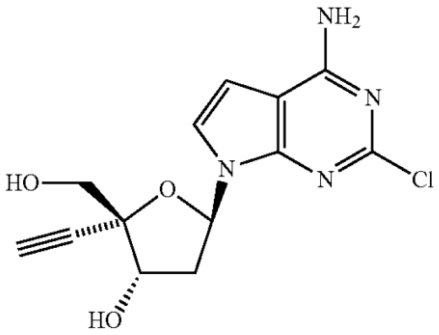
significant need for improved treatment and prevention of HIV infections using long-acting RT inhibitors.

## SUMMARY

**[0005]** The present disclosure is directed to prodrugs of 4'-substituted nucleoside derivatives and their use in the inhibition of HIV reverse transcriptase. The present disclosure is further directed to the use of these compounds in the prophylaxis of infection by HIV, the treatment of infection by HIV, and the prophylaxis, treatment, and delay in the onset or progression of AIDS and/or ARC, in a subject in need thereof. The present disclosure provides compounds that are solubility-limiting, cleavable prodrugs of NRTIs that may be adapted for extended dosing regimens for a subject in need thereof.

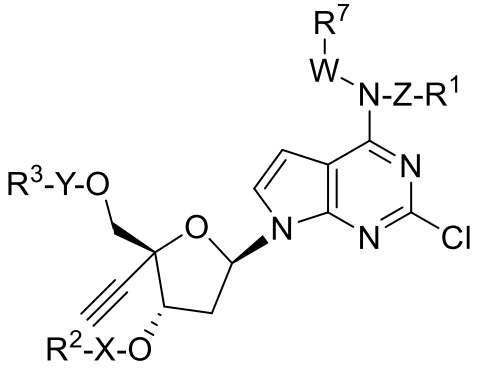
**[0006]** In some examples, the disclosure provides 4'-substituted fused heterocyclic compounds. In some examples, the disclosure provides compounds that are cleavable prodrugs of Compound A:




(A).

**[0007]** Compound A is a 4′-substituted heterocyclic nucleoside analogue. The synthesis and ability of Compound A to inhibit HIV reverse transcriptase is described in PCT International Application WO 2015/148746, published on October 1, 2015, to Merck Sharp & Dohme Corp., which is hereby incorporated by reference in its entirety.

**[0008]** In an aspect, provided herein is a compound having the Formula VI:




(VI)

or a pharmaceutically acceptable salt thereof, wherein:

**X** is selected from -C(=O)-, -C(=O)-O-, -$CR^5R^6$-O-C(=O)-, -$CR^5R^6$-O-C(=O)-O-, and a bond;

**Y** is selected from -C(=O)-, -C(=O)-O-, -$CR^5R^6$-O-C(=O)-, -$CR^5R^6$-O-C(=O)-O-, -P(=O)(O-$C_{6-12}$ aryl)-NH-$CR^4$C(=O)-O-, and a bond;

**Z** is selected from -C(=O)-, -C(=O)-O-, and a bond;

**W** is selected from -C(=O)-, -C(=O)-O-, and a bond;

**$R^1$** is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy;

**$R^2$** is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, and $(CR^5R^6)_z$-$C_{1-6}$ alkyl ester, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, oxo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy;

**$R^3$** is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, and $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, oxo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl, or hydroxy, and wherein said aryl can be optionally substituted with one to three groups independently selected from halo, oxo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl, hydroxy, and $C_{1-6}$ alkyl ester;

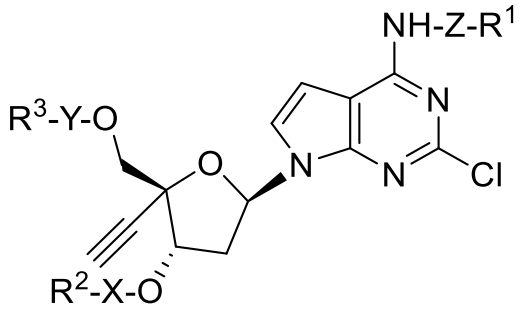
**$R^4$** is selected from the group consisting of hydrogen, $C_{1-3}$ alkyl, and $(CH_2)_z$-cycloalkyl;

**$R^5$** and **$R^6$** are each independently selected from hydrogen, a halogen, $C_{1-3}$ alkyl, and $C_{3-6}$ cycloalkyl; and

**$R^7$** is selected from hydrogen, $C_{1-21}$ alkyl and $(CR^5R^6)_z$-$C_{5-12}$cycloalkyl,
wherein at least one of $R^1$, $R^2$ and $R^3$ is not hydrogen; and z is 0, 1, 2, 3, 4, 5, or 6.

**[0009]** In an example of this disclosure are compounds of Formula VI having structural Formula I, or a pharmaceutically acceptable salt thereof:

**[0010]** Accordingly, in some examples, provided herein are compounds having the Formula I:




(I)

or a pharmaceutically acceptable salt thereof, wherein:

**X** is selected from -C(=O)-, -C(=O)-O-, -$CR^5R^6$-O-C(=O)-, -$CR^5R^6$-O-C(=O)-O- or a bond;

**Y** is selected from -C(=O)-, -C(=O)-O-, -$CR^5R^6$-O-C(=O)-, -$CR^5R^6$-O-C(=O)-O-, -P(=O)(O-$C_{6-12}$ aryl)-NH-$CR^4$C(=O)-O- or a bond;

**Z** is selected from -C(=O)-, or a bond;

**$R^1$** is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$ cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy;

**$R^2$** is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$ cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy;

**$R^3$** is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$ cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy;

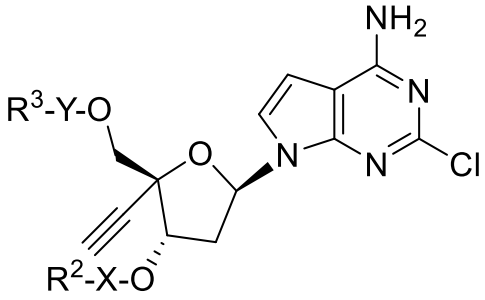
**$R^4$** is selected from the group consisting of hydrogen, $C_{1-3}$ alkyl or $(CH_2)_z$-cycloalkyl;

**$R^5$** and **$R^6$** are each independently selected from hydrogen, a halogen, $C_{1-3}$ alkyl, and $C_{3-6}$ cycloalkyl; and wherein at least one of $R^1$, $R^2$ and $R^3$ is not hydrogen; and

z is 0, 1, 2, 3, 4, 5, or 6.

**[0011]** In some examples of Formula I and Formula VI, where X is -$CR^5R^6$-O-C(=O)- and/or Y is -$CR^5R^6$-O-C(=O)-, neither $R^5$nor $R^6$ is a halogen.

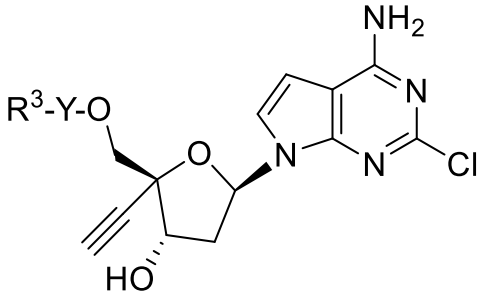
**[0012]** In an example of this disclosure are compounds of Formula I and Formula VI having structural Formula II or a pharmaceutically acceptable salt thereof:




II,

wherein all variables therein ($R^2$, $R^3$, X, Y, etc.) are as defined in Formula I and Formula VI.

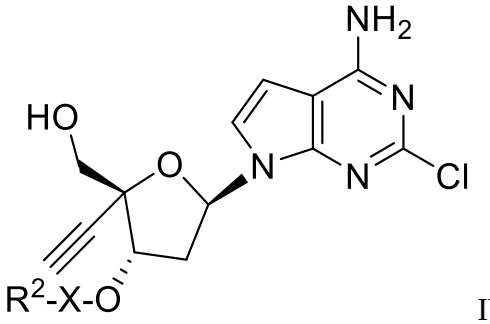
**[0013]** In another example of this disclosure are compounds of Formula I and Formula VI having structural Formula III or a pharmaceutically acceptable salt thereof:




III,

wherein all variables therein ($R^3$, Y, etc.) are as defined in Formula I and Formula VI.

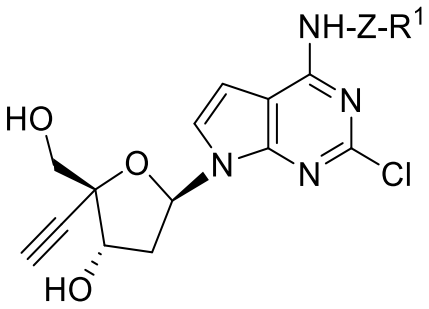
**[0014]** In another example of this disclosure are compounds of Formula I and Formula VI having structural Formula IV or a pharmaceutically acceptable salt thereof:




IV,

wherein all variables therein ($R^2$, X, etc.) are as defined in Formula I and Formula VI.

**[0015]** In another example of this disclosure are compounds of Formula I and Formula VI having structural Formula V or a pharmaceutically acceptable salt thereof:




V,

wherein all variables therein ($R^1$, Z, etc.) are as defined in Formula I and Formula VI.

**[0016]** Accordingly, in various examples, provided herein are cleavable prodrugs of Compound A that are substituted at the 3' (or 3-) position, the 5' (or 5-) position, or both positions, of the tetrahydrofuran ("THF") ring (which also may be referred to herein as the sugar moiety).

**[0017]** Further provided herein are cleavable prodrugs of Compound A that are substituted at the 5' position of the THF ring, the 4-amino position of the pyrrolopyrimidine core, or both positions. Further provided herein are cleavable prodrugs of Compound A that are substituted at the 3' position of the THF ring, the 5' position of the THF ring, the 4-amino position of the pyrrolopyrimidine core, or all three positions.

**[0018]** All structural Formulas, embodiments (or examples) and classes thereof described herein include the pharmaceutically acceptable salts of the compounds defined therein. Reference to the compounds of Formula I and Formula VI herein encompasses the compounds of each of Formulas I, II, III, IV, V, and VI, and all embodiments (or examples) and classes thereof. Reference to the compounds of this invention (or disclosure) as those of a specific formula or embodiment (or example), e.g., Formula I, II, III, IV, V or VI, or embodiments (or examples) thereof, or any other generic structural formula or specific compound described or claimed herein, is intended to encompass the specific compound or compounds falling within the scope of the Formula or embodiment (or example), including salts thereof, particularly pharmaceutically acceptable salts, solvates (including hydrates) of such compounds and solvated salt forms thereof, where such forms are possible, unless specified otherwise.

**[0019]** The present disclosure includes each of the Examples described herein, and pharmaceutically acceptable salts thereof. The disclosure also encompasses pharmaceutical compositions comprising an effective amount of a compound of the disclosure or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

**[0019a]** In another aspect, there is provided a pharmaceutical composition comprising a compound or salt as described herein, and a pharmaceutically acceptable carrier.

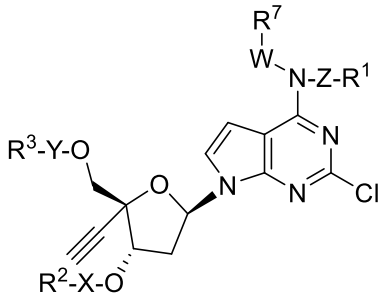
**[0019b]** In another aspect, there is provided use of the compound or salt as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for the inhibition of HIV reverse transcriptase in a subject in need thereof.

**[0019c]** In another aspect, there is provided use of the compound or salt as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for the treatment or prophylaxis of infection by HIV or the treatment, prophylaxis, or delay in the onset or progression of AIDS in a subject in need thereof.

**[0019d]** In another aspect, there is provided the compound or salt as described herein, or the pharmaceutical composition as described herein, for use in therapy.

WHAT IS CLAIMED IS:

1. A compound of Formula (VI):




(VI)

or a pharmaceutically acceptable salt thereof, wherein:

**X** is selected from -C(=O)-, -C(=O)-O-, -$CR^5R^6$-O-C(=O)-, -$CR^5R^6$-O-C(=O)-O-, and a bond;aryl

**Y** is selected from -C(=O)-, -C(=O)-O-, -$CR^5R^6$-O-C(=O)-, -$CR^5R^6$-O-C(=O)-O-, -P(=O)(O-$C_{6-12}$ aryl)-NH-$CR^4$C(=O)-O-, and a bond;

**Z** is selected from -C(=O)-, -C(=O)-O-, and a bond;

**W** is selected from -C(=O)-, -C(=O)-O-, and a bond;

**$R^1$** is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy;

**$R^2$** is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, and $(CR^5R^6)_z$-$C_{1-6}$ alkyl ester, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, oxo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy;

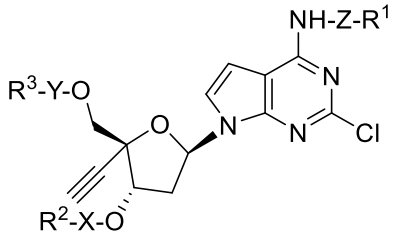
**$R^3$** is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, and $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, oxo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl, or hydroxy, and wherein said aryl can be optionally substituted with one to three groups independently selected from halo, oxo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl, hydroxy, and $C_{1-6}$ alkyl ester;

**$R^4$** is selected from the group consisting of hydrogen, $C_{1-3}$ alkyl, and $(CH_2)_z$-cycloalkyl;

**$R^5$** and **$R^6$** are each independently selected from hydrogen, a halogen, $C_{1-3}$ alkyl, and $C_{3-6}$ cycloalkyl; and

**$R^7$** is selected from hydrogen, $C_{1-21}$ alkyl and $(CR^5R^6)_z$-$C_{5-12}$cycloalkyl, wherein at least one of $R^1$, $R^2$ and $R^3$ is not hydrogen; and z is 0, 1, 2, 3, 4, 5, or 6.

2. A compound of Formula (I):




(I)

or a pharmaceutically acceptable salt thereof, wherein:

**X** is selected from -C(=O)-, -C(=O)-O-, -$CR^5R^6$-O-C(=O)-, -$CR^5R^6$-O-C(=O)-O-, and a bond;

**Y** is selected from -C(=O)-, -C(=O)-O-, -$CR^5R^6$-O-C(=O)-, -$CR^5R^6$-O-C(=O)-O-, -P(=O)(O-$C_{6-12}$ aryl)-NH-$CR^4$C(=O)-O-, and a bond;

**Z** is selected from -C(=O)- and a bond;

**$R^1$** is selected from the group consisting of hydrogen, $C_1$-$_{21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$ cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, and $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy;

**$R^2$** is selected from the group consisting of hydrogen, $C_1$-$_{21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$ cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, and $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy;

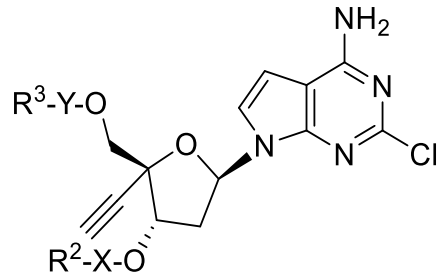
**$R^3$** is selected from the group consisting of hydrogen, $C_1$-$_{21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$ cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, and $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy;

**$R^4$** is selected from the group consisting of hydrogen, $C_{1-3}$ alkyl and $(CH_2)_z$-cycloalkyl;

**$R^5$** and **$R^6$** are each independently selected from hydrogen, a halogen, $C_{1-3}$ alkyl, and $C_{3-6}$ cycloalkyl; and

wherein at least one of $R^1$, $R^2$ and $R^3$ is not hydrogen; and z is 0, 1, 2, 3, 4, 5, or 6.

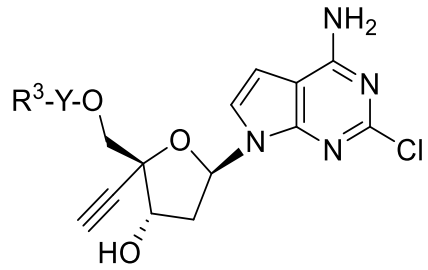
3. The compound of claim 1 or 2, wherein the compound is of Formula (II):




(II)

or a pharmaceutically acceptable salt thereof.

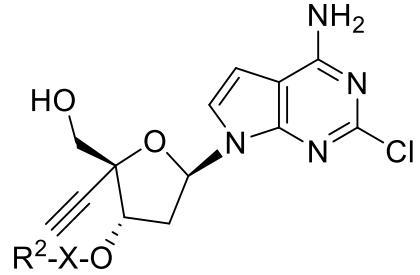
4. The compound of claim 1 or 2, wherein the compound is of Formula (III):




(III)

or a pharmaceutically acceptable salt thereof.

5. The compound of claim 1 or 2, wherein the compound is of Formula (IV):




(IV)

or a pharmaceutically acceptable salt thereof.

6. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein

**X** is selected from -C(=O)-, -$CR^5R^6$-O-C(=O)-, and a bond;

**Y** is selected from -C(=O)-, -$CR^5R^6$-O-C(=O)-, and a bond;

**Z** is a bond, and $\mathbf{R^1}$ is hydrogen;

$\mathbf{R^2}$ is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$ cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, and $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy; and

$\mathbf{R^3}$ is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$ cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, and $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy,

wherein z is 0, 1, 2, 3, 4, 5, or 6.

7. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein

**X** is selected from -C(=O)-O-, -$CR^5R^6$-O-C(=O)-O-, and a bond;

**Y** is selected from -C(=O)-O-, -$CR^5R^6$-O-C(=O)-O-, and a bond;

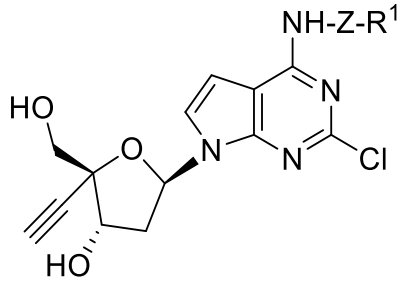
**Z** is a bond, and $\mathbf{R^1}$ is hydrogen;

$\mathbf{R^2}$ is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$ cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, and $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy; and

$\mathbf{R^3}$ is selected from the group consisting of hydrogen, $C_{1-21}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$ cycloalkyl, $(CR^5R^6)_z$-$C_{5-12}$heterocyclyl, $(CR^5R^6)_z$-$C_{6-12}$ aryl, and $(CR^5R^6)_z$-$C_{5-12}$ heteroaryl, wherein said alkyl, cycloalkyl, heterocyclyl, aryl or heteroaryl group can be optionally substituted with one to three groups independently selected from halo, $C_{1-6}$ alkyl, $C_{3-12}$ cycloalkyl and hydroxy,

wherein z is 0, 1, 2, 3, 4, 5, or 6.

8. The compound of claim 1 or 2, wherein the compound is of Formula (V):




(V)

or a pharmaceutically acceptable salt thereof.

9. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, wherein:

**X** is selected from -C(=O)-, -C(=O)-O-, and a bond;

**Y** is selected from -C(=O)-, -C(=O)-O-, and a bond;

**Z** is a bond, and $\mathbf{R^1}$ is hydrogen;

$\mathbf{R^1}$ is selected from hydrogen and $C_{1-14}$ alkyl;

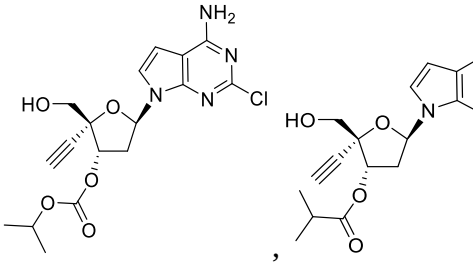
$\mathbf{R^2}$ is selected from $C_{1-10}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$cycloalkyl, and $(CR^5R^6)_z$-$C_6$ aryl, wherein said aryl can be optionally substituted with a halo; and

$\mathbf{R^3}$ is selected from $C_{1-10}$ alkyl, $(CR^5R^6)_z$-$C_{3-12}$cycloalkyl, and $(CR^5R^6)_z$-$C_6$ aryl, wherein said aryl can be optionally substituted with a halo, and

wherein $\mathbf{R^5}$ and $\mathbf{R^6}$ are hydrogen,

wherein z is 0, 1, 2, 3, 4, 5, or 6.

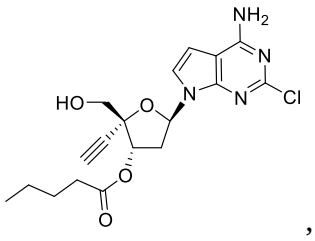
10. The compound of any one of claims 1-9 having the structure:



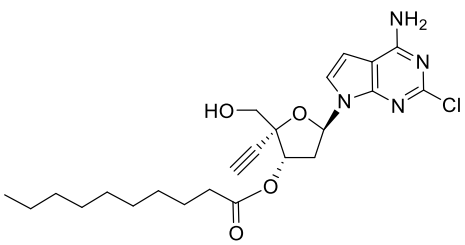

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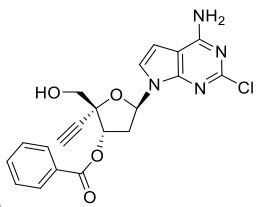

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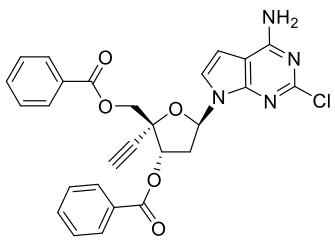

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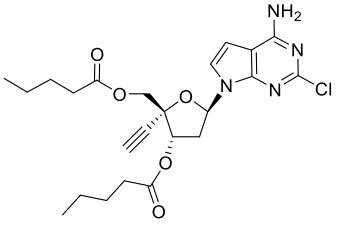
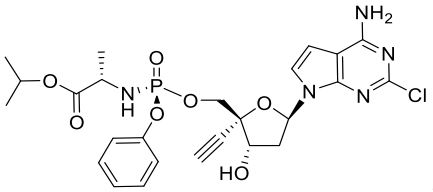
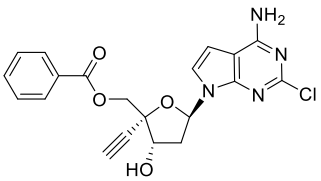

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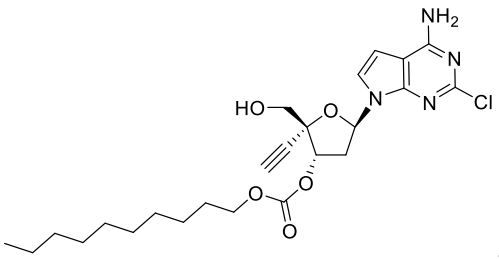
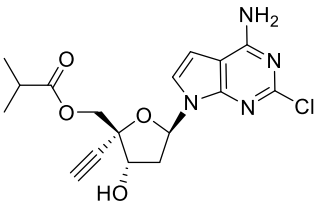
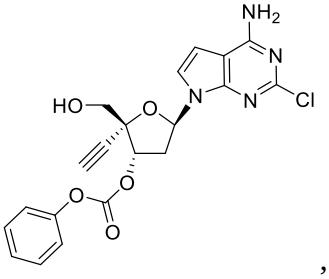


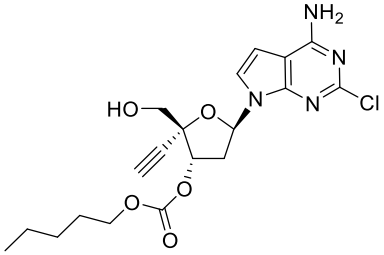
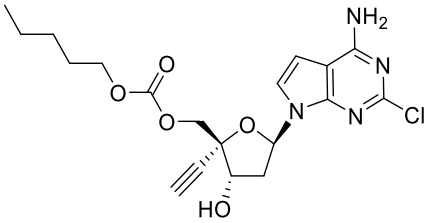
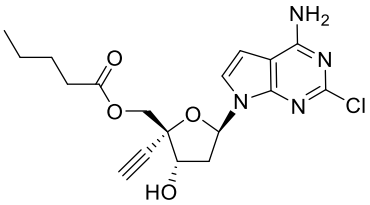

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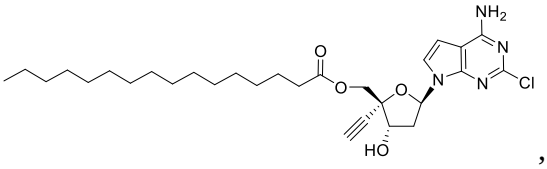
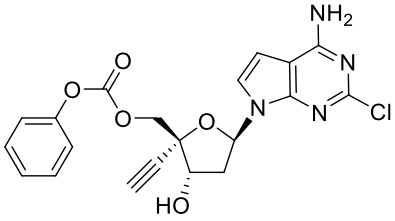


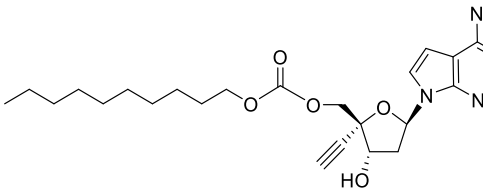
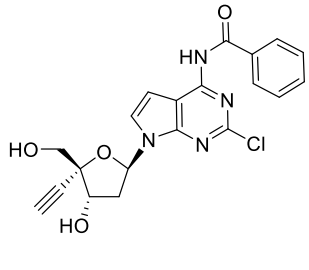

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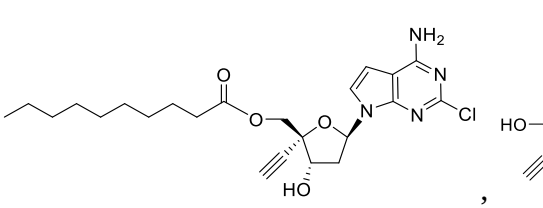
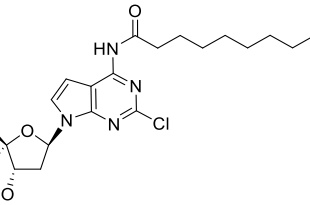

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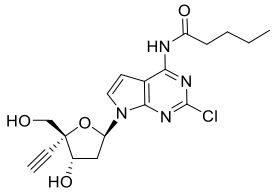

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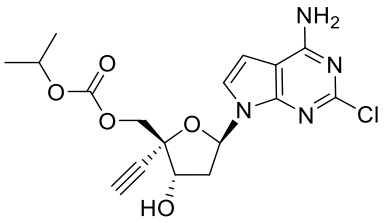
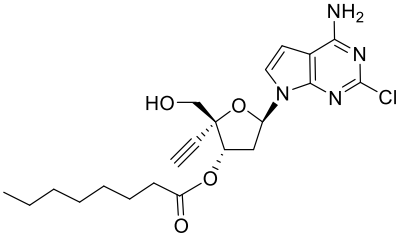
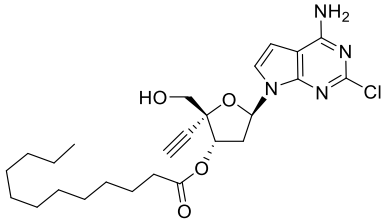

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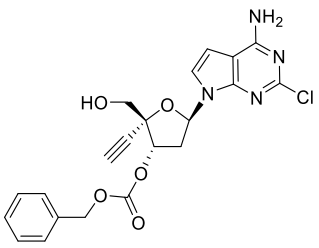
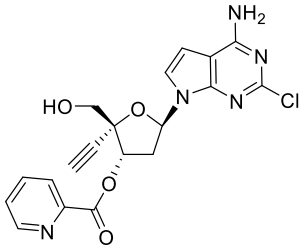
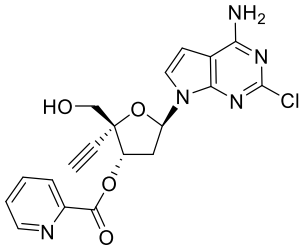
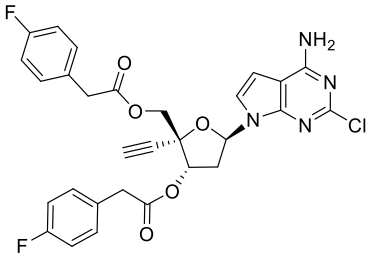
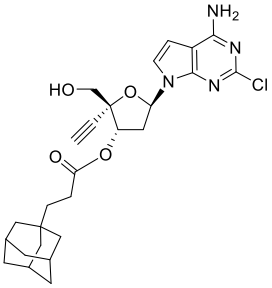
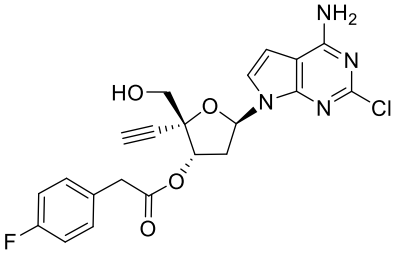
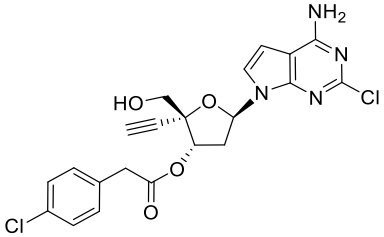
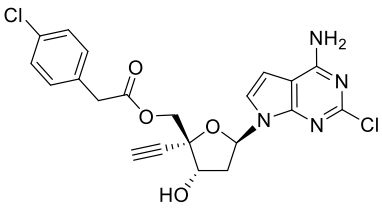
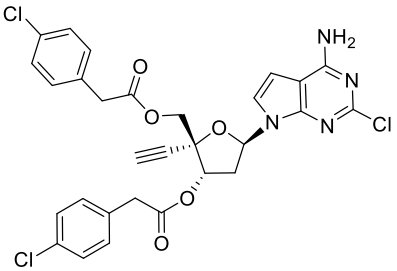
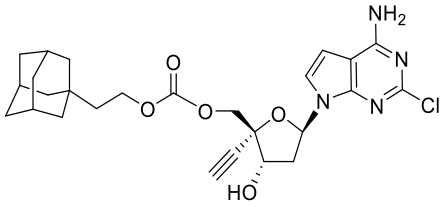
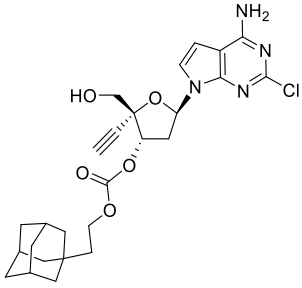
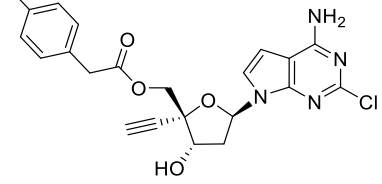
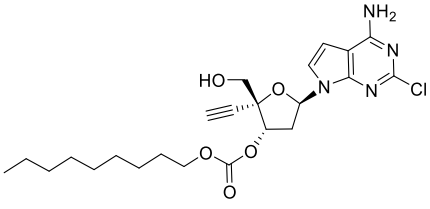
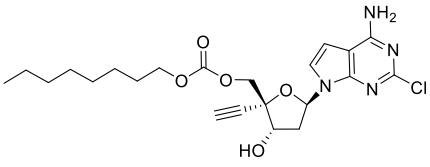

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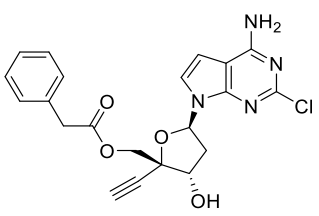
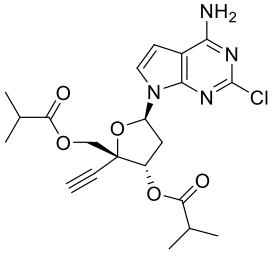
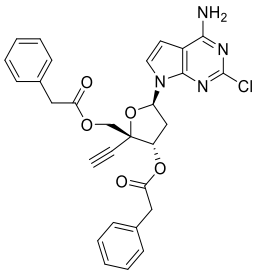
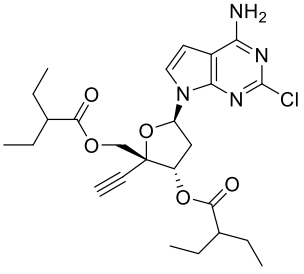

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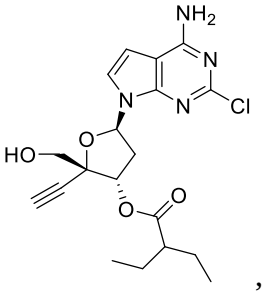
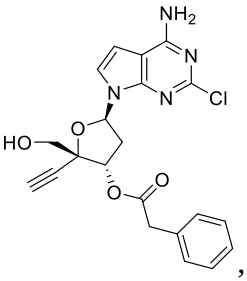
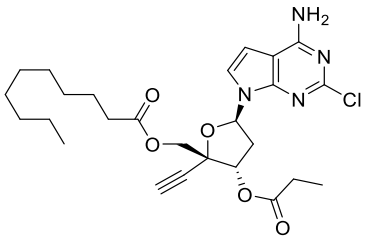
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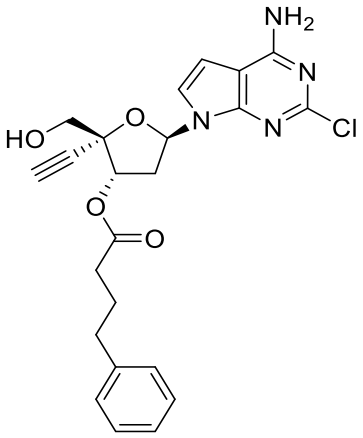
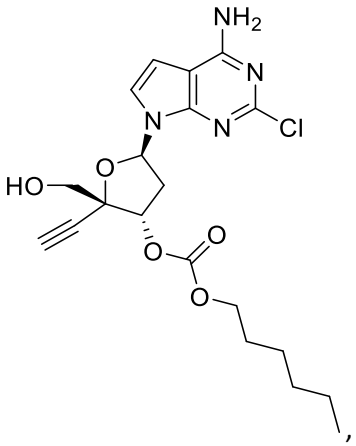
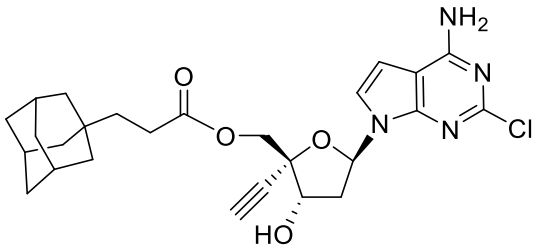
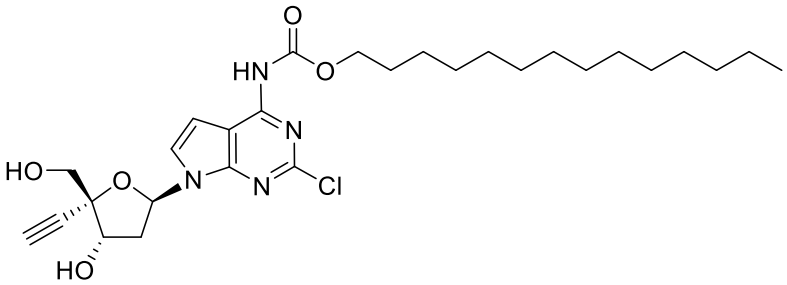
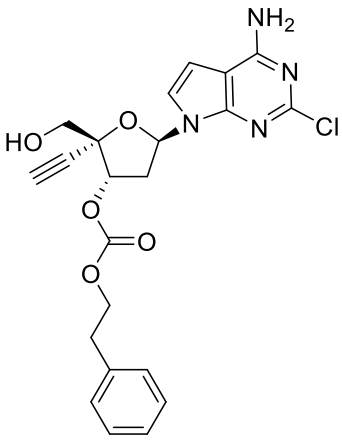
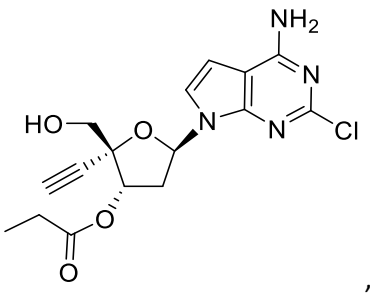
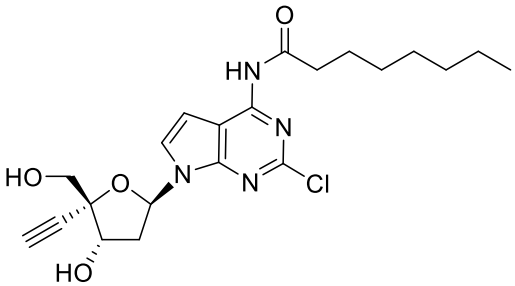
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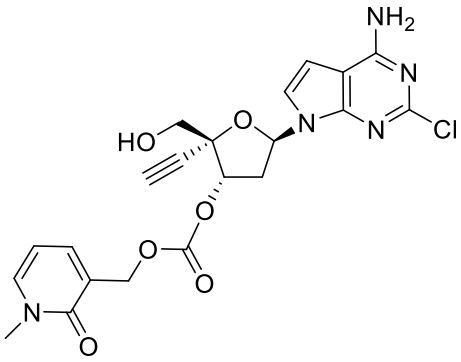
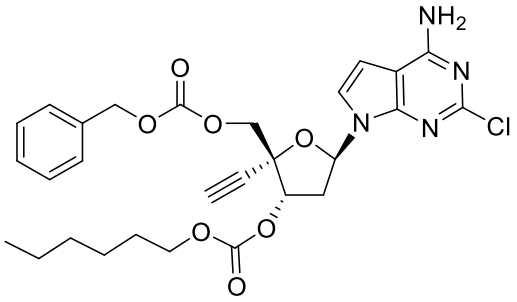
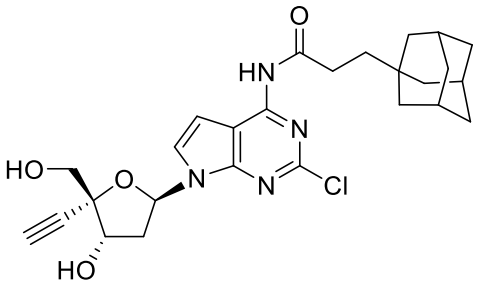
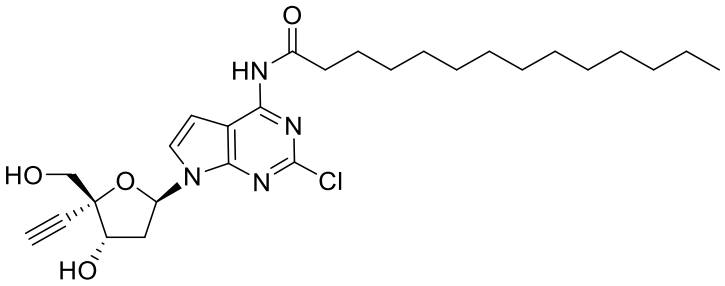
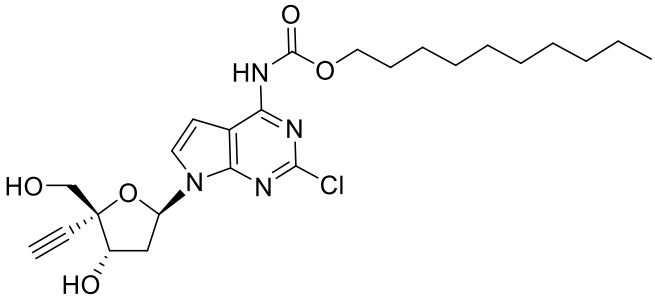
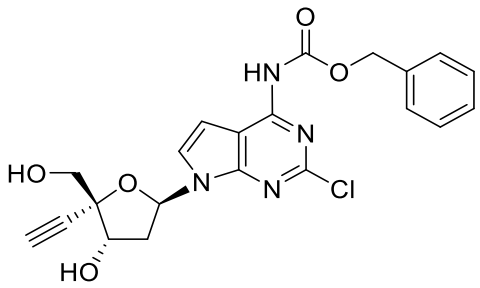
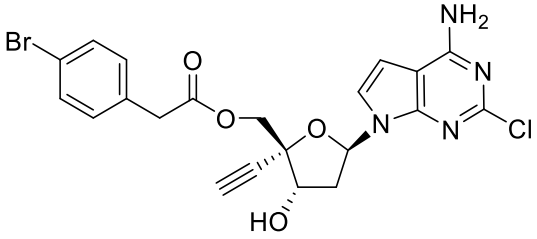
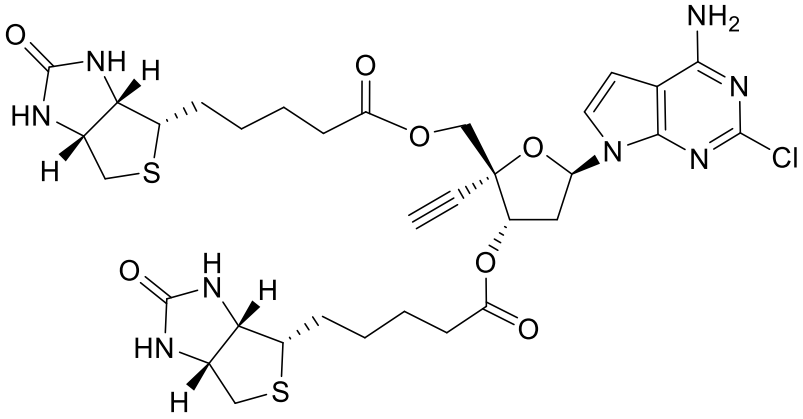
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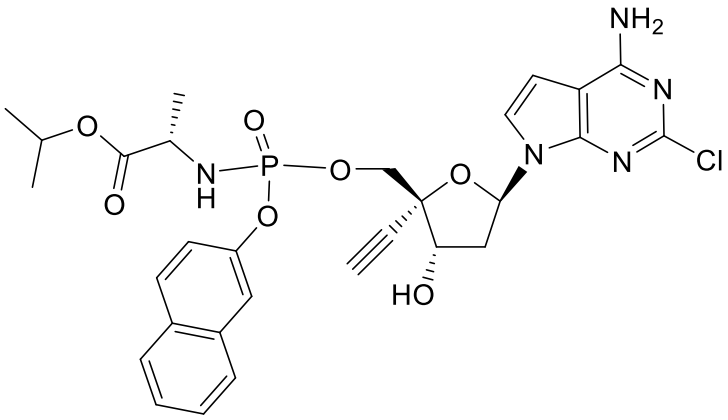
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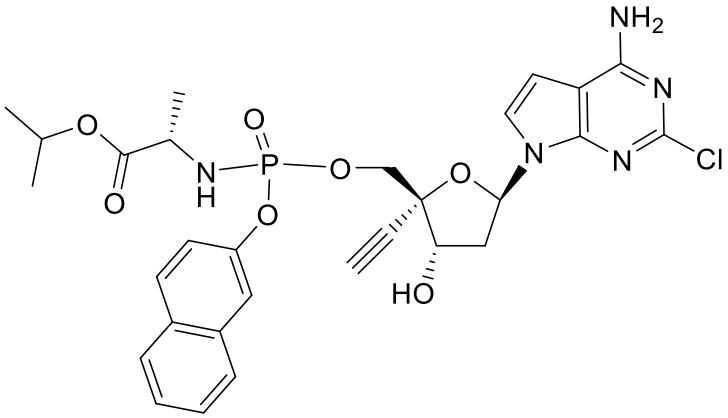

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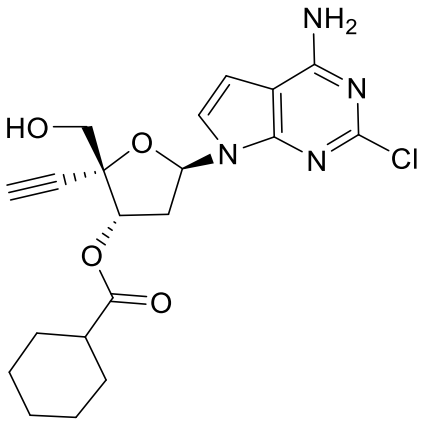

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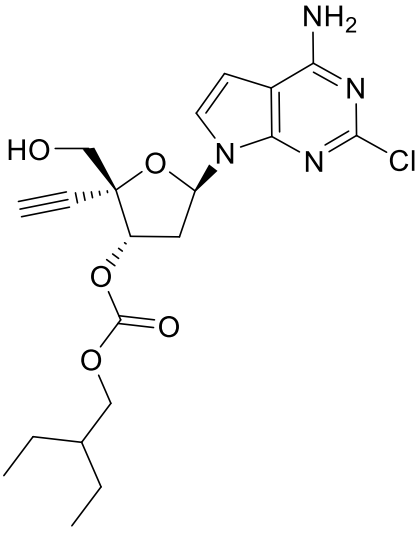
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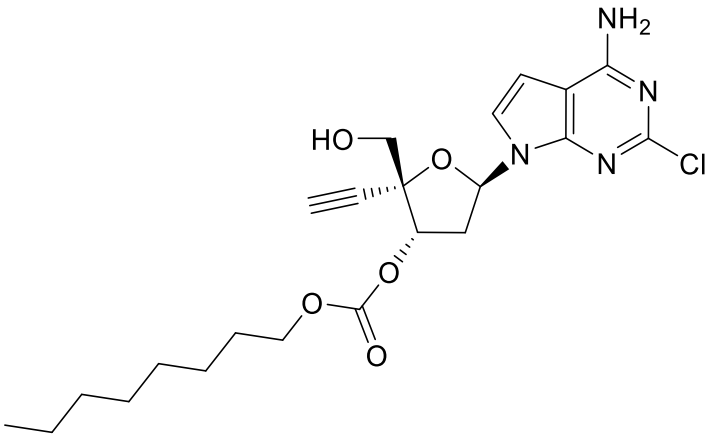
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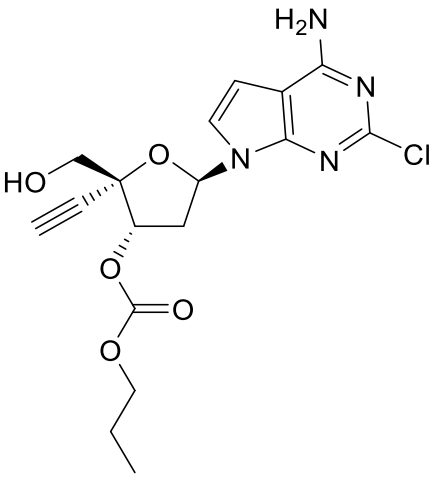
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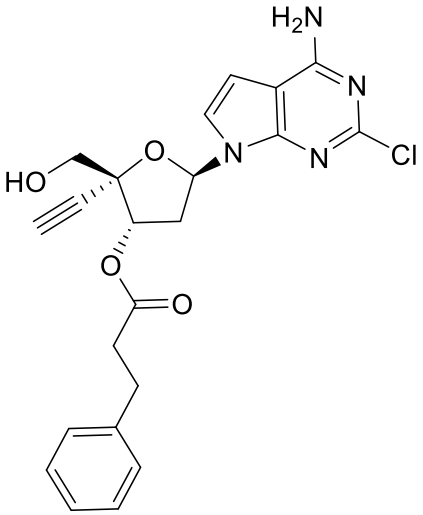
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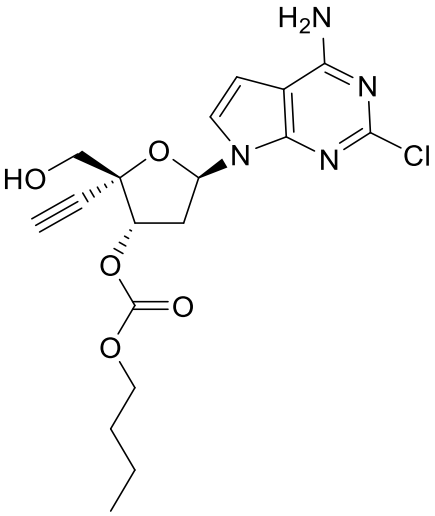
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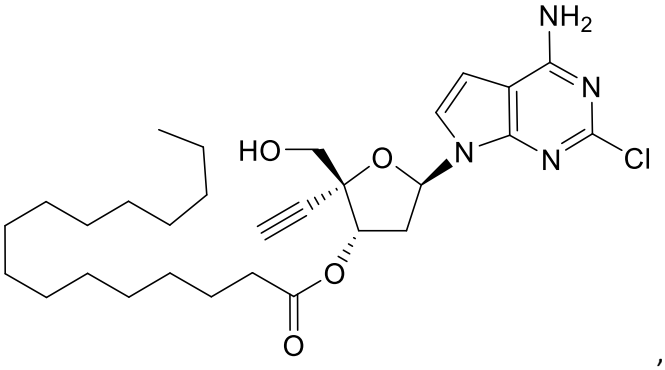
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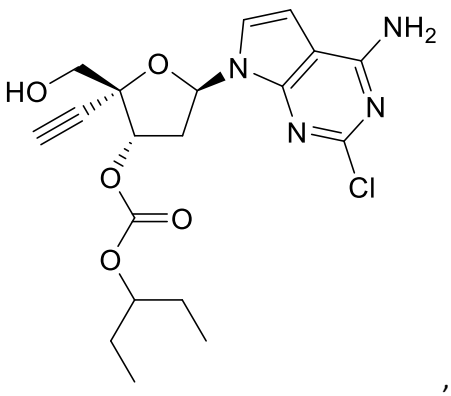
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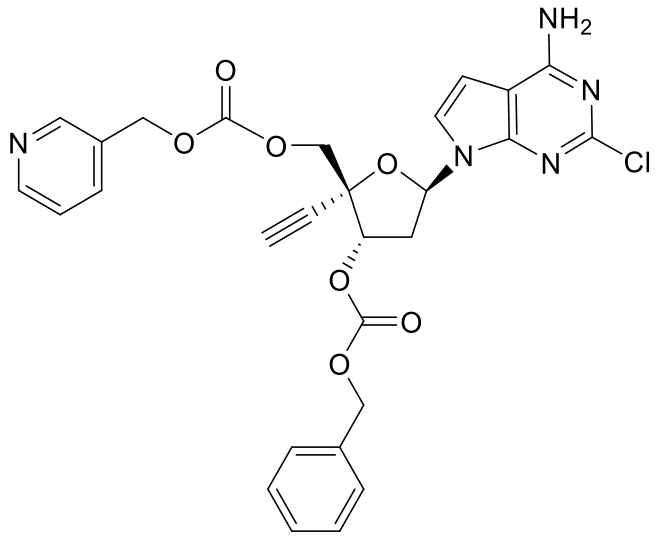
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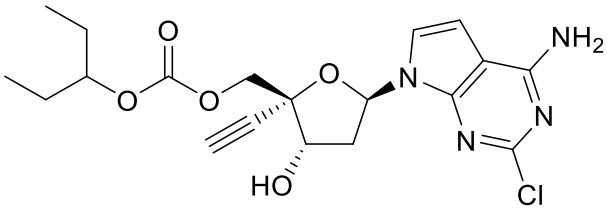
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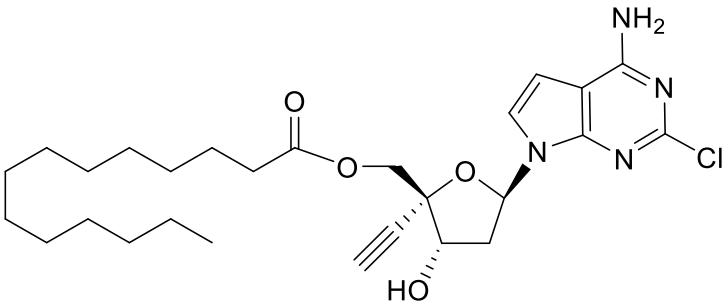
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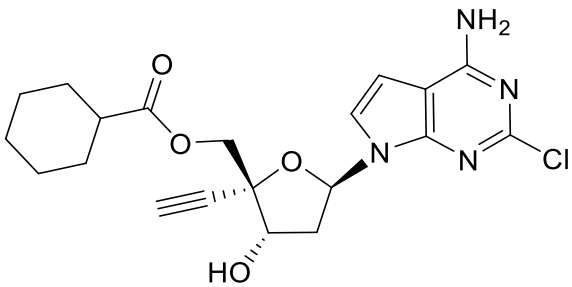
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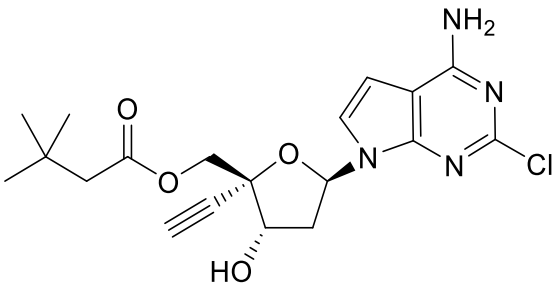
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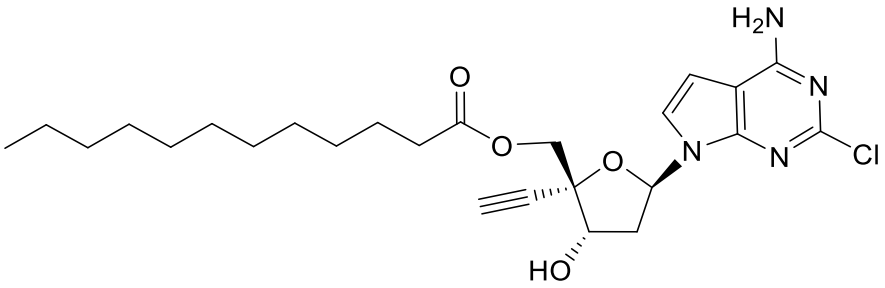
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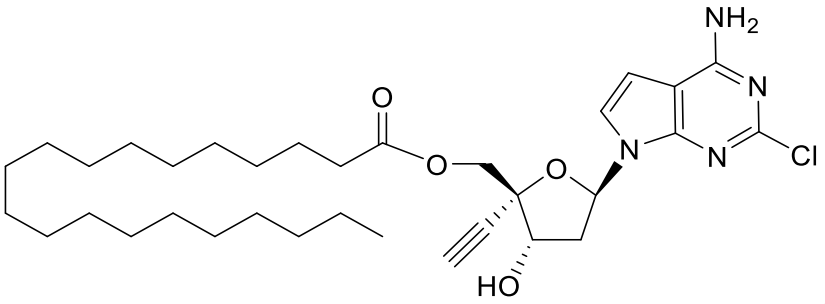
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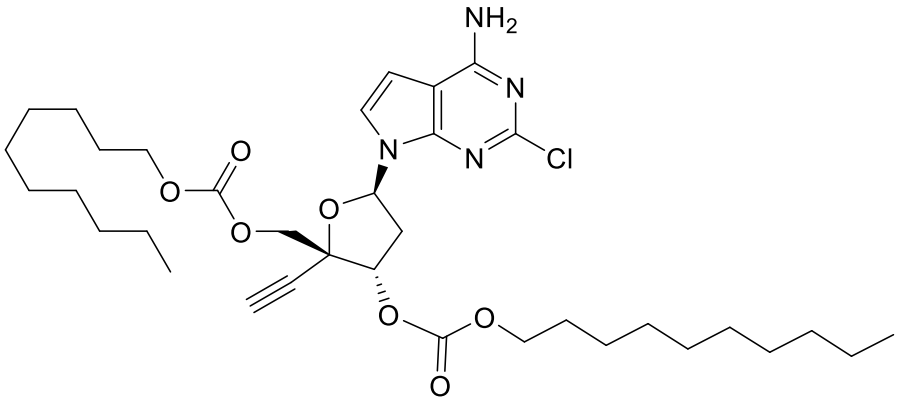
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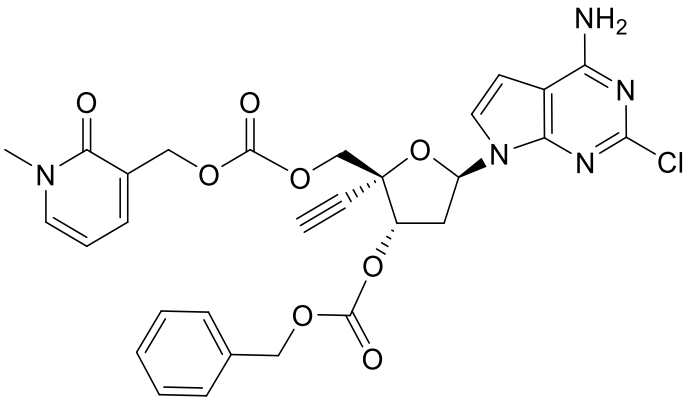
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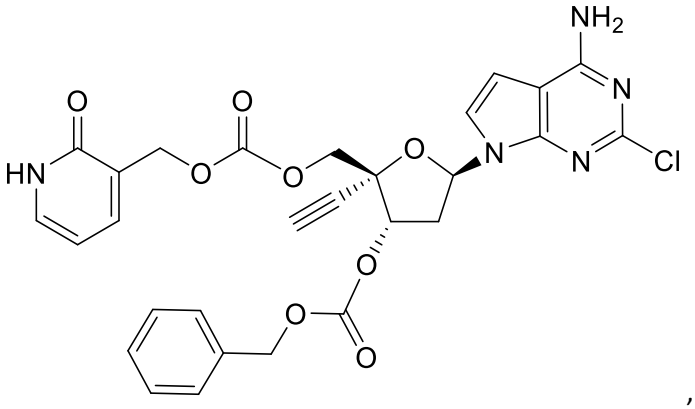
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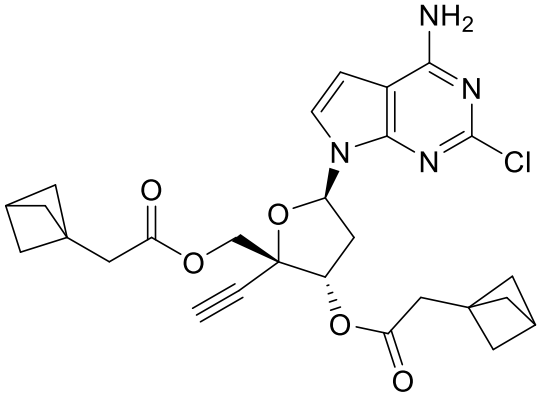
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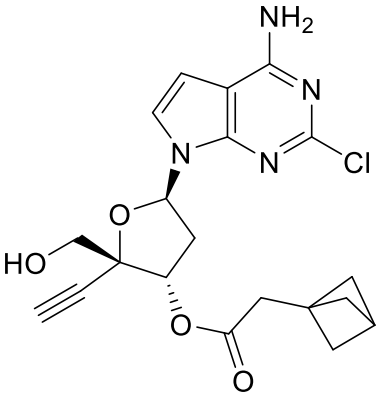
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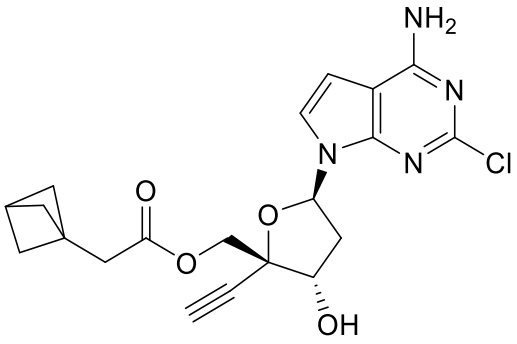
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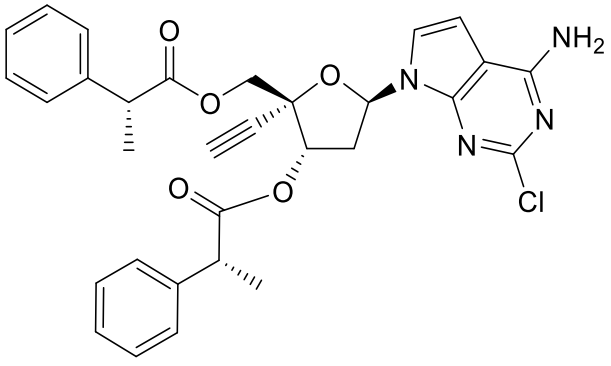
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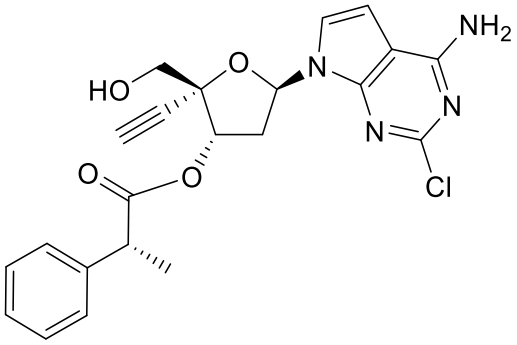
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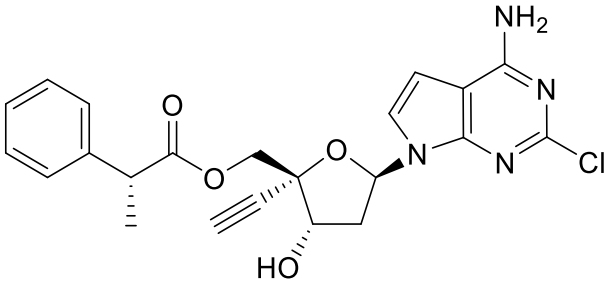
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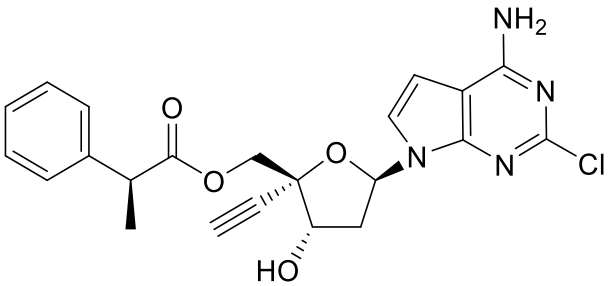
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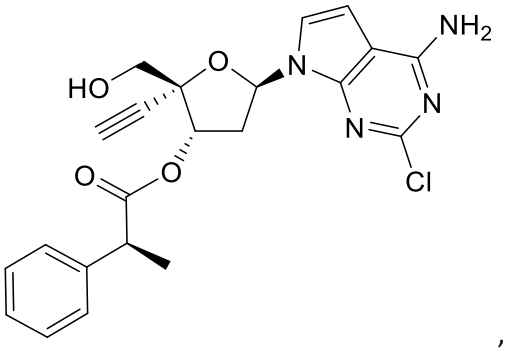
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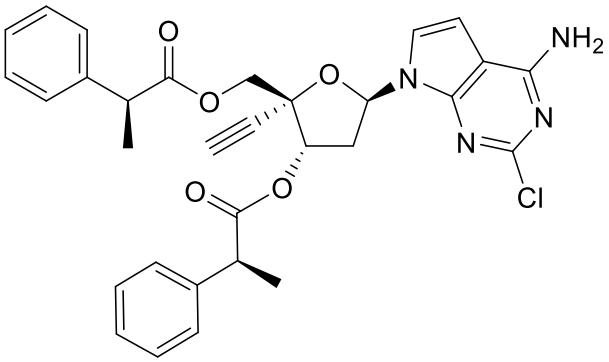
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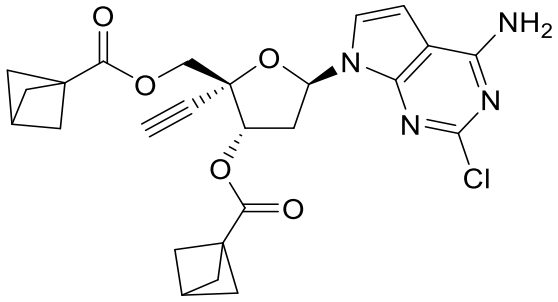
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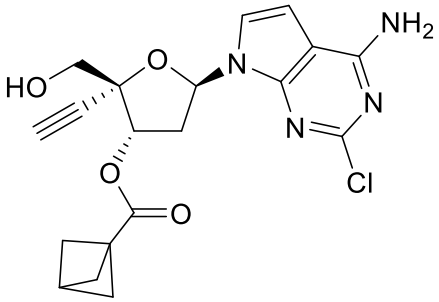
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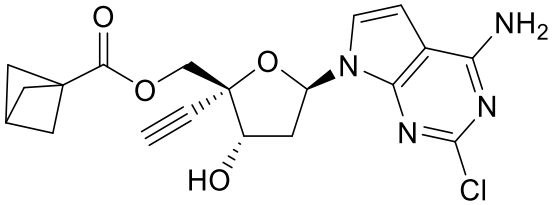
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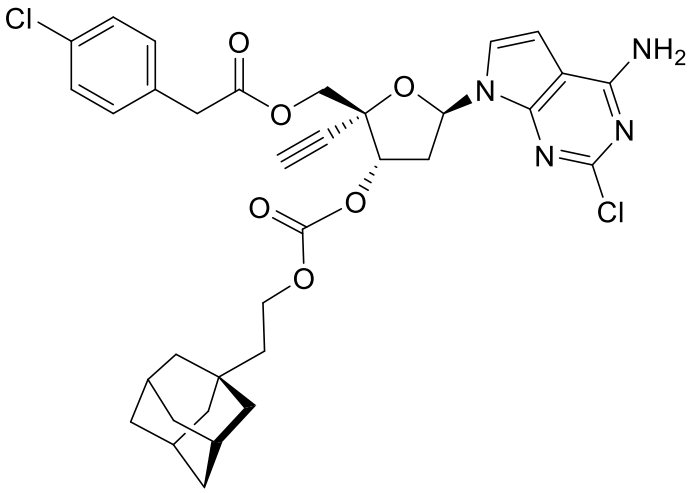
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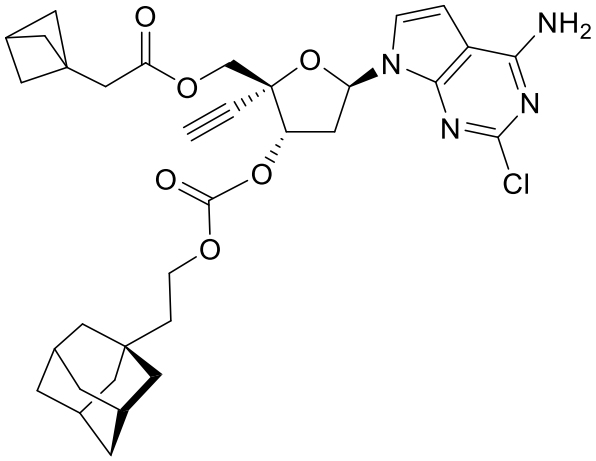
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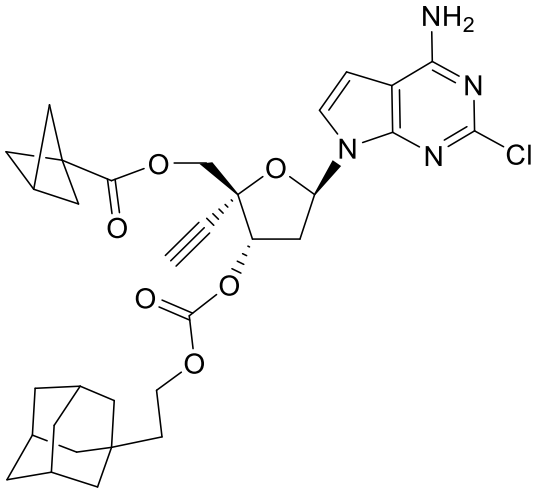
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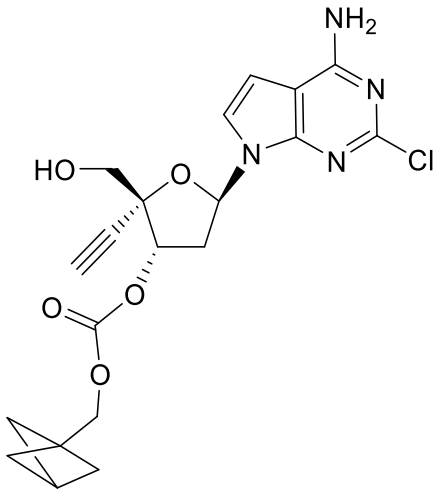
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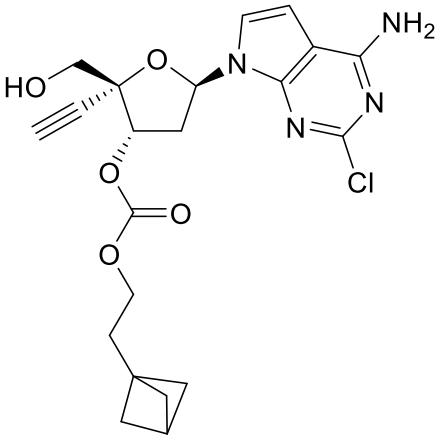
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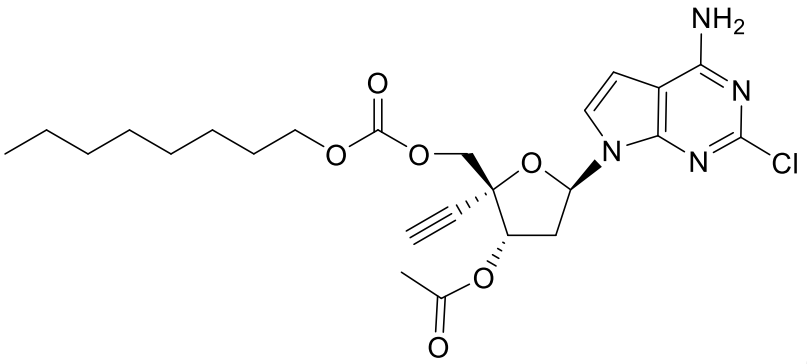
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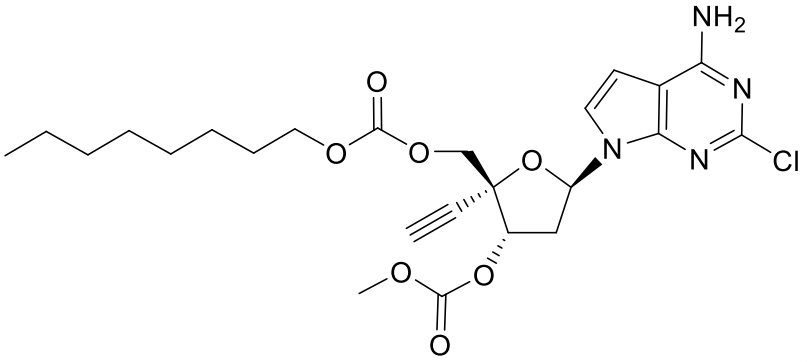
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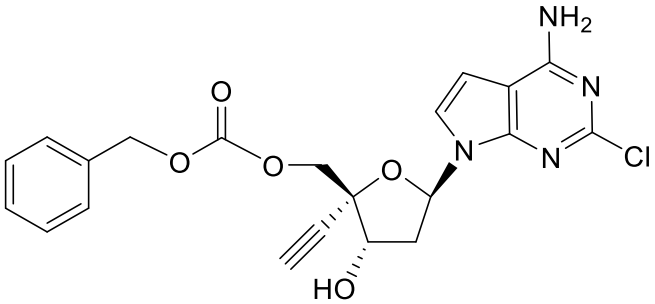
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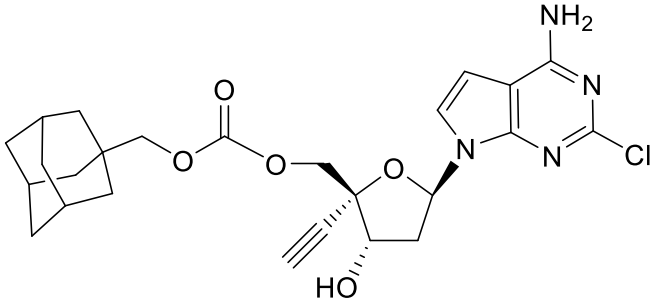
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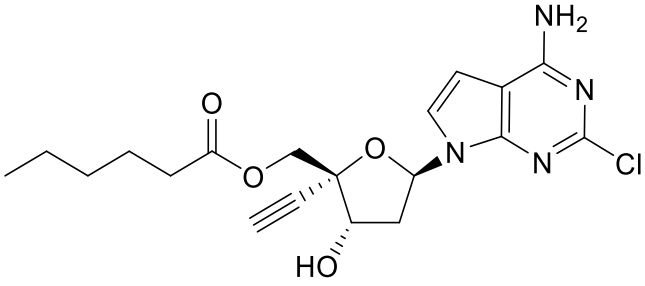
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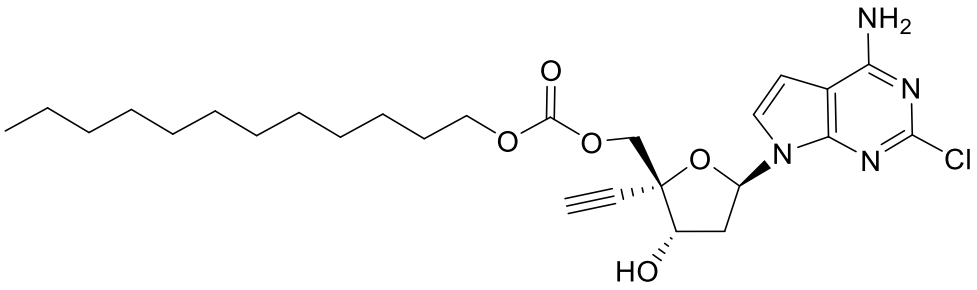
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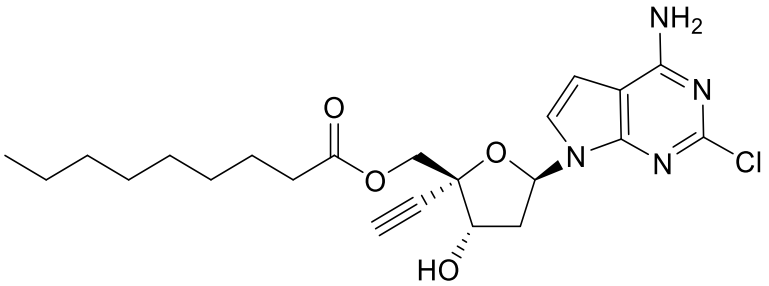
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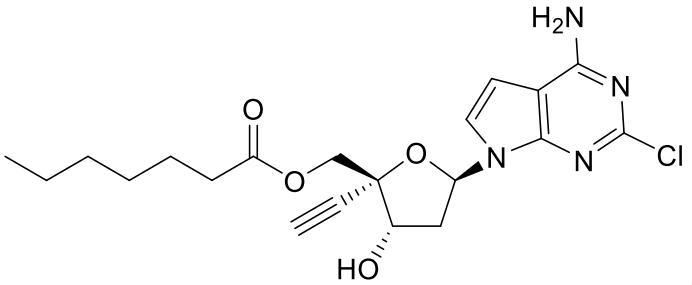
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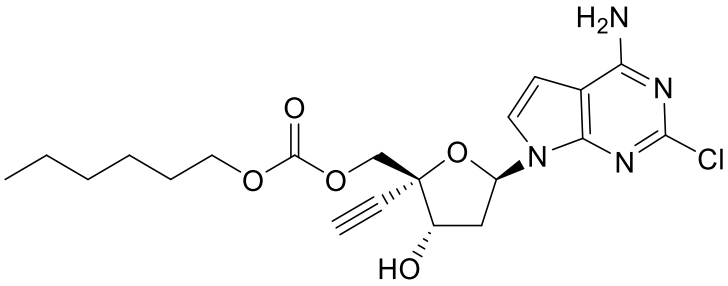
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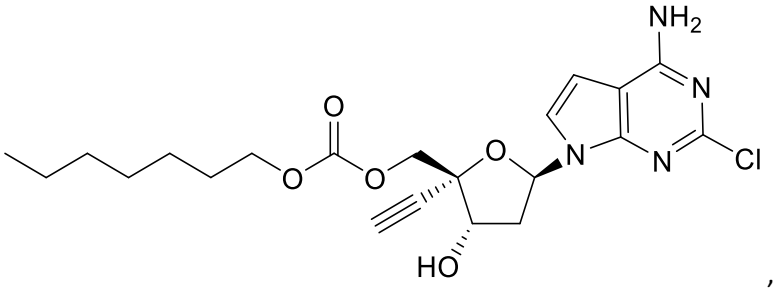
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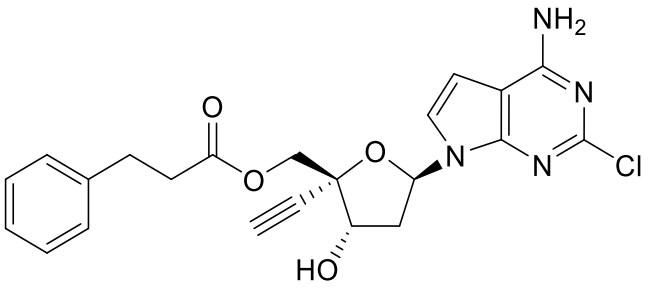
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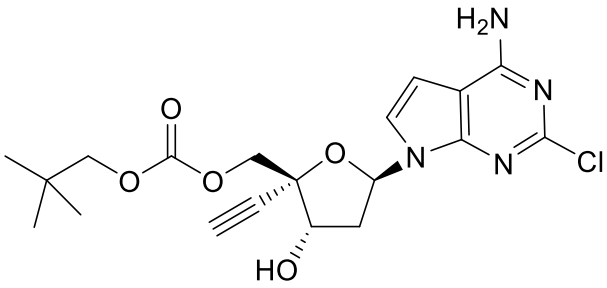
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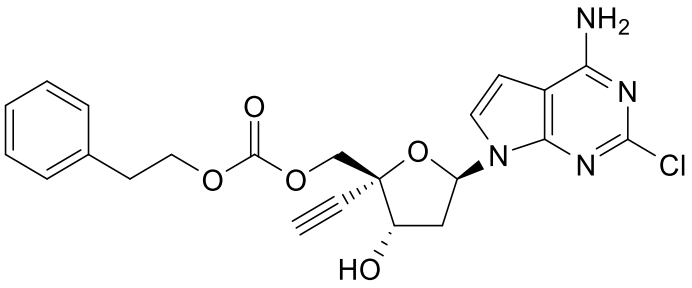
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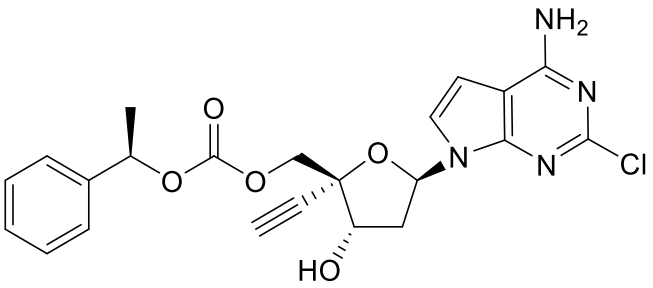
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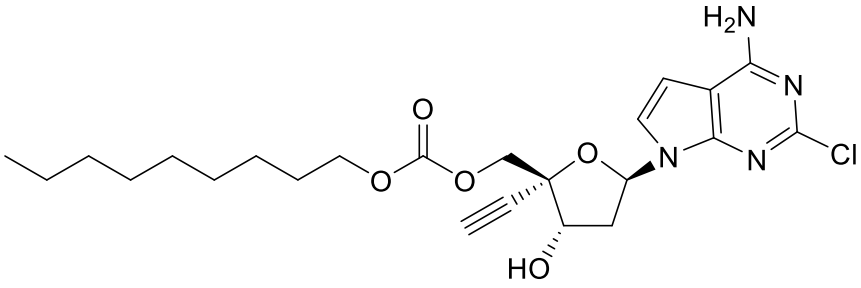
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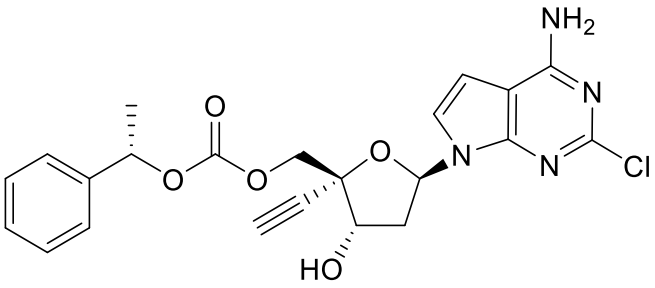
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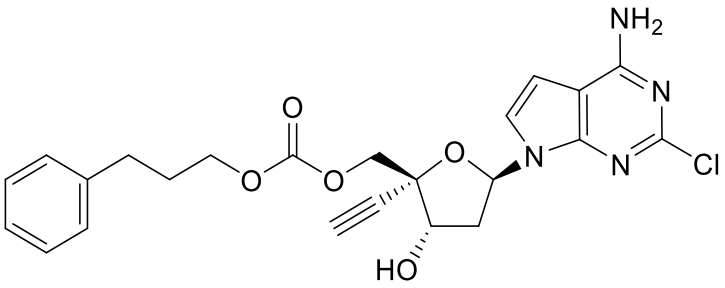
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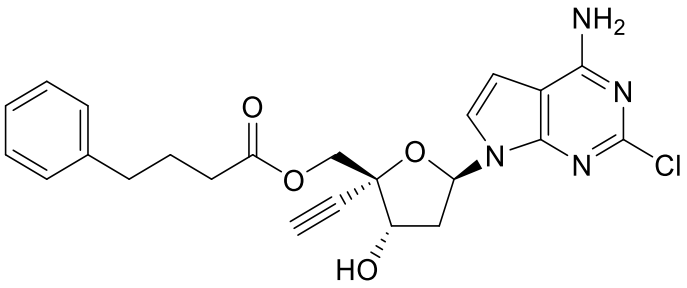
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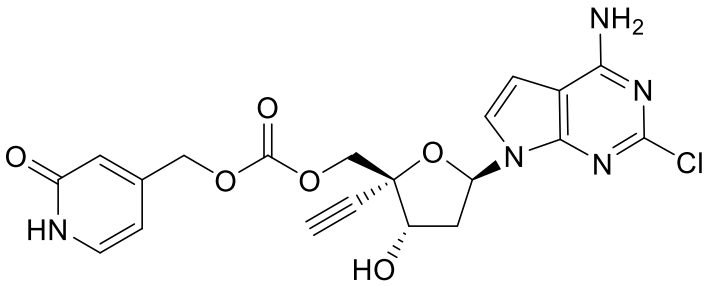
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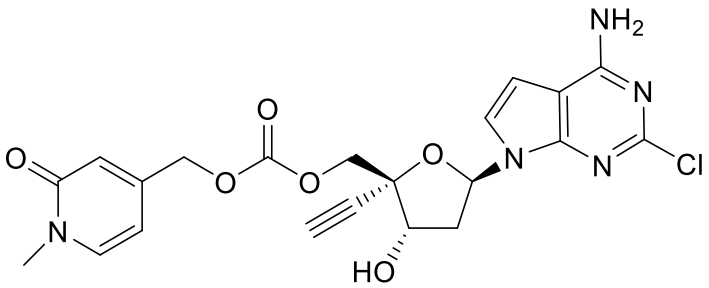
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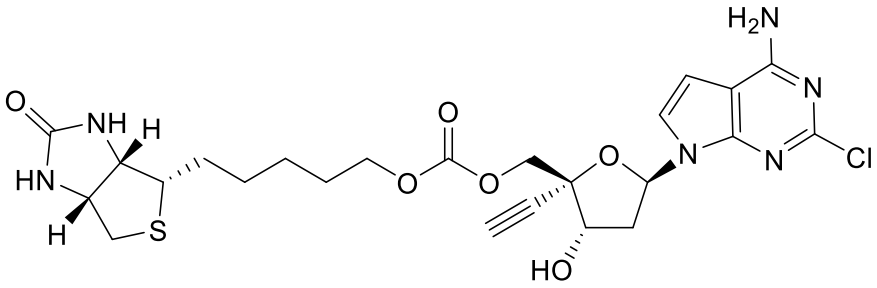
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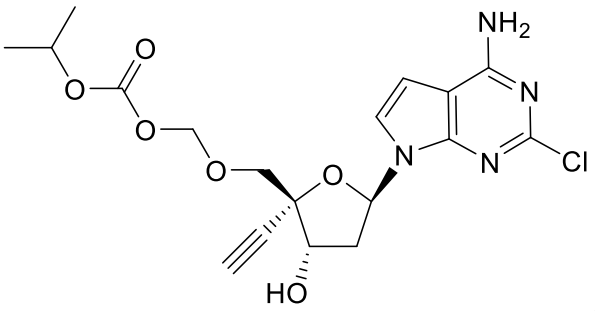
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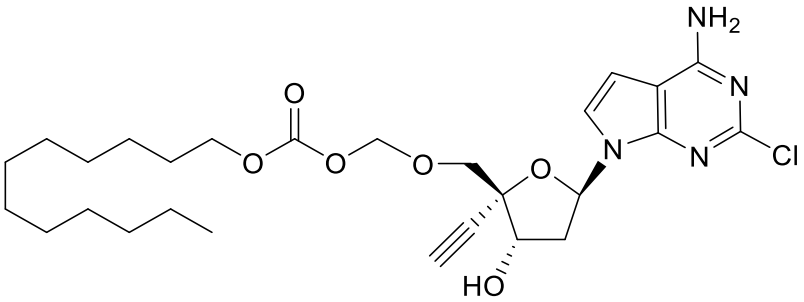
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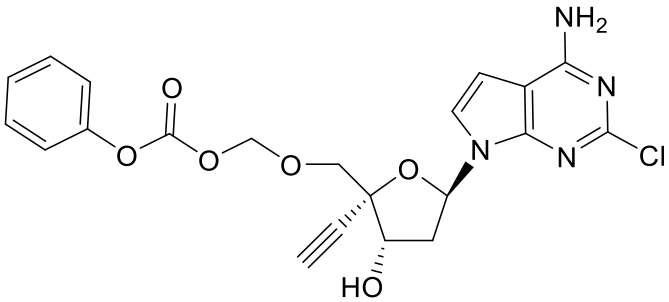
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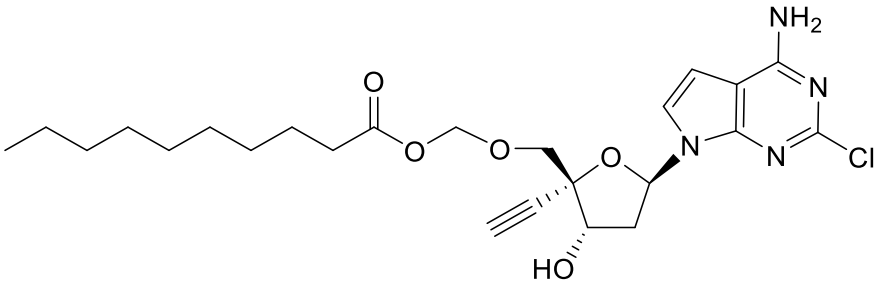
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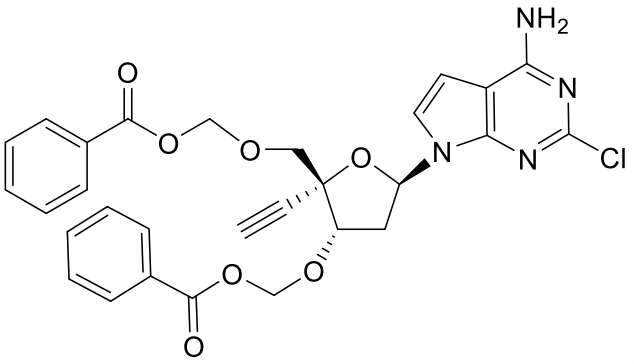
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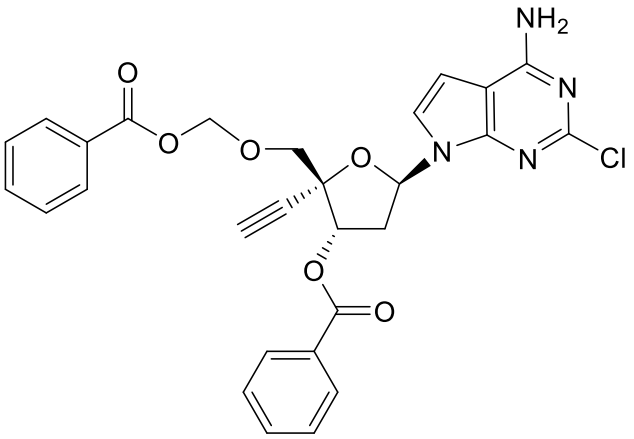
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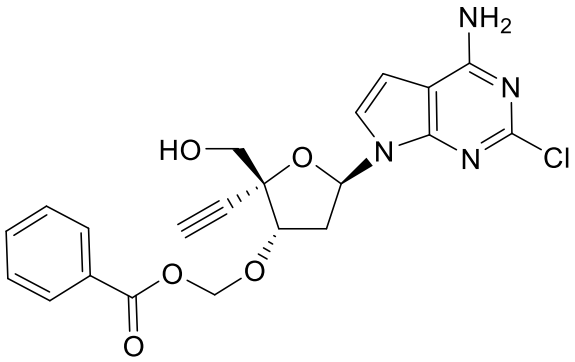
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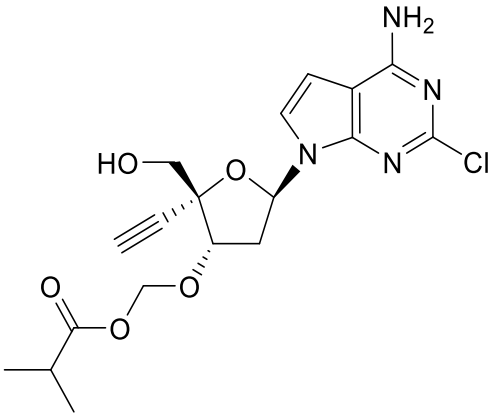
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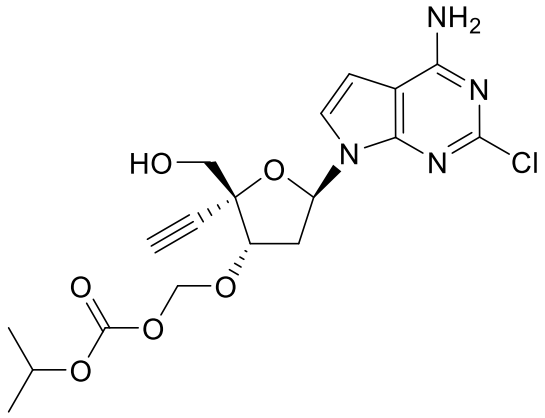
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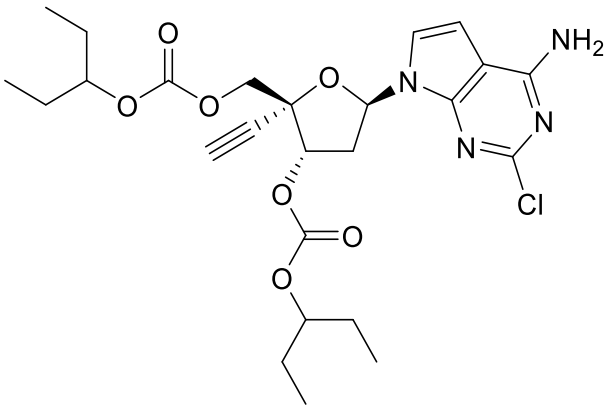
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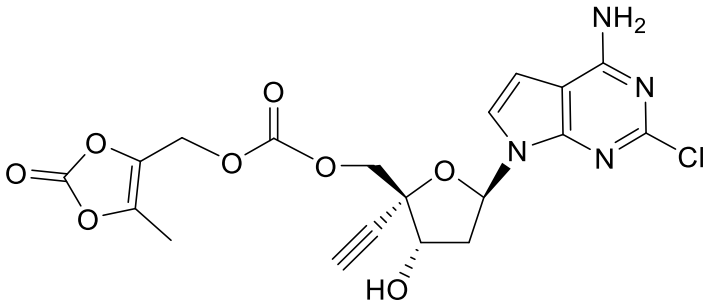
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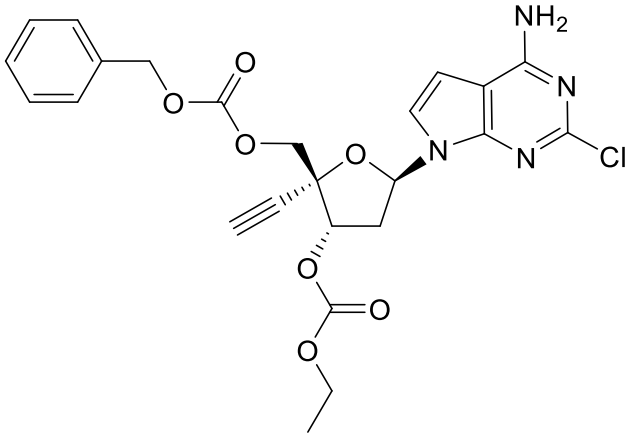
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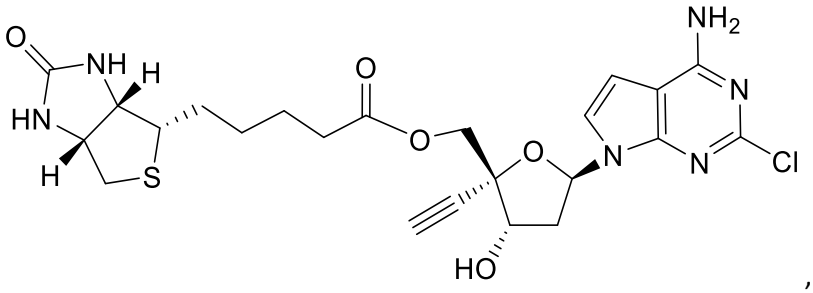
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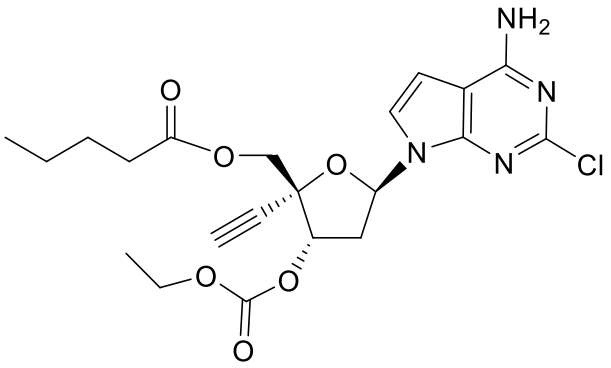
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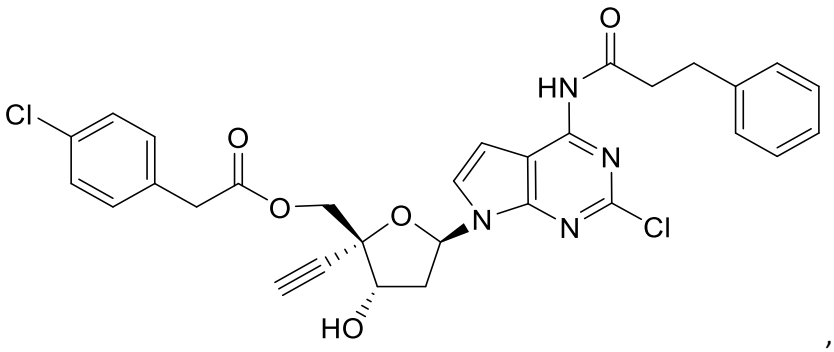
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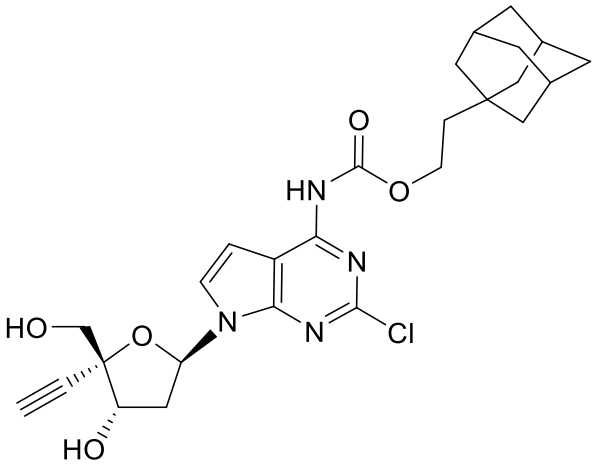
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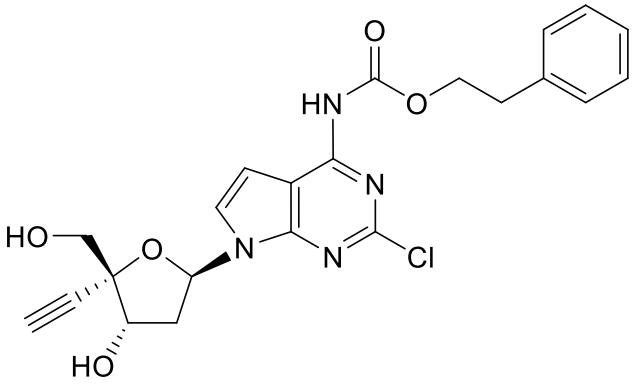
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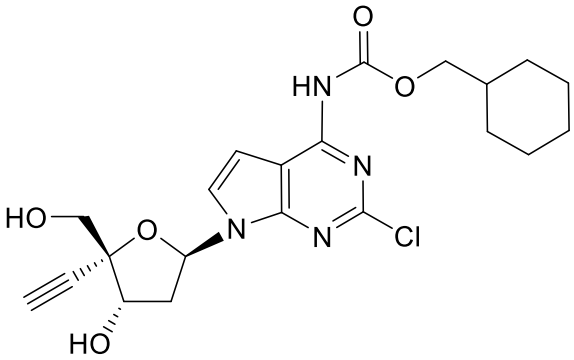
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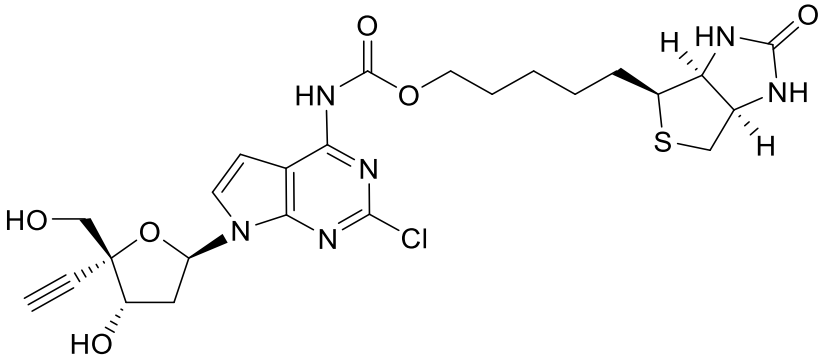
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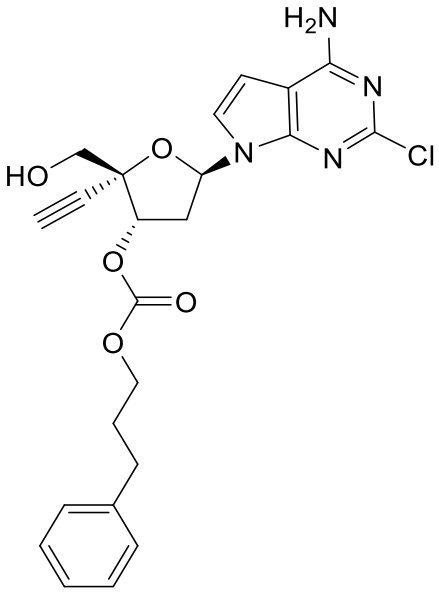
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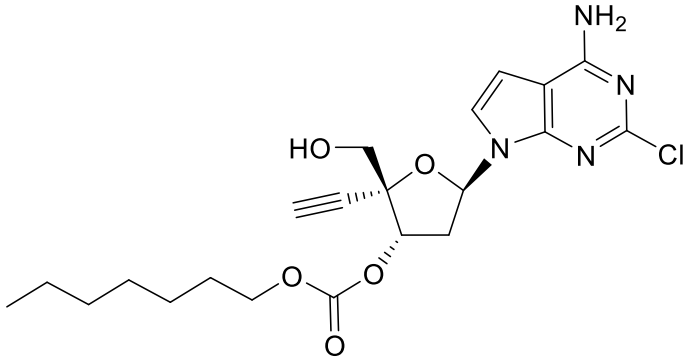
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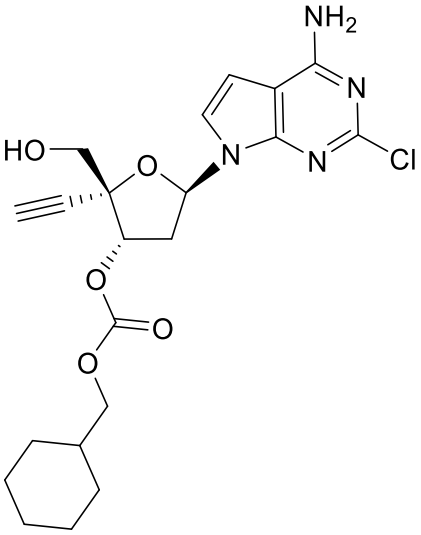
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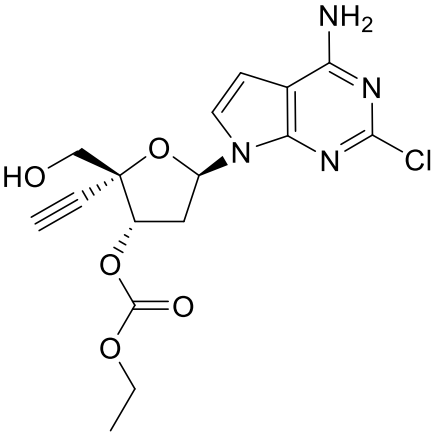
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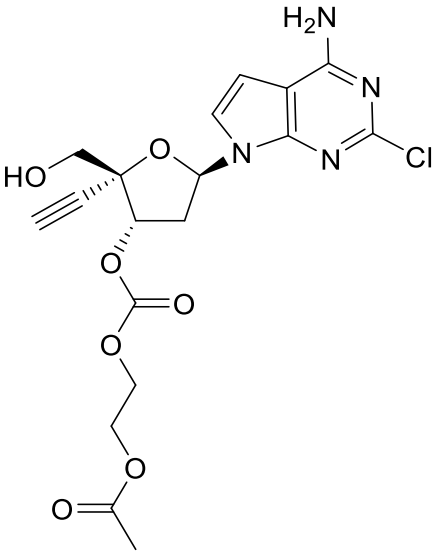
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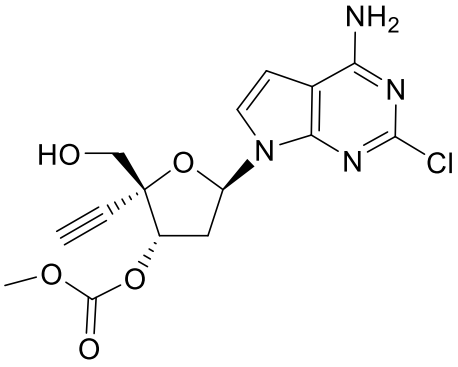
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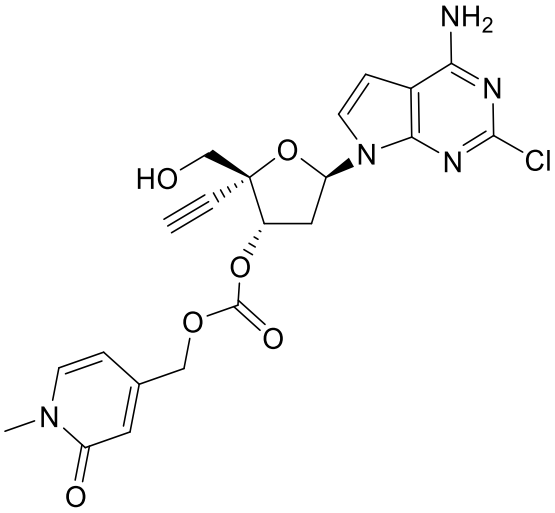
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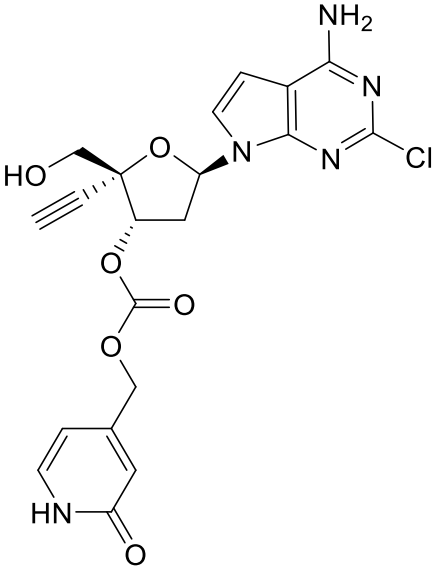
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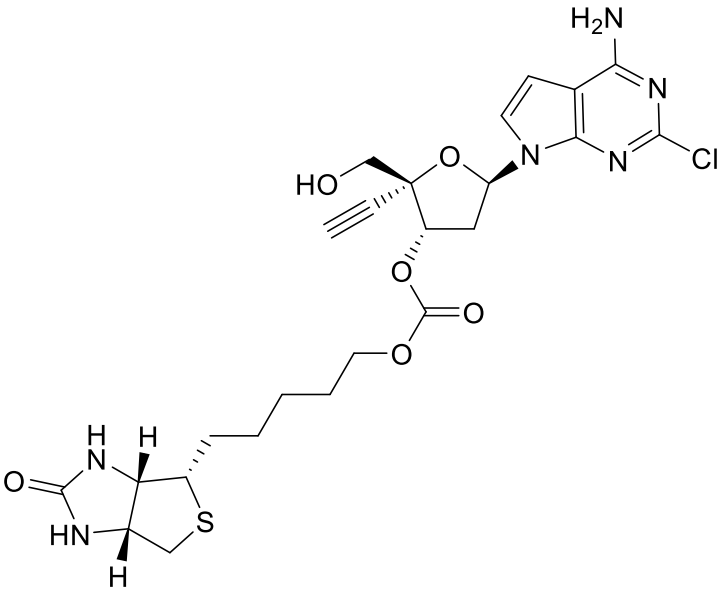
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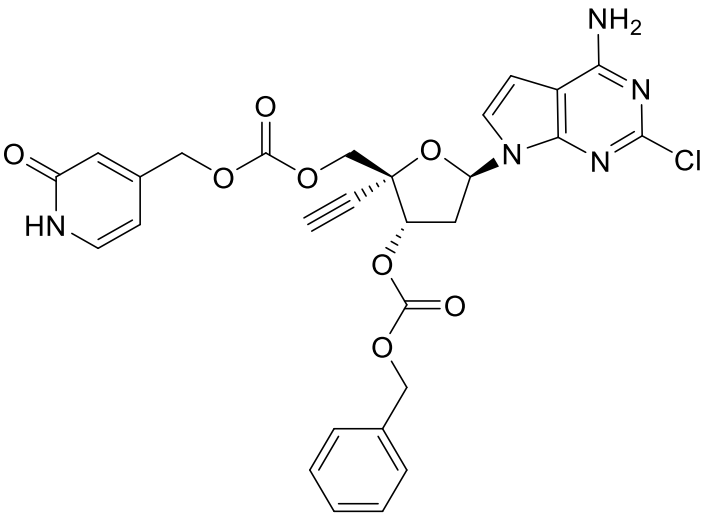
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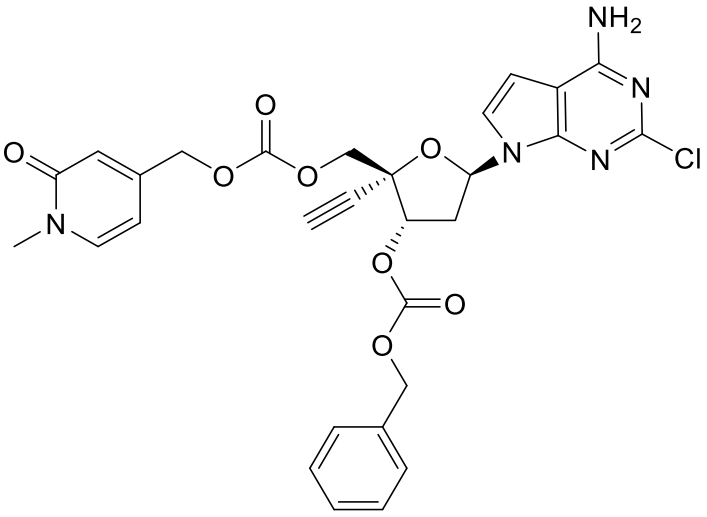
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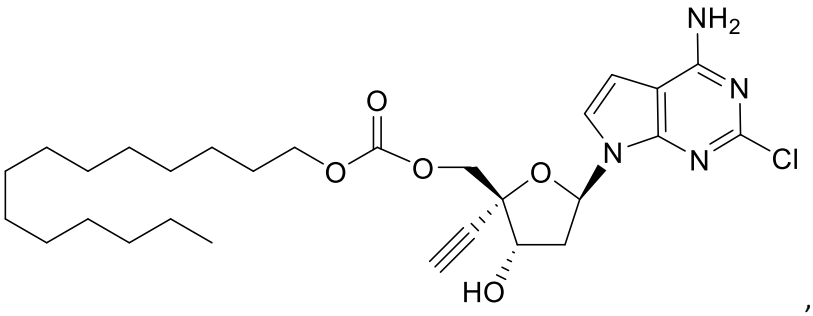
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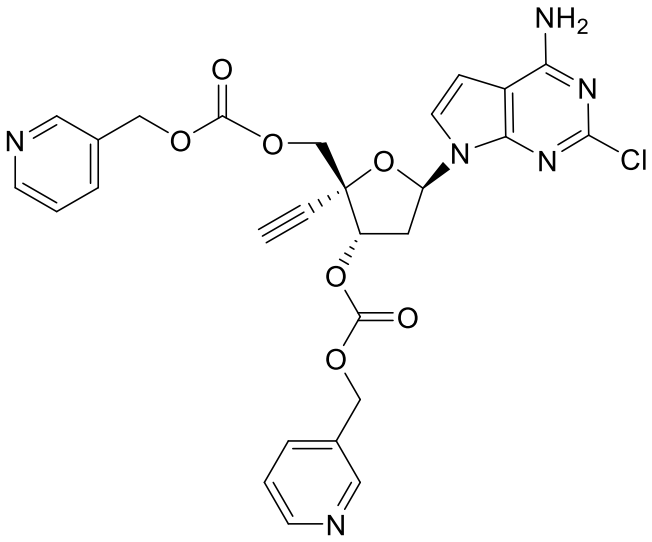
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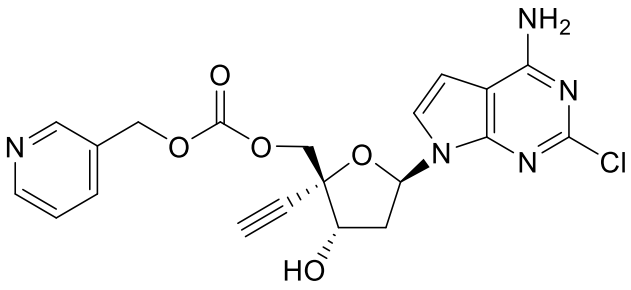
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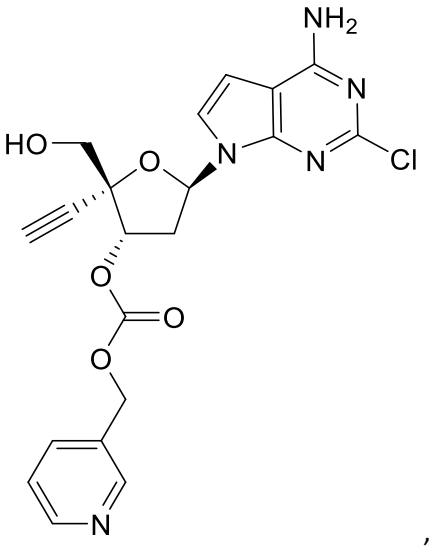
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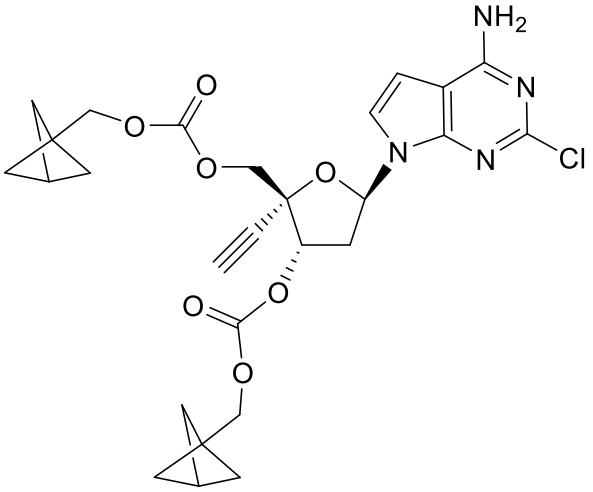
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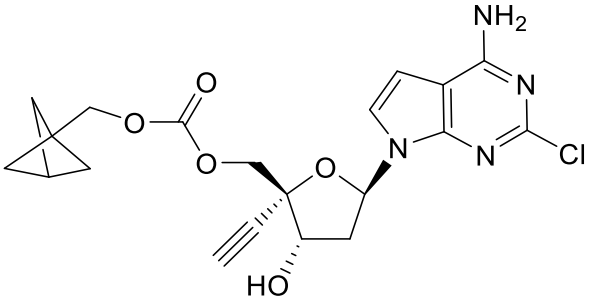
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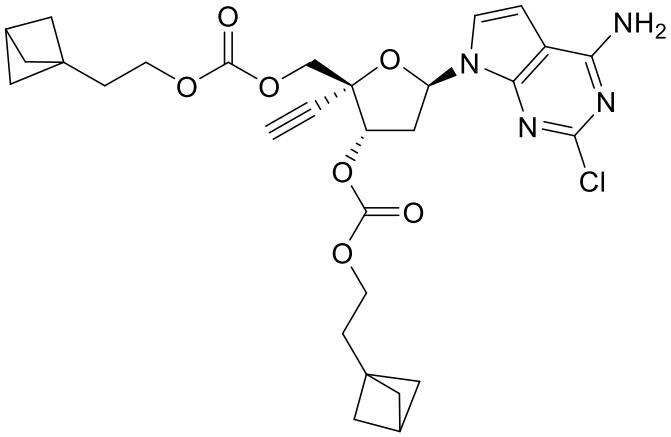
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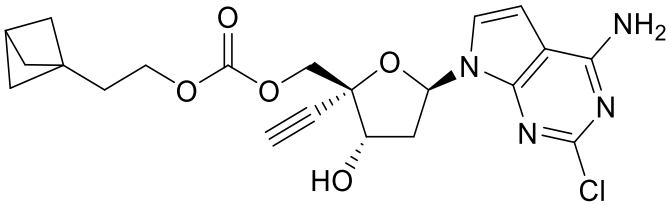
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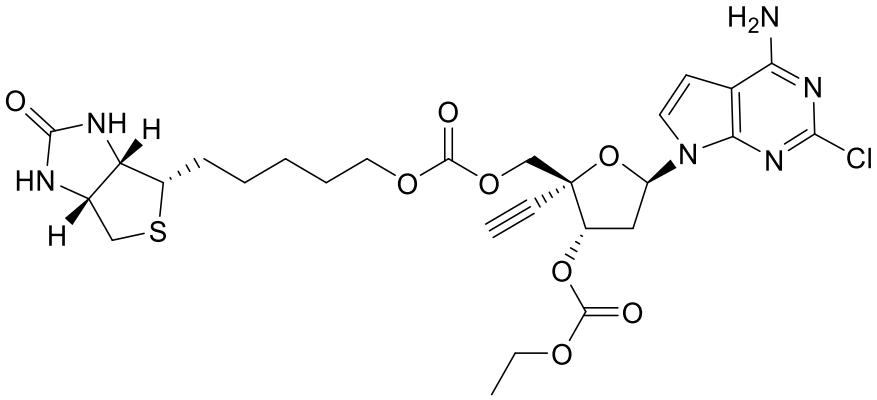
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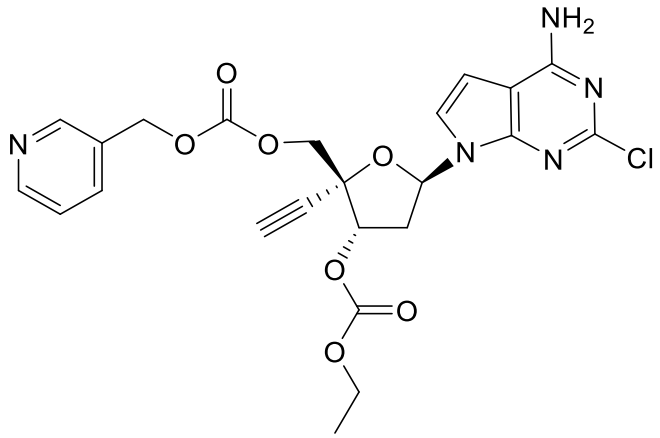
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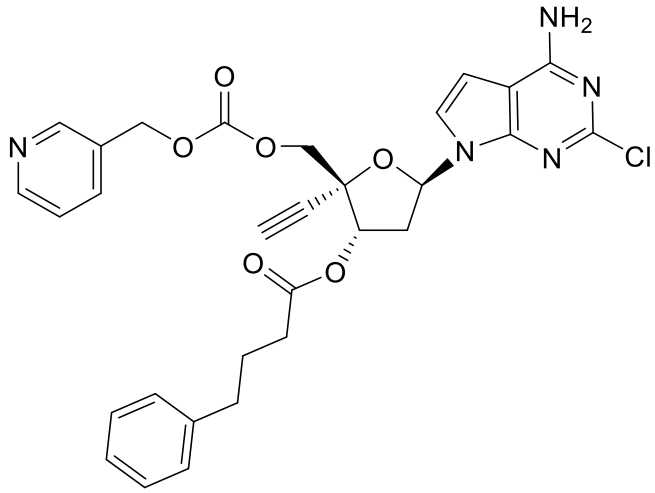
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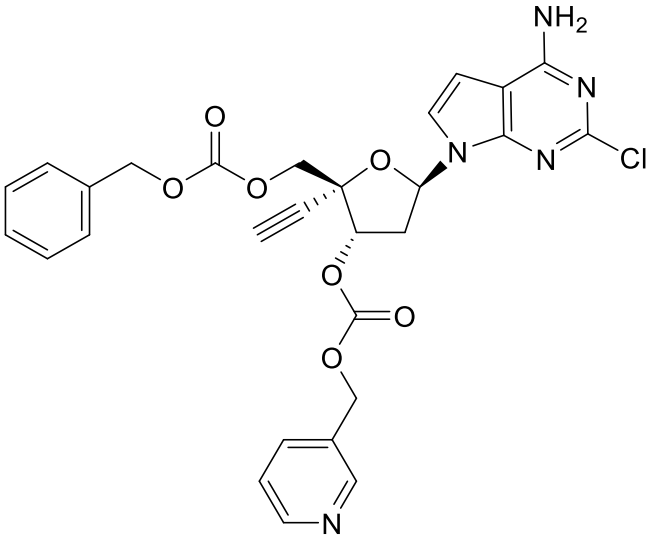
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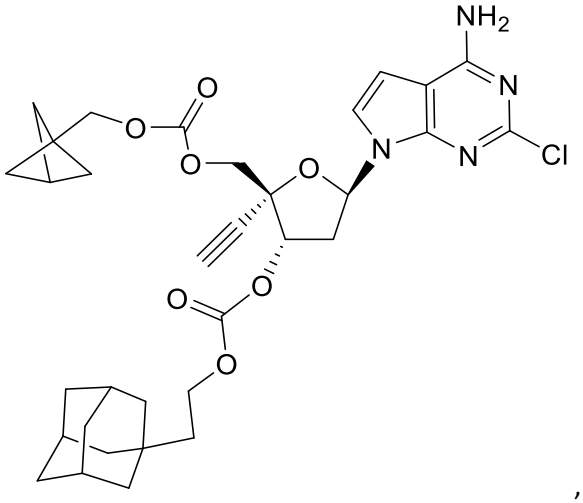
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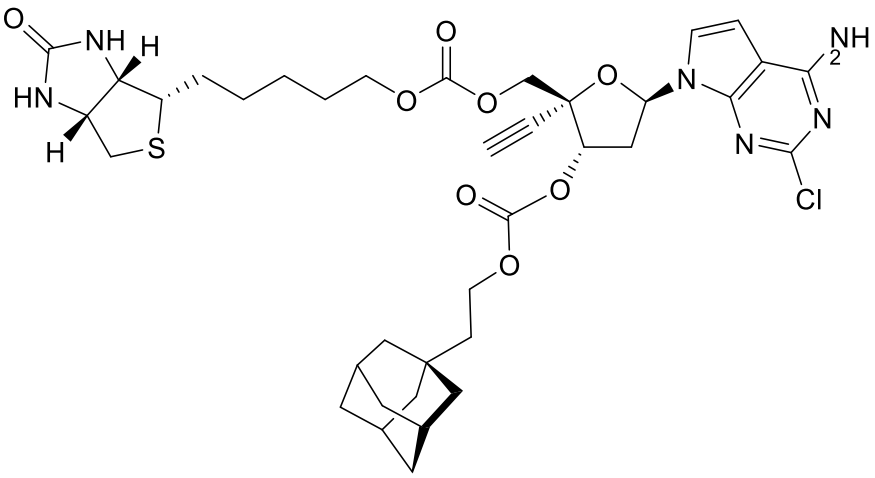
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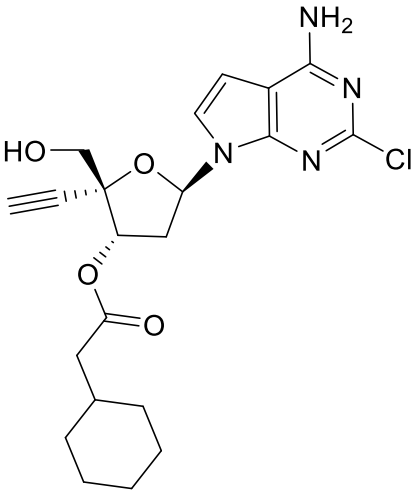
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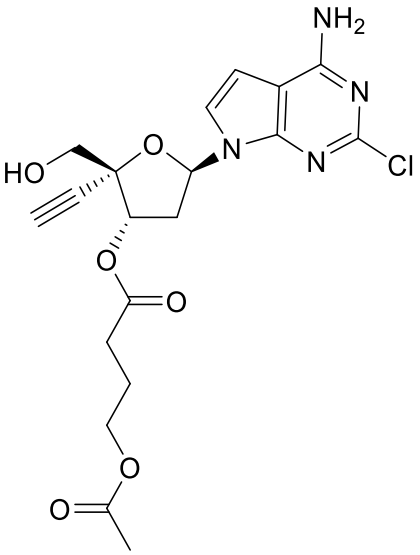
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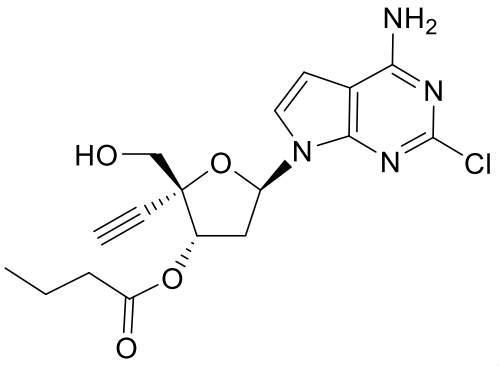
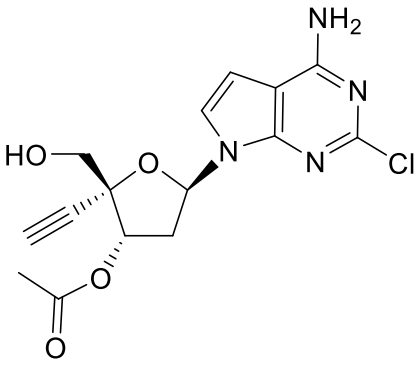
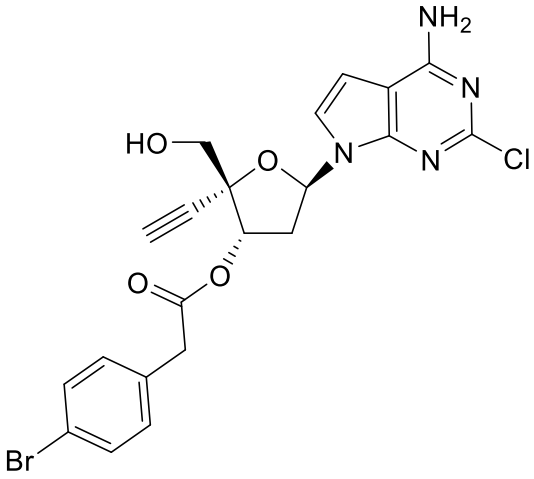
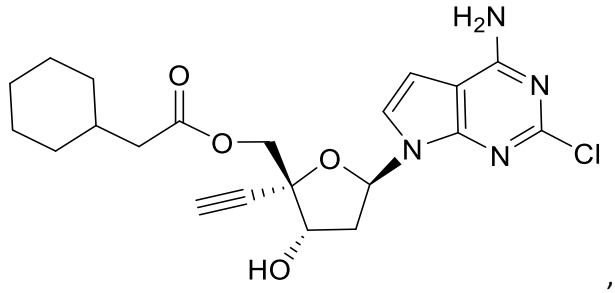
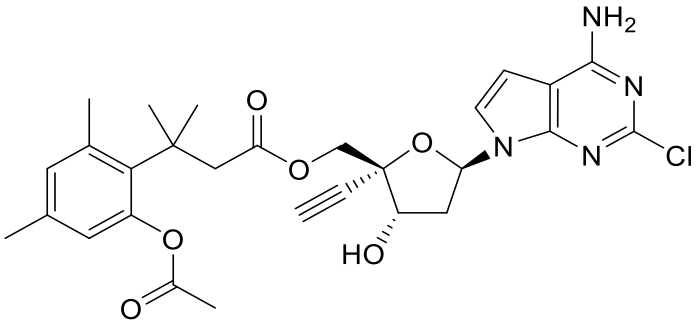
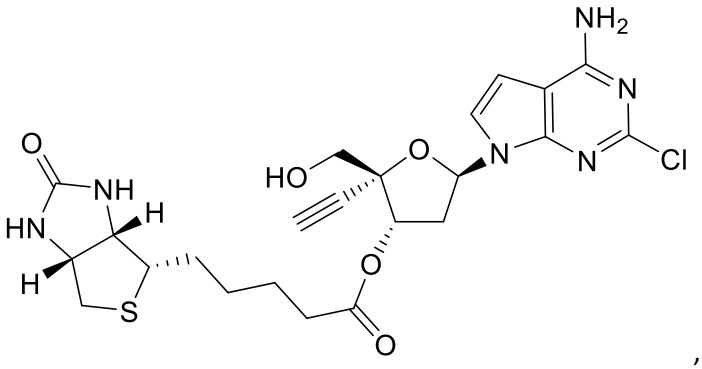
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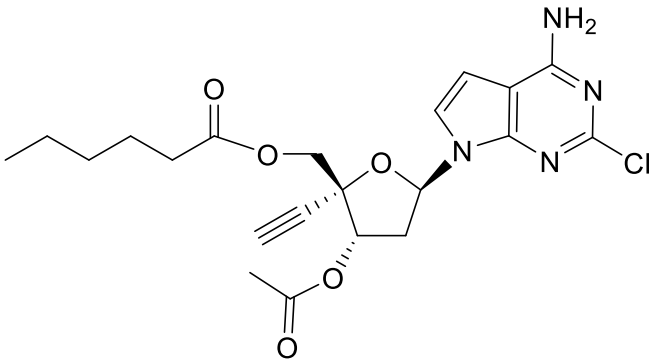


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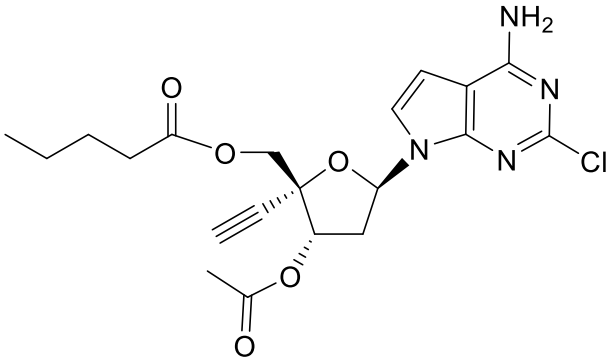


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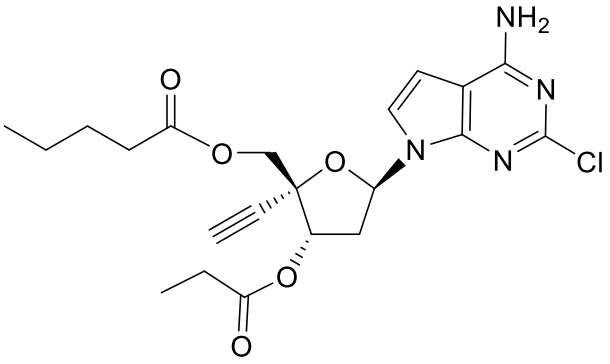








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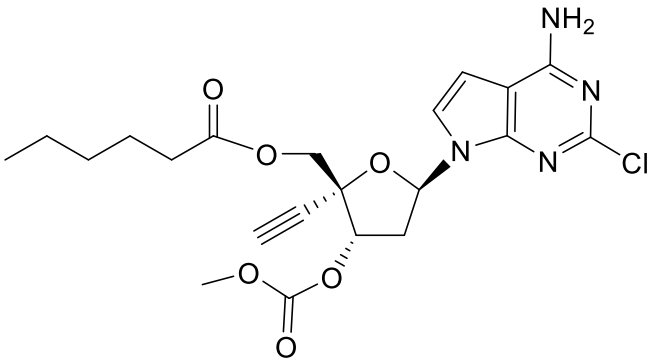
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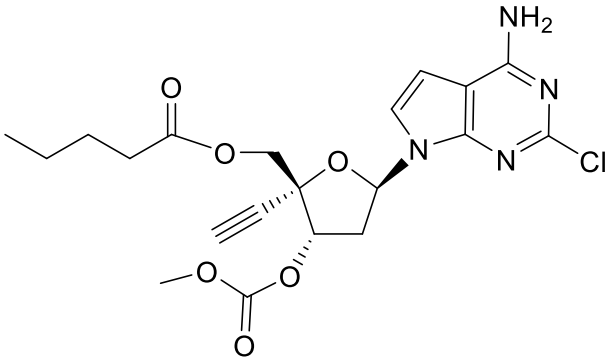
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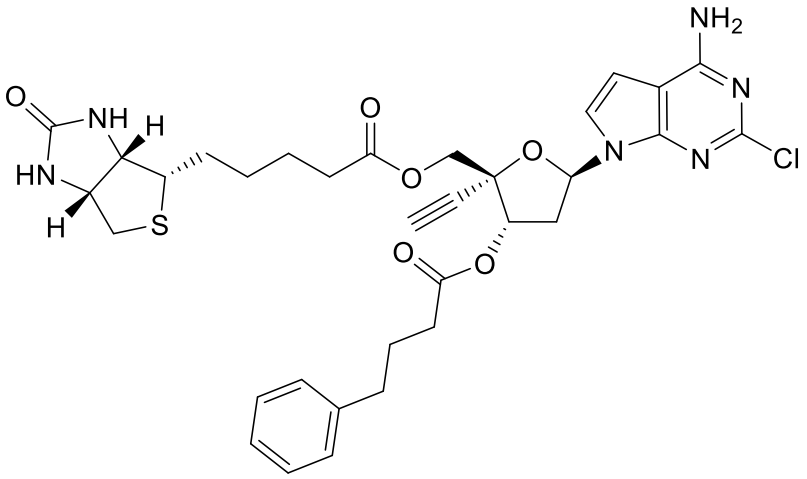
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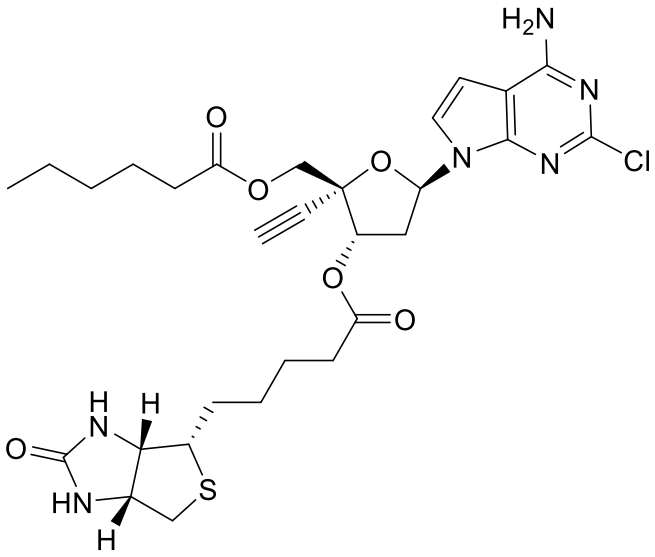
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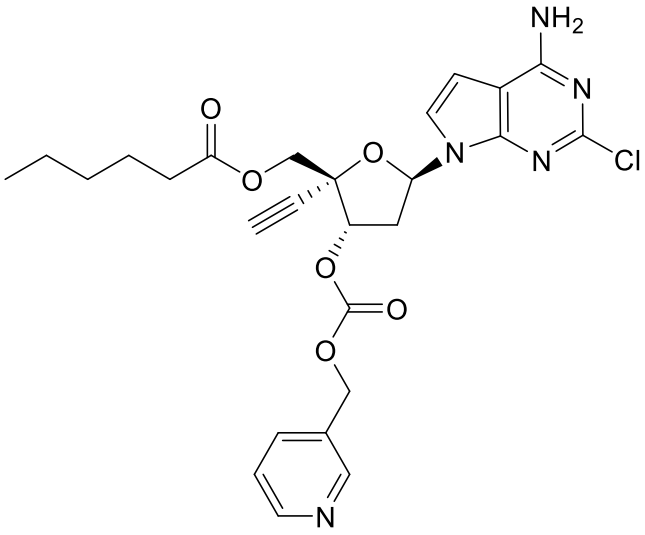
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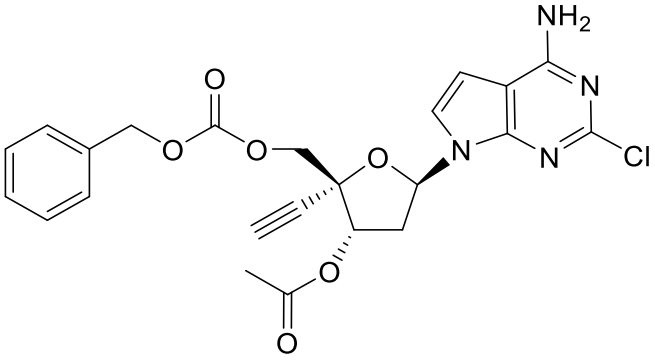
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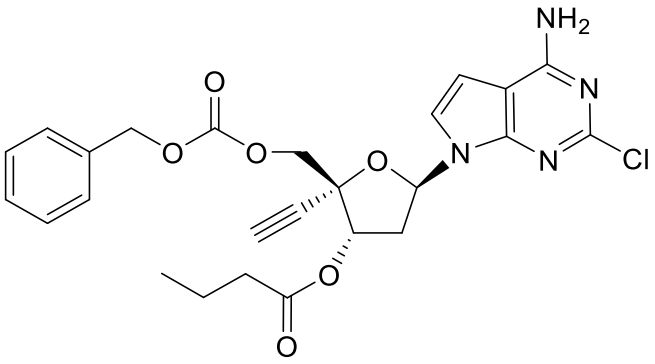
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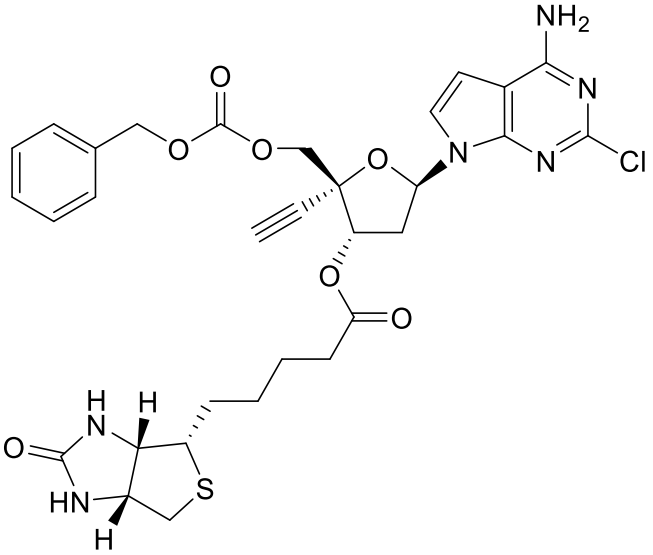
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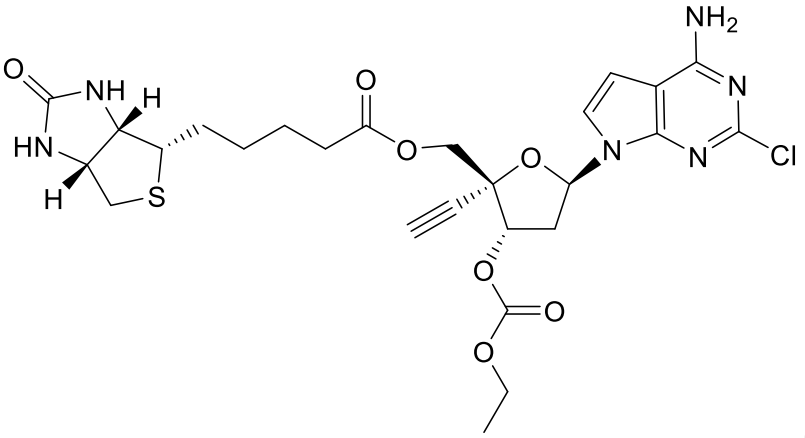
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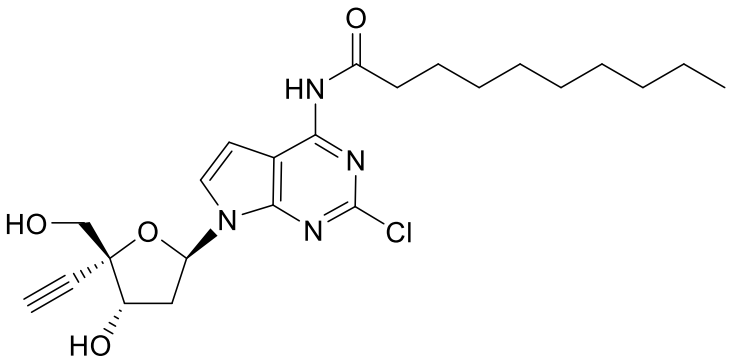
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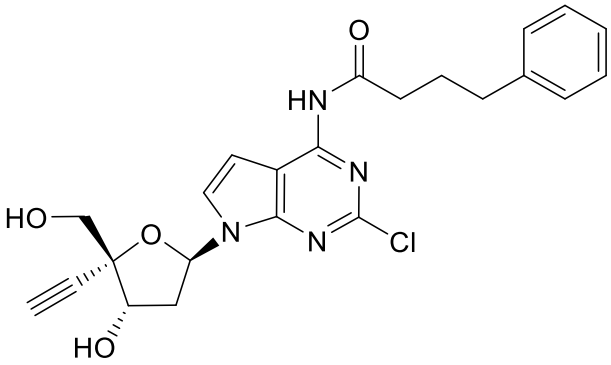
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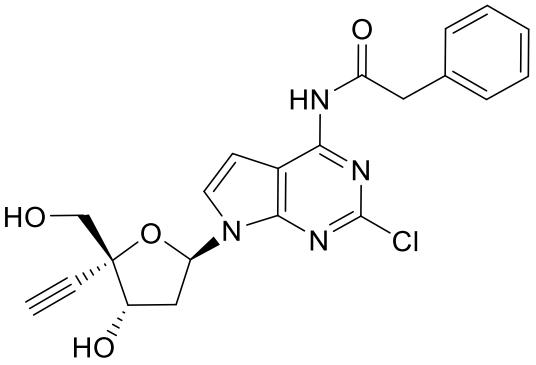
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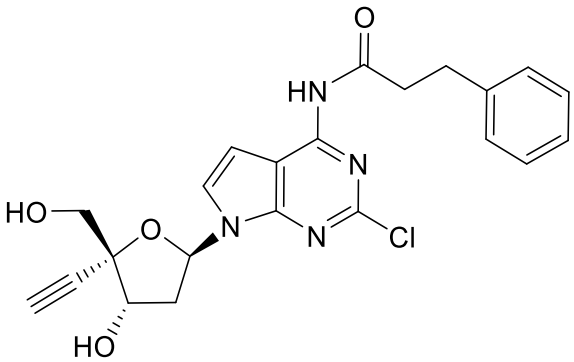
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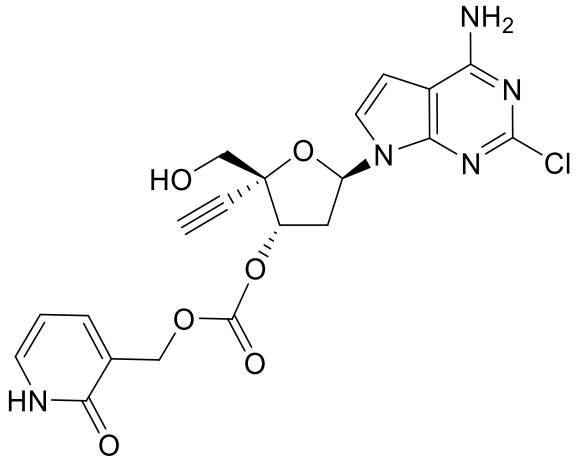
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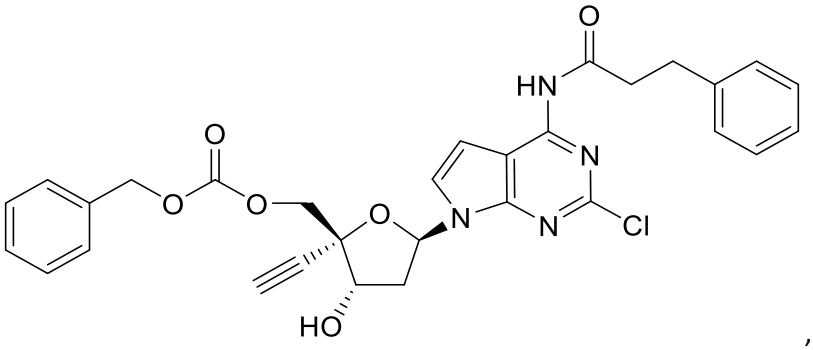
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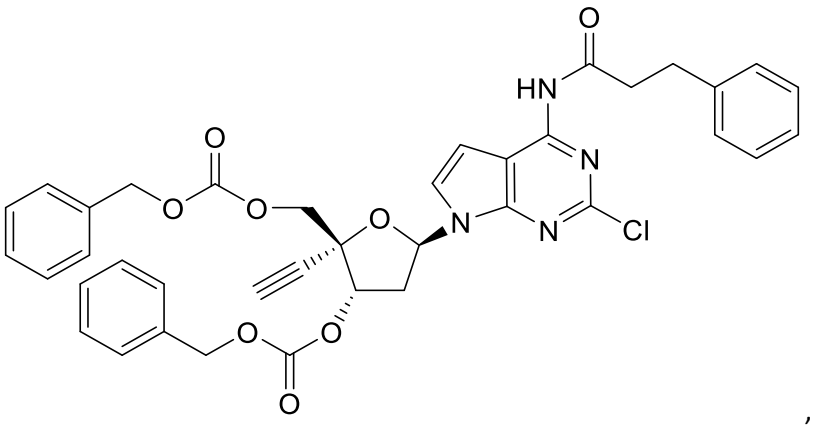
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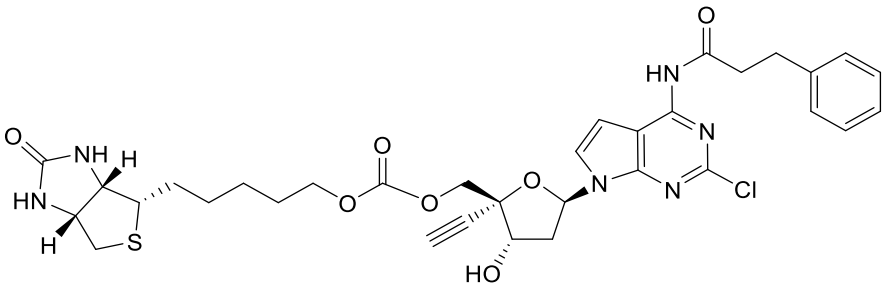
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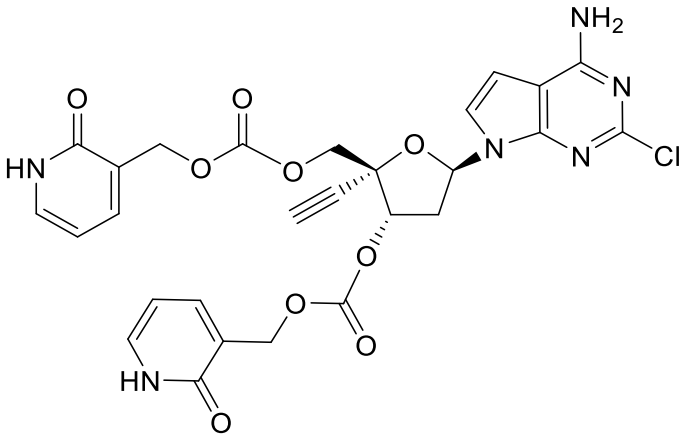
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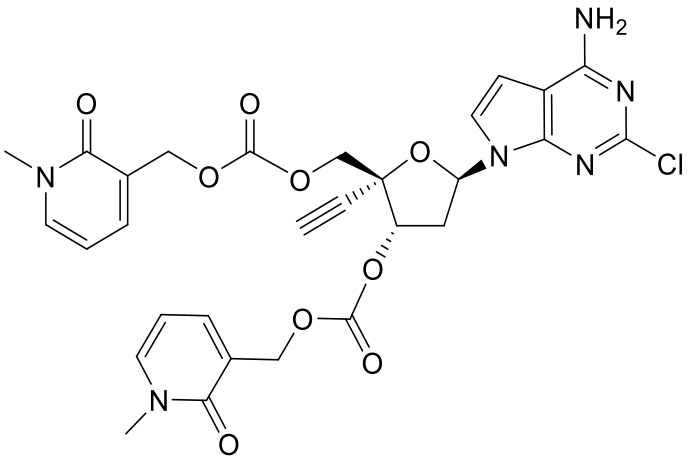
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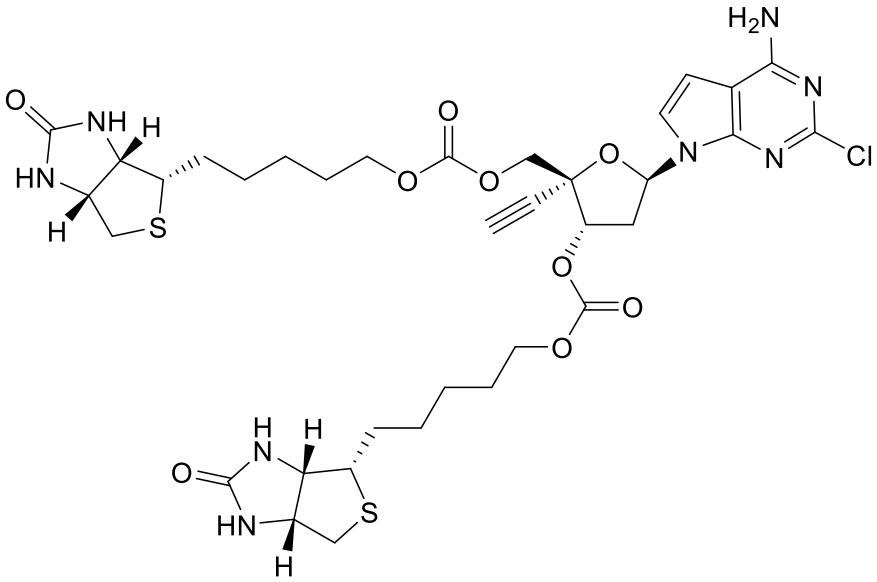
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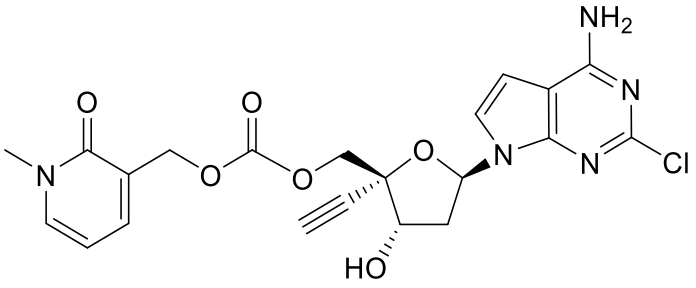
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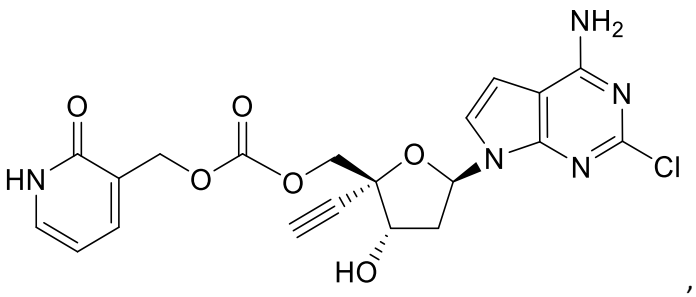
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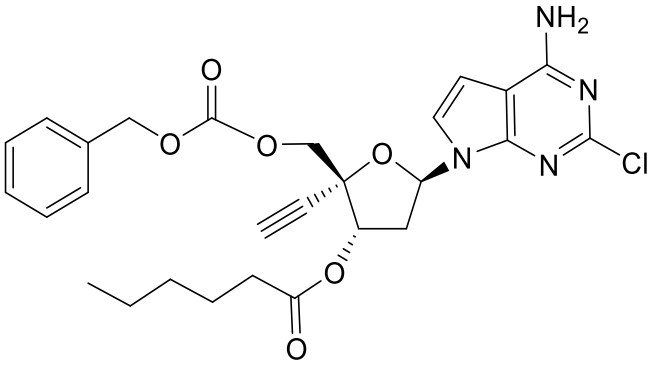
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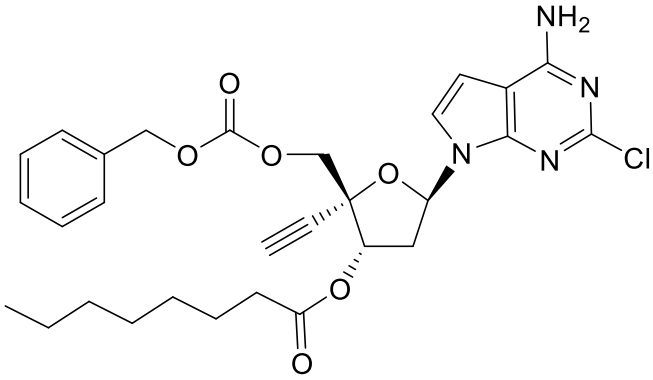
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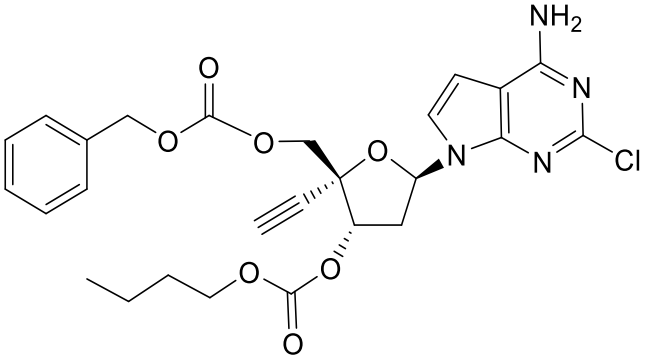
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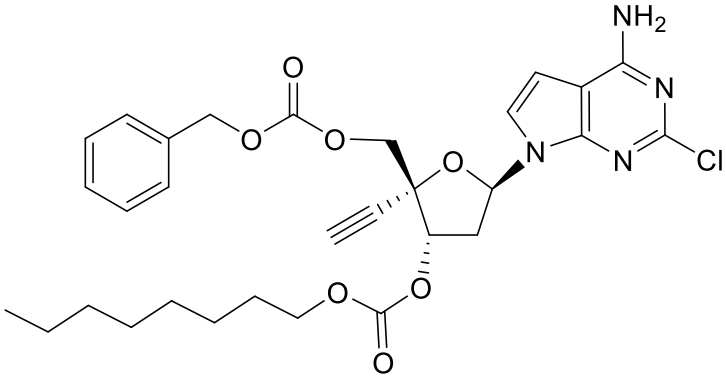
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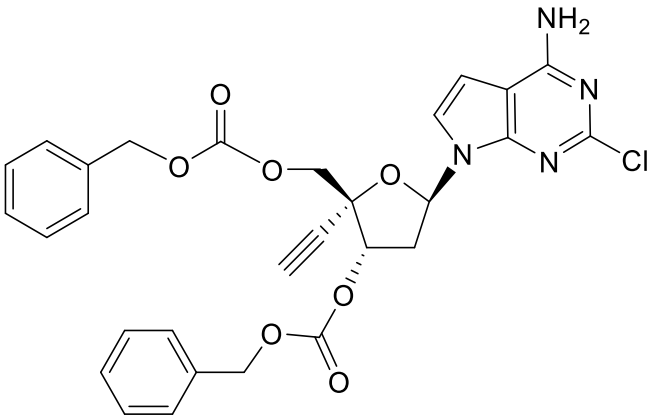
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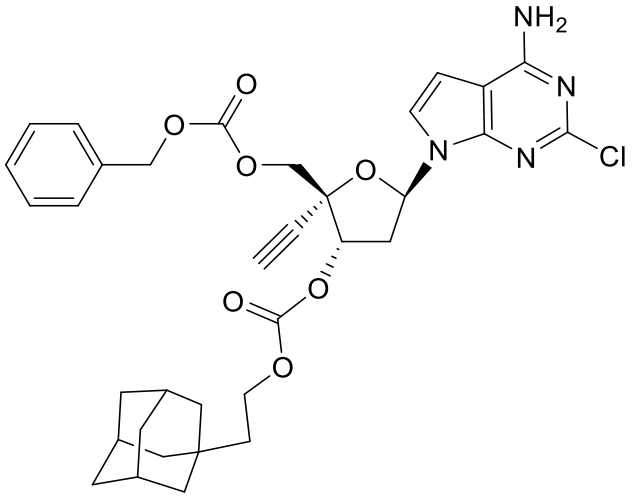
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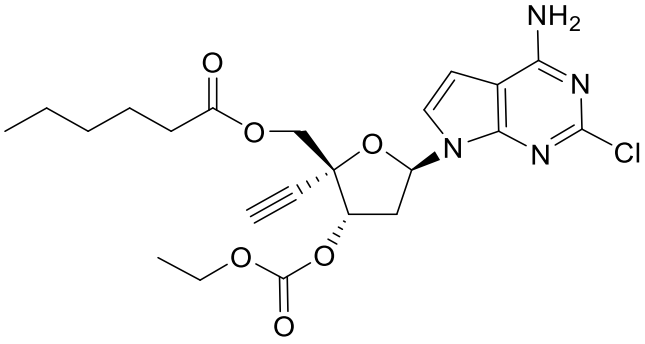
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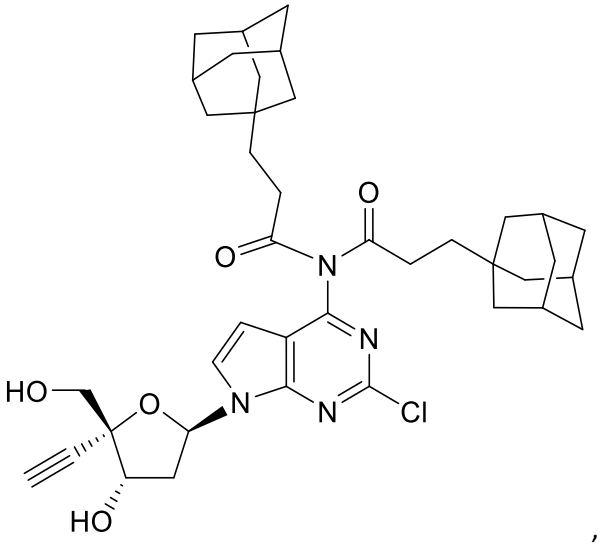
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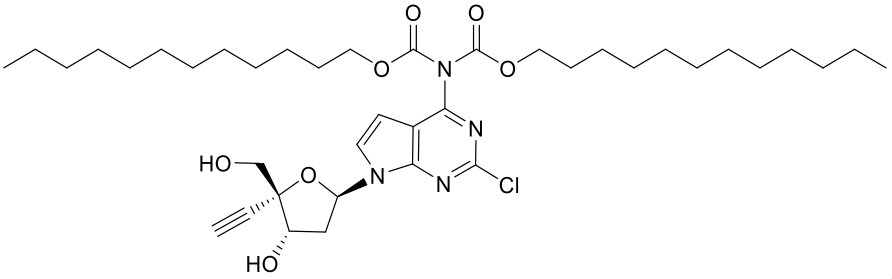
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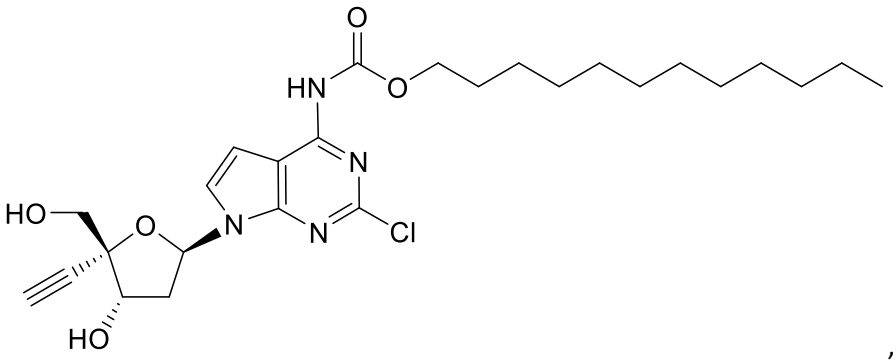
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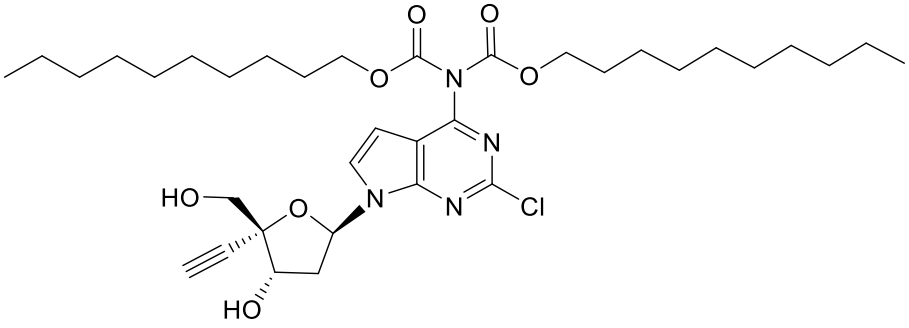
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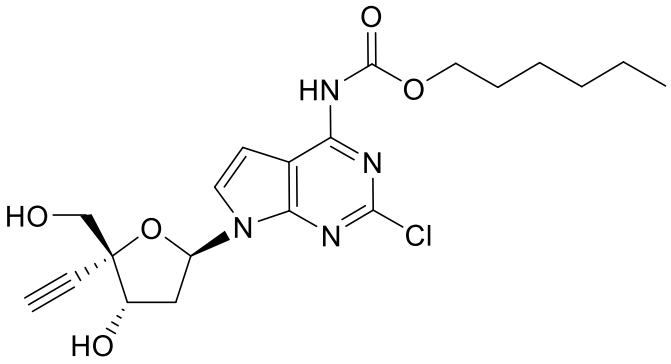
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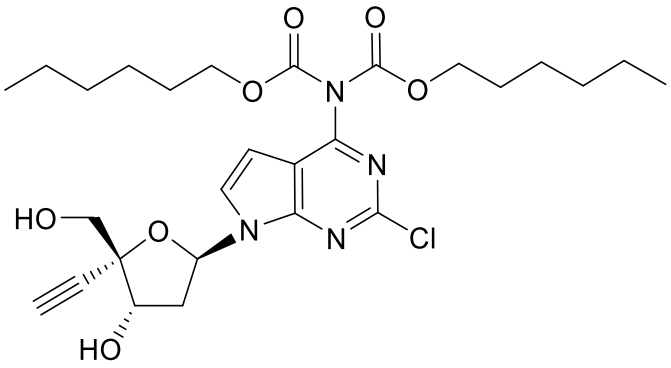
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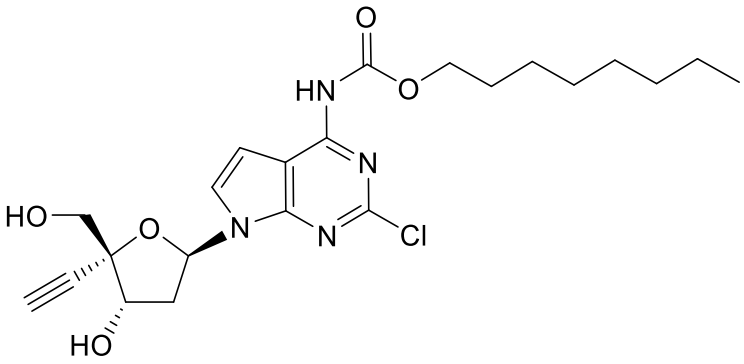
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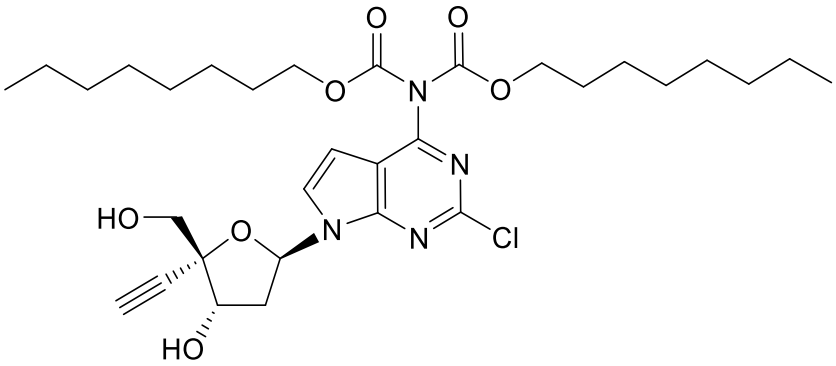
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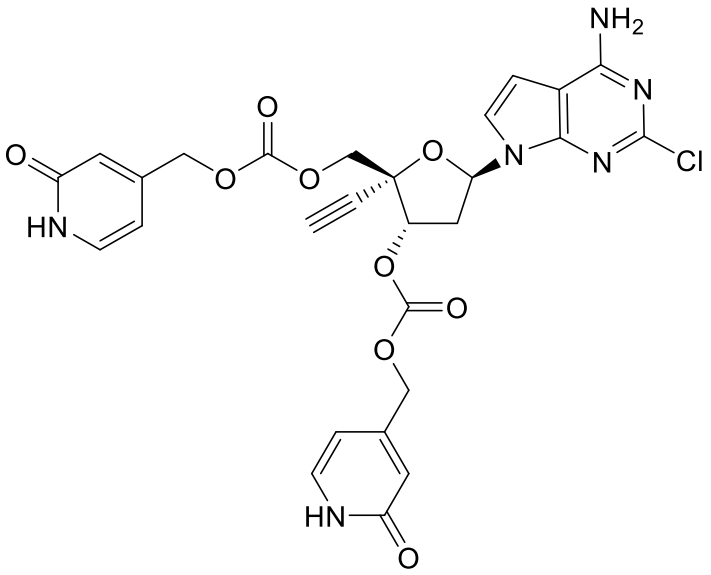
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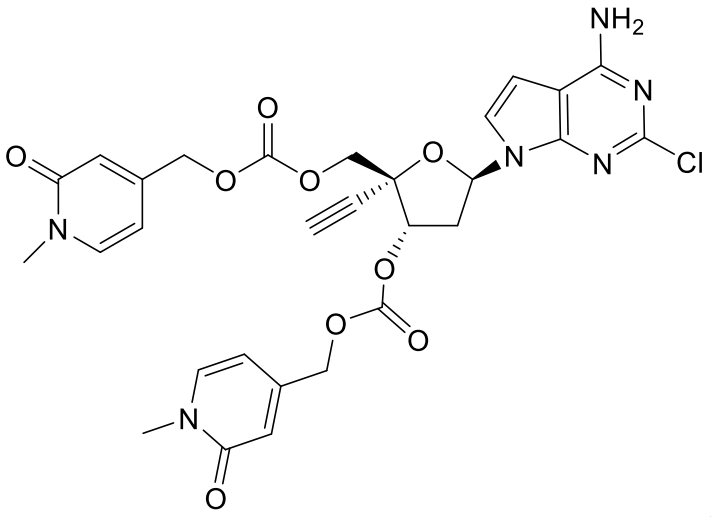
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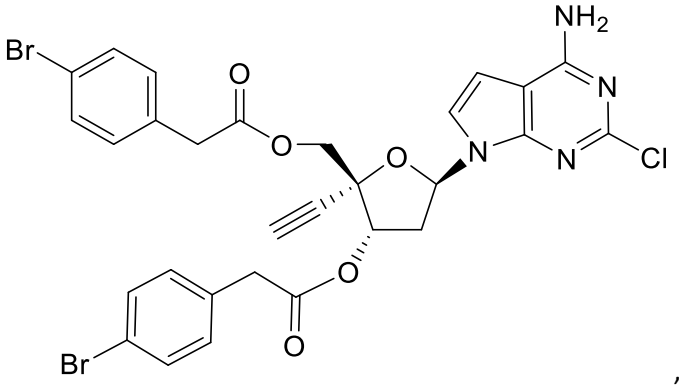
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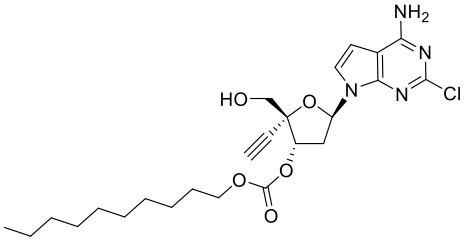
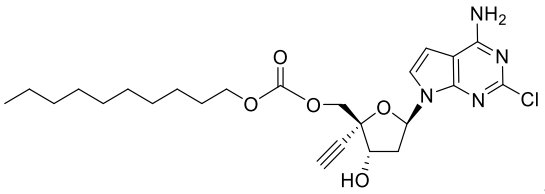
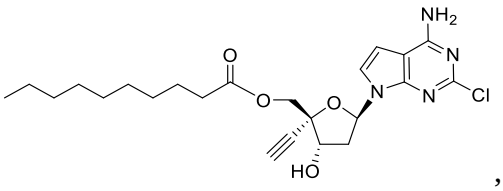
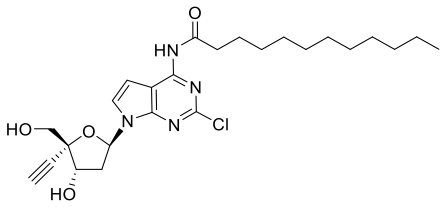
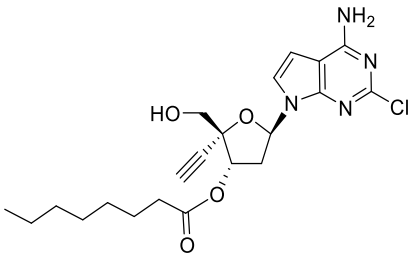
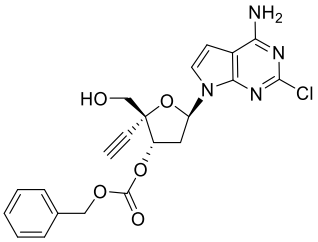
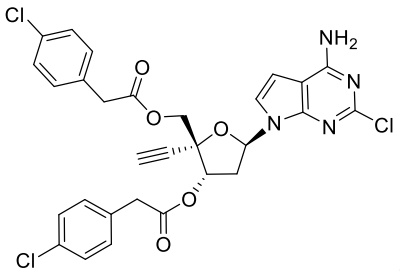
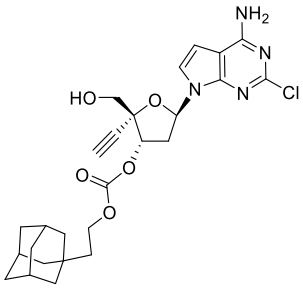
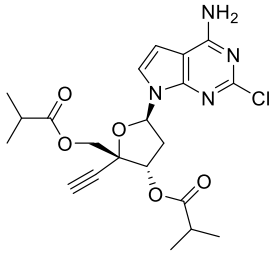
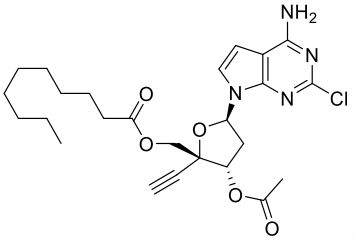
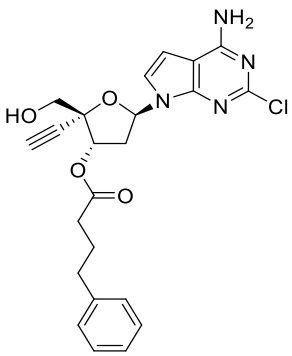
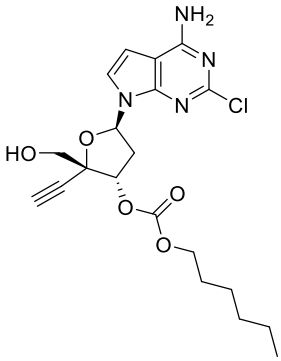
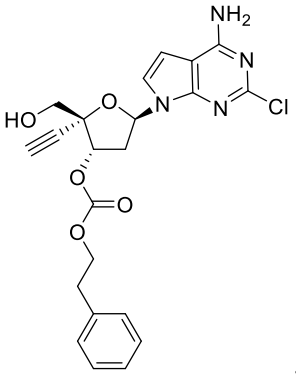
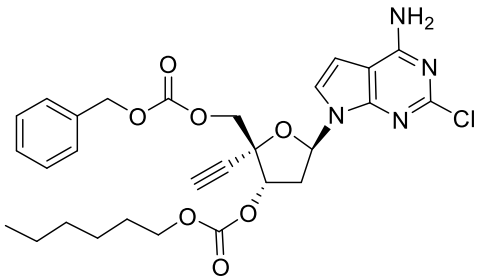

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or a pharmaceutically acceptable salt thereof.

11. The compound of any one of claims 1-9 having the structure:


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, or a pharmaceutically acceptable salt thereof.

12. A pharmaceutical composition comprising a compound or salt of any one of claims 1-11, and a pharmaceutically acceptable carrier.

13. The pharmaceutical composition of claim 12, wherein the composition is injectable, or adapted for injection.

14. A pharmaceutical composition of claim 12 or 13, further comprising one or more additional therapeutic agents selected from the group consisting of lenacapavir, raltegravir, lamivudine, abacavir, ritonavir, dolutegravir, darunavir, atazanavir, emtricitabine, tenofovir, elvitegravir, rilpivirine, lopinavir, doravirine and islatravir.

15. Use of the compound or salt of any one of claims 1-11, or the pharmaceutical composition of any one of claims 12-14 in the manufacture of a medicament for the inhibition of HIV reverse transcriptase in a subject in need thereof.

16. Use of the compound or salt of any one of claims 1-11, or the pharmaceutical composition of any one of claims 12-14 in the manufacture of a medicament for the treatment or prophylaxis of infection by HIV or the treatment, prophylaxis, or delay in the onset or progression of AIDS in a subject in need thereof.

17. The use according to claim 16, wherein the prophylaxis of infection by HIV is pre-exposure prophylaxis of infection by HIV.

18. The use according to any one of claims 15 to 17, further comprising one or more additional therapeutic agents selected from capsid inhibitors, nucleoside reverse transcriptase inhibitors (NRTIs), and non-nucleoside reverse transcriptase inhibitors (NNRTIs) to be administered to the subject.

19. The use of claim 18, wherein the one or more additional therapeutic agents is selected from lenacapavir, raltegravir, lamivudine, abacavir, ritonavir, dolutegravir, darunavir, atazanavir, emtricitabine, tenofovir, elvitegravir, rilpivirine, lopinavir, and doravirine.

20. The use of claim 19, wherein the additional therapeutic agent is lenacapavir.

21. The use of any one of claims 15-20, wherein the compound or salt is to be administered in accordance with a dosing interval range from about once per month to about once per every twelve months.

22. The use of claim 21, wherein the dosing interval range is about once per every three months, once per every six months, or once per every twelve months.

23. The compound or salt of any one of claims 1-11, or the pharmaceutical composition of any one of claims 12-14, for use in therapy.