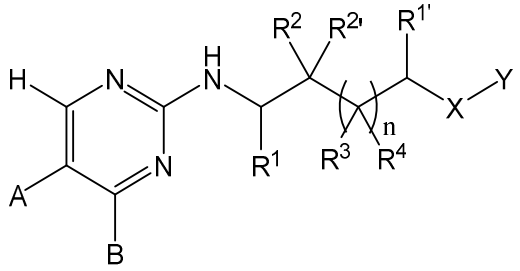
Claims:

1. An inhibitor of PCSK9 that binds to a binding pocket defined by amino acid residues Val589 and Ser636 of human PCSK9 for use in inhibiting PCSK9, wherein the inhibitor is a compound of formula (I):



(I)

wherein:

A is selected from halo, hydroxy, alkyl, thioalkyl, alkenyl, alkoxy, acyloxy, cyano, cycloalkyl, -C(O)OR^6, and -C(O)NR^{6}R^7;

B is selected from H, alkyl, and halo, or

A and B are taken together with the carbon atoms to which they are attached to form a 5- or 6-membered heteroaryl;

X is NR^5;

n is 0;

R^1 and R$^{1'}$ are each independently selected from H and alkyl; or R^1 and R$^{1'}$, together with the atoms to which they are attached, form a 4-8 membered cycloalkyl or cycloalkenyl ring;

R^2 is selected from H, halo, alkyl, alkoxy, amidoalkyl, aminoalkyl, hydroxyalkyl, alkylamino, cyano, and hydroxy; or

R^1 and R^2, together with the atoms to which they are attached, form a 3-8 membered cycloalkyl or heterocyclyl ring; or

R$^{1'}$ and R^2, together with the atoms to which they are attached, form a 3-8 membered cycloalkyl or heterocyclyl ring;

$R^{2'}$ is selected from H, halo, alkyl, alkoxy, amidoalkyl, aminoalkyl, and cyano, or

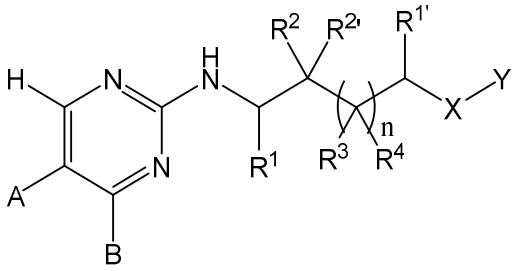
R^2 and $R^{2'}$, taken together with the carbon atom to which they are attached, form a 3- to 8-membered cycloalkyl or heterocyclyl ring;

R^5 is H;

each R^6 and R^7 is independently H or alkyl; and

Y is selected from aryl and heteroaryl.

2. Use of an inhibitor of PCSK9 that binds to a binding pocket defined by amino acid residues Val589 and Ser636 of human PCSK9 in the manufacture of a medicament for the treatment of cardiovascular disease, wherein the inhibitor is a compound of formula (I):



(I)

wherein:

A is selected from halo, hydroxy, alkyl, thioalkyl, alkenyl, alkoxy, acyloxy, cyano, cycloalkyl, $-C(O)OR^6$, and $-C(O)NR^6R^7$;

B is selected from H, alkyl, and halo, or

A and B are taken together with the carbon atoms to which they are attached to form a 5- or 6-membered heteroaryl;

X is NR^5;

n is 0;

R^1 and $R^{1'}$ are each independently selected from H and alkyl; or R^1 and $R^{1'}$, together with the atoms to which they are attached, form a 4-8 membered cycloalkyl or cycloalkenyl ring;

R^2 is selected from H, halo, alkyl, alkoxy, amidoalkyl, aminoalkyl, hydroxyalkyl, alkylamino, cyano, and hydroxy; or

R^1 and R^2, together with the atoms to which they are attached, form a 3-8 membered cycloalkyl or heterocyclyl ring; or

$R^{1'}$ and R^2, together with the atoms to which they are attached, form a 3-8 membered cycloalkyl or heterocyclyl ring;

$R^{2'}$ is selected from H, halo, alkyl, alkoxy, amidoalkyl, aminoalkyl, and cyano, or

R^2 and $R^{2'}$, taken together with the carbon atom to which they are attached, form a 3- to 8-membered cycloalkyl or heterocyclyl ring;

R^5 is H;

each R^6 and R^7 is independently H or alkyl; and

Y is selected from aryl and heteroaryl.

3. The inhibitor for use of claim 1 or the use of claim 2, wherein A is selected from hydroxy, thioalkyl, alkyl, alkoxy, acyloxy, cyano, cycloalkyl, $-C(O)OR^6$, and $-C(O)NR^6R^7$.

4. The inhibitor for use or the use of claim 3, wherein A is alkoxy.

5. The inhibitor for use or the use of claim 3, wherein A is cycloalkyl.

6. The inhibitor for use of any one of claims 1 or 3 to 5, or the use of any one of claims 2 to 5, wherein B is H.

7. The inhibitor for use of any one of claims 1 or 3 to 6, or the use of any one of claims 2 to 6, wherein Y is heteroaryl.

8. The inhibitor for use of any one of claims 1 or 3 to 7 or the use of any one of claims 2 to 7, wherein R^2 is selected from H, halo, alkyl, alkoxy, amidoalkyl, aminoalkyl, alkylamino, cyano, and hydroxy.

9. The inhibitor for use of any one of claims 1 or 3 to 8 or the use of any one of claims 2 to 8, wherein $R^{2'}$ is H.

10. The inhibitor for use of any one of claims 1 or 3 to 9 or the use of any one of claims 2 to 9, wherein Y is monocyclic heteroaryl.

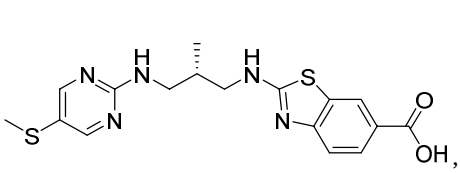
11. The inhibitor for use or the use of claim 10, wherein Y is selected from pyridyl, pyridinyl, pyrazinyl, pyrimidinyl, and thiazolyl.

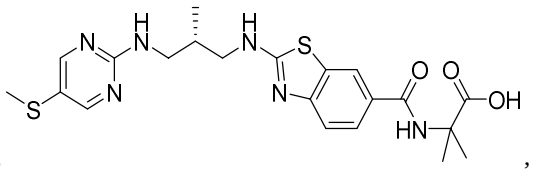
12. The inhibitor for use or the use of claim 10, wherein Y is selected from oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, and triazolyl.

13. The inhibitor for use or the use of any one of claims 10 to 12, wherein the monocyclic heteroaryl is unsubstituted or substituted with one or more substituents selected from alkyl, thioalkyl, alkoxy, alkoxycarbonyl, amido, carboxy, cyano, halo, aryl, heteroaryl, heterocyclyl, nitro, sulfonamido, and thioalkyl.

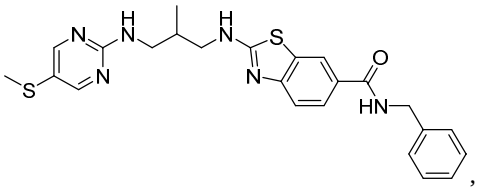
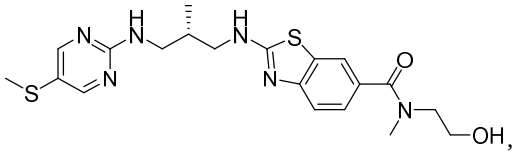
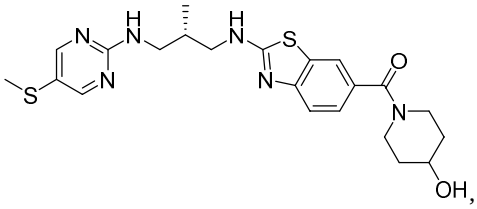
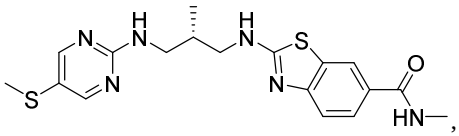
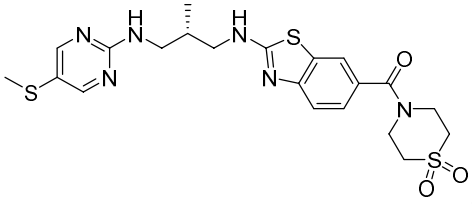
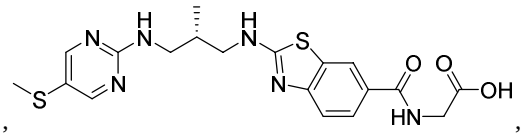
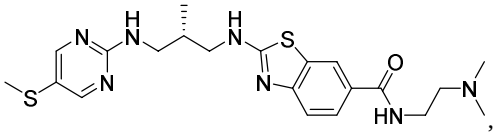
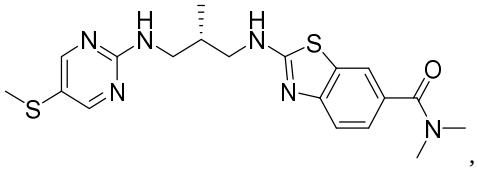
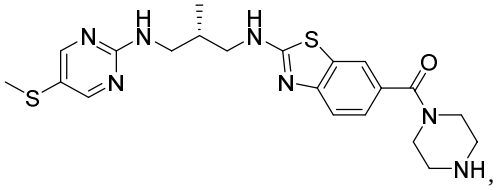
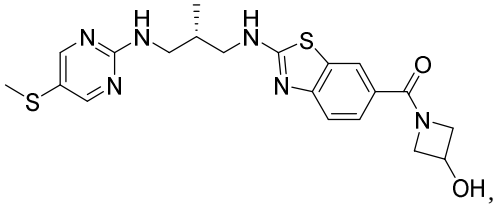
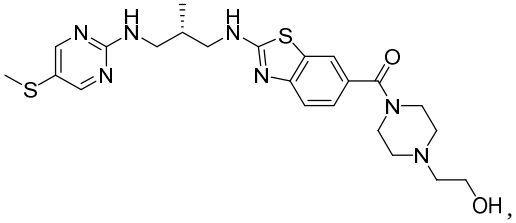
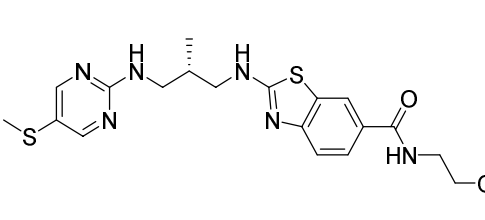
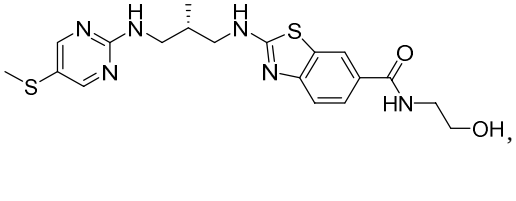
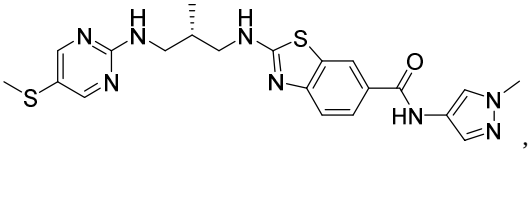
14. The inhibitor for use or the use of claim 13, wherein the monocyclic heteroaryl is substituted with a 6-membered aryl, heteroaryl or heterocyclyl selected from phenyl, pyridinyl, 2-hydroxypyridinyl, piperidinonyl, 2-hydroxy-1-methylpyridinyl, triazolyl, imidazolidinonyl, pyrimidonyl, 2-hydroxyisoquinolinyl, 3-hydroxypyridazinyl, pyrrolidinonyl, pyrazolyl, and morpholinonyl.

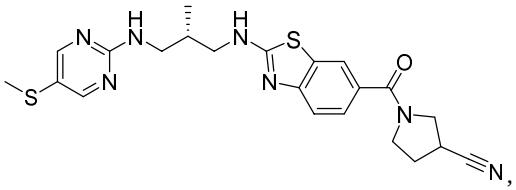
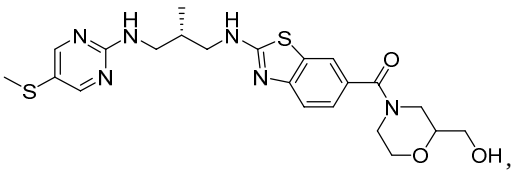
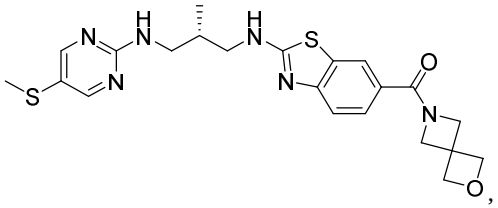
15. The inhibitor for use of claim 1 or the use of claim 2, wherein the inhibitor is selected from

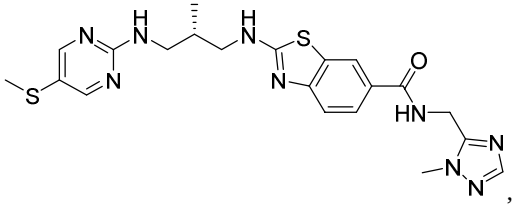
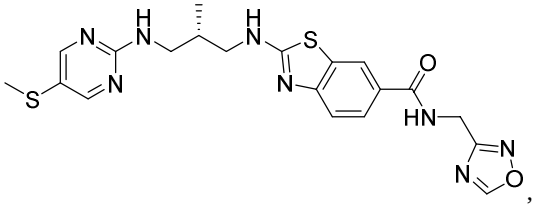
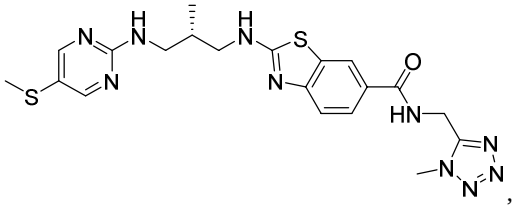
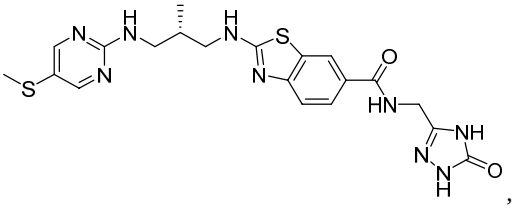
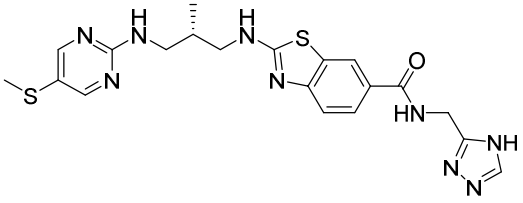
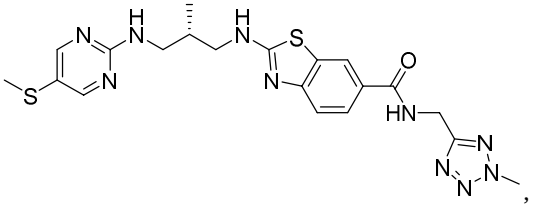
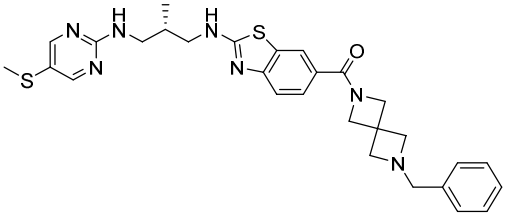
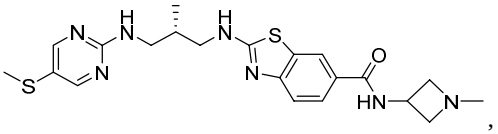
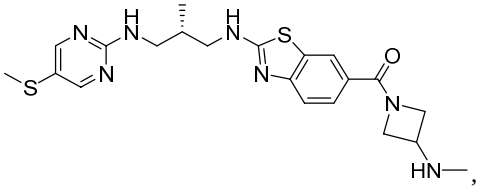
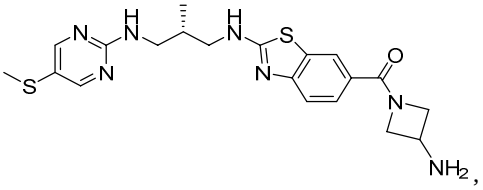
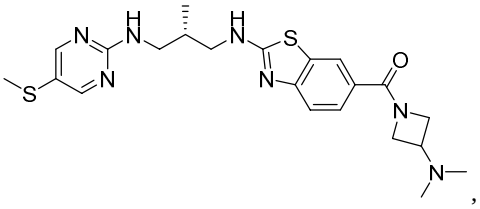
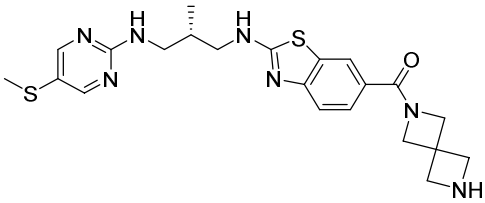


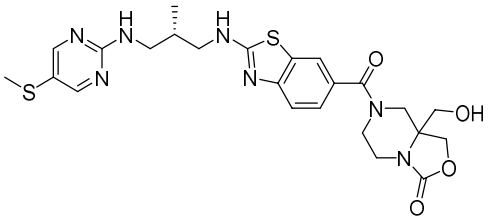
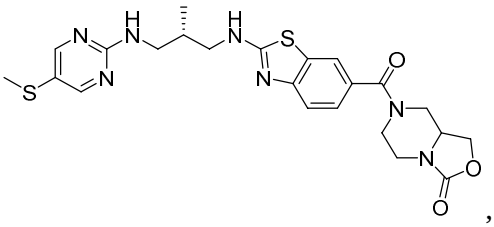
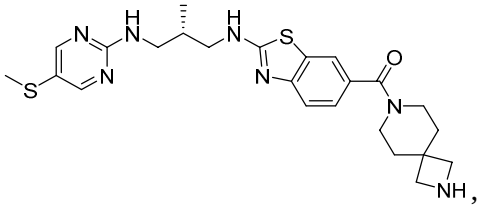
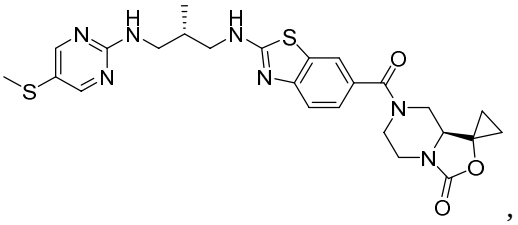
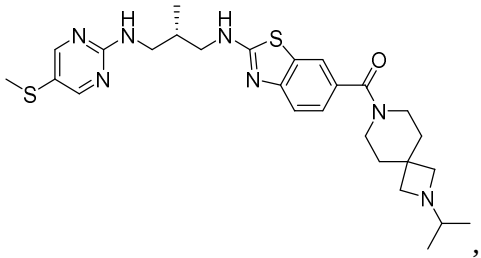
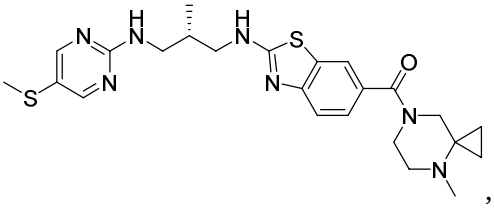
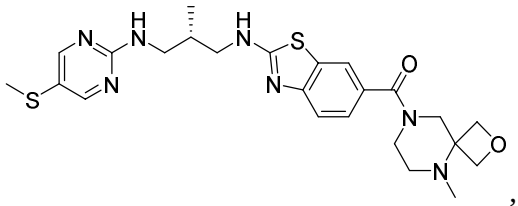
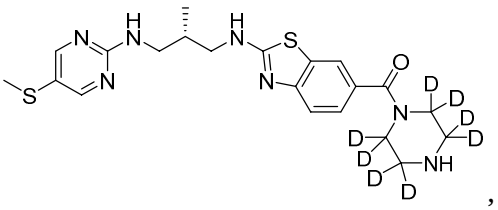
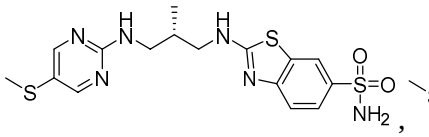
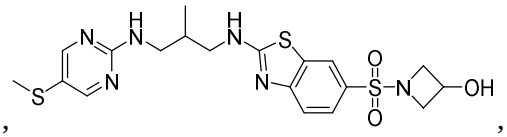
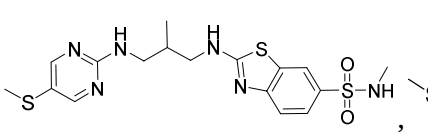
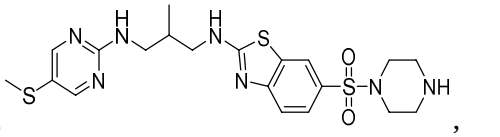
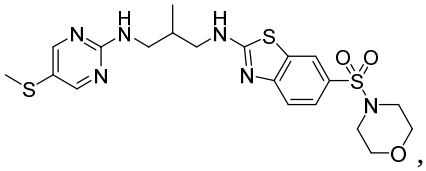
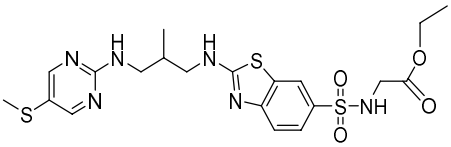
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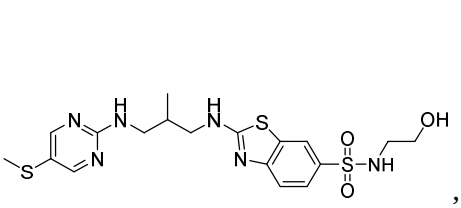
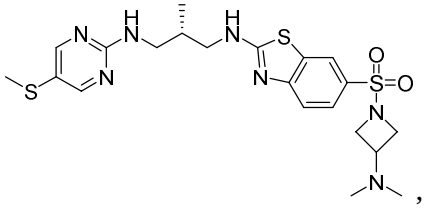
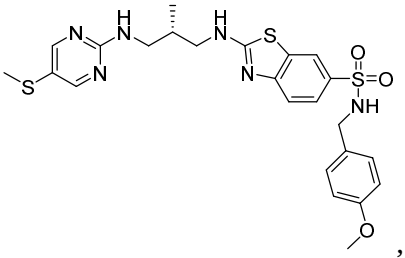
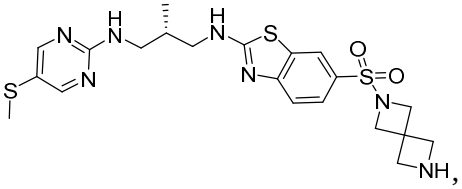
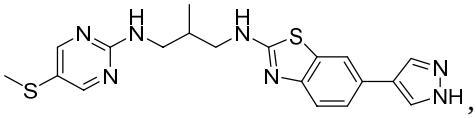
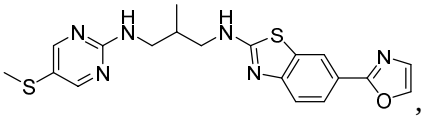
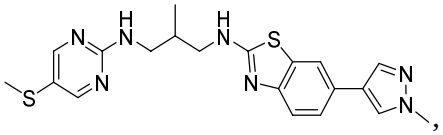
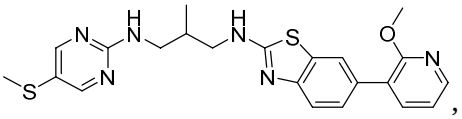
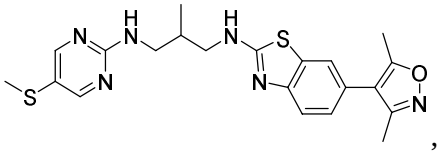
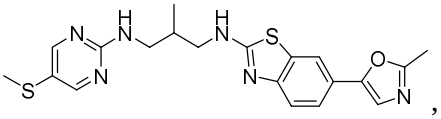
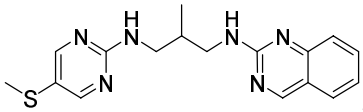
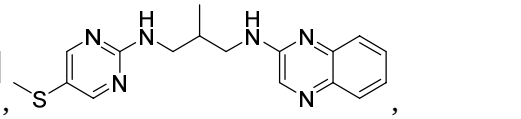
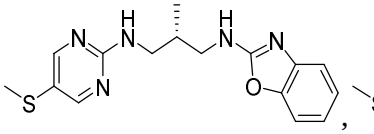
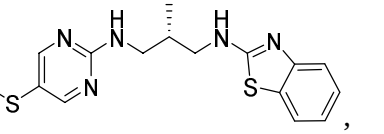
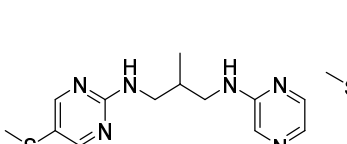
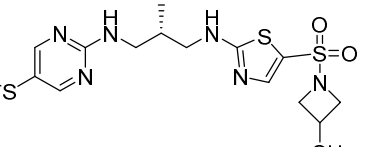
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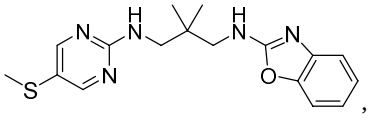
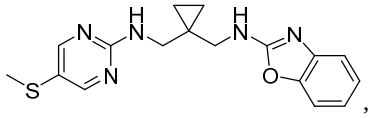
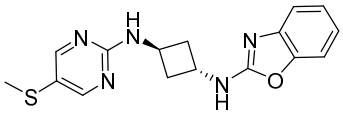
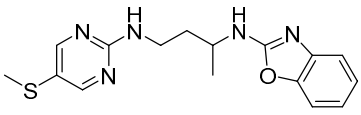
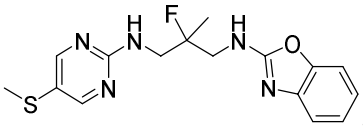
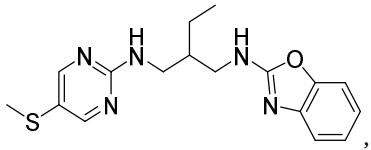
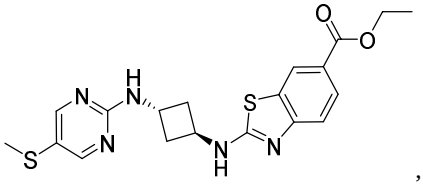
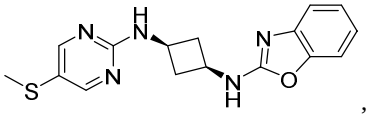
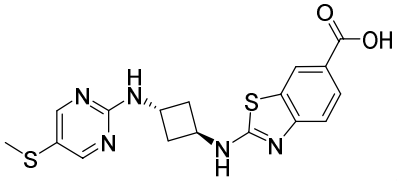
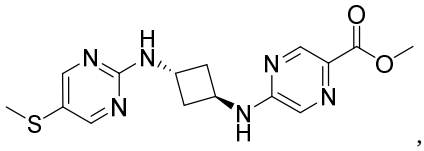
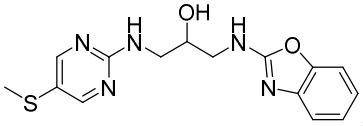
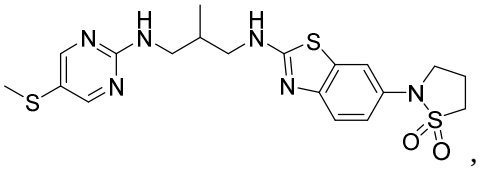
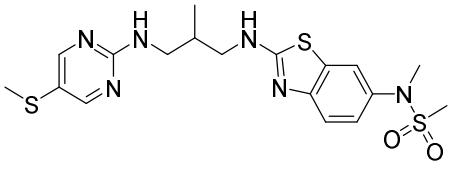
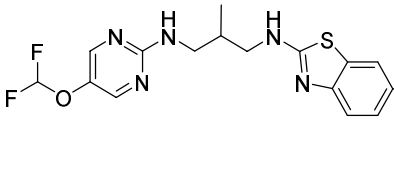
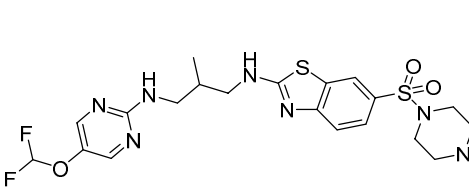
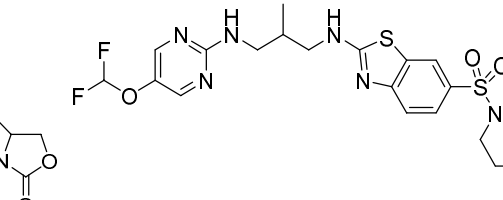
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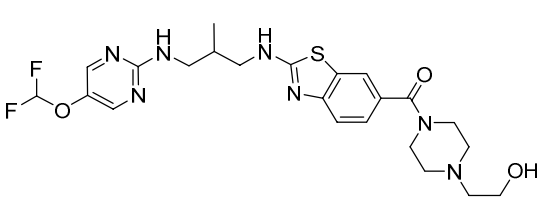
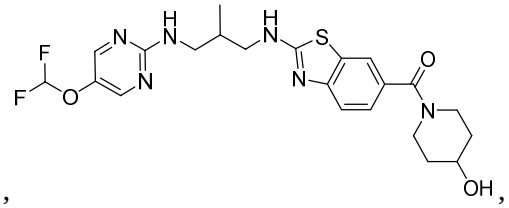
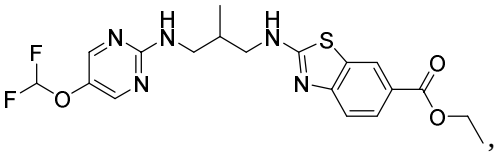
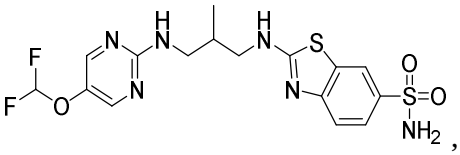
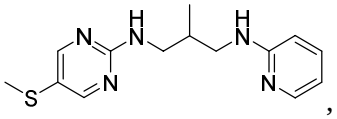
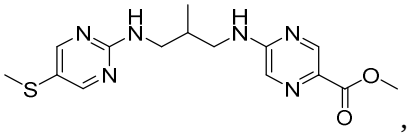
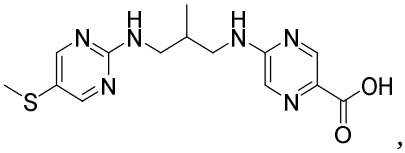
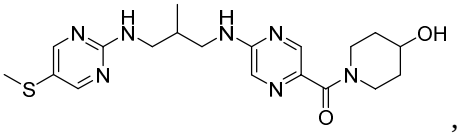
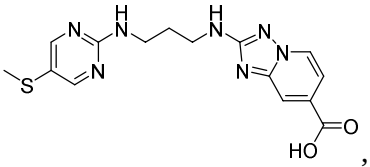
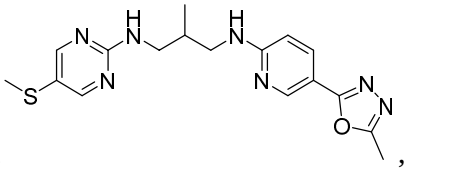
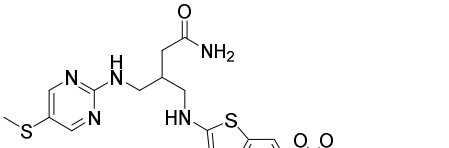
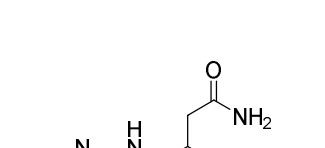

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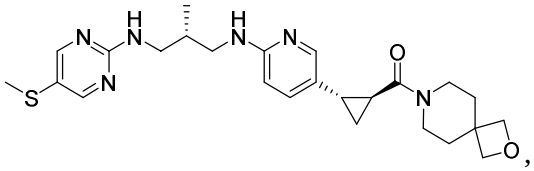
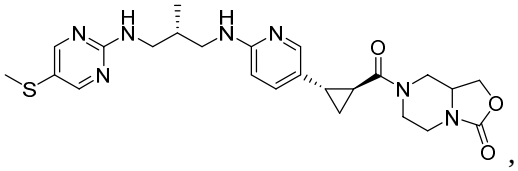
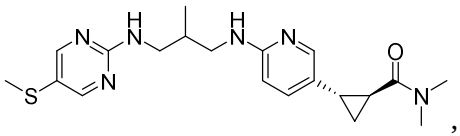
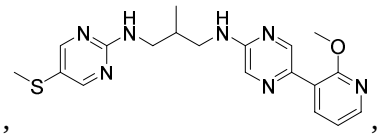
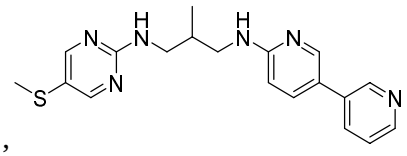
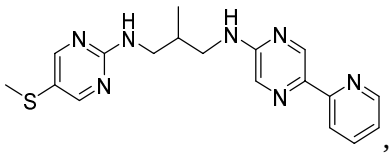
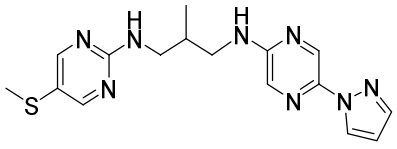
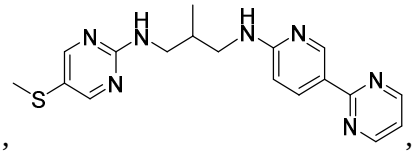
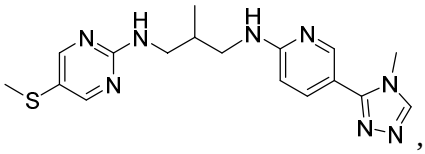
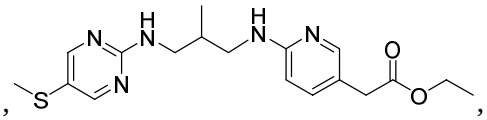
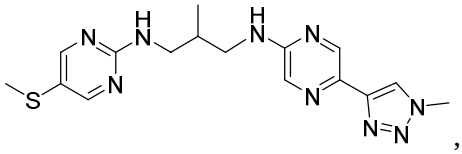
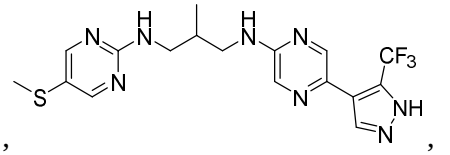
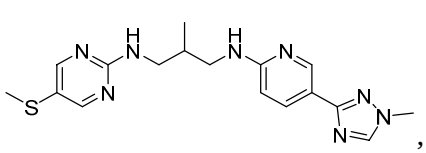
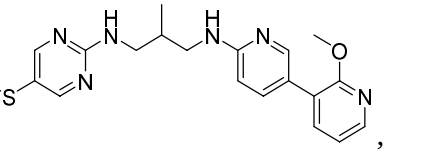
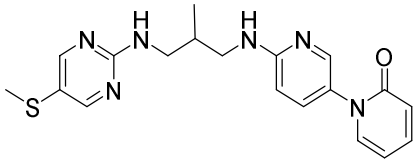
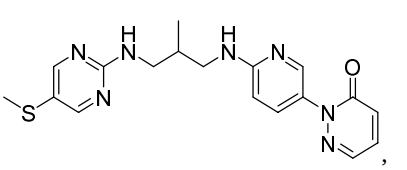
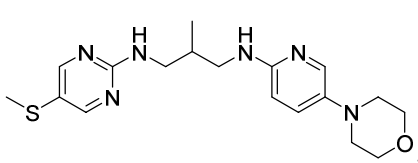
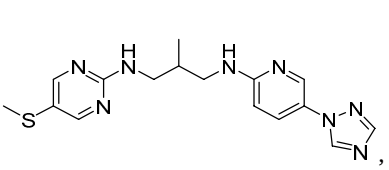
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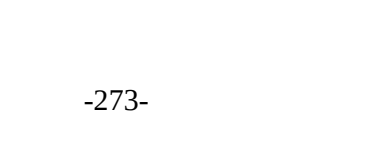
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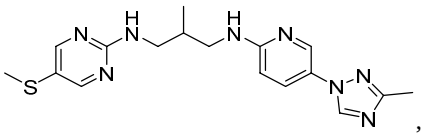
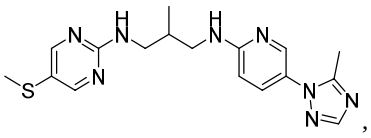
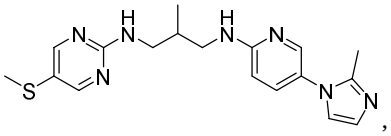
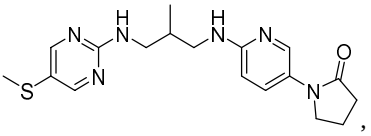
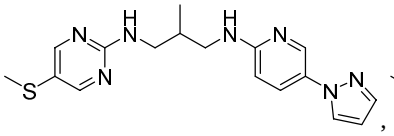
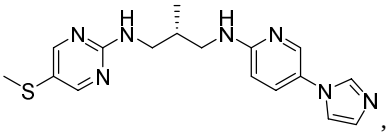
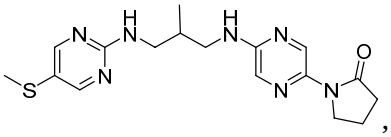
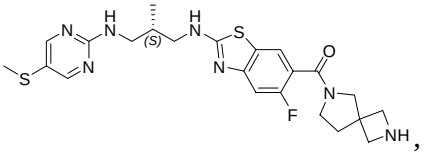
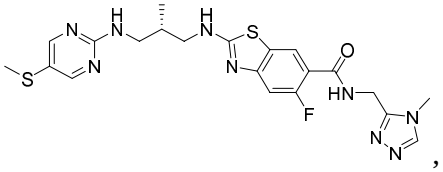
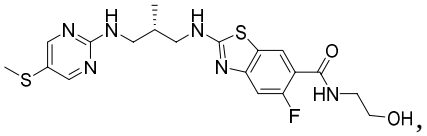
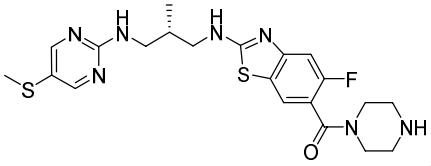
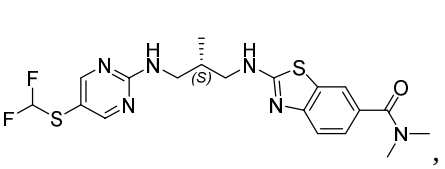
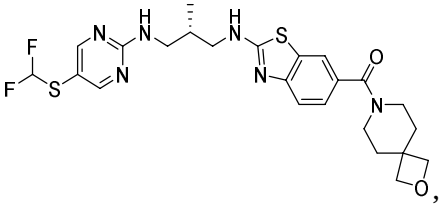
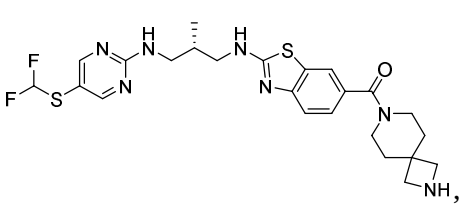
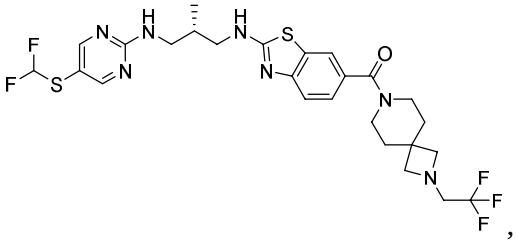
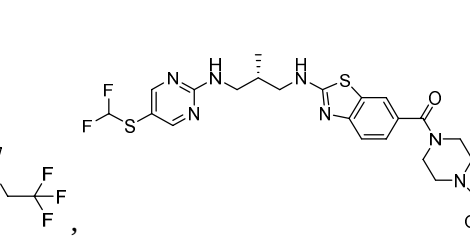

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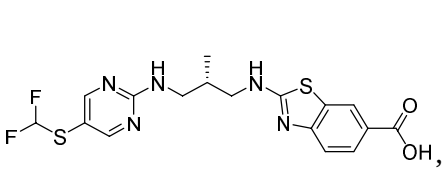
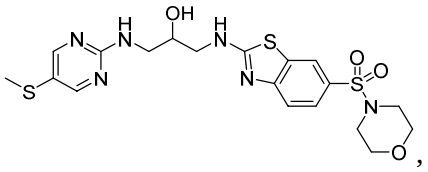
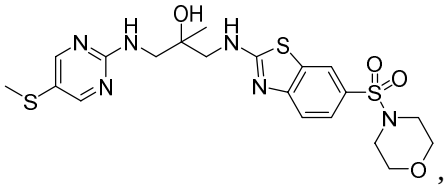
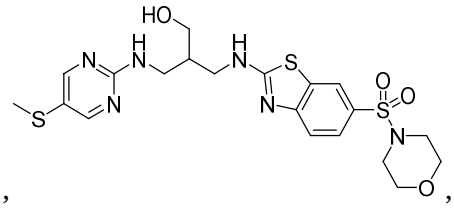
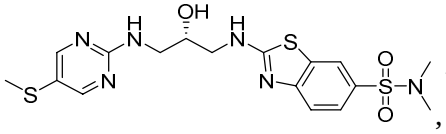
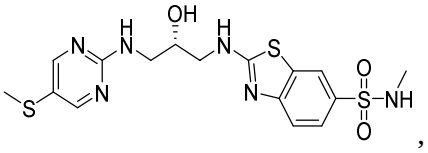
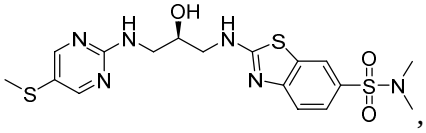
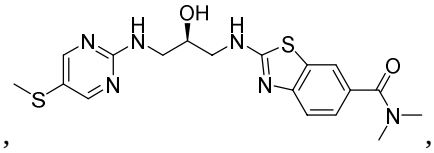
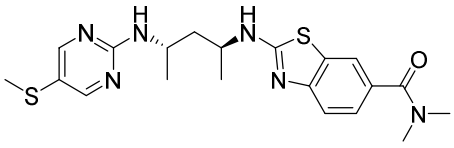
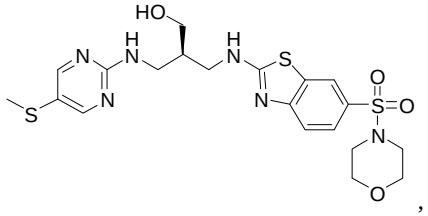
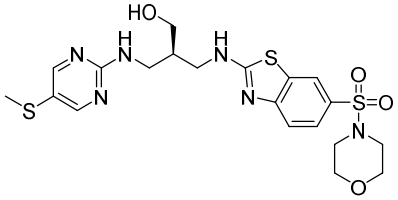
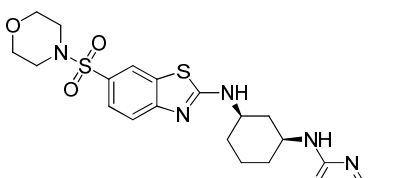
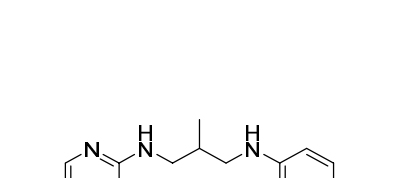


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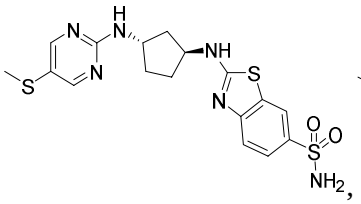
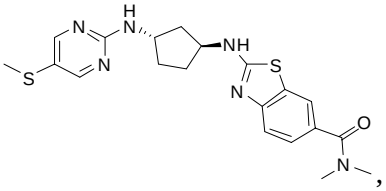
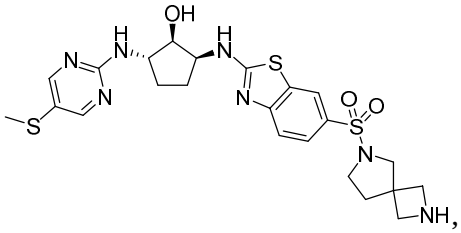
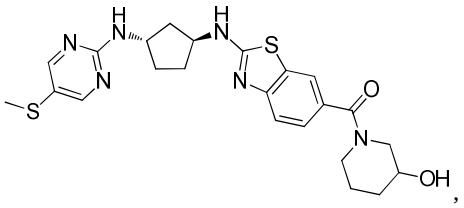
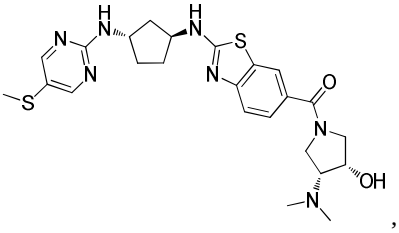
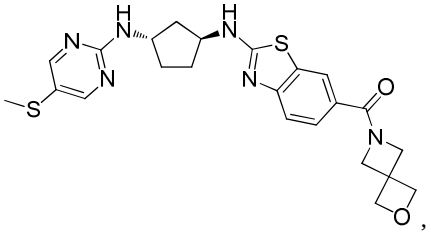
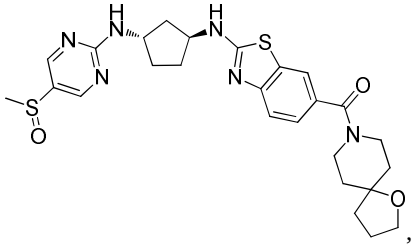
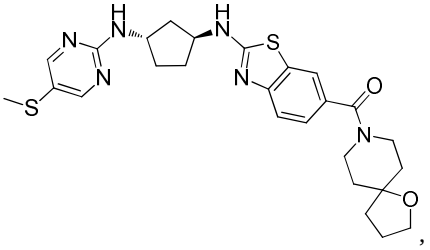
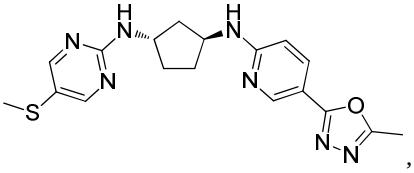
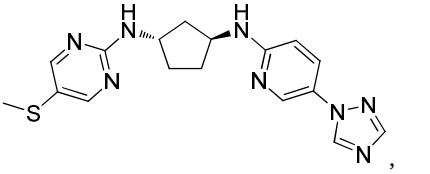
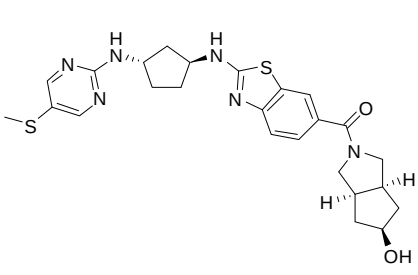
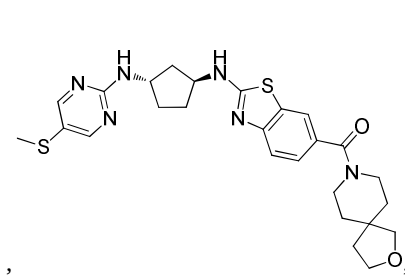
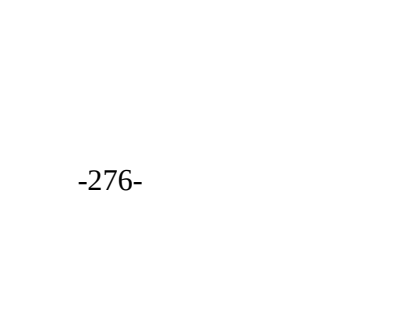
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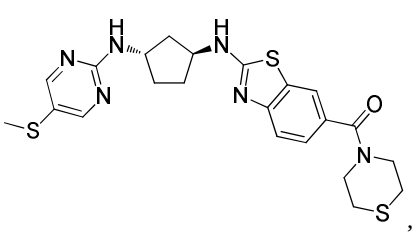
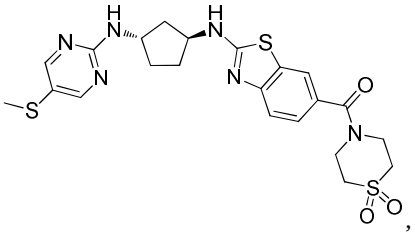
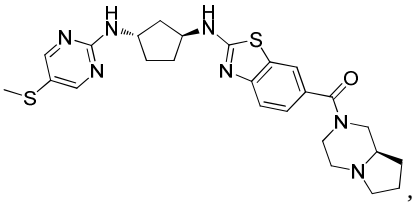
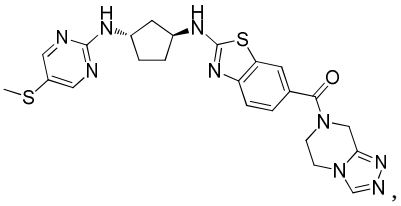
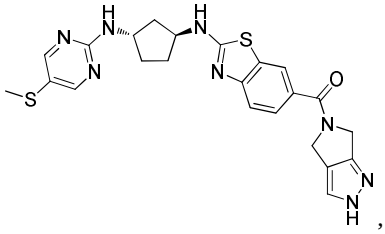
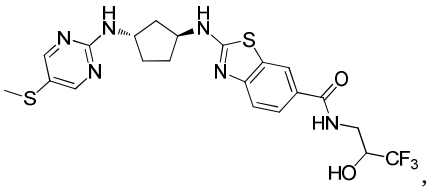
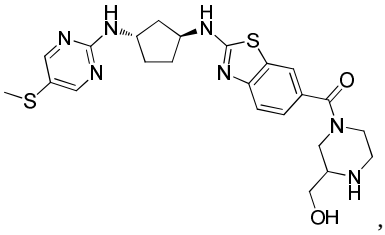
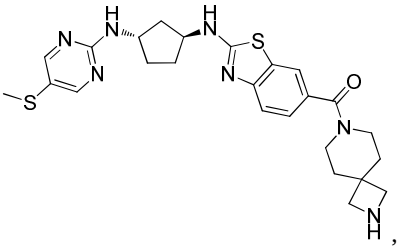
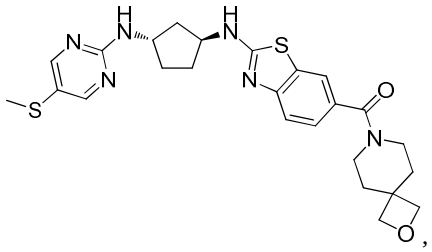
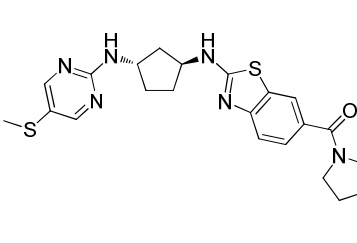
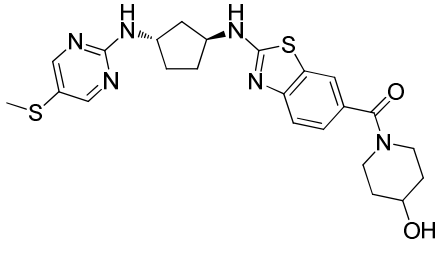
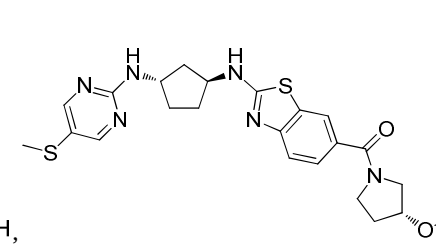
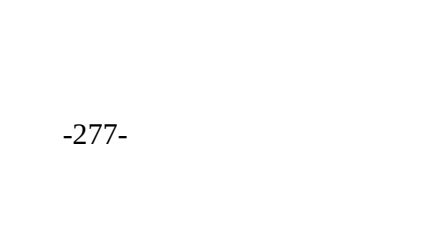
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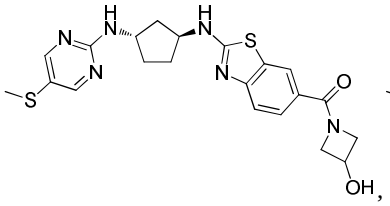
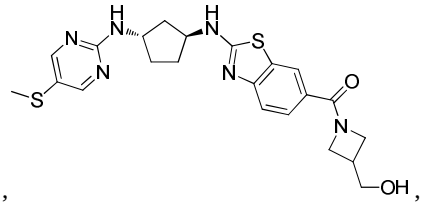
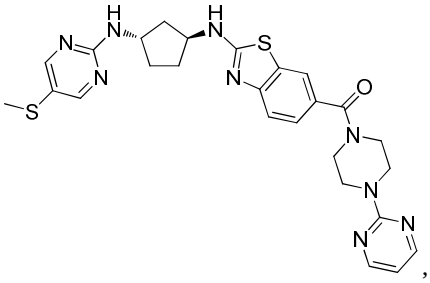
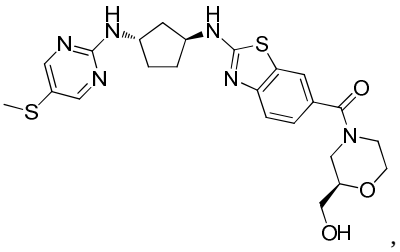
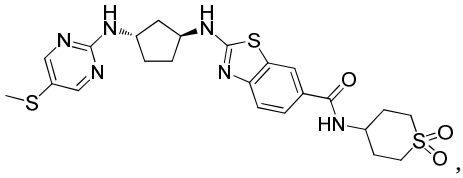
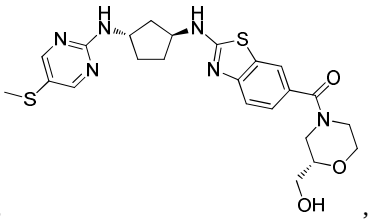
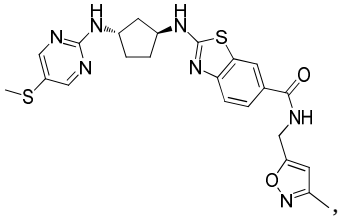
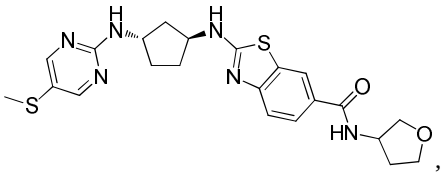
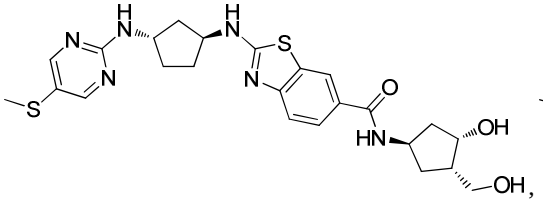
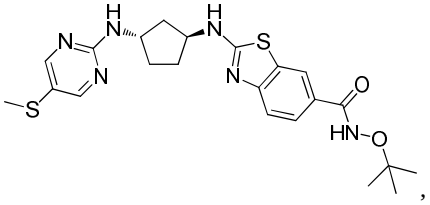
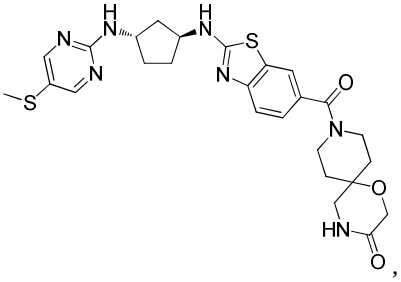
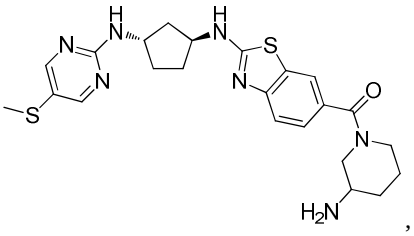
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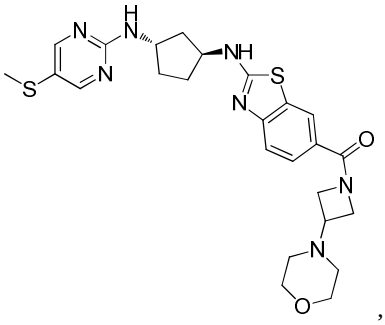
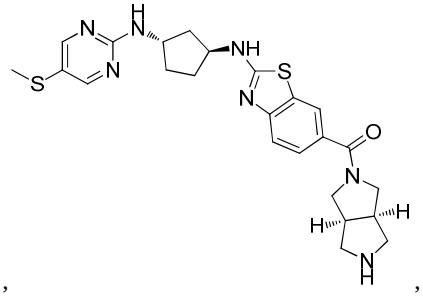
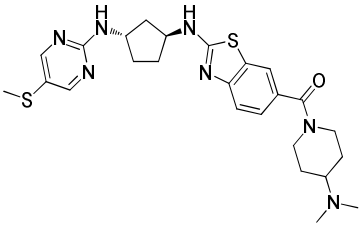
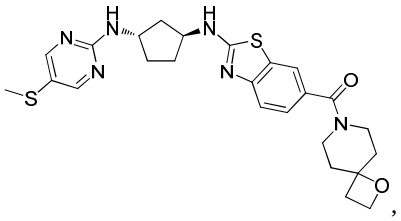
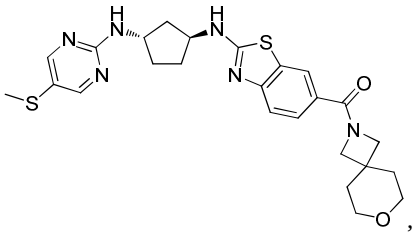
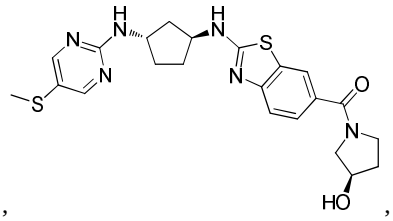
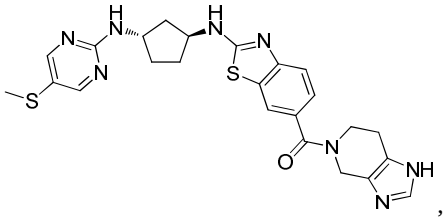
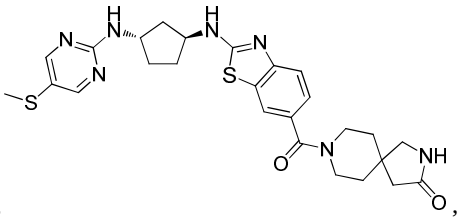
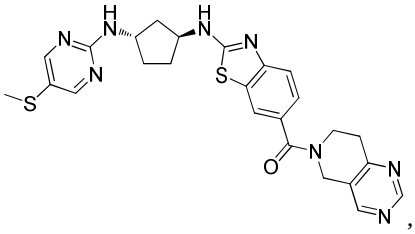
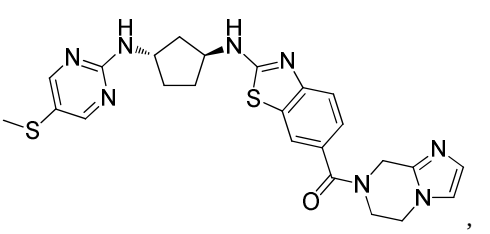

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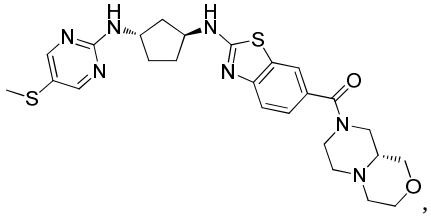
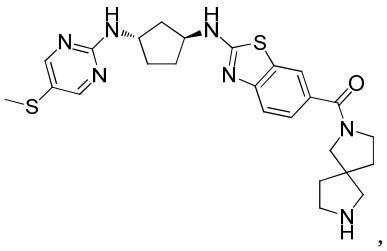
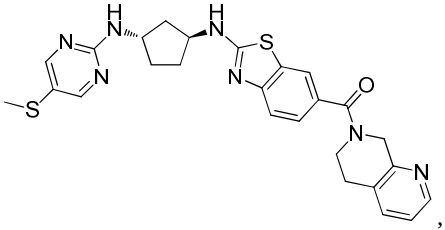
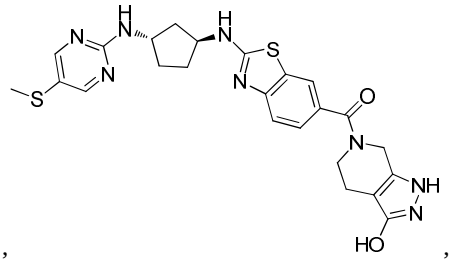
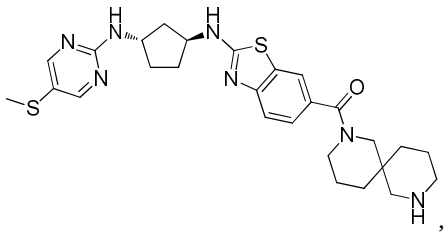
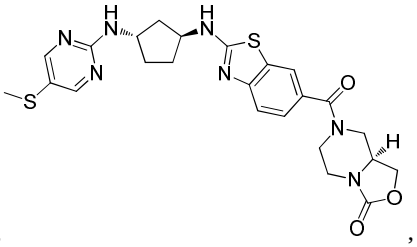
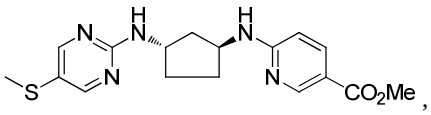
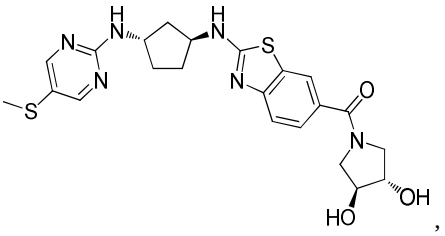
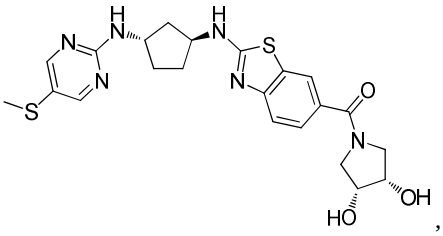
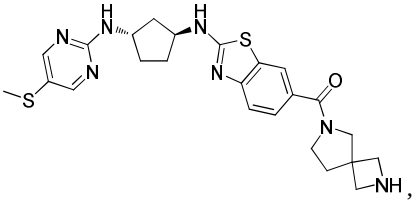
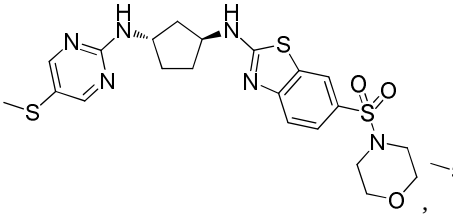
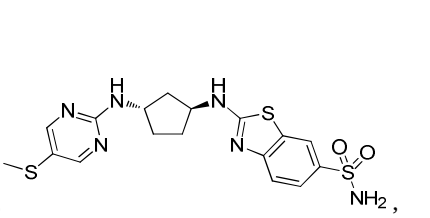
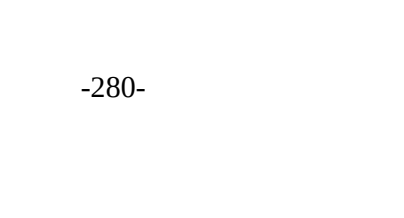
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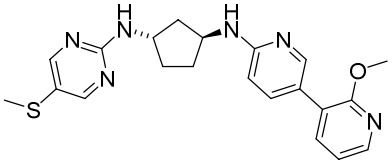
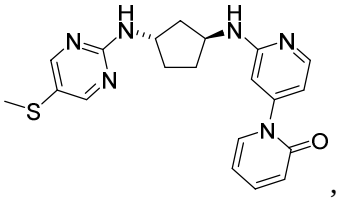
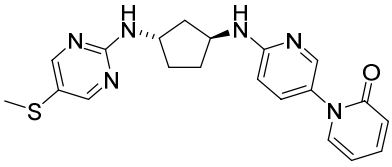
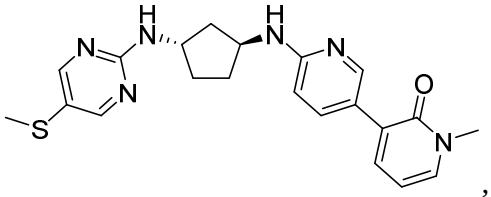
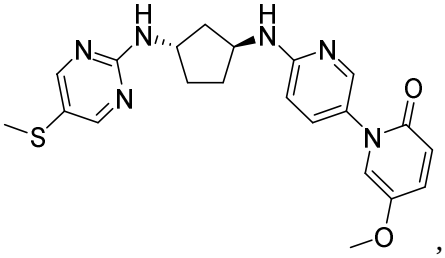
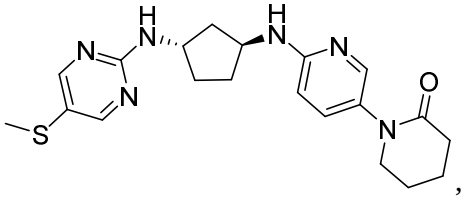
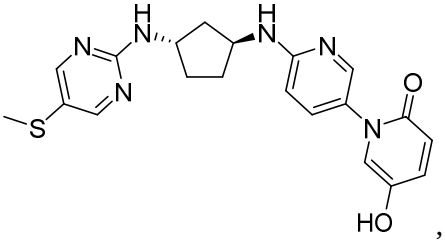
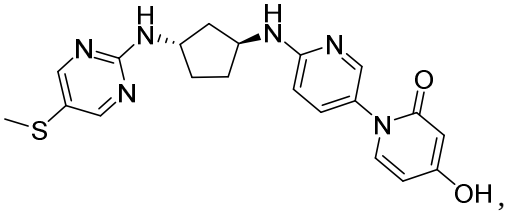
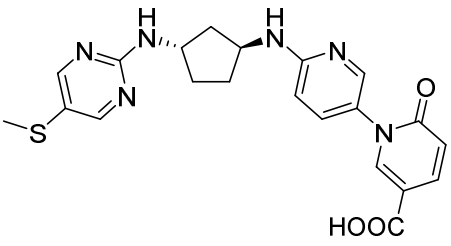
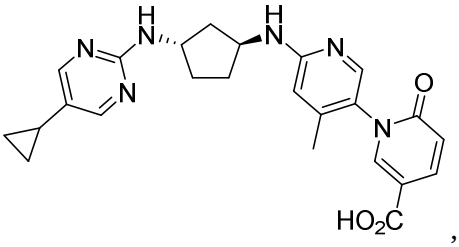
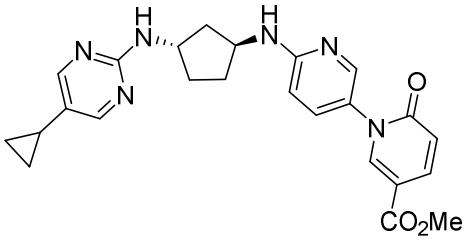
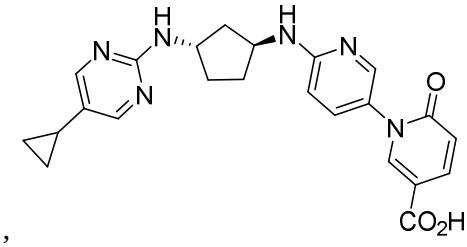

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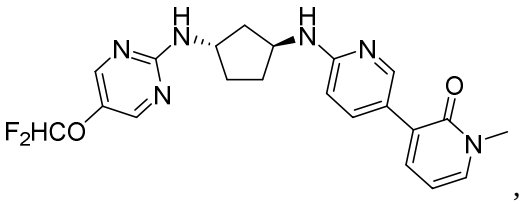
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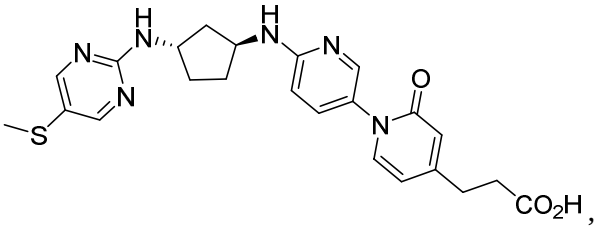
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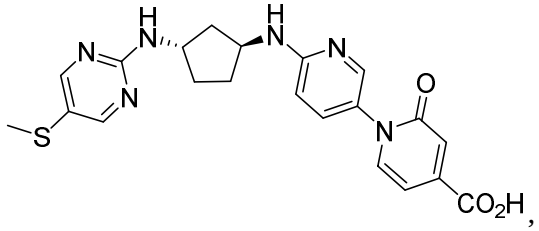

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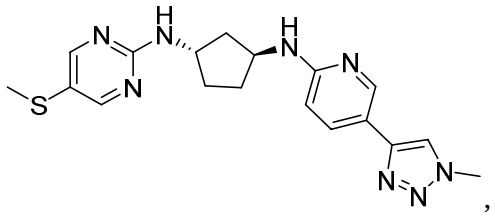
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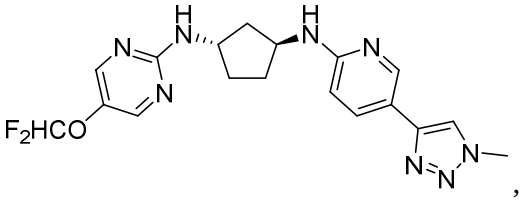
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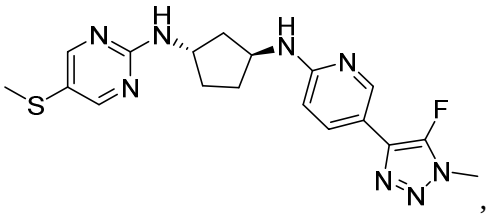

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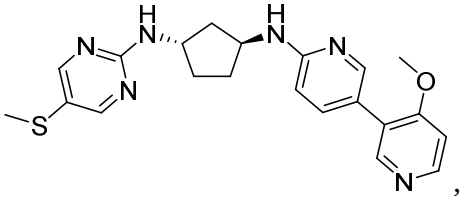

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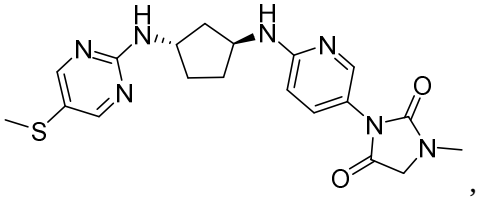

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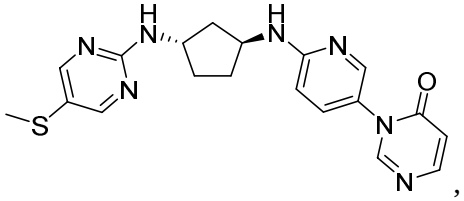

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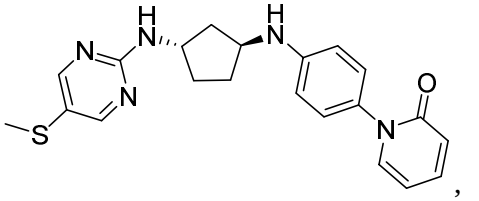

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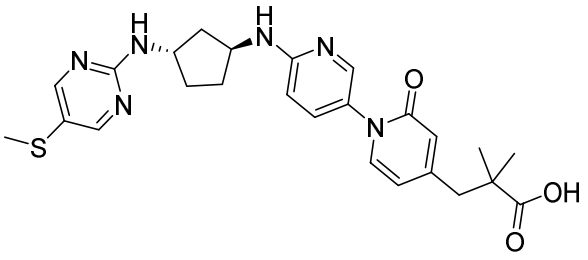

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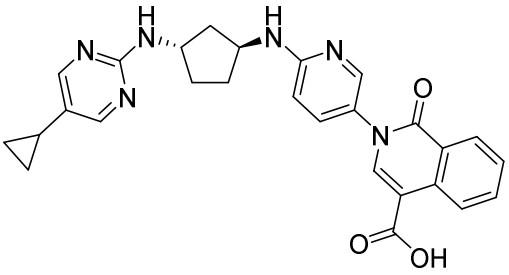

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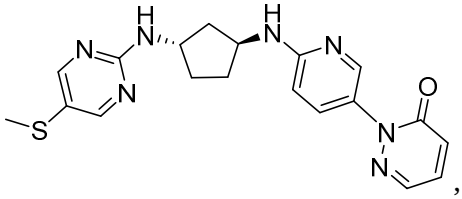

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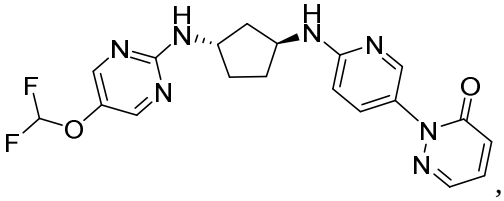
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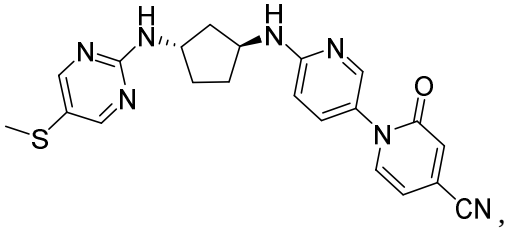
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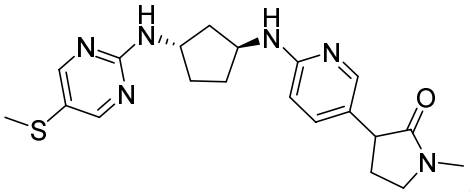
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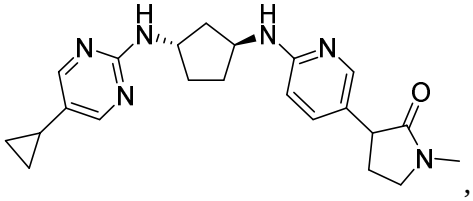
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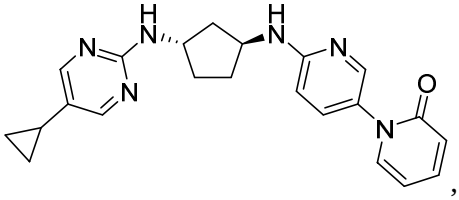
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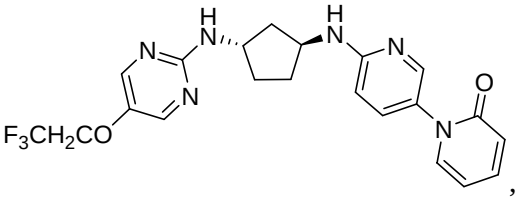
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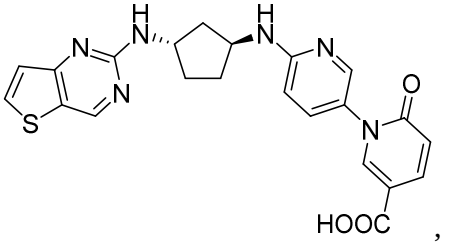
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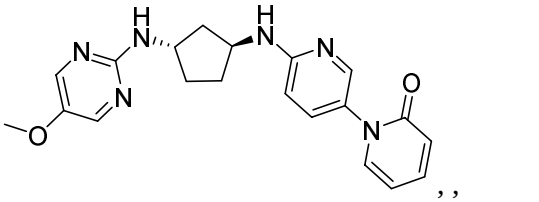
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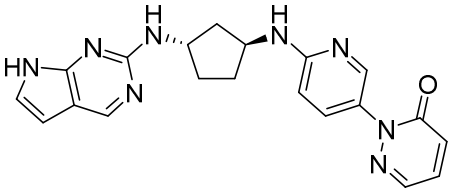
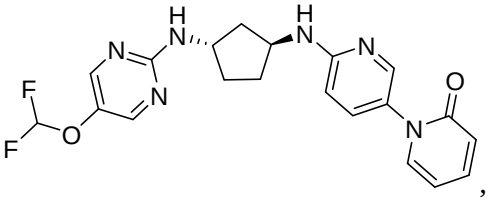
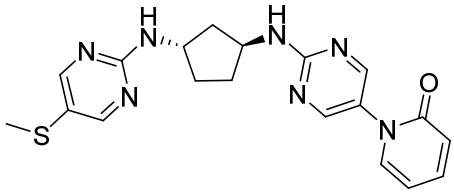
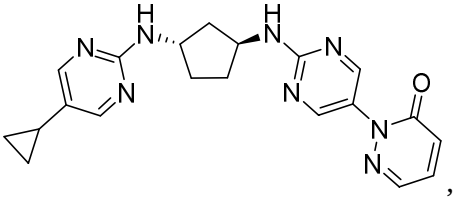
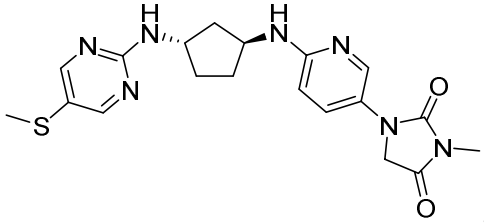
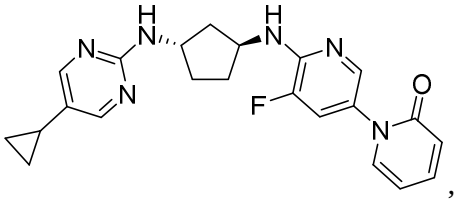
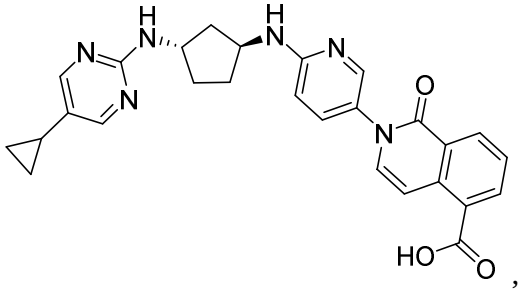
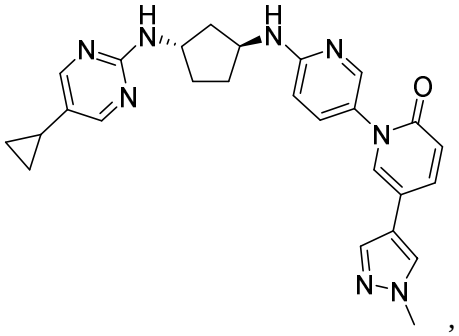
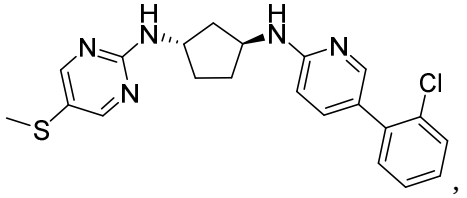
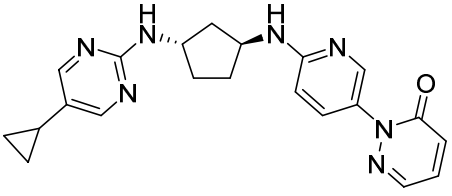
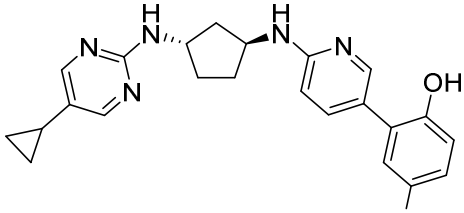
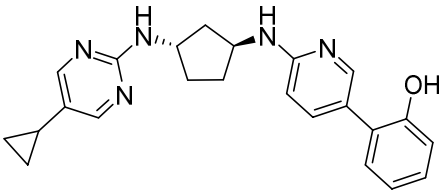
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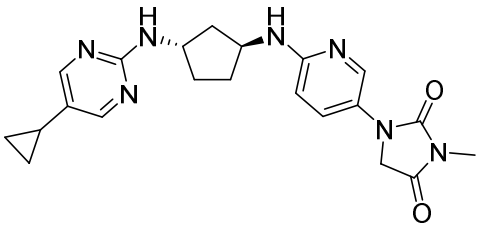
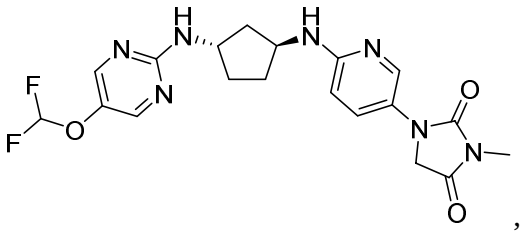
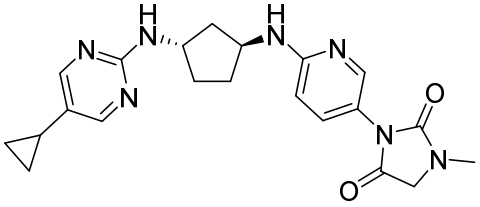
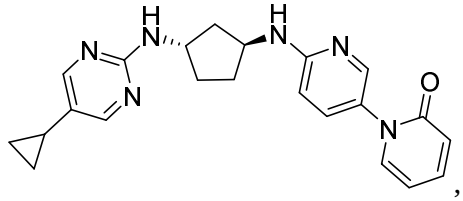
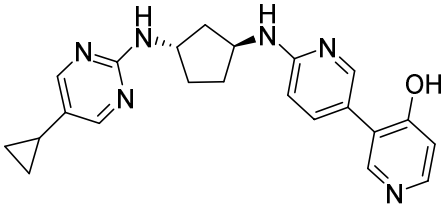
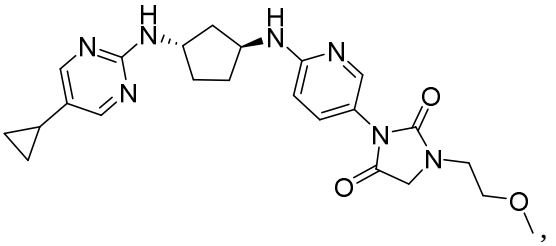
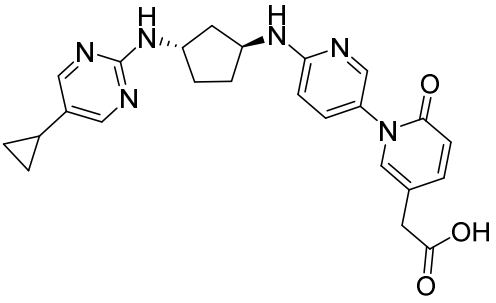
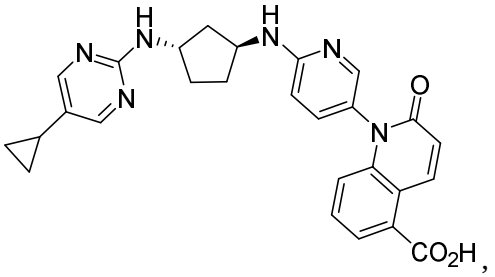
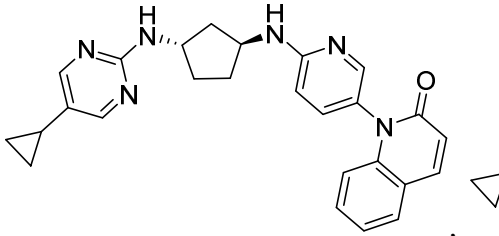
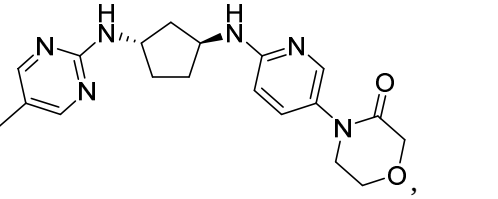

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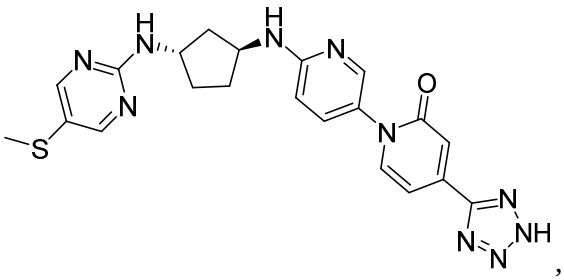
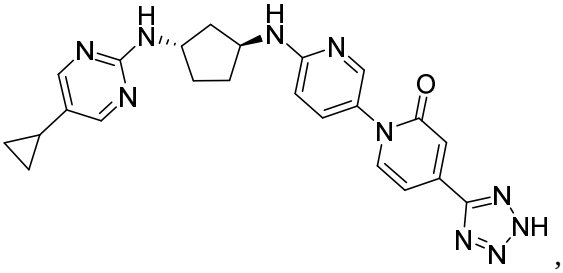
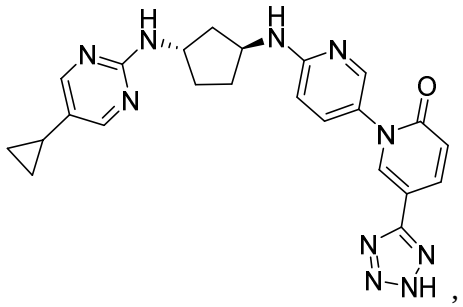
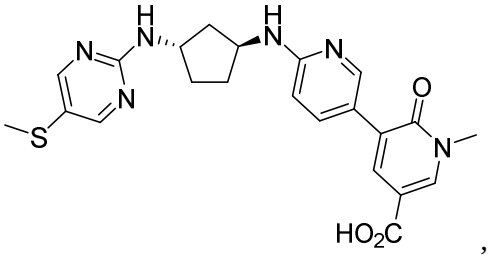
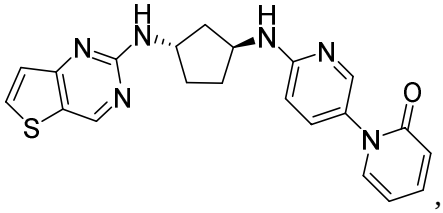
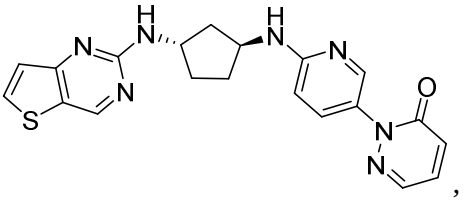
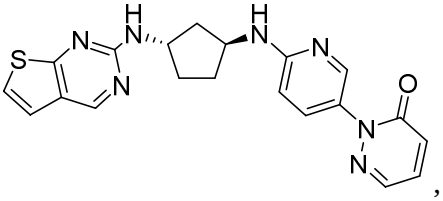
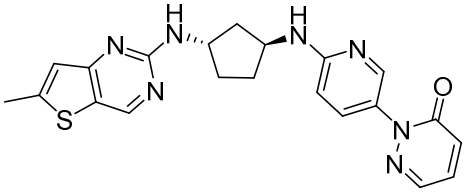
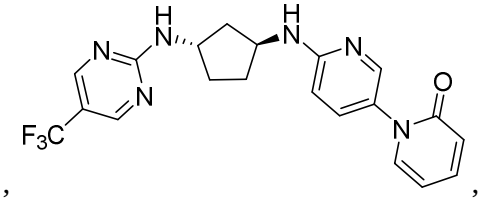
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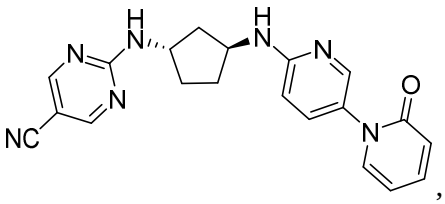
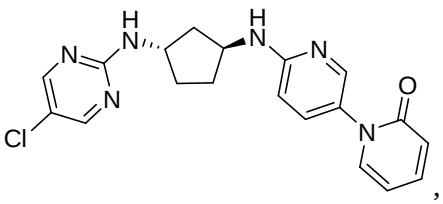
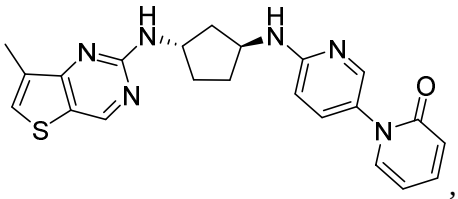
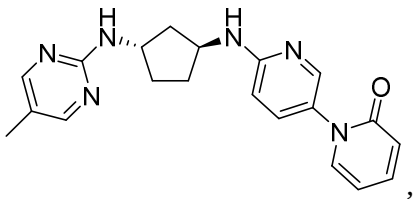
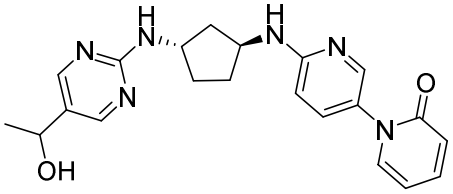
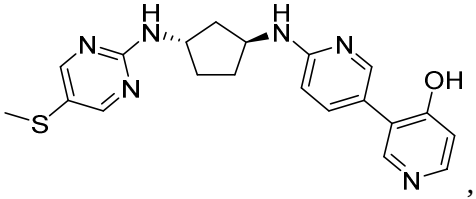
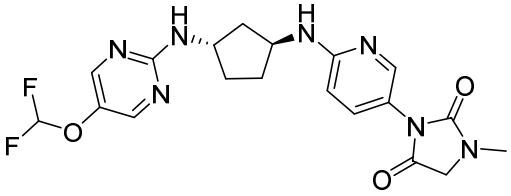
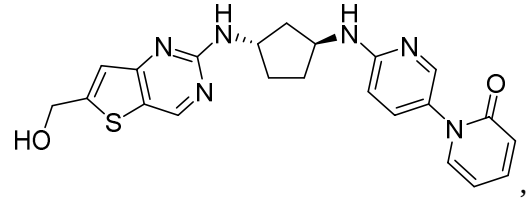
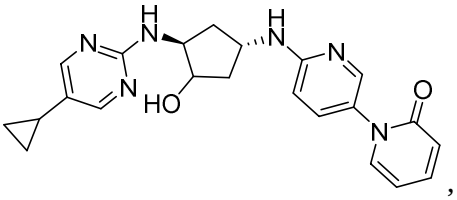
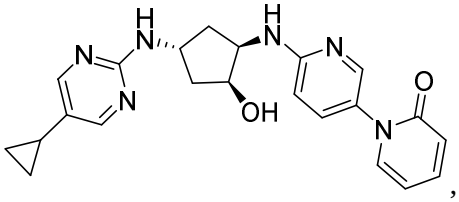
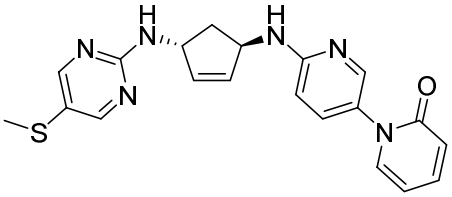
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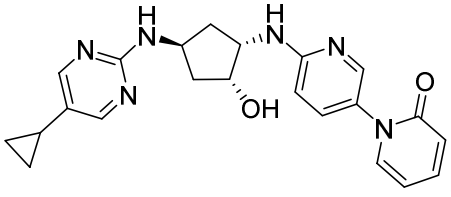
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16. The use of any one of claims 2 to 15, wherein the cardiovascular disease is dyslipidemia, dyslipoproteinemia, hypercholesterolemia, hypertriglyceridemia, hyperlipidemia, hyperlipoproteinemia, hypoalphalipoproteinemia, metabolic syndrome, diabetic complications, atherosclerosis, stroke, vascular dimensia, chronic kidney disease, hepatic steatosis, coronary heart disease, coronary artery disease, retinopathy, inflammation, thrombosis, metabolic syndrome, peripheral vascular disease or congestive heart failure.

17. The use of claim 16, wherein the hypercholesterolemia is familial hypercholesterolemia or autosomal dominant hypercholesterolemia.