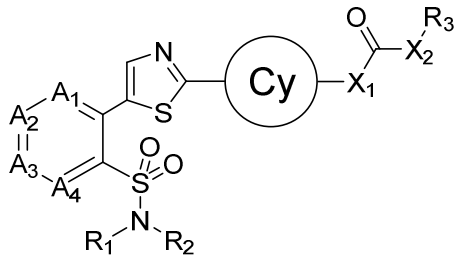
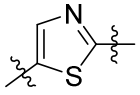
CLAIMS

1. A compound of Formula I:



(I),

or a pharmaceutically acceptable salt or solvate thereof, wherein:

the thiazolyl ring  is optionally substituted with F or Cl;

the ring Cy is C_3-C_7 cycloalkyl, bridged C_6-C_{12} cycloalkyl, or saturated heterocyclyl comprising one or two 3- to 7-membered rings and 1-3 heteroatoms selected from N, O, and S, wherein the cycloalkyl or heterocyclyl moiety is optionally substituted with one or more groups selected from halogen, OH, CN, NH_2, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy;

X_1 is NR_8 or O, or, when X_1 is bonded to a nitrogen atom in the ring Cy, X_1 is absent;

X_2 is NR_8 or O;

R_1 is H or C_1-C_6 alkyl optionally substituted with halogen, OH, C_1-C_6 alkoxy, or C_6-C_{10} aryloxy;

R_2 is H or C_1-C_6 alkyl optionally substituted with halogen, OH, C_1-C_6 alkoxy, or C_6-C_{10} aryloxy;

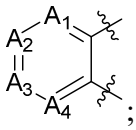
or R_1 and R_2, together with the nitrogen atom to which they are attached, form a heterocyclyl comprising one or two 3- to 7-membered rings and 1-3 heteroatoms selected from N, O, and S;

R_3 is C_1-C_6 alkyl optionally substituted with one or more groups selected from halogen, OH, and CN, phenyl, CH_2-phenyl, C_3-C_7 cycloalkyl, CH_2-(C_3-C_7) cycloalkyl, heterocyclyl, or CH_2-heterocyclyl, wherein the heterocyclyl comprises one or two 3- to 7-membered rings and 1-3 heteroatoms selected from N, O, and S, wherein the cycloalkyl, phenyl, or heterocyclyl moiety is optionally substituted with one or more groups selected from halogen, OH, CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy;

A_1, A_2, A_3, and A_4 are each independently N or C(R_4);

each R_4 is independently H, halogen, CN, OH, N(R_6')$_2$, C_1-C_6 alkoxy, C(=O)N(R_6)$_2$, C(=O)OR_6, C(=O)R_6, Q-T, C_6-C_{10} aryl, or heteroaryl comprising one or two 5- or 6-

membered rings and 1-3 heteroatoms selected from N, O, and S, wherein the aryl or heteroaryl moiety is optionally substituted with one or more R_9;

each Q is independently C_1-C_4 alkylene or O-(C_1-C_4) alkylene wherein the oxygen atom is bonded to the ring ;

each T is independently C_1-C_4 alkoxy, OH, $N(R_6)_2$, $N(R_5)C(=O)R_6$, $N(R_5)C(=O)OR_6$, $C(=O)N(R_6)_2$, $C(=O)OR_6$, $C(=O)R_6$, C_6-C_{10} aryl, or heteroaryl comprising one or two 5- or 6-membered rings and 1-3 heteroatoms selected from N, O, and S, wherein the aryl or heteroaryl moiety is optionally substituted with one or more R_9;

each R_5 is independently H or C_1-C_4 alkyl;

each R_6' is independently H, C_1-C_6 alkyl optionally substituted with one or more R_7, C_1-C_6 haloalkyl, C_3-C_7 cycloalkyl, heterocyclyl comprising one or two 3- to 7-membered rings and 1-3 heteroatoms selected from N, O, and S, C_6-C_{10} aryl, or heteroaryl comprising one or two 5- or 6-membered rings and 1-3 heteroatoms selected from N, O, and S, wherein the cycloalkyl, heterocyclyl, aryl, or heteroaryl moiety is optionally substituted with one or more R_9, wherein at least one R_6' is not H;

or two R_6' together with the atoms to which they are attached form a 3- to 10-membered heterocyclyl comprising 1-3 heteroatoms selected from N, O, and S, wherein the heterocyclyl is optionally substituted with one or more R_9;

each R_6 is independently H, C_1-C_6 alkyl optionally substituted with one or more R_7, C_1-C_6 haloalkyl, C_6-C_{10} aryl, or heteroaryl comprising one or two 5- or 6-membered rings and 1-3 heteroatoms selected from N, O, and S, wherein the aryl or heteroaryl moiety is optionally substituted with one or more R_9;

or two R_6 together with the atoms to which they are attached form a 3- to 10-membered heterocyclyl comprising 1-3 heteroatoms selected from N, O, and S, wherein the heterocyclyl is optionally substituted with one or more R_9;

each R_7 is independently $N(R_8)_2$, OR_8, C_6-C_{10} aryl, or heteroaryl comprising one or two 5- or 6-membered rings and 1-3 heteroatoms selected from N, O, and S;

each R_8 is independently H or C_1-C_6 alkyl; and

each R_9 is independently oxo, halogen, OH, CN, NH_2, $N(C_1$-C_4 alkyl$)_2$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, or C_1-C_6 haloalkoxy, wherein the C_1-C_6 alkyl is optionally substituted with one or more oxo, OH, O(C_1-C_4 alkyl), CN, NH_2, NH(C_1-C_4 alkyl), or N(C_1-C_4 alkyl)$_2$.

2. The compound of claim 1, wherein the ring Cy is C_3-C_7 cycloalkyl or saturated heterocyclyl comprising one or two 3- to 7-membered rings and 1-3 heteroatoms selected from N, O, and S, wherein the cycloalkyl or heterocyclyl is optionally substituted with one or more groups selected from halogen, OH, CN, NH_2, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy.

3. The compound of claim 1 or 2, wherein A_1, A_2, A_3, and A_4 are each $C(R_4)$.

4. The compound of claim 1 or 2, wherein one, two, or three of A_1, A_2, A_3, and A_4 are N.

5. The compound of any one of claims 1-4, wherein X_1 is NR_8 and X_2 is NR_8.

6. The compound of any one of claims 1-4, wherein X_1 is NR_8 and X_2 is O.

7. The compound of any one of claims 1-4, wherein X_1 is O and X_2 is NR_8.

8. The compound of any one of claims 1-4, wherein X_1 is absent and X_2 is NR_8.

9. The compound of any one of claims 1-4, wherein X_1 is absent and X_2 is O.

10. The compound of any one of claims 1-9, wherein R_3 is C_1-C_6 alkyl optionally substituted with one or more groups selected from halogen, OH, and CN.

11. The compound of any one of claims 1-9, wherein R_3 is phenyl or CH_2-phenyl, wherein the phenyl moiety is optionally substituted with one or more groups selected from halogen, OH, CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy.

12. The compound of any one of claims 1-9, wherein R_3 is C_3-C_7 cycloalkyl or CH_2-(C_3-C_7) cycloalkyl, wherein the cycloalkyl moiety is optionally substituted with one or more groups selected from halogen, OH, CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy.

13. The compound of any one of claims 1-9, wherein R_3 is heterocyclyl or CH_2-heterocyclyl, wherein the heterocyclyl moiety is optionally substituted with one or more groups selected from halogen, OH, CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy.

14. The compound of any one of claims 1-13, wherein R_1 is H.

15. The compound of any one of claims 1-13, wherein R_1 is C_1-C_6 alkyl optionally substituted with halogen, OH, C_1-C_6 alkoxy, or C_6-C_{10} aryloxy.

16. The compound of any one of claims 1-15, wherein R_2 is H.

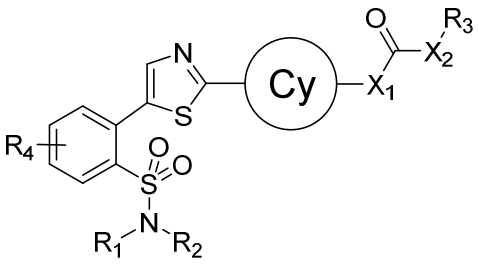
17. The compound of any one of claims 1-15, wherein R_2 is C_1-C_6 alkyl optionally substituted with halogen, OH, C_1-C_6 alkoxy, or C_6-C_{10} aryloxy.

18. The compound of any one of claims 1-15, wherein R_1 and R_2, together with the nitrogen atom to which they are attached, form a heterocyclyl.

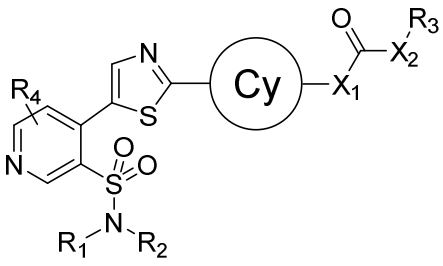
19. The compound of any one of claims 1-18, wherein each R_4 is H.

20. The compound of any one of claims 1-18, wherein at least one R_4 is halogen, CN, OH, $N(R_6')_2$, C_1-C_4 alkoxy, $C(=O)N(R_6)_2$, $C(=O)OR_6$, $C(=O)R_6$, Q-T, C_6-C_{10} aryl, or heteroaryl comprising one or two 5- or 6-membered rings and 1-3 heteroatoms selected from N, O, and S, wherein the aryl or heteroaryl moiety is optionally substituted with one or more R_9.

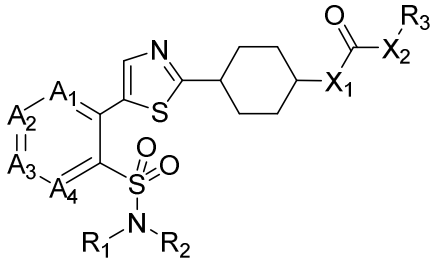
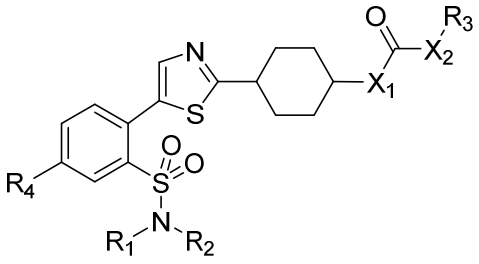
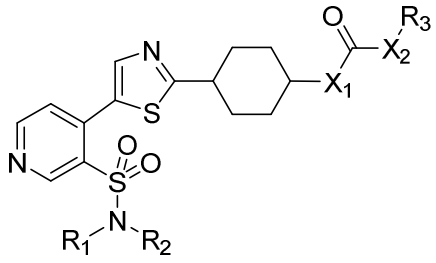
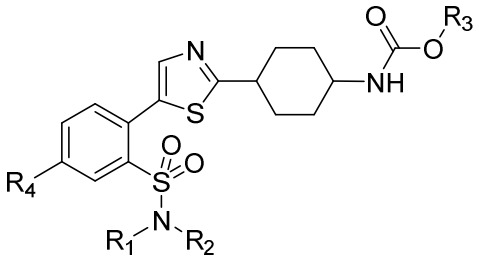
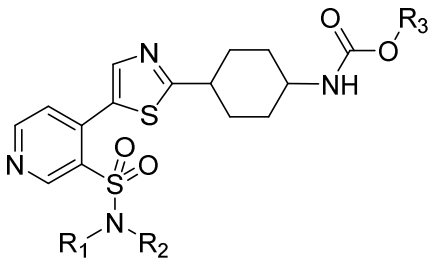
21. The compound of claim 1, wherein the compound is of Formula Ia, Ib, Ic, Id, Ie, If or Ig:



(Ia),

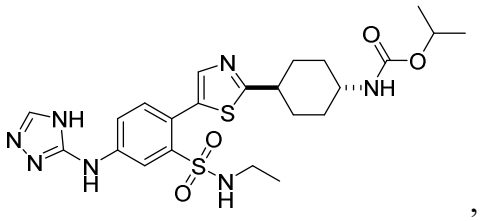


(Ib),


(Ic),

(Id),

(Ie),

(If),

or (Ig),

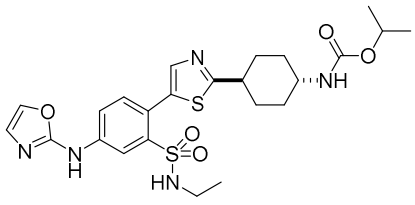
or a pharmaceutically acceptable salt or solvate thereof.

22. The compound of claim 1, wherein the compound is


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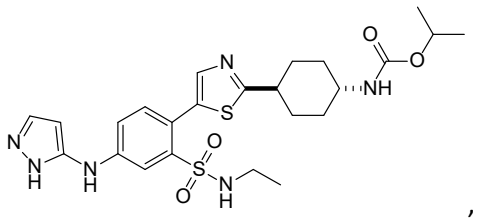
or a pharmaceutically acceptable salt or solvate thereof.

23. The compound of claim 1, wherein the compound is


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or a pharmaceutically acceptable salt or solvate thereof.

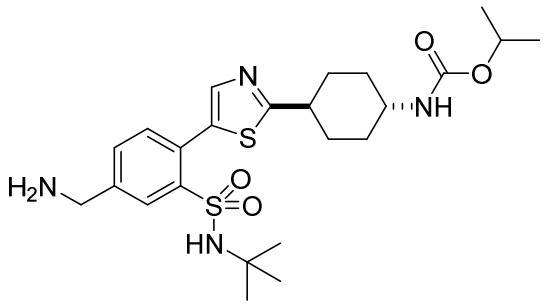
24. The compound of claim 1, wherein the compound is



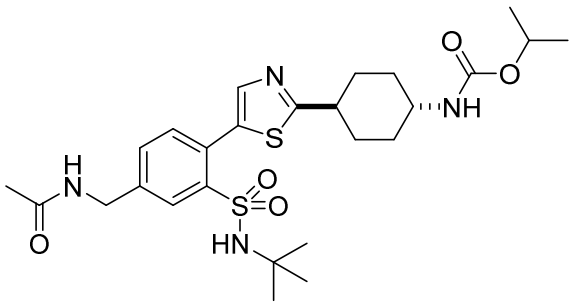
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or a pharmaceutically acceptable salt or solvate thereof.

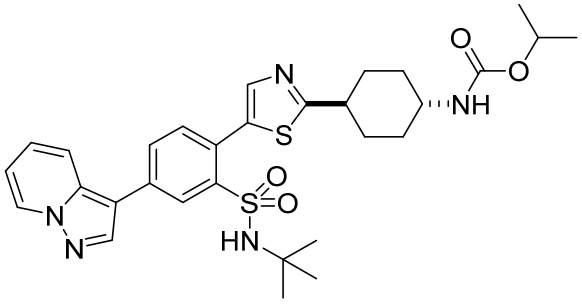
25. A compound selected from:



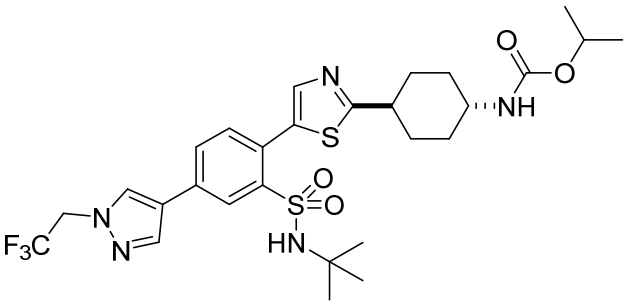
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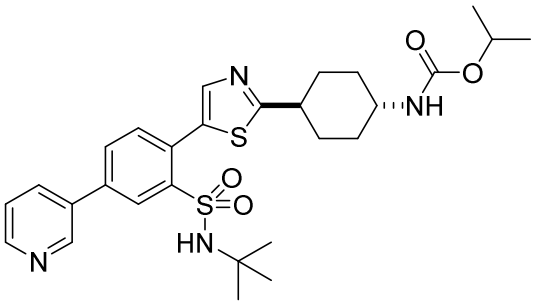
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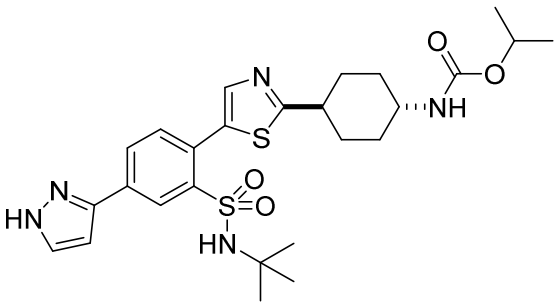
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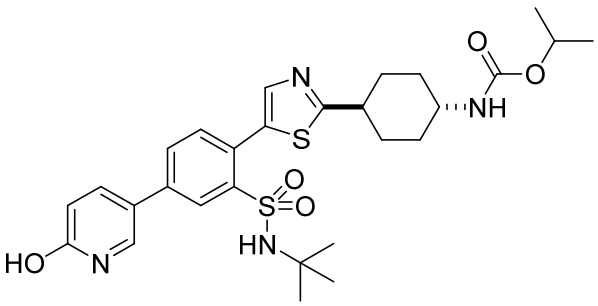
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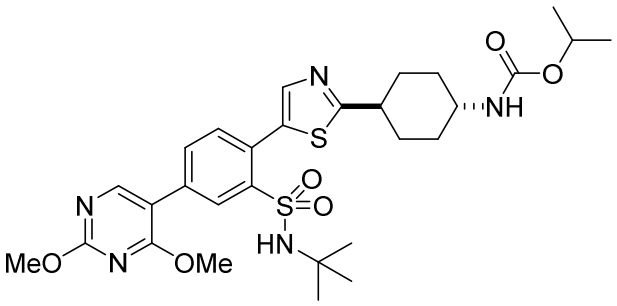
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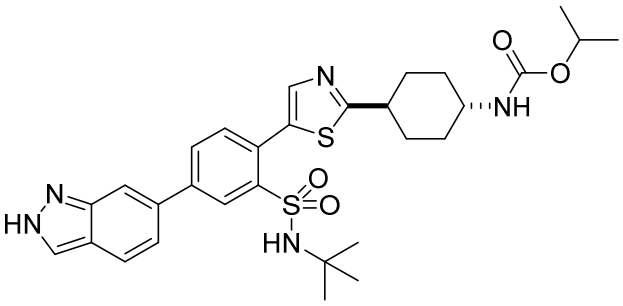
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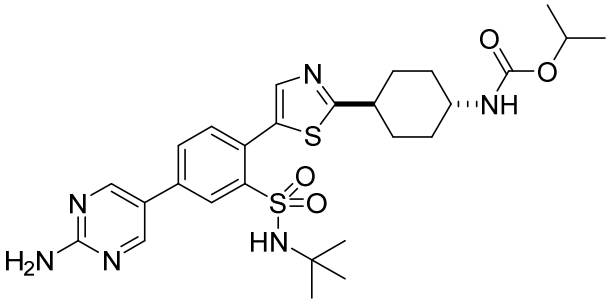
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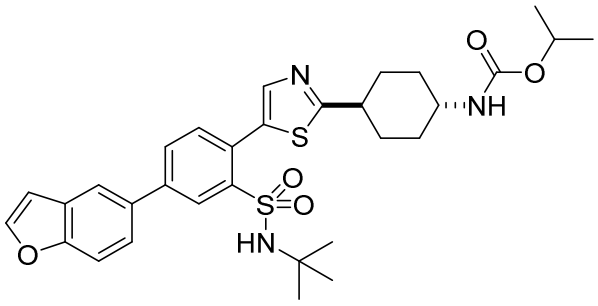
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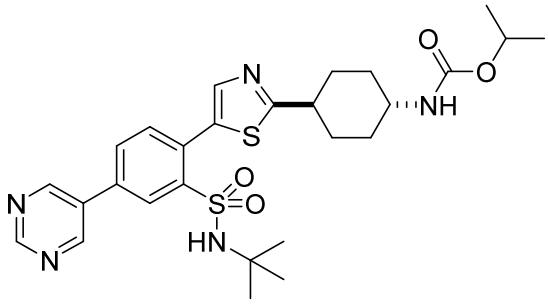
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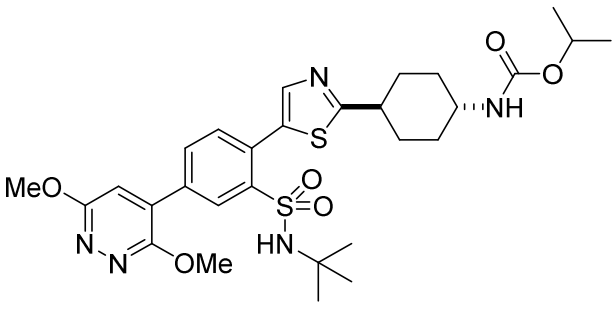
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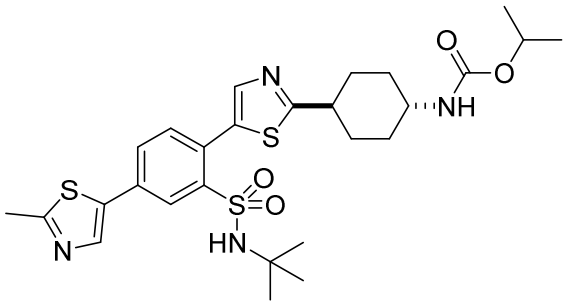
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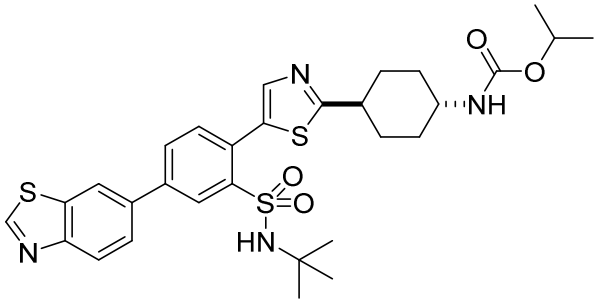
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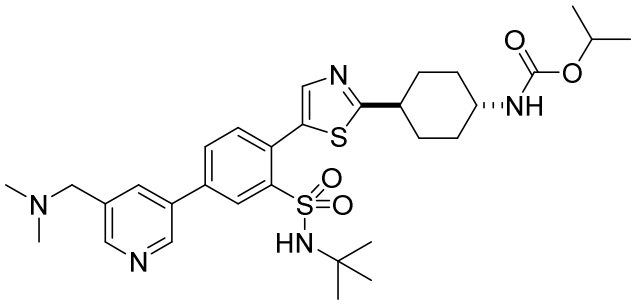
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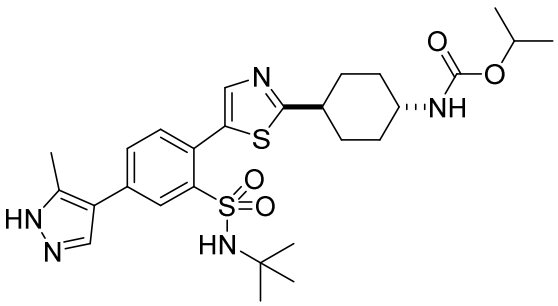
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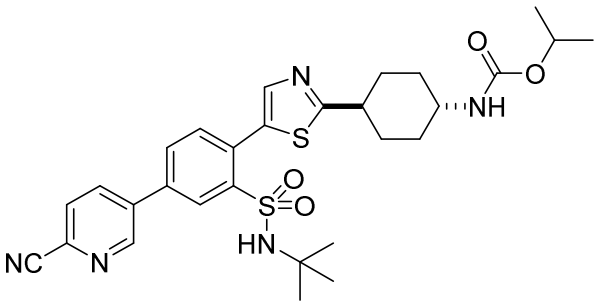
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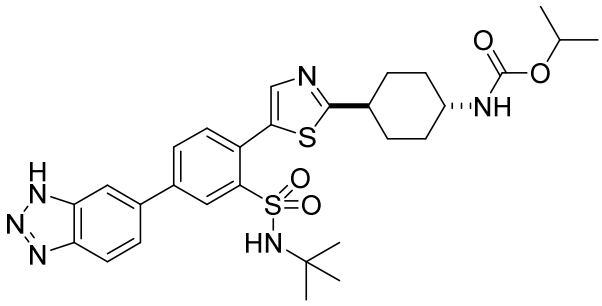
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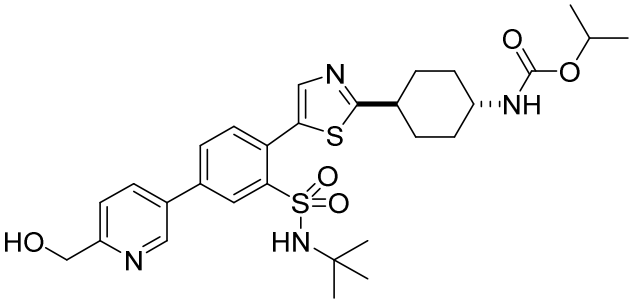
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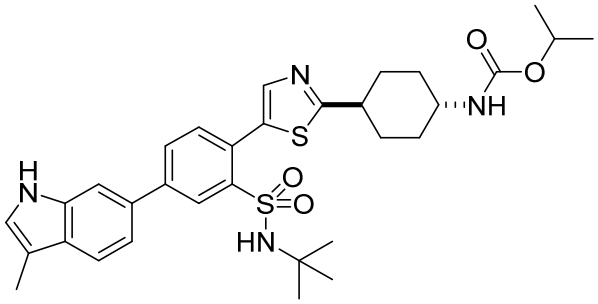
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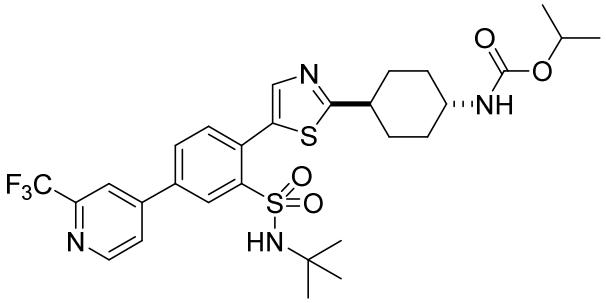
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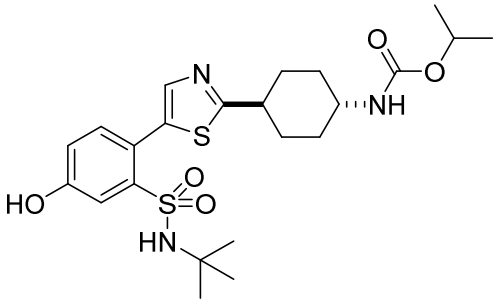
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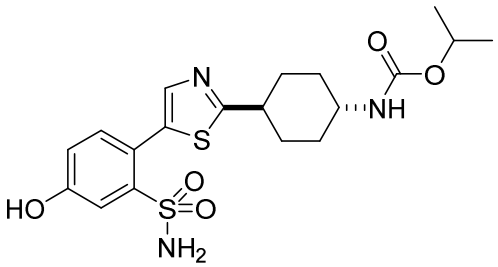
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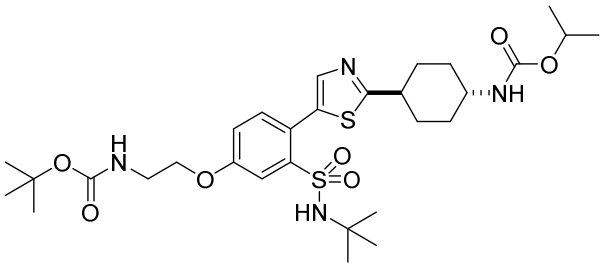
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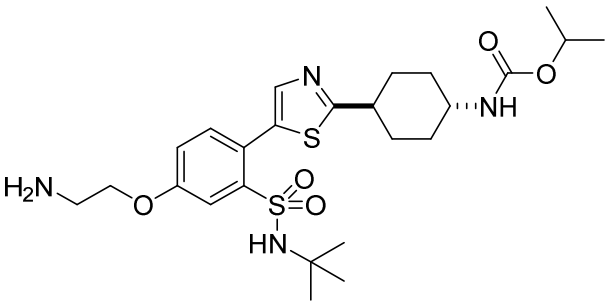
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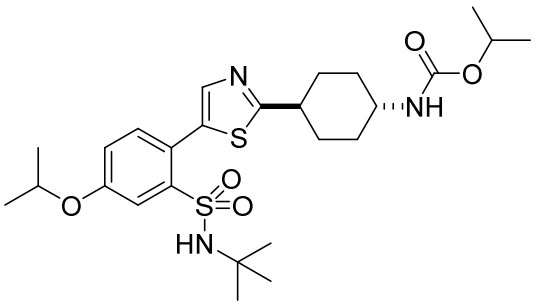
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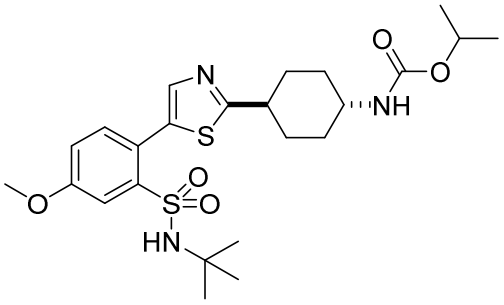
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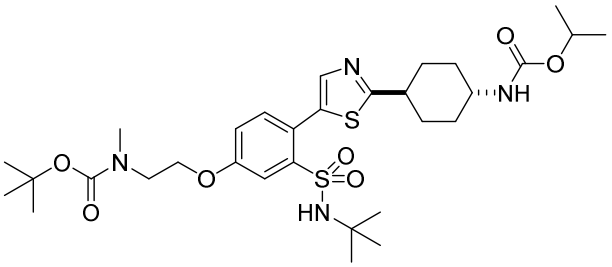
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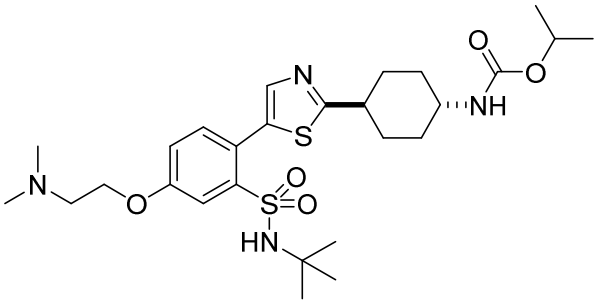
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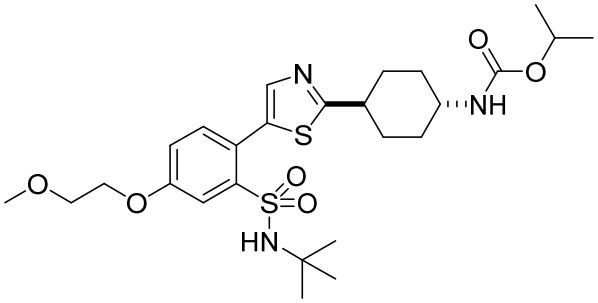
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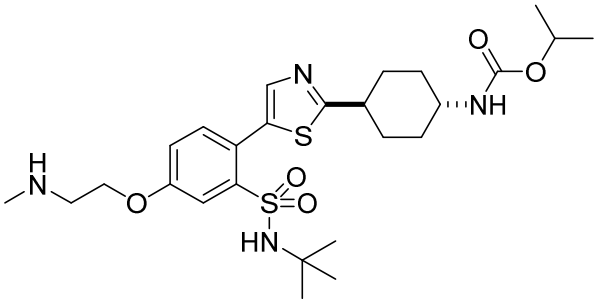
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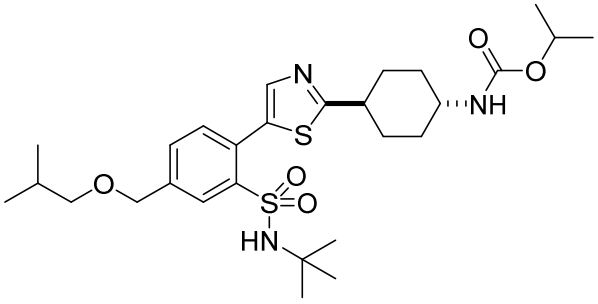
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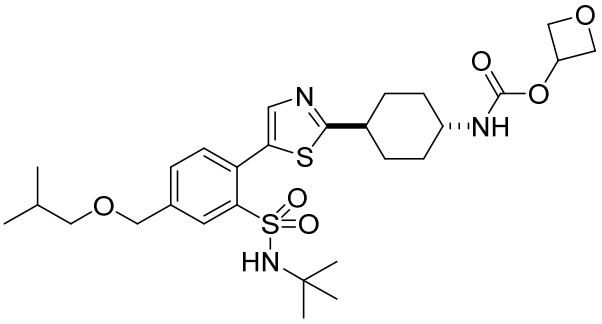
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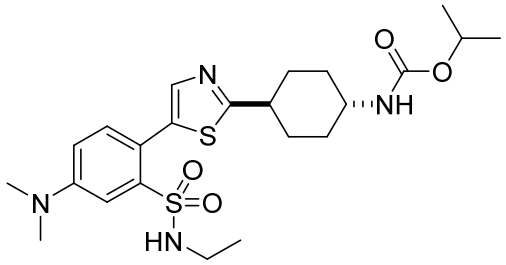
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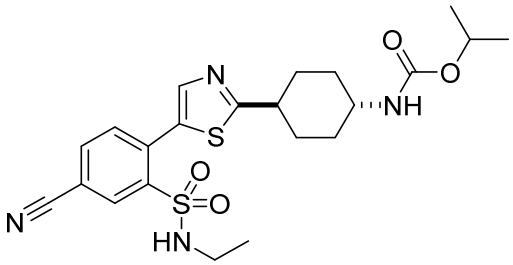
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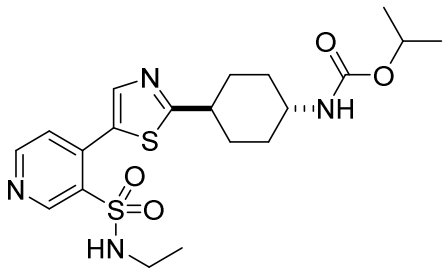
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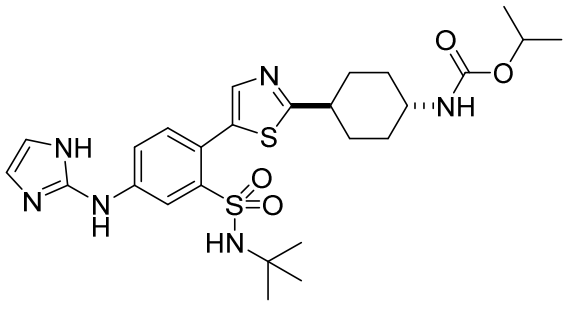
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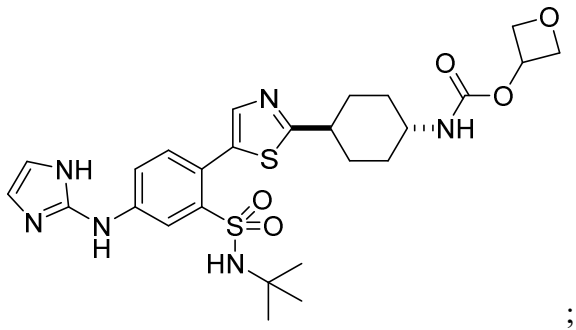
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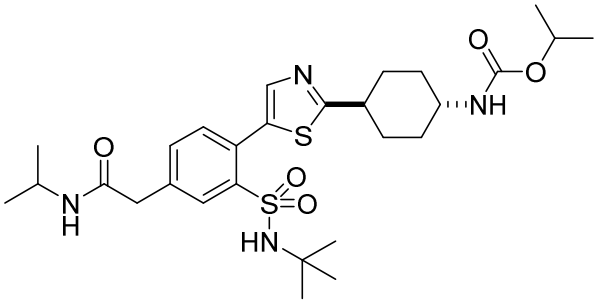
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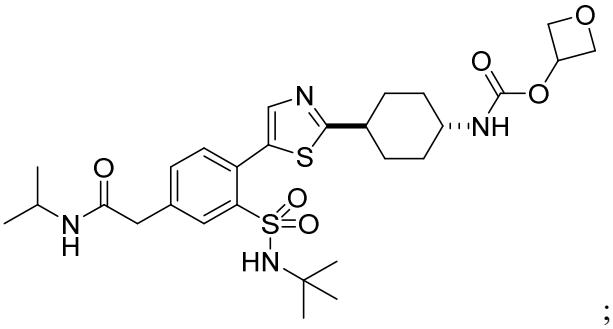
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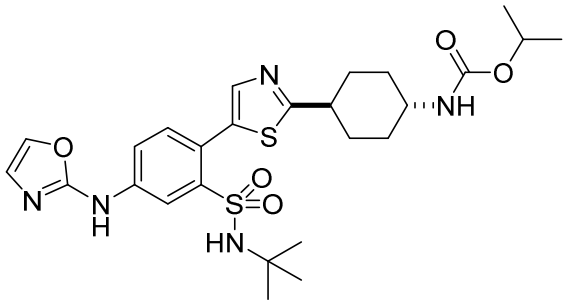
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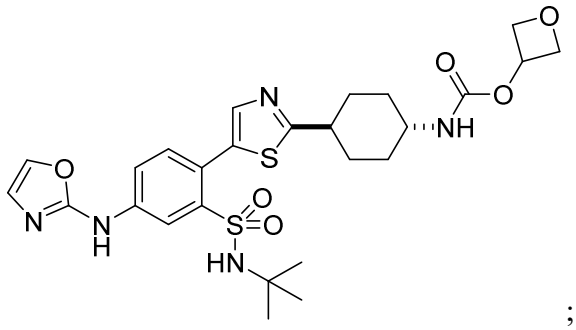
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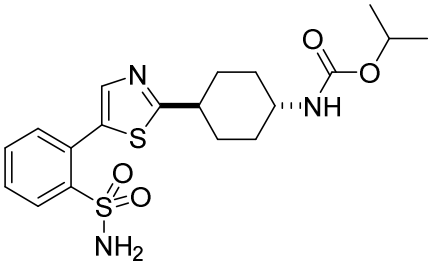
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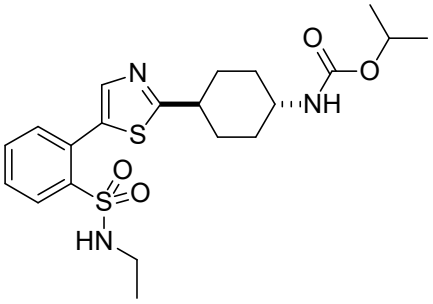
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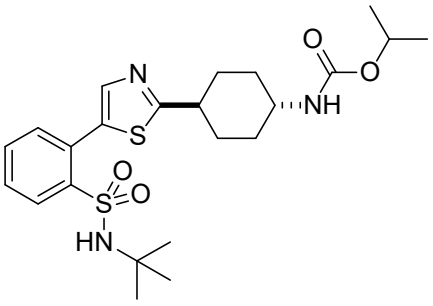
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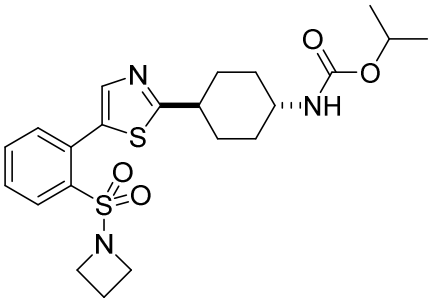
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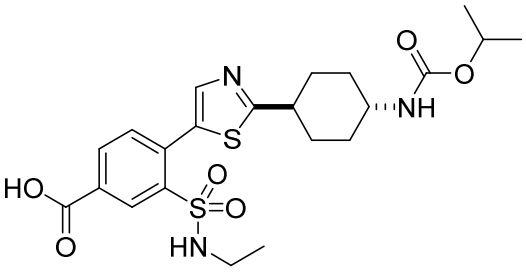
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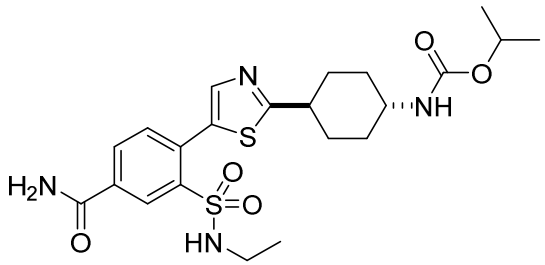
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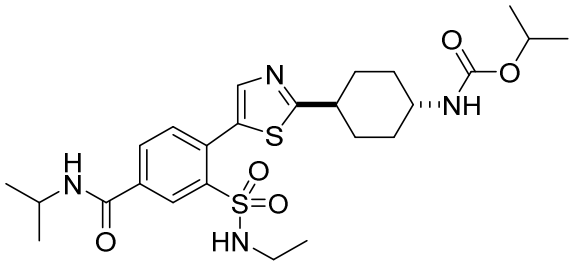
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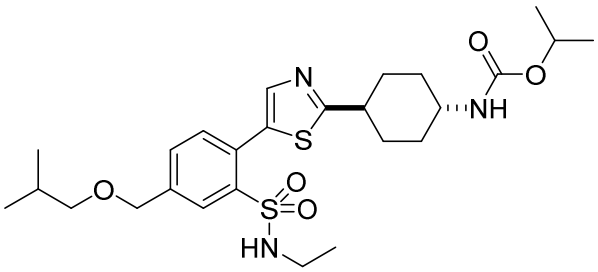
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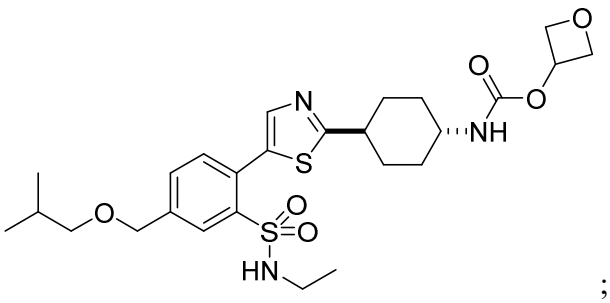
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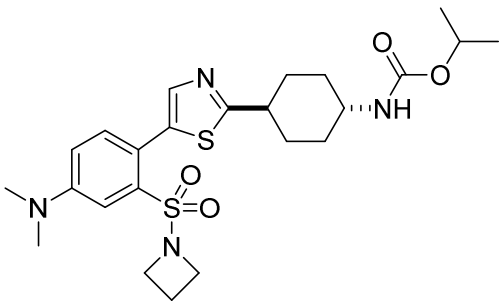
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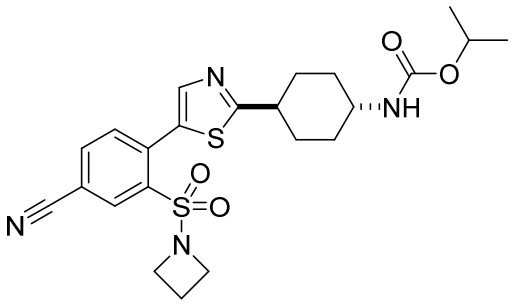
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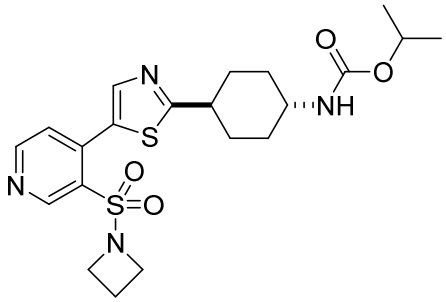
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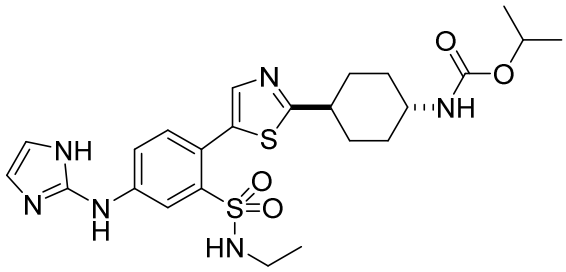
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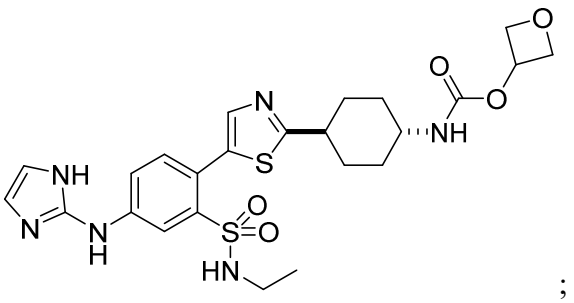
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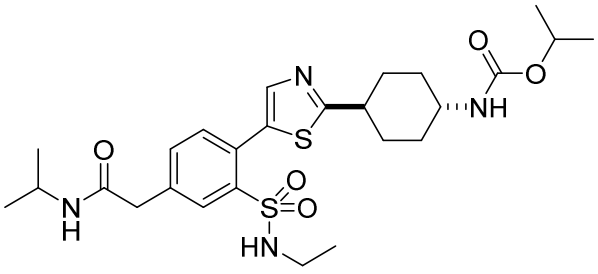
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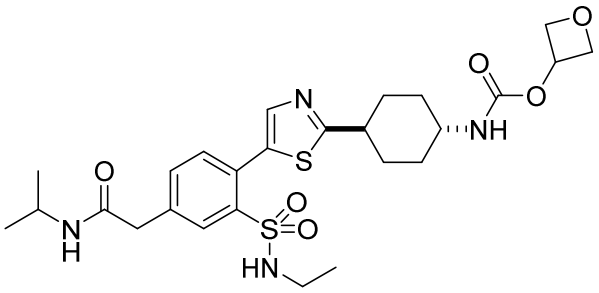
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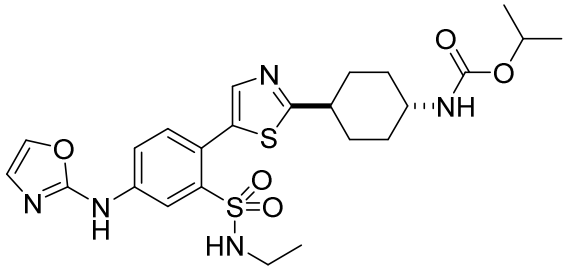
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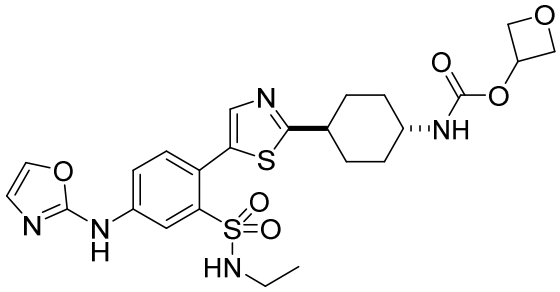
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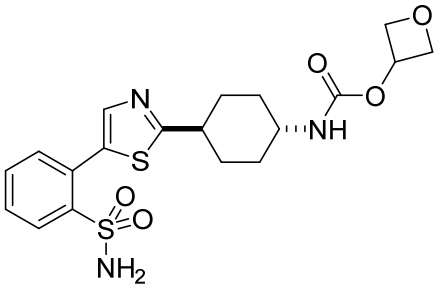
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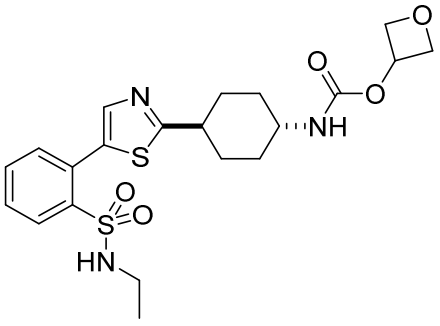
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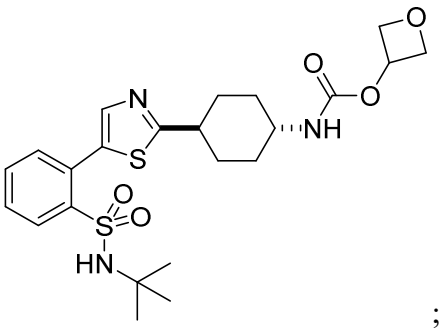
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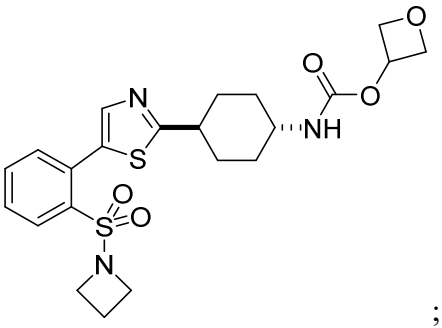
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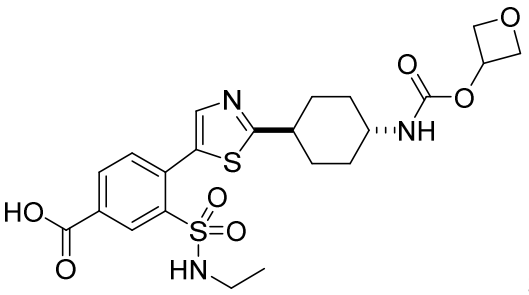
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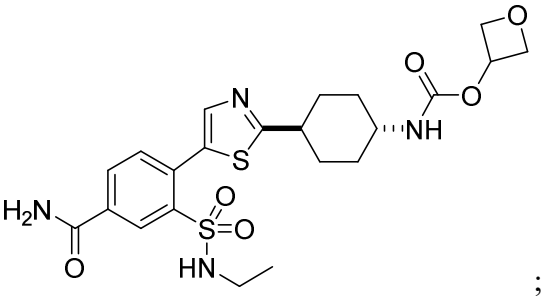
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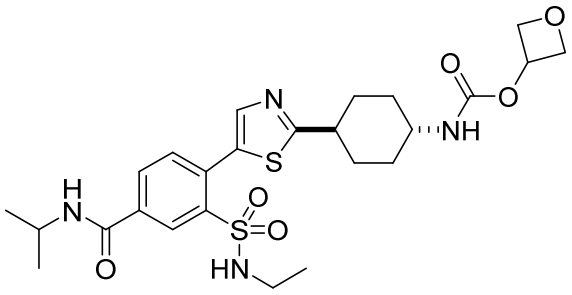
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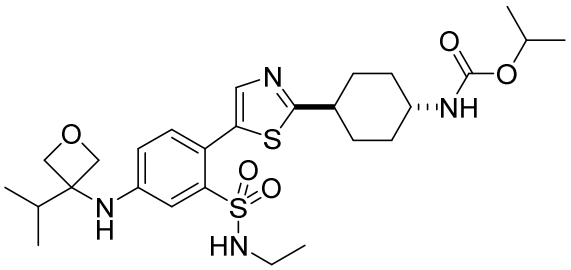
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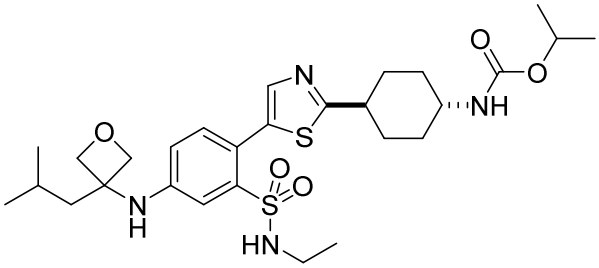


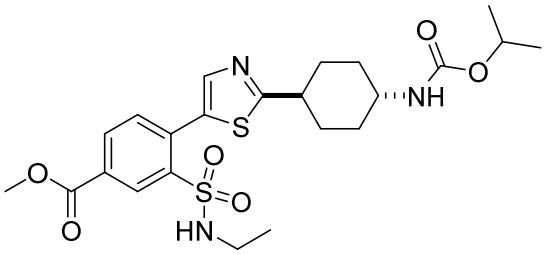
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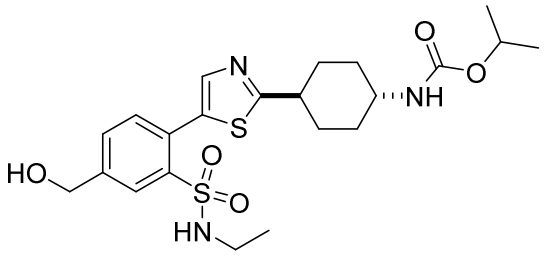


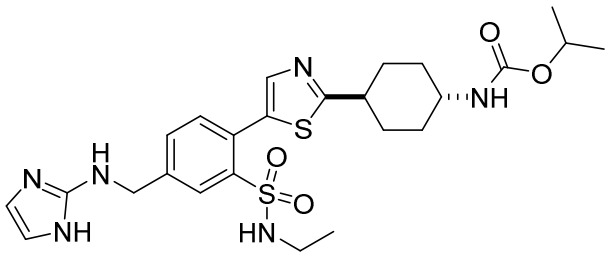
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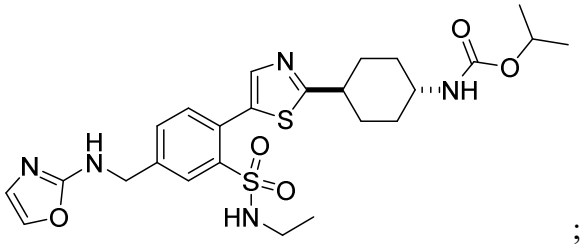

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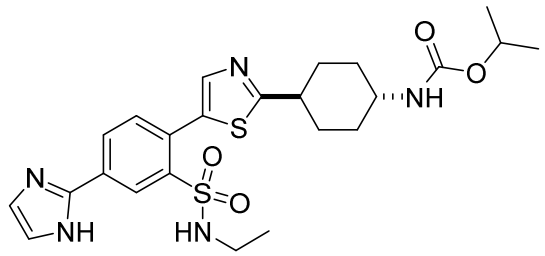

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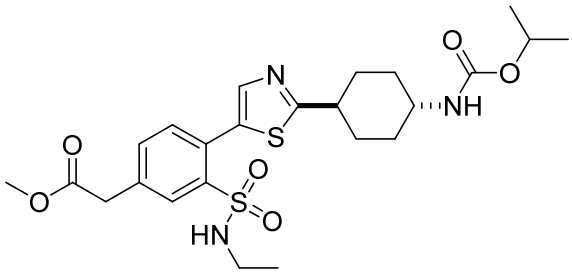

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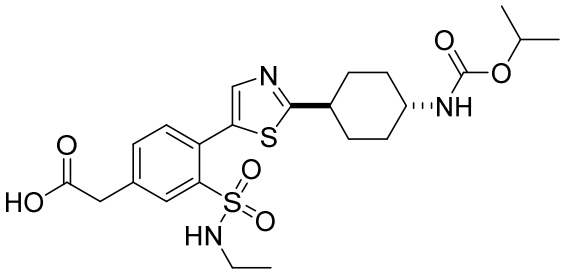

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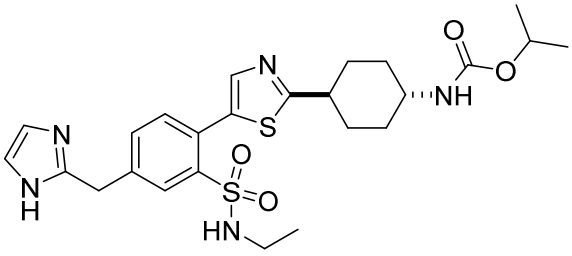

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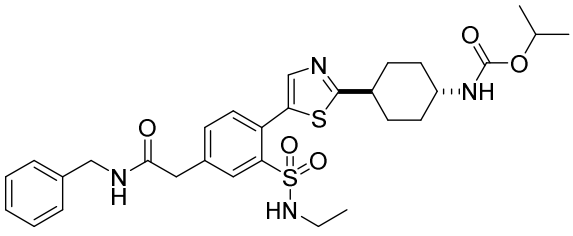

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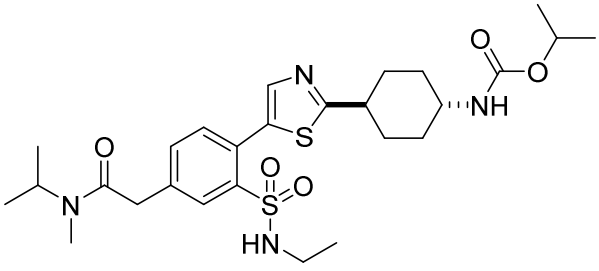

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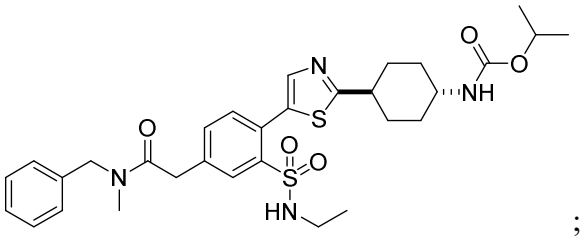

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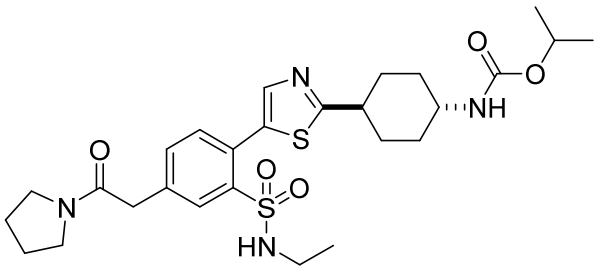

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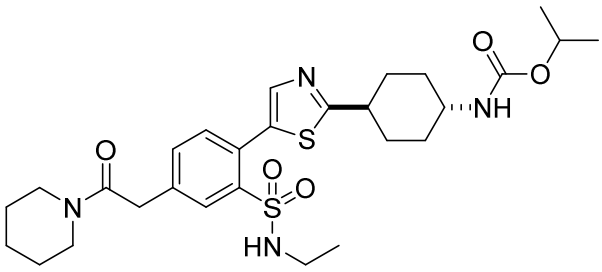

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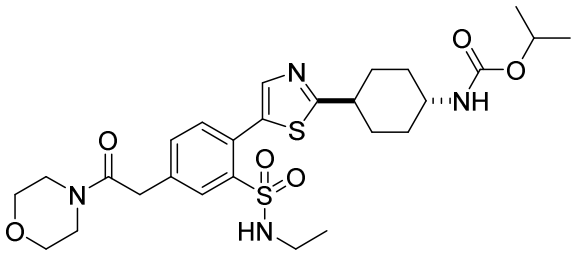

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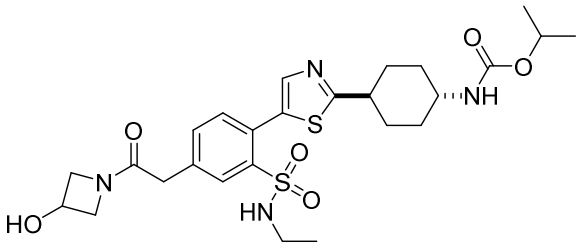

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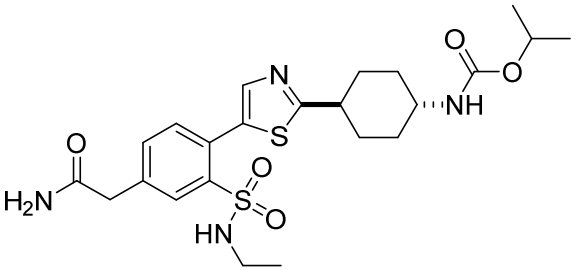

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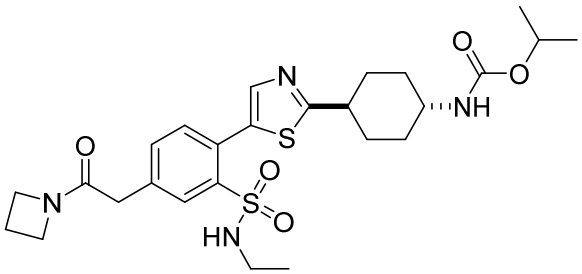

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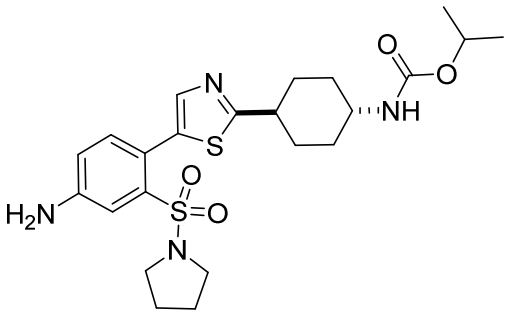

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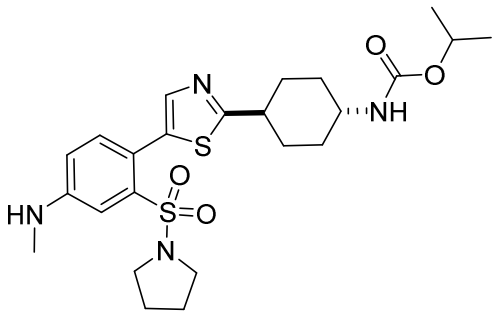

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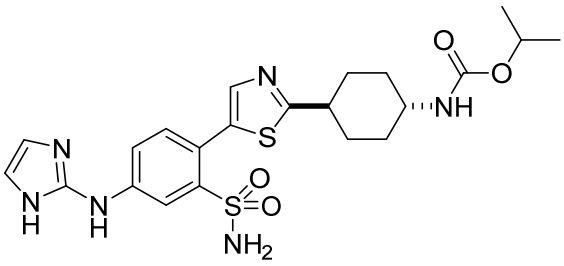
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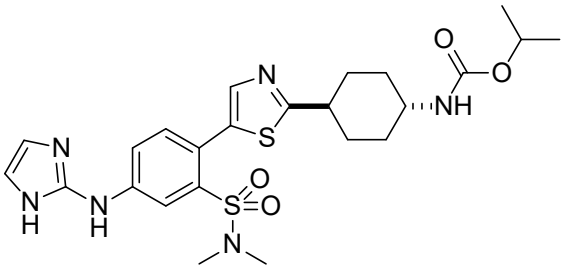
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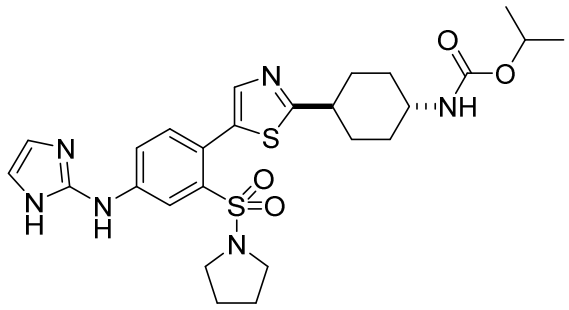
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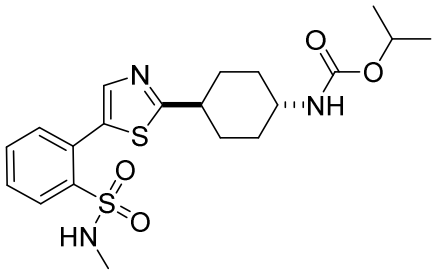
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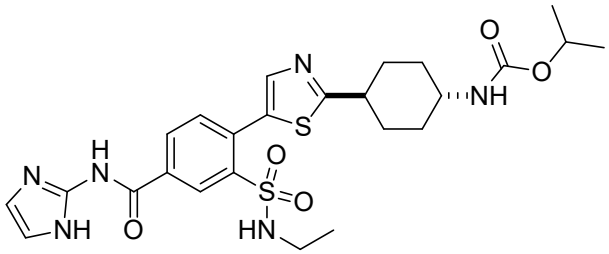
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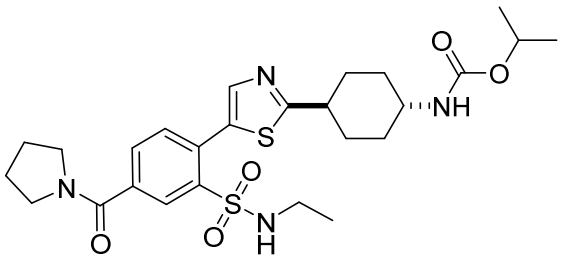
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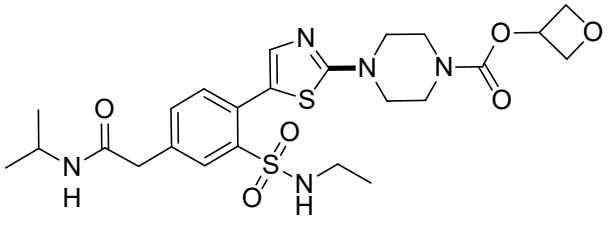
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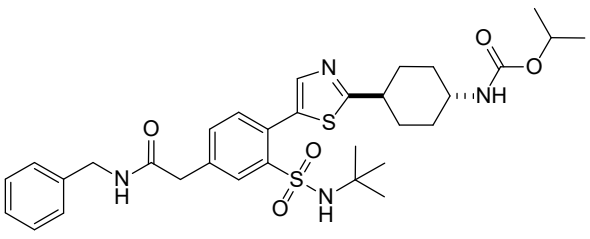
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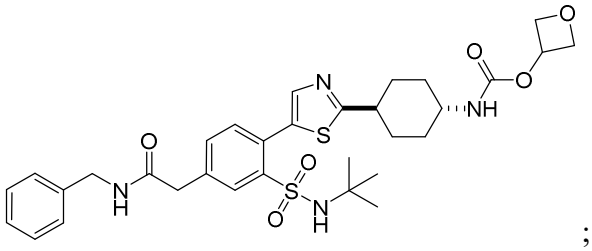
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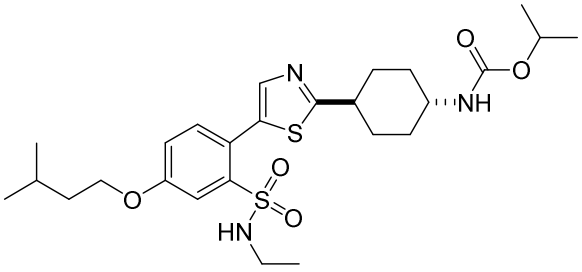
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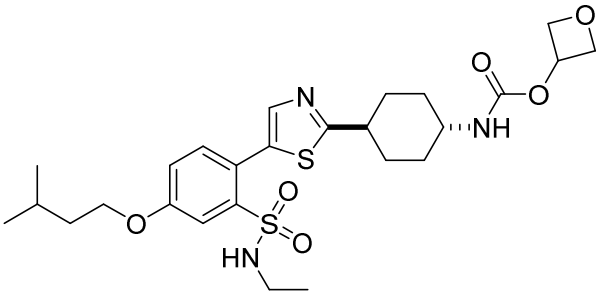
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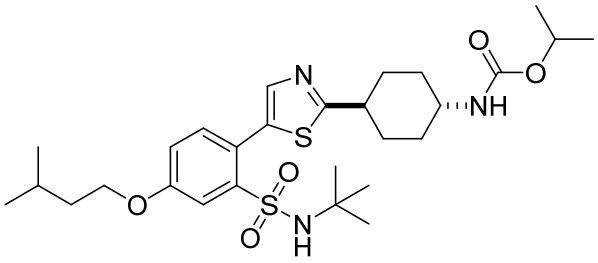
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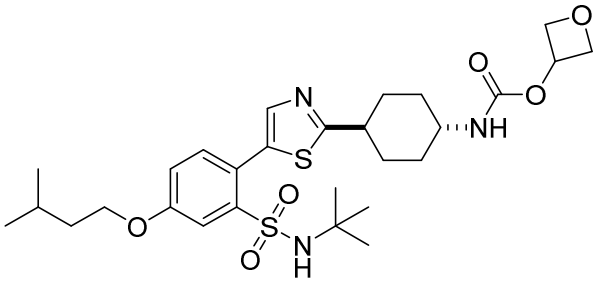
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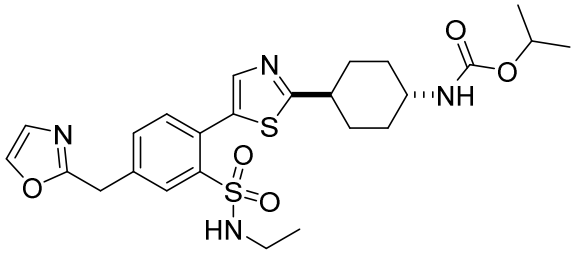
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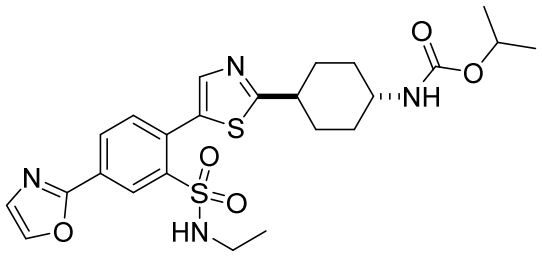
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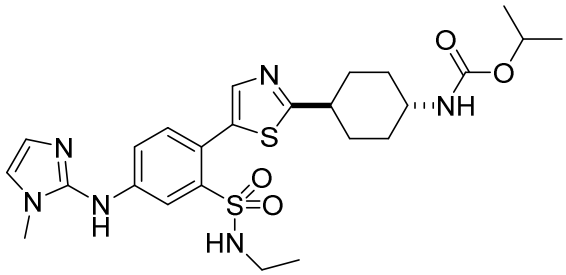
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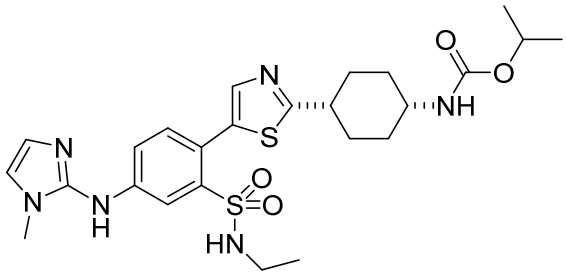
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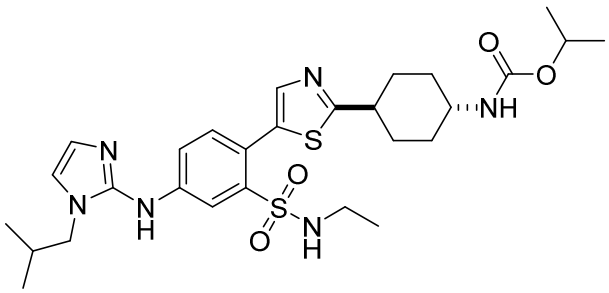
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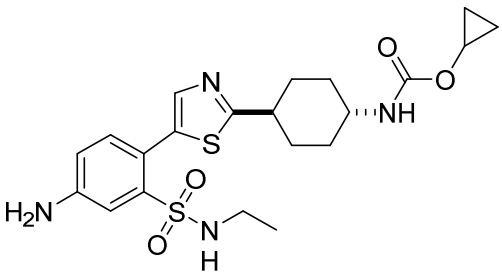
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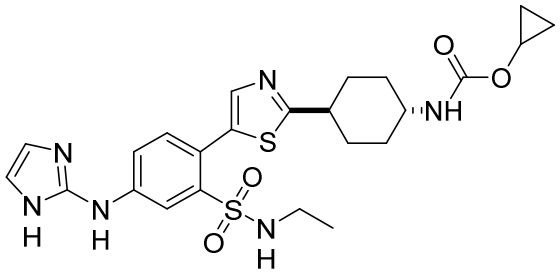
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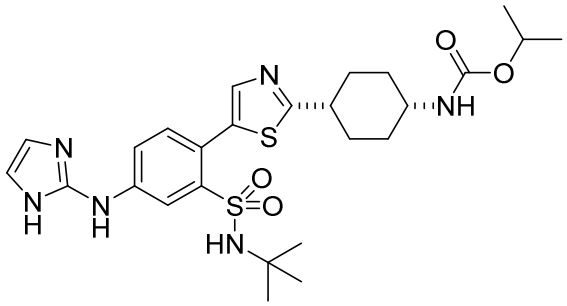
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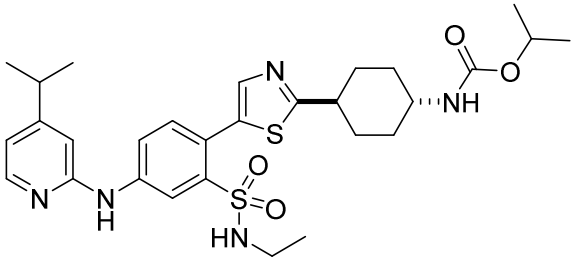
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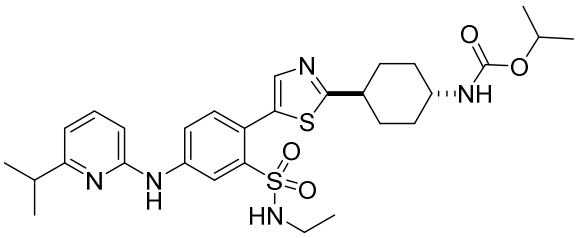
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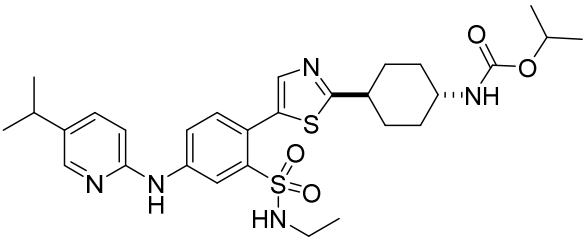
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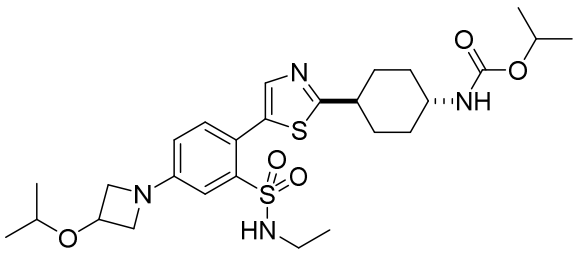
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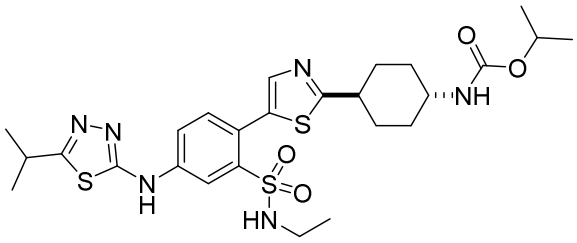
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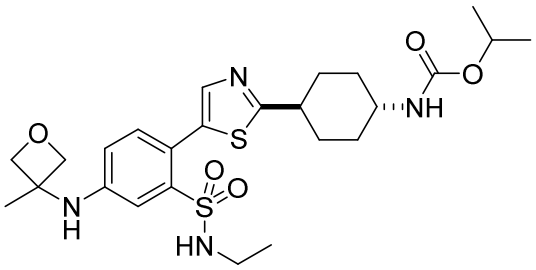


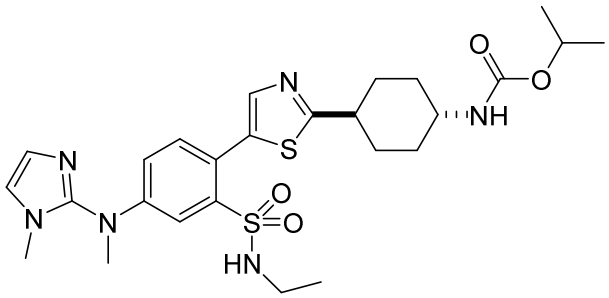
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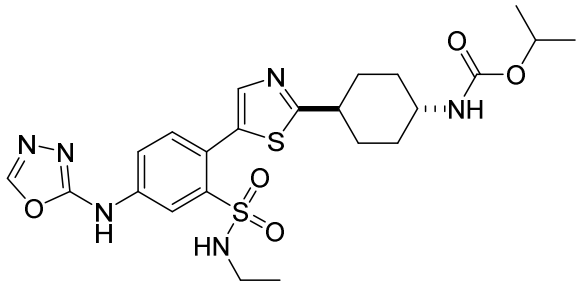


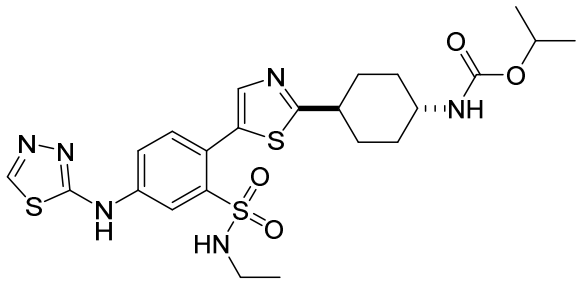
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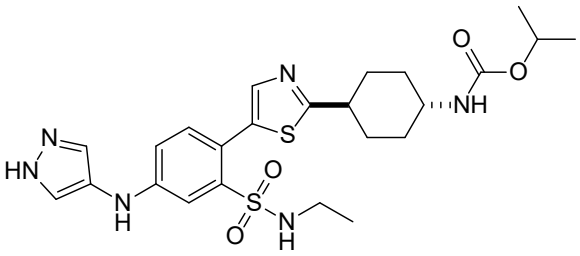

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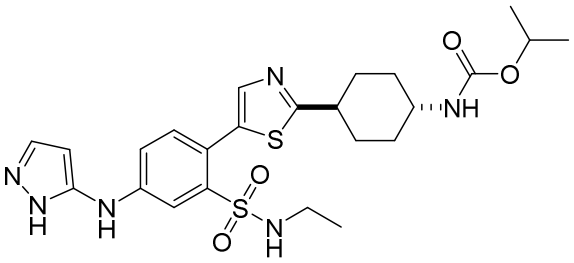

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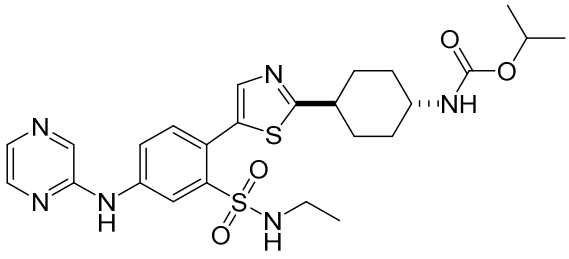

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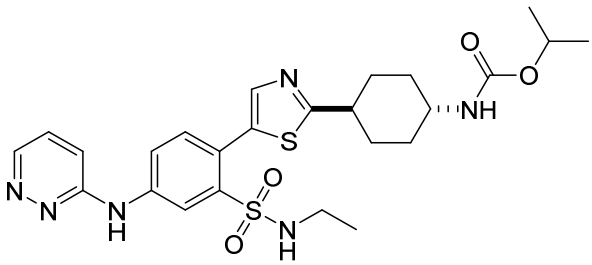

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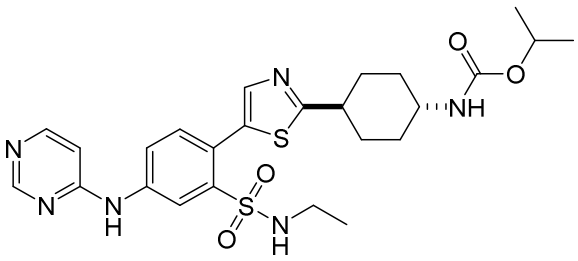

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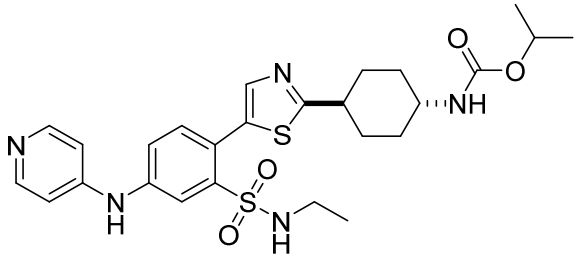

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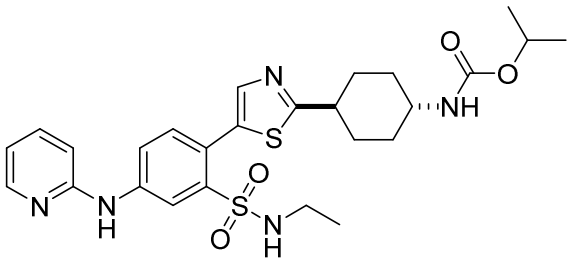

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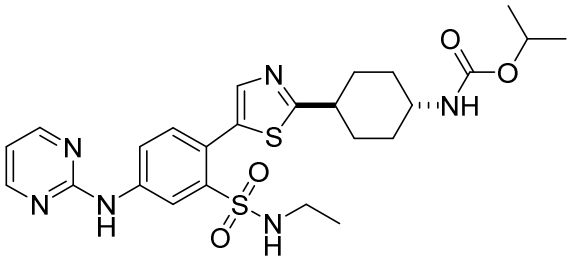

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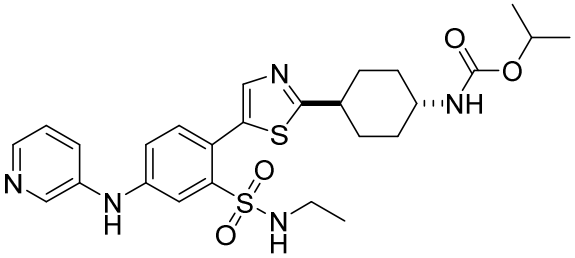

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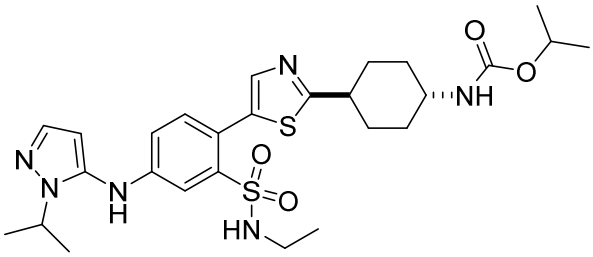

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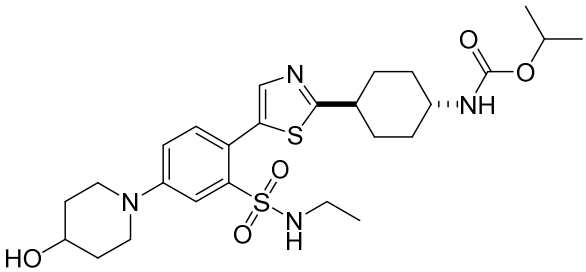

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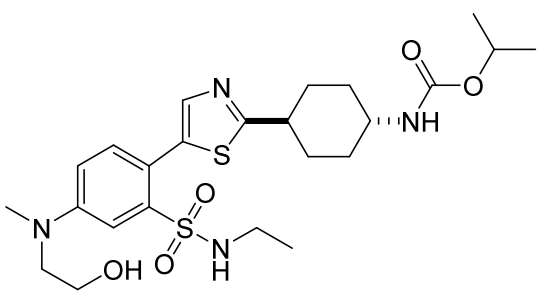

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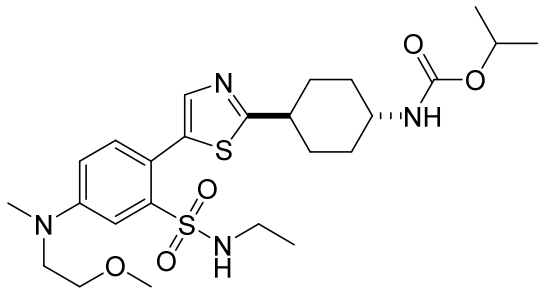

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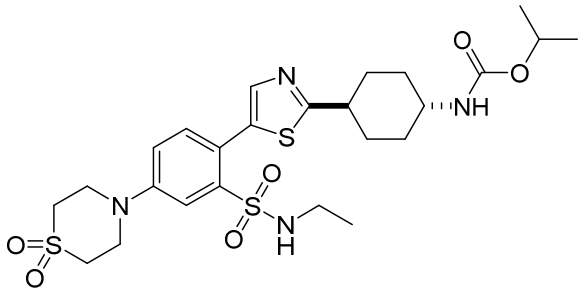

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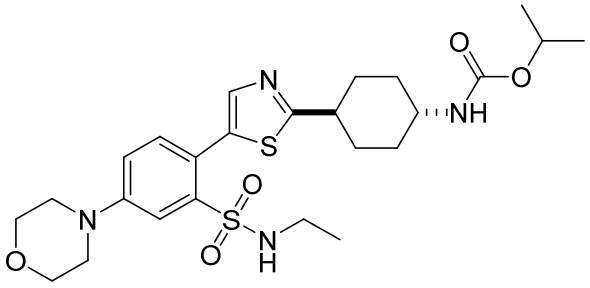

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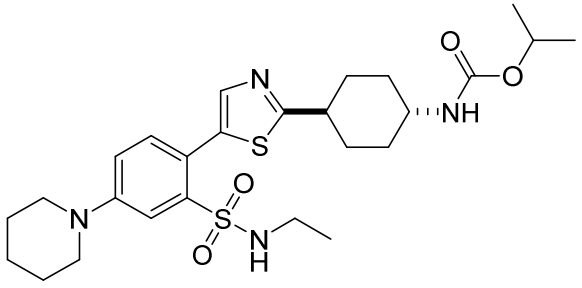
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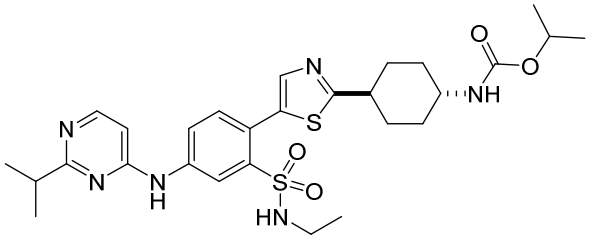
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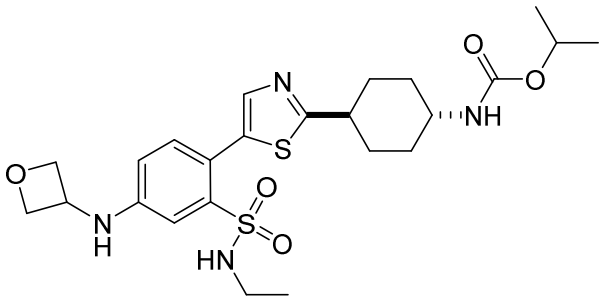
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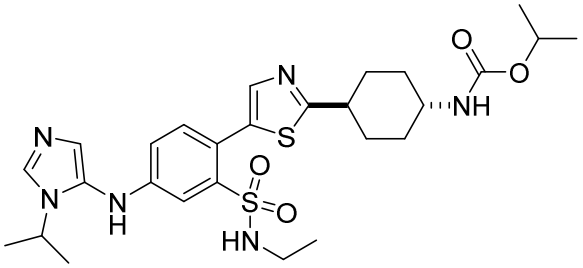
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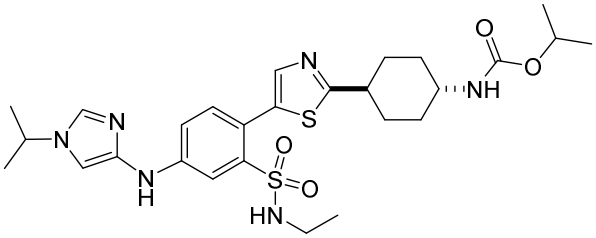
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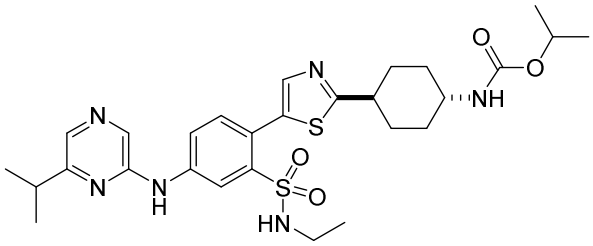
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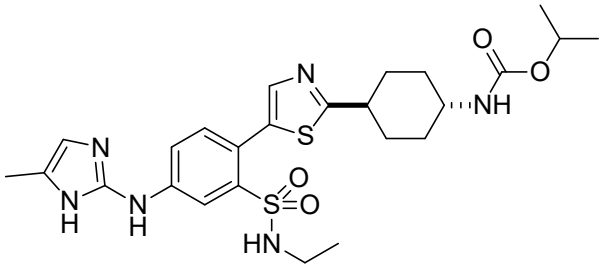
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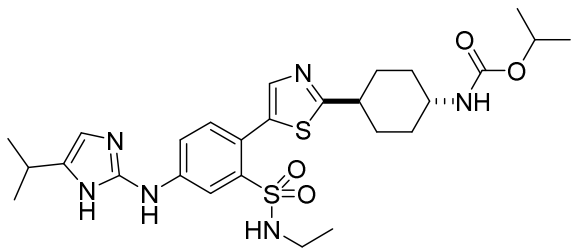
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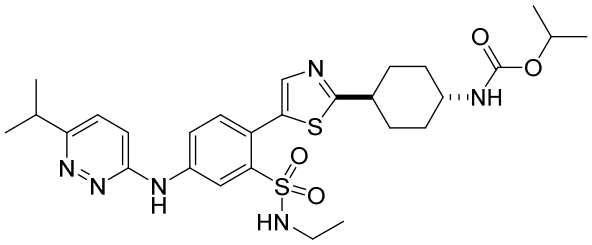
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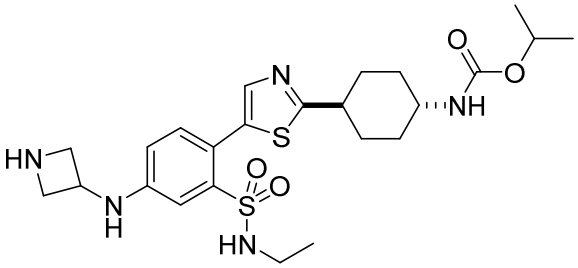
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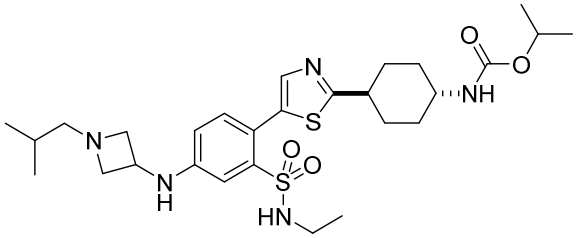
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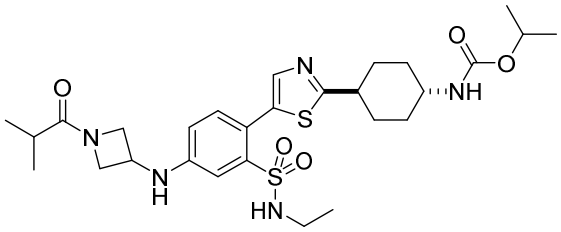
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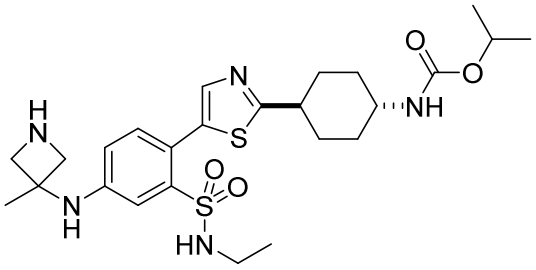
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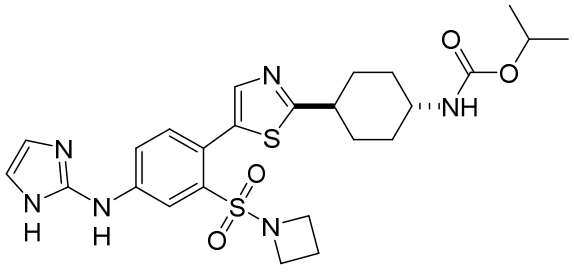
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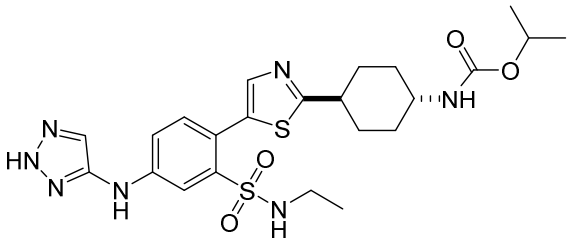
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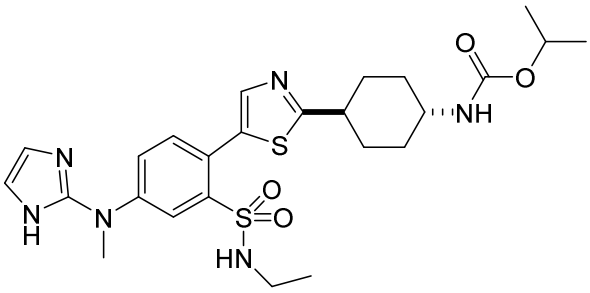
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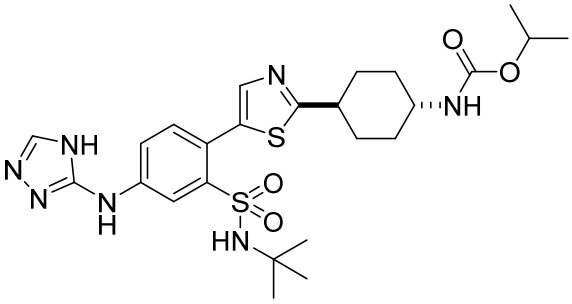
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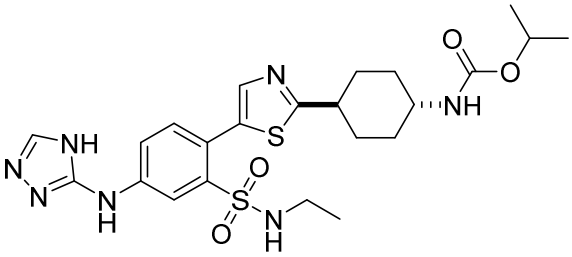
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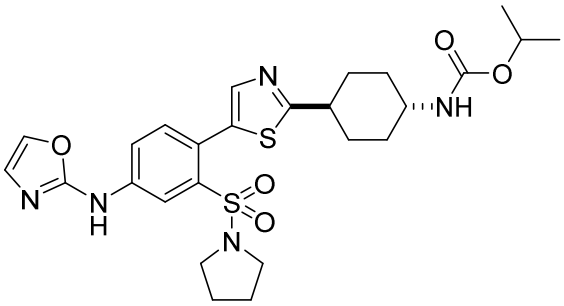
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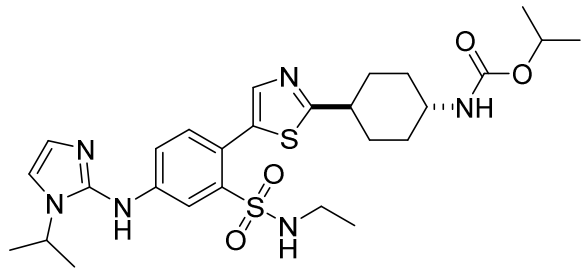
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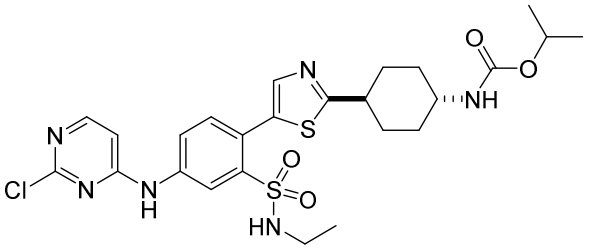


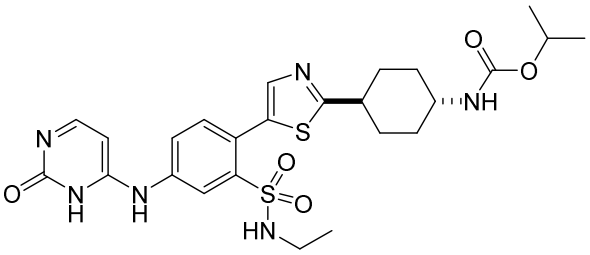
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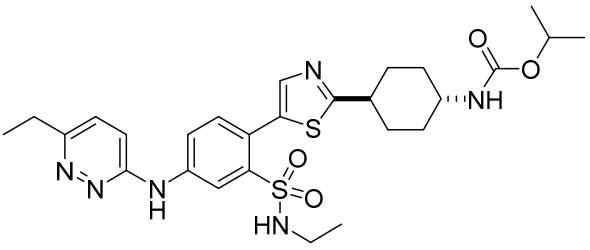


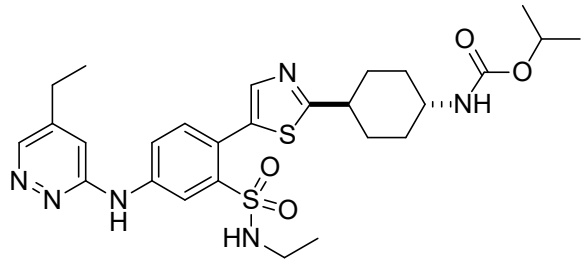
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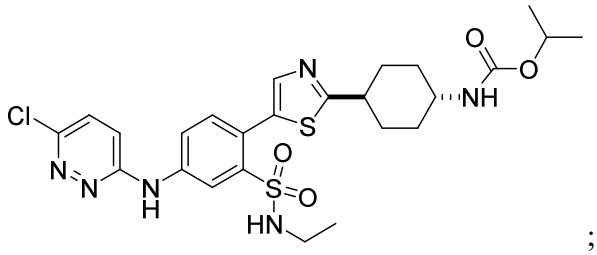

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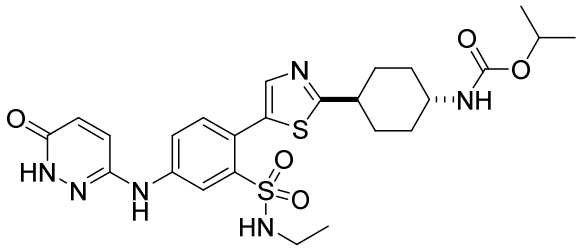

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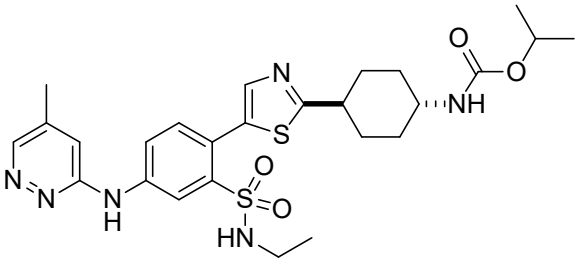

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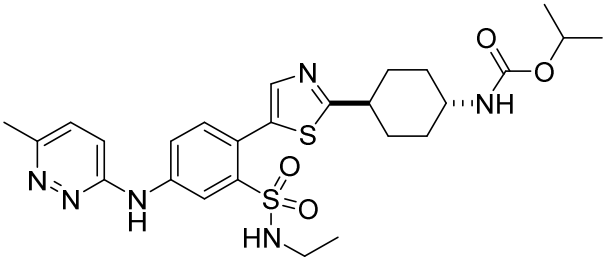

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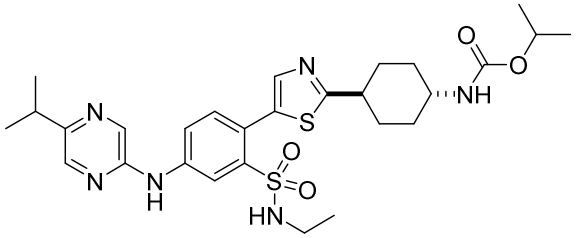

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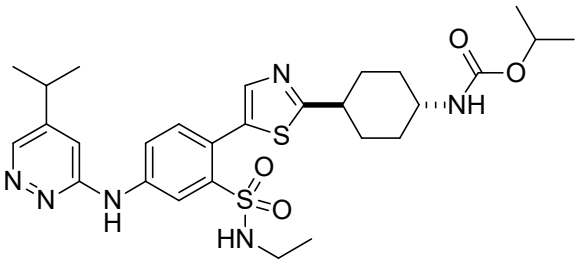

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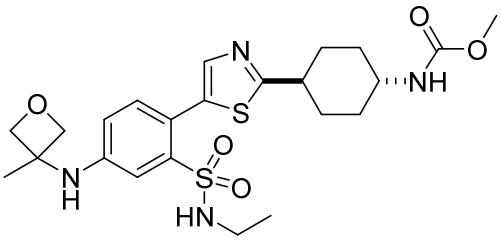

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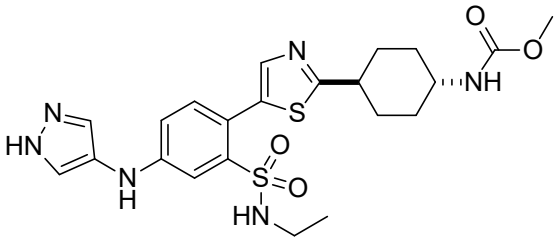

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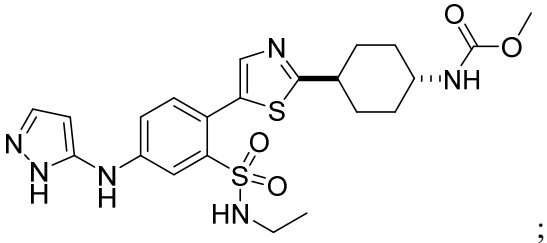

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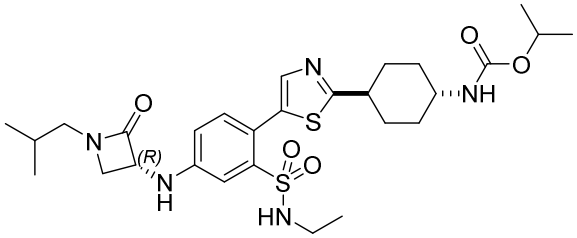

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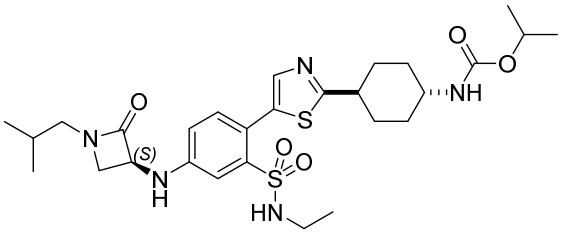

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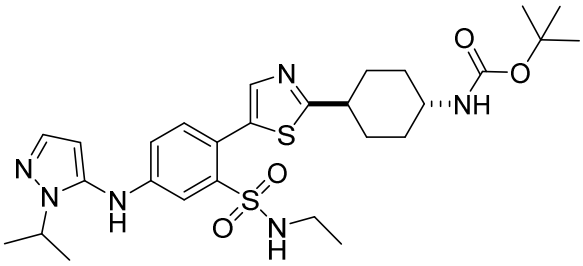

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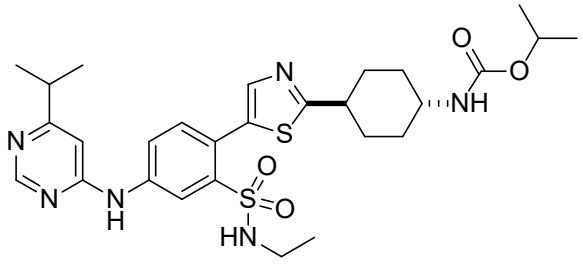

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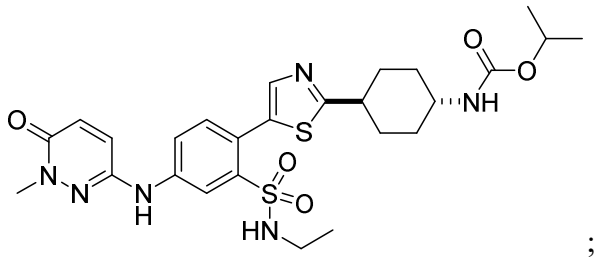

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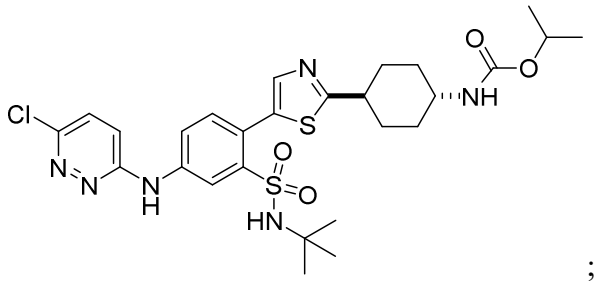

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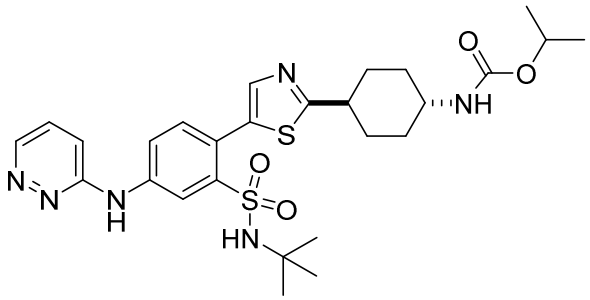


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and



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or a pharmaceutically acceptable salt or solvate thereof.

26. A pharmaceutical composition comprising the compound of any one of claims 1-25 or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier or diluent.

27. Use of the compound of any one of claims 1-25 or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for the treatment of a disease or disorder selected from cancer, an autoimmune disease, an immune deficiency, and a neurodegenerative disease,

wherein treatment is an improvement in at least one symptom of the disease or disorder.