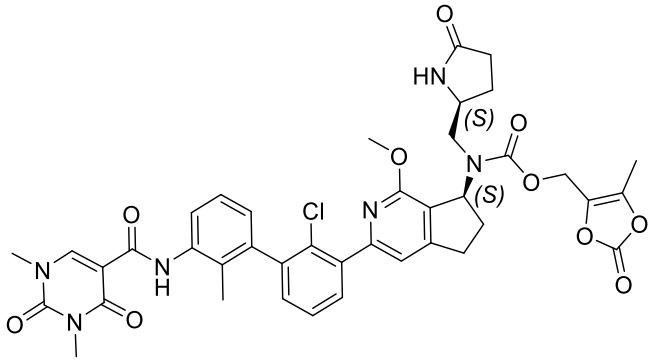
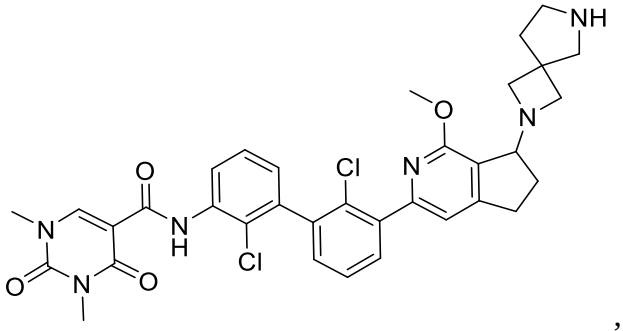
B-1	 ,
B-2	 ,
B-3	 ,
B-4	 ,
C-1	 ,

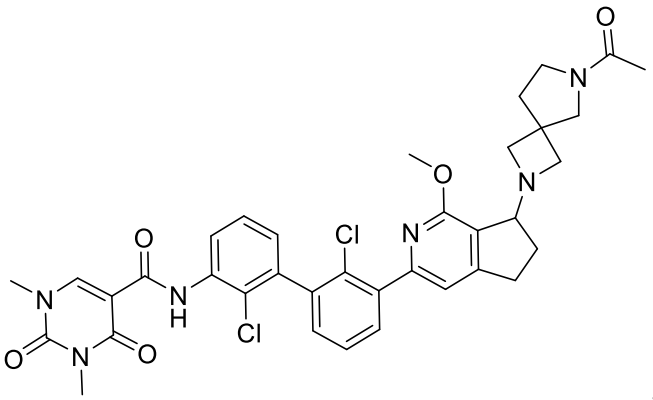
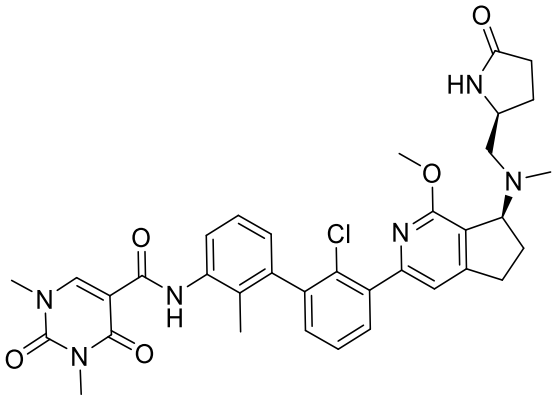
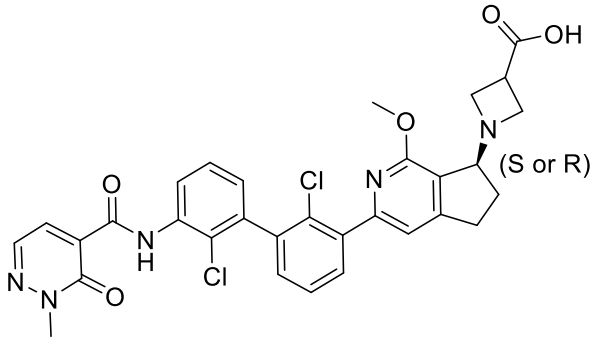
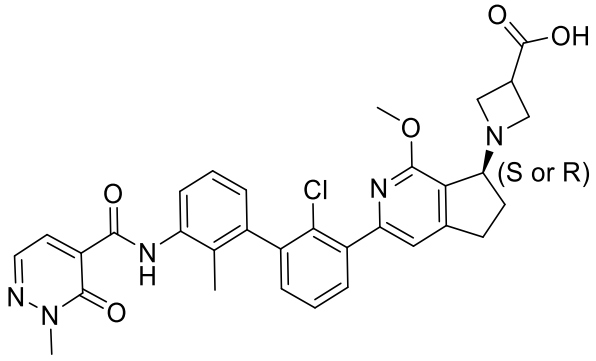
D-1	 ,
D-2	 ,
D-3	 ,
D-4	 ,
D-5	 ,

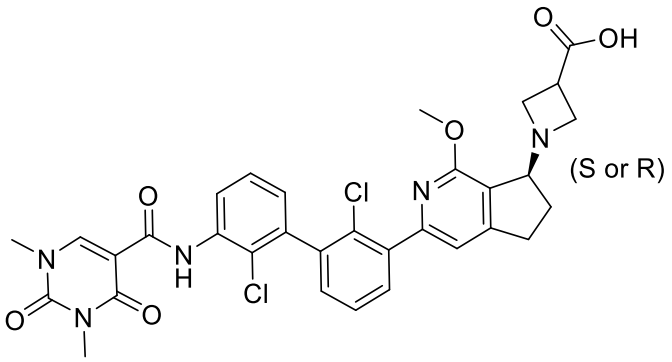
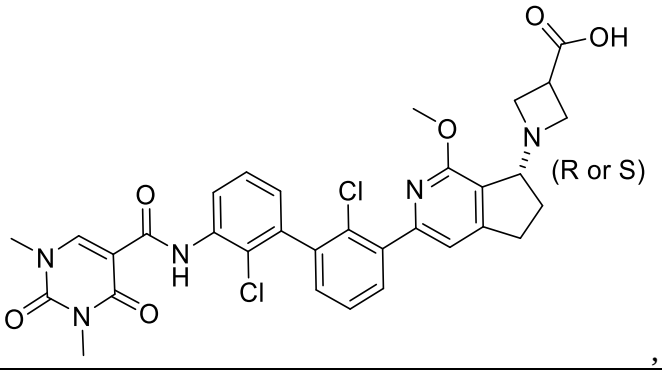
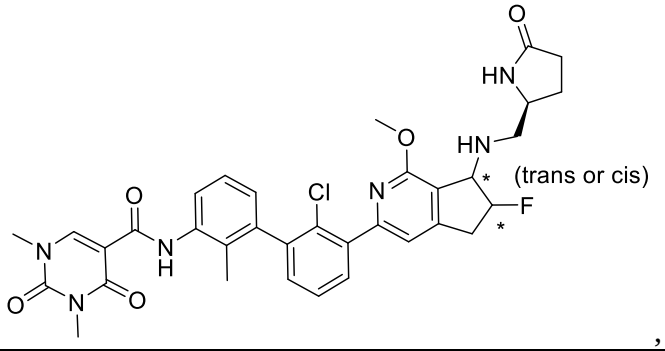
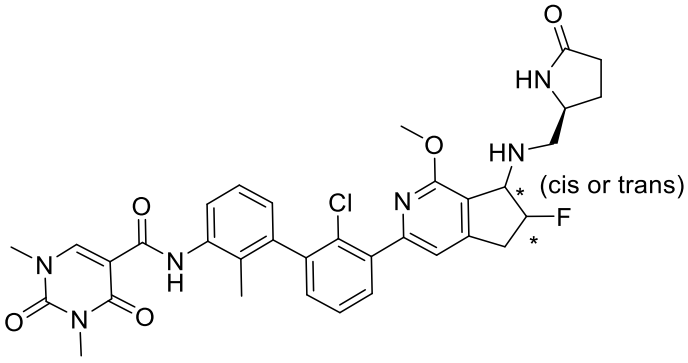
D-6	 ,
D-7	 ,
D-8a	 ,
D-8b	 ,
D-9	 ,

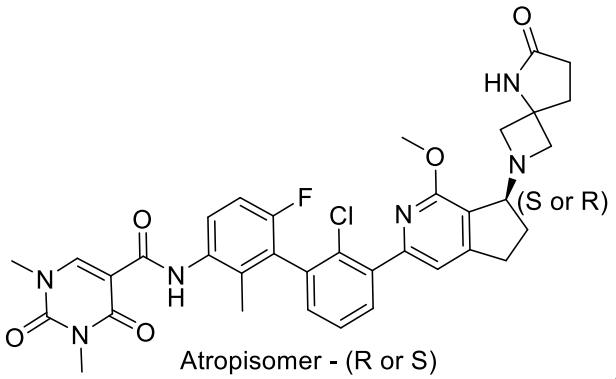
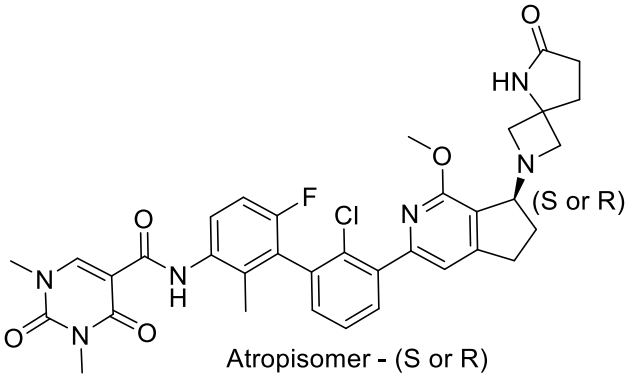
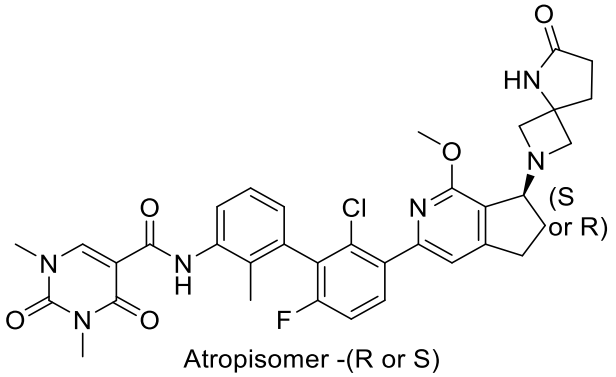
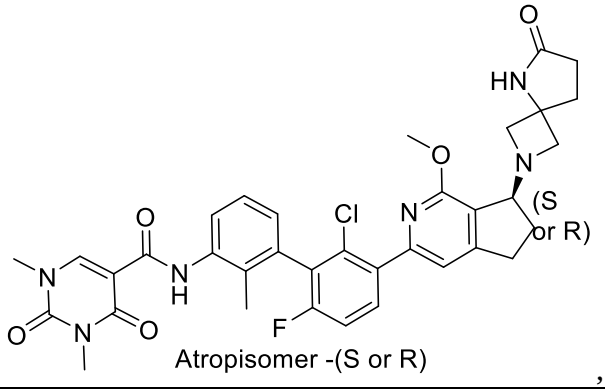
D-10	 ,
D-11	 ,
D-12	 ,
D-13	 ,
D-14	 ,

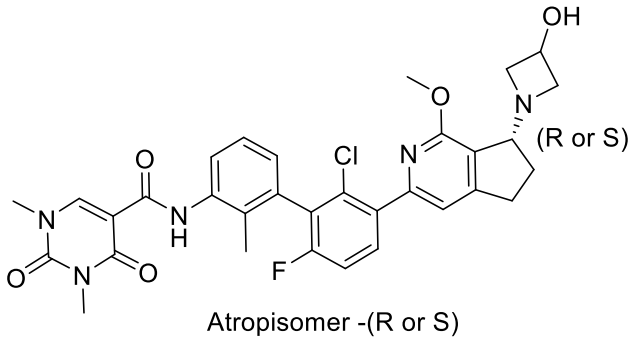
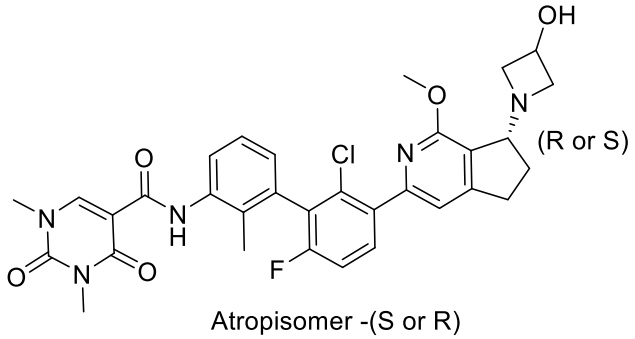
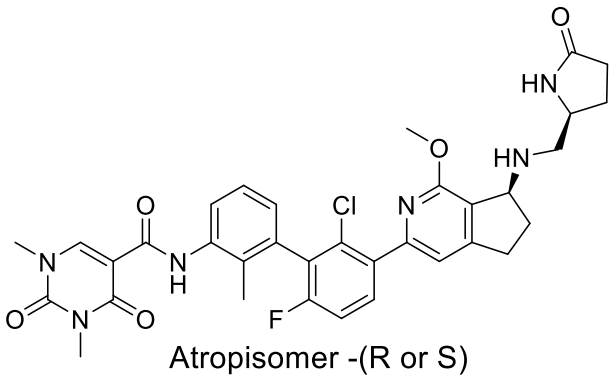
D-15	 ,
D-16	 ,
D-17	 ,
D-18	 ,
D-19	 ,

E-1	 ,
E-2	 ,
E-3	 ,
F-1	 ,
G-1	 ,

H-1	 ,
I-1	 ,
J-1	 ,
J-2	 ,

J-3	 ,
J-4	 ,
K-1a	 ,
K-1b	 ,

L-1a	 Atropisomer - (R or S) ,
L-1b	 Atropisomer - (S or R) ,
M-1a	 Atropisomer -(R or S) ,
M-1b	 Atropisomer -(S or R) ,

M-2a	 Atropisomer -(R or S) ,
M-2b	 Atropisomer -(S or R) ,
M-3a	 Atropisomer -(R or S) ,
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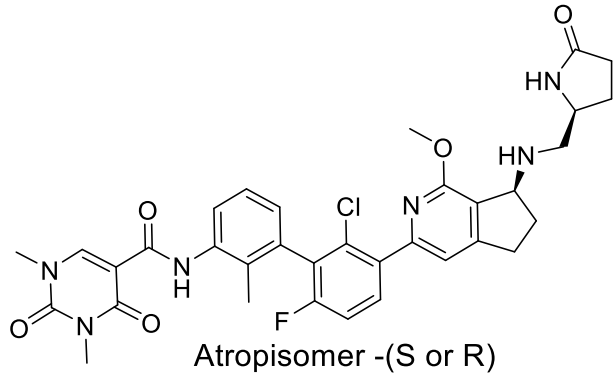
M-3b	 Atropisomer -(S or R)

, or a pharmaceutically acceptable salt of any of the foregoing.

149. A pharmaceutical composition comprising an effective amount of a compound of any one of Claims 1-148, or a pharmaceutically acceptable salt thereof, and excipient.

150. A compound of any one of Claims 1-148, or a pharmaceutically acceptable salt thereof, for use in treating hepatitis B.

151. A compound of any one of Claims 1-148, or a pharmaceutically acceptable salt thereof, for use in treating hepatocellular carcinoma (HCC).

152. The compound for use of any one of Claims 150-151, wherein the compound is to be used in combination with surgery, radiation therapy, chemotherapy, targeted therapy, immunotherapy, hormonal therapy, or antiviral therapy.

153. Use of an effective amount of a compound of any one of Claims 1-148, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating hepatitis B.

154. Use of an effective amount of a compound of any one of Claims 1-148, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating hepatocellular carcinoma (HCC).

155. The use of any one of Claims 153-154, wherein surgery, radiation therapy, chemotherapy, targeted therapy, immunotherapy, hormonal therapy, or antiviral therapy is to be further used.

156. A compound of any one of Claims 1-148, or a pharmaceutically acceptable salt thereof, for use in therapy.