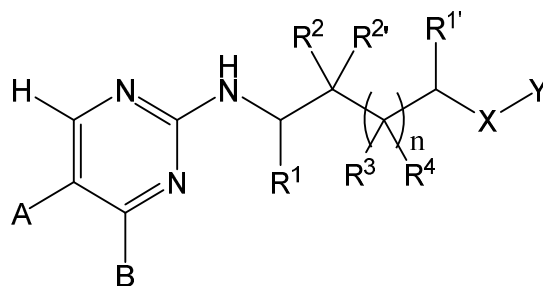


Claims:

1. A compound of Formula (I);



(I)

wherein:

A is selected from H, halo, hydroxy, alkyl, thioalkyl, alkenyl, alkoxy, acyloxy, cyano, cycloalkyl, -C(O)OR⁶, and -C(O)NR⁶R⁷;

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 NR⁵ or O;

~~R¹ and R¹² are each independently selected from H and alkyl; or~~

~~if n is 0, and R¹ and R¹², together with the atoms to which they are attached, form a 4-8 membered cycloalkyl or cycloalkenyl ring;~~

R² is selected from H, halo, alkyl, alkoxy, amidoalkyl, aminoalkyl, hydroxyalkyl, alkylamino, cyano, and hydroxy; or

~~R¹ and R², together with the atoms to which they are attached, form a 3-8 membered cycloalkyl or heterocyclyl ring; or~~

~~R¹² and R², 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

~~R² and R²², taken together with the carbon atom to which they are attached, form a 3-8 membered cycloalkyl or heterocyclyl ring;~~

each R³ and R⁴ is independently H or alkyl; or

~~R² and R³, together with the atoms to which they are attached, form a 3-8 membered cycloalkyl or heterocyclyl ring; and~~

R⁵ is H or alkyl; ~~or~~

~~R¹ and R⁵, together with the atoms to which they are attached, form a 6-8 membered cycloalkyl or heterocyclyl ring; or~~

~~R² and R⁵, together with the atoms to which they are attached, form a 5-8 membered cycloalkyl or heterocyclyl ring;~~

each R⁶ and R⁷ is independently H or alkyl;

Y is selected from aryl; and heteroaryl ~~and heterocyclyl~~;

~~and~~

n is 0 or 1.

2. The compound of claim 1, wherein A is selected from H, hydroxy, thioalkyl, alkyl, alkoxy, acyloxy, cyano, cycloalkyl, -C(O)OR⁶, and -C(O)NR⁶R⁷.

3. The compound of claim 1, wherein A is alkoxy.

4. The compound of claim 1, wherein A is cycloalkyl.

5. The compound of any preceding claim, wherein B is H.

~~6. The compound of any preceding claim, wherein X is NR⁵.~~

~~7. The compound of any preceding claim, wherein Y is heteroaryl or heterocyclyl.~~

~~8. The compound of any one of claims 1-7, wherein n is 0, and R¹ and R^{1'}, together with the atoms to which they are attached, form a 4- to 8-membered monocyclic or bicyclic cycloalkyl or cycloalkenyl ring which is unsubstituted or substituted, e.g., with one or more hydroxy.~~

~~9. The compound of claim 8, wherein R¹ and R^{1'}, together with the atoms to which they are attached, form a 4- to 8-membered monocyclic or bicyclic cycloalkyl.~~

~~10. The compound of claim 8, wherein the cycloalkyl ring is a cyclopentyl ring.~~

~~1417.~~ The compound of any preceding claim, wherein R² is selected from H, halo, alkyl, alkoxy, amidoalkyl, aminoalkyl, alkylamino, cyano, and hydroxyl.

~~1428.~~ The compound of any one of claims 1-~~1417~~, wherein R^{2'} is H.

~~1439.~~ The compound of any preceding claim, wherein Y is monocyclic heteroaryl.

~~14410.~~ The compound of claim ~~1439~~, wherein Y is selected from pyridyl, pyridinyl, pyrazinyl, pyrimidinyl, and thiazolyl.

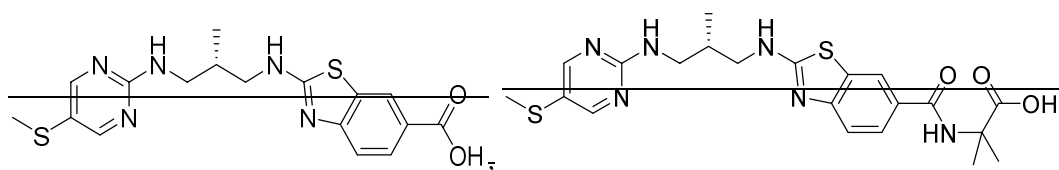
~~14511.~~ The compound of claim ~~1439~~, wherein Y is selected from ~~triazenyl~~, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, and triazolyl.

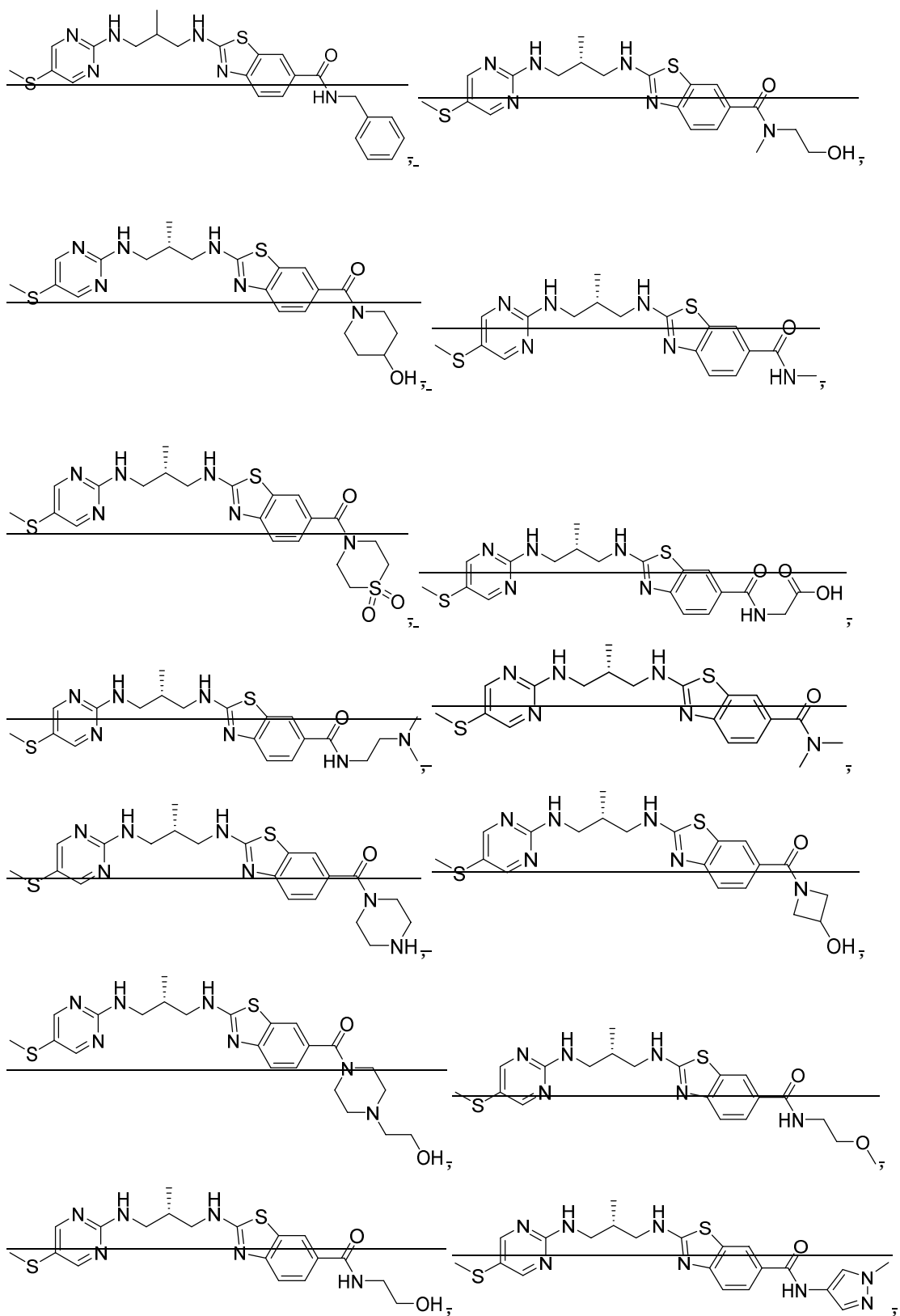
~~14612.~~ The compound of any one of claims ~~1439-14511~~, wherein the monocyclic heteroaryl is unsubstituted or substituted with one or more substituents selected from alkyl, thioalkyl, alkoxy, alkoxy carbonyl, amido, carboxy, cyano, halo, aryl, heteroaryl, heterocyclyl, nitro, sulfonamido, and thioalkyl.

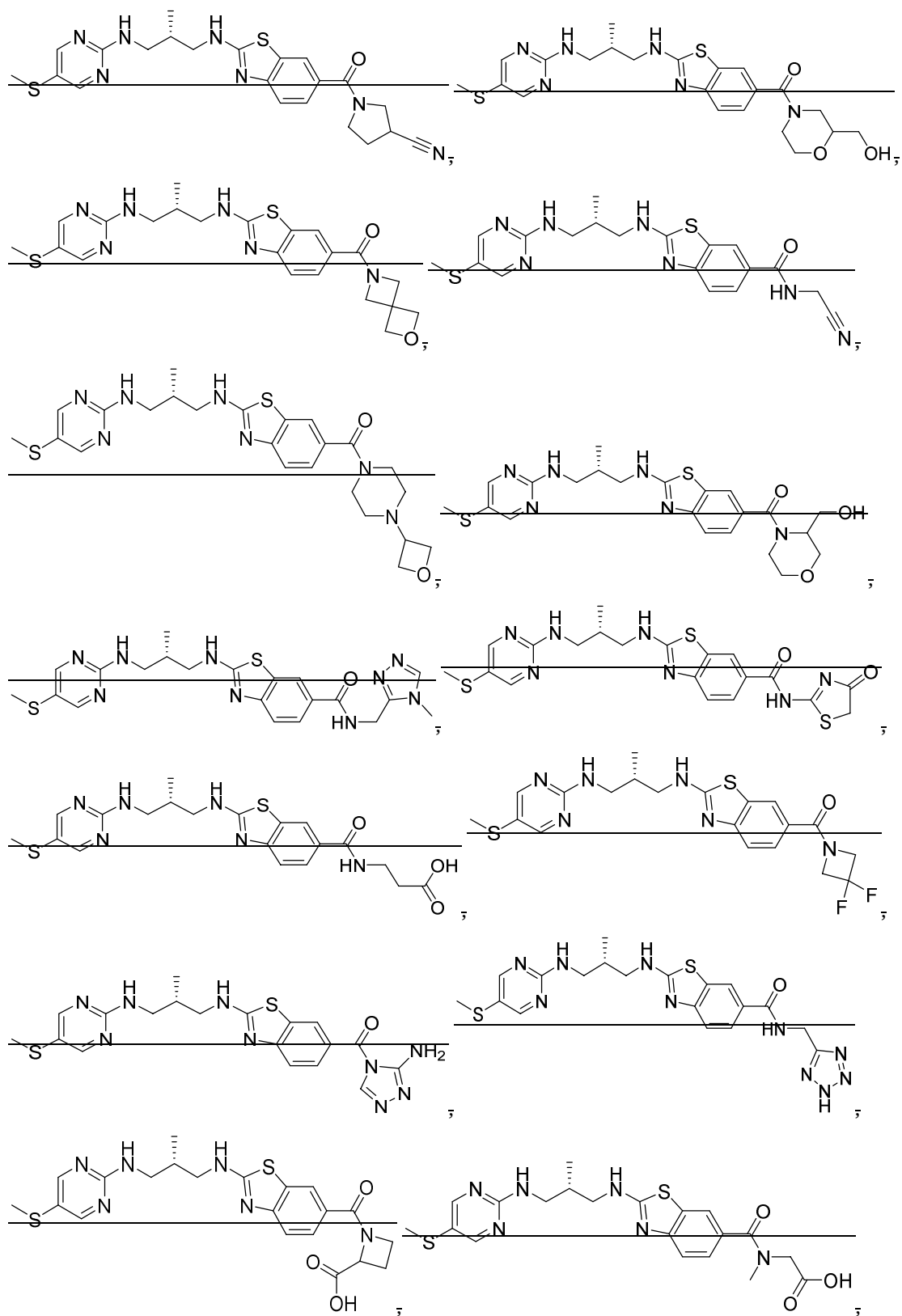
~~14713.~~ The compound of claim ~~14612~~, wherein the monocyclic heteroaryl is substituted with a 6-membered aryl, heteroaryl or heterocyclyl selected from phenyl, pyridinyl, 2-hydroxypyridinyl, piperidinonyl, 2-hydroxy-1-methylpyridinyl, triazolyl, imidazolidinonyl, pyrimidinonyl, 2-hydroxyisoquinolinyl, 3-hydroxypyridazinyl, pyrrolidinonyl, pyrazolyl, and morpholinonyl.

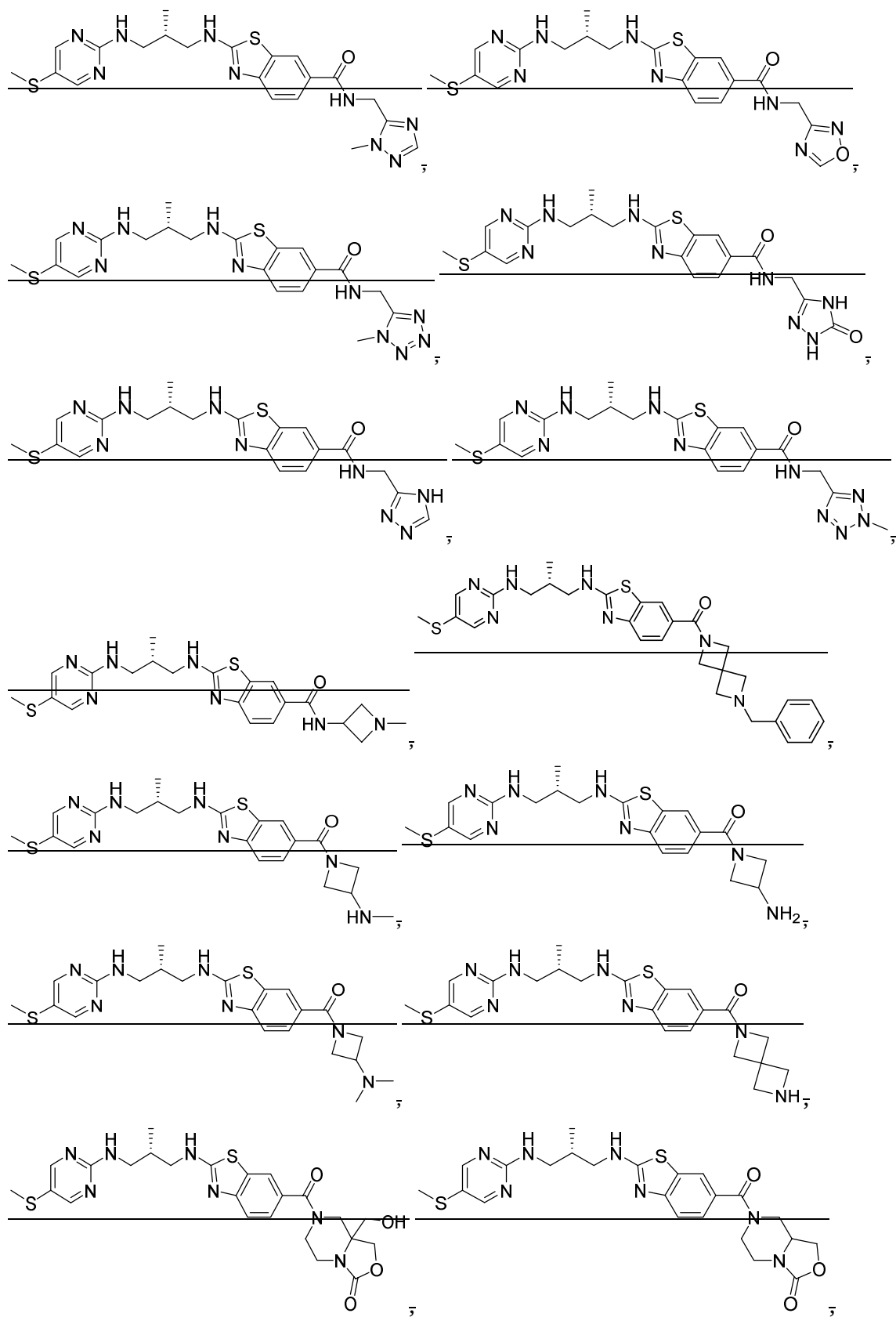
~~14814.~~ The compound of claim ~~14713~~, wherein the ~~monocyclic heteroaryl~~ is substituted with ~~an~~ heteroaryl or heterocyclyl ~~that~~ is substituted with one or more substituents selected from halo, CN, alkyl, alkoxy, hydroxy, carboxy, -CO₂alkyl, and tetrazolyl.

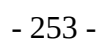
~~14915.~~ A compound selected from

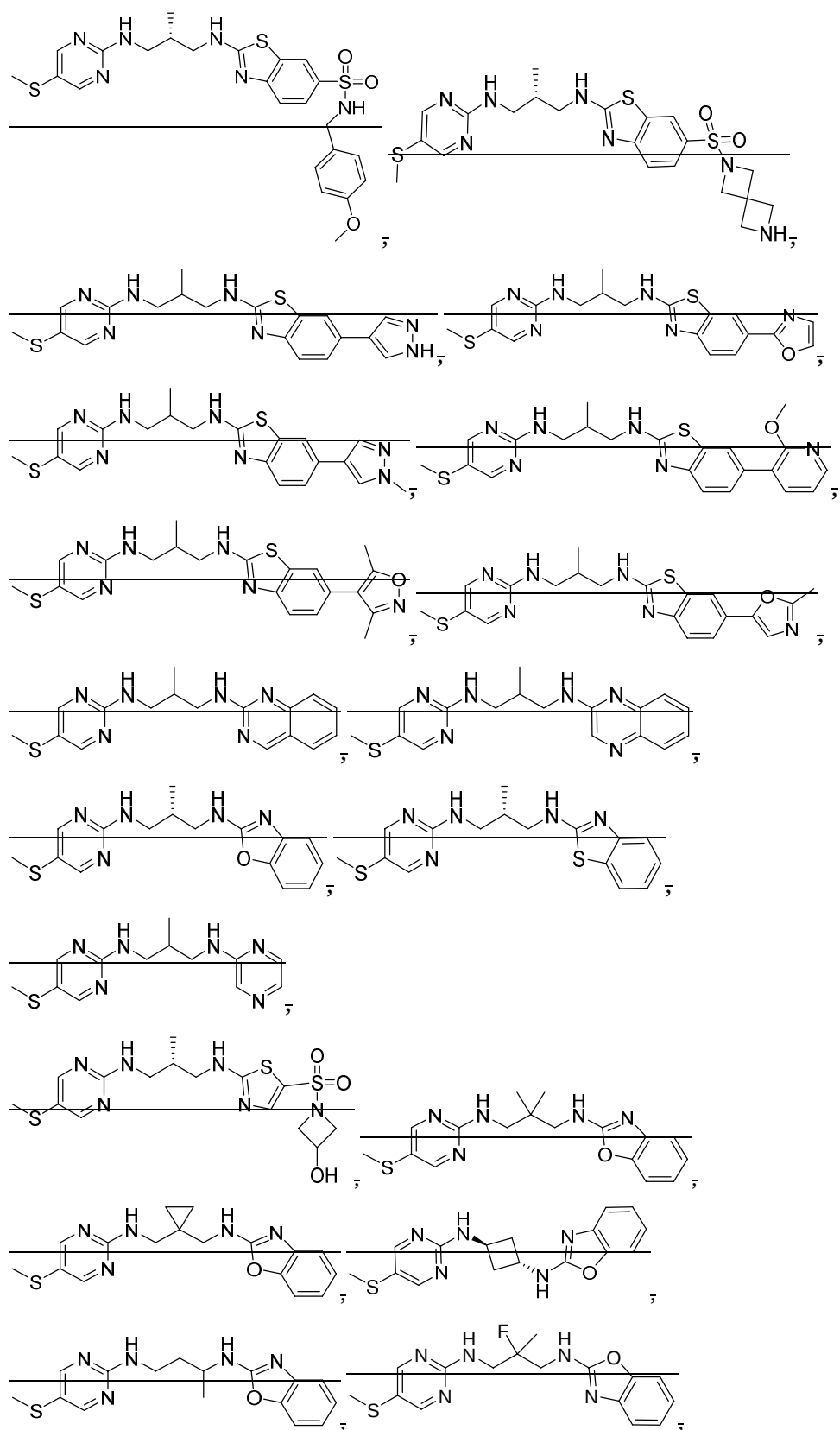


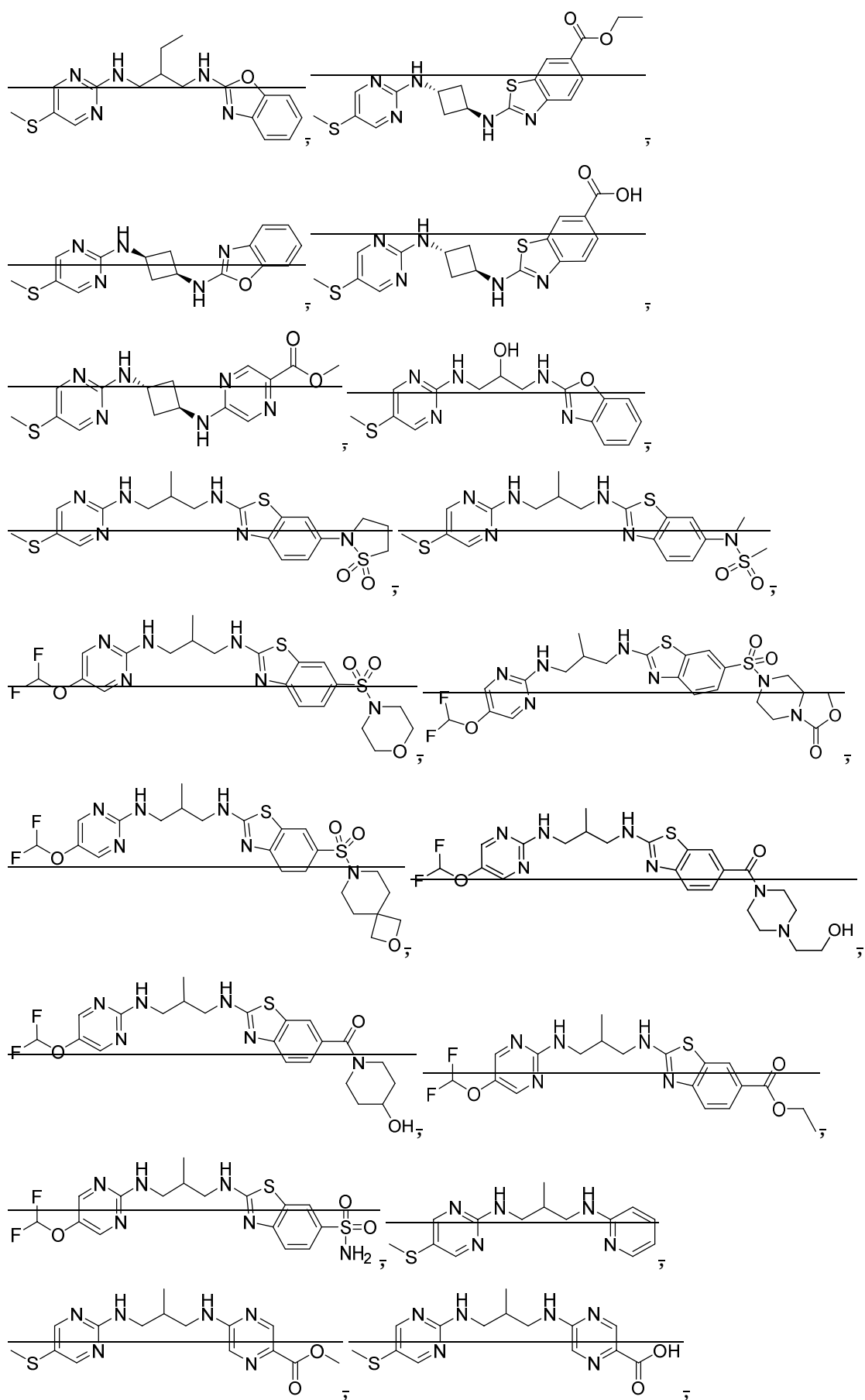


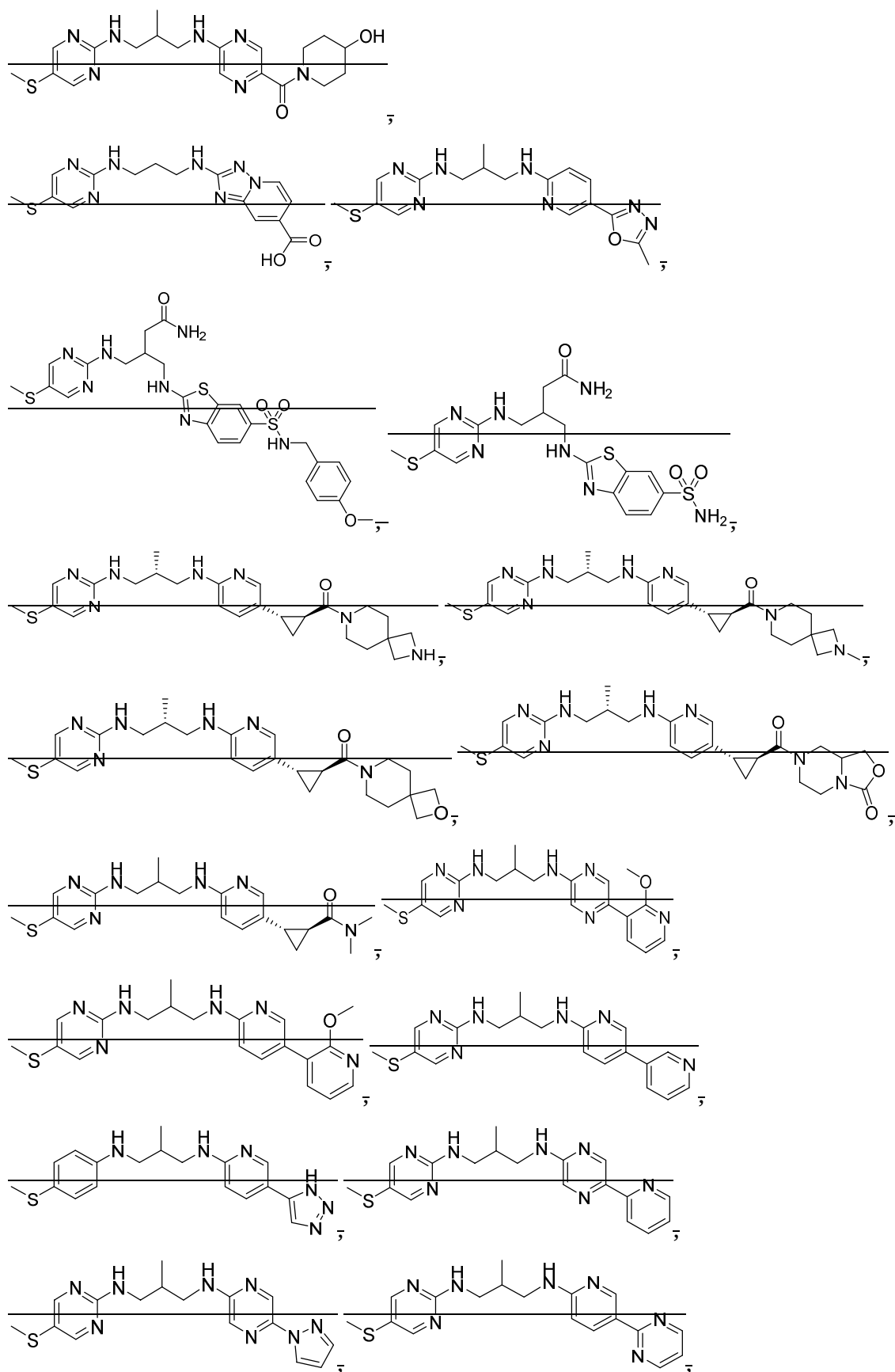


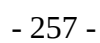


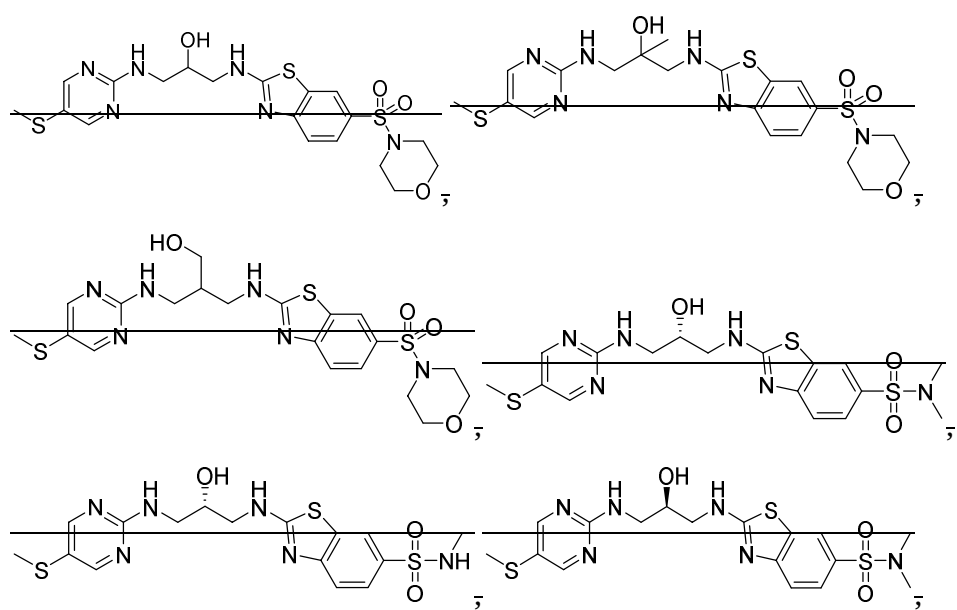


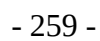


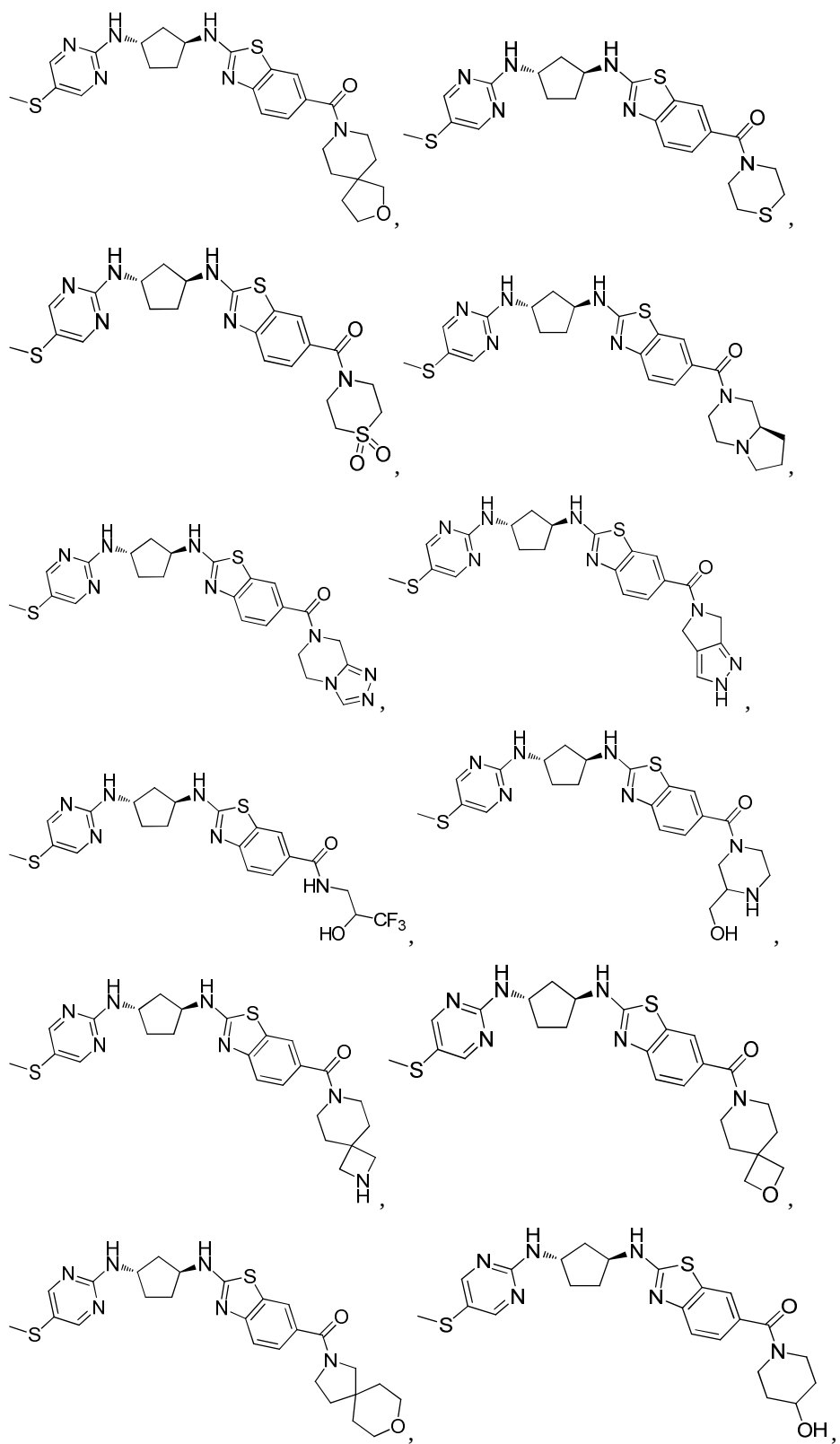


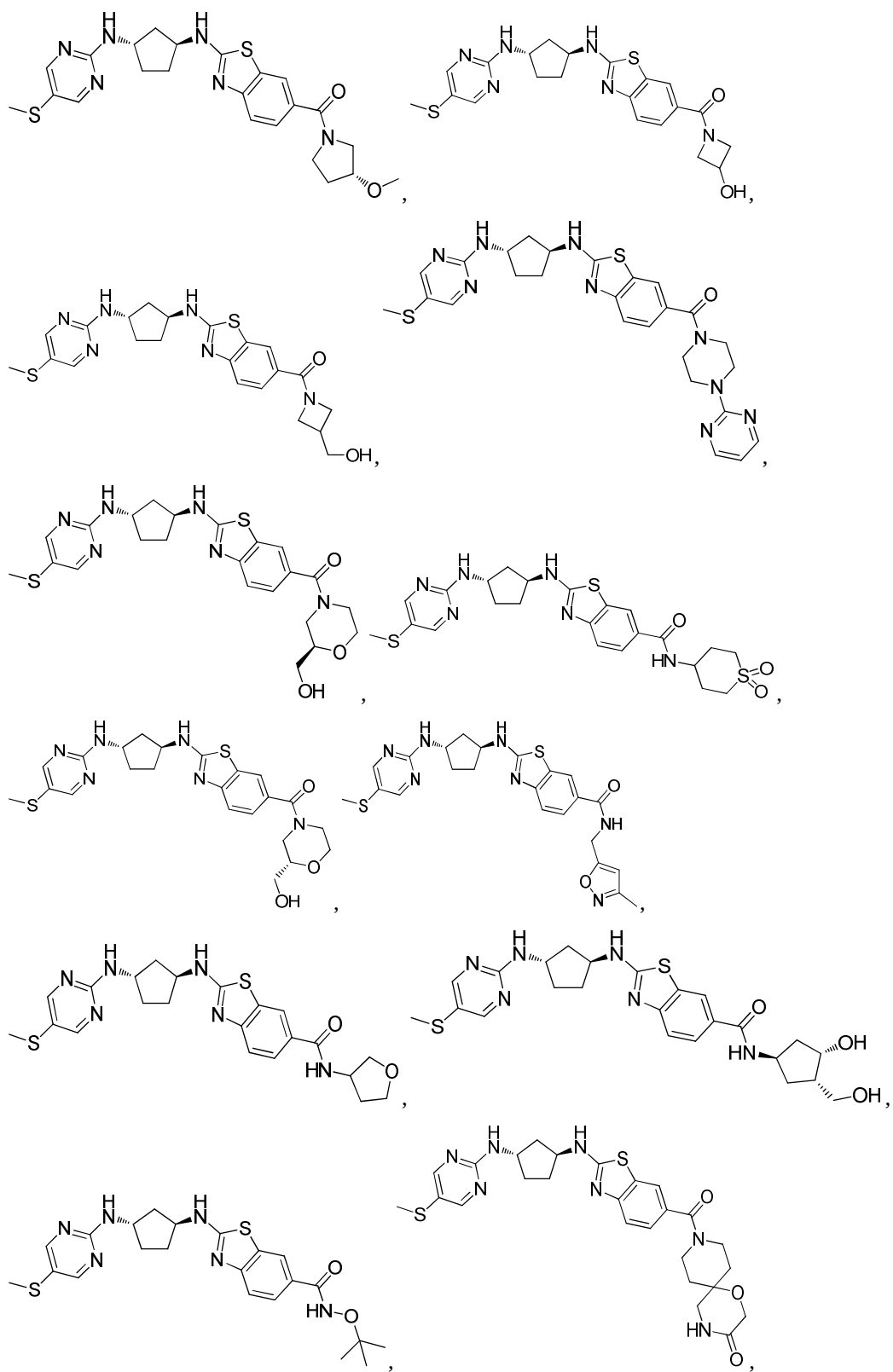


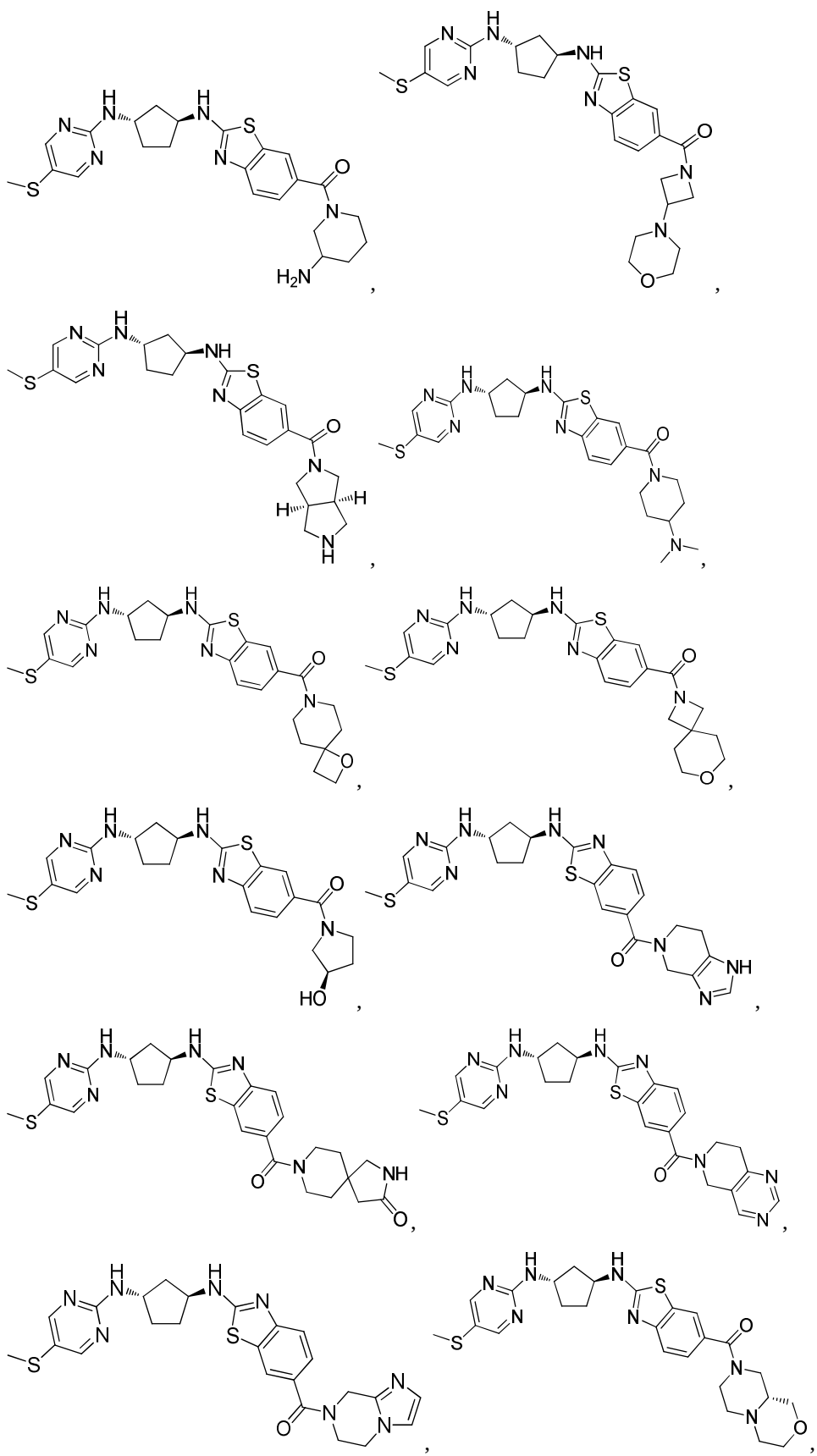


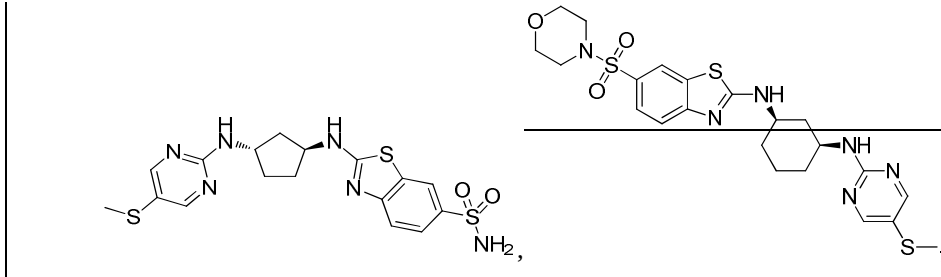


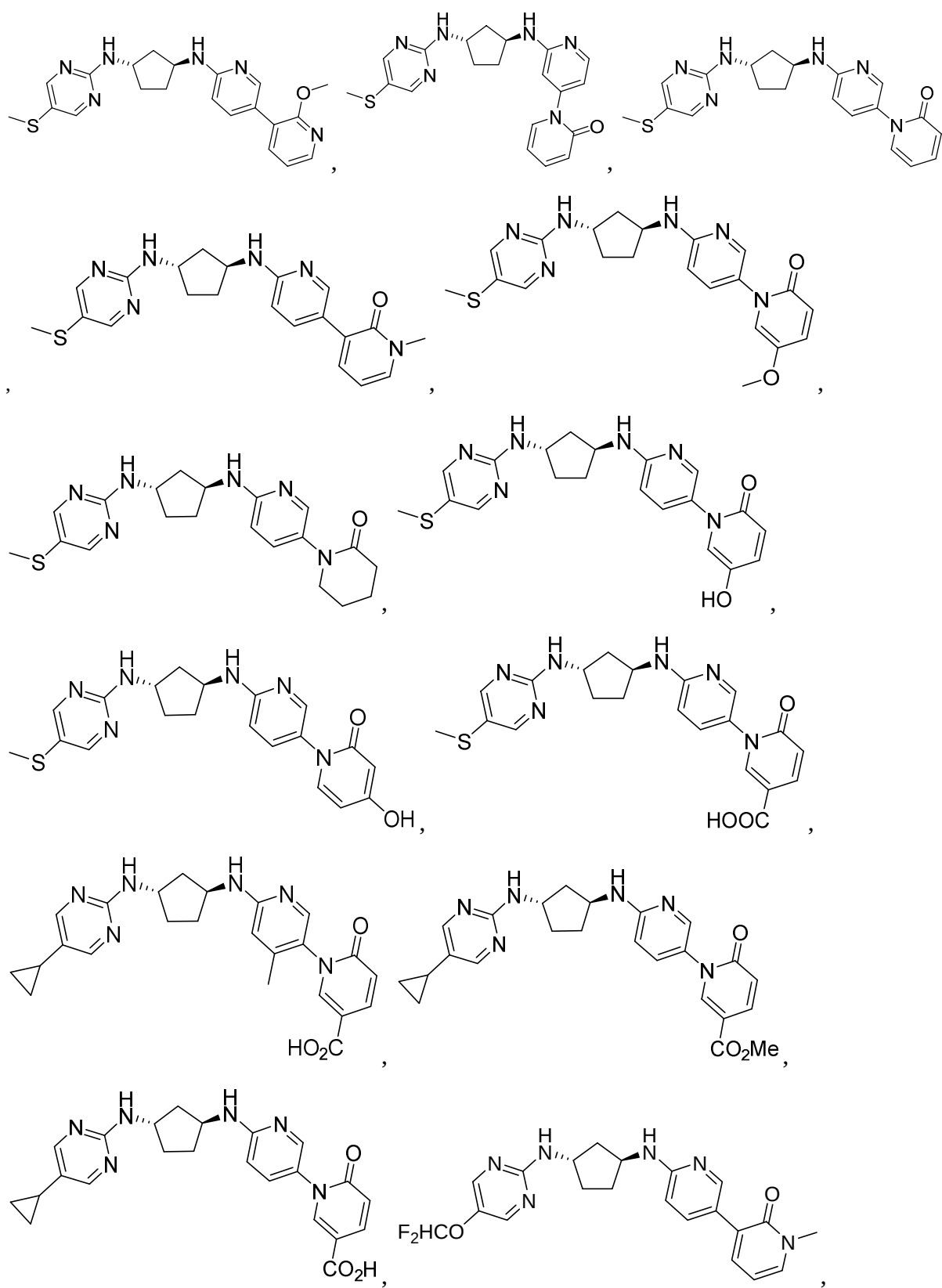


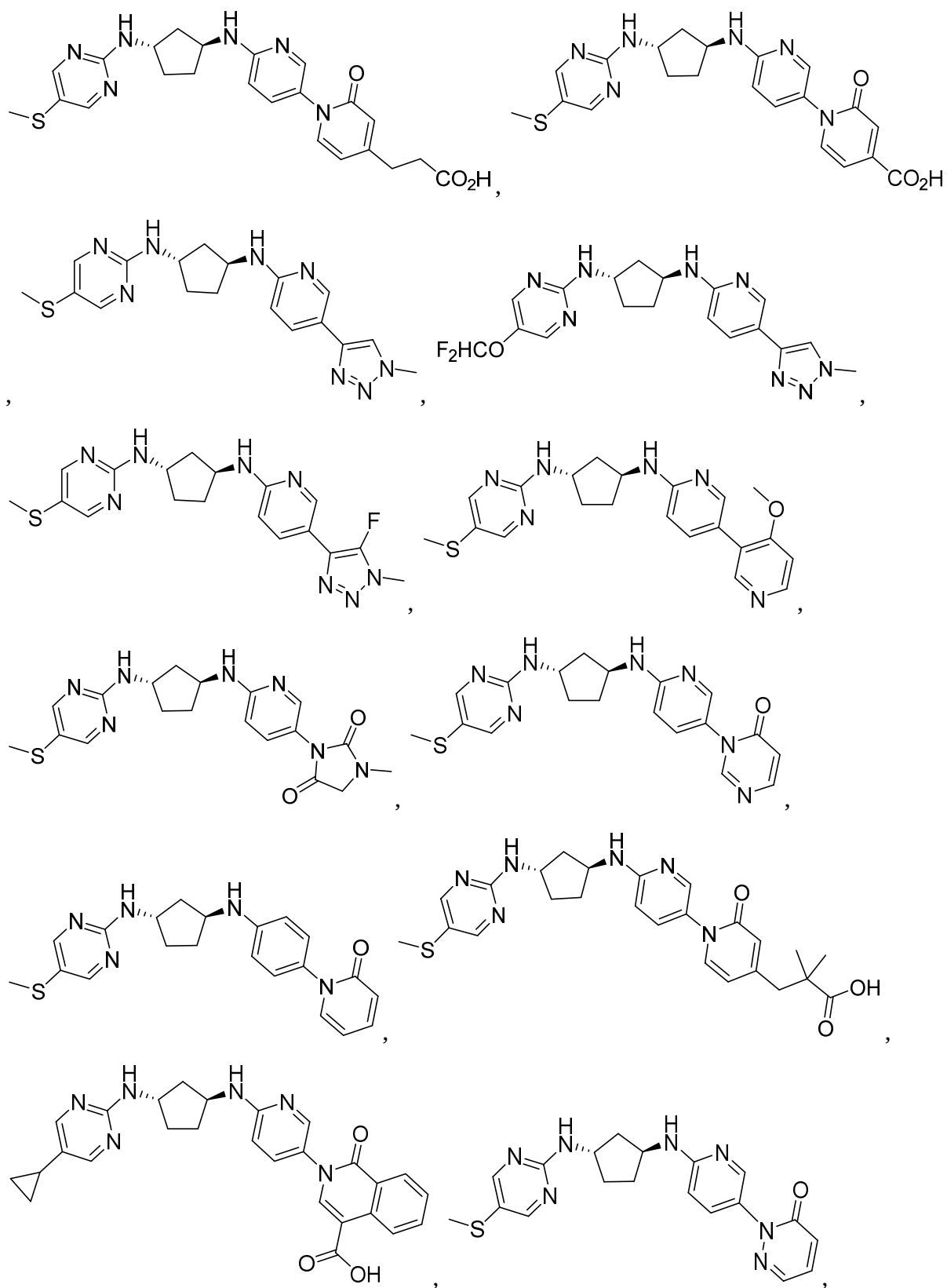


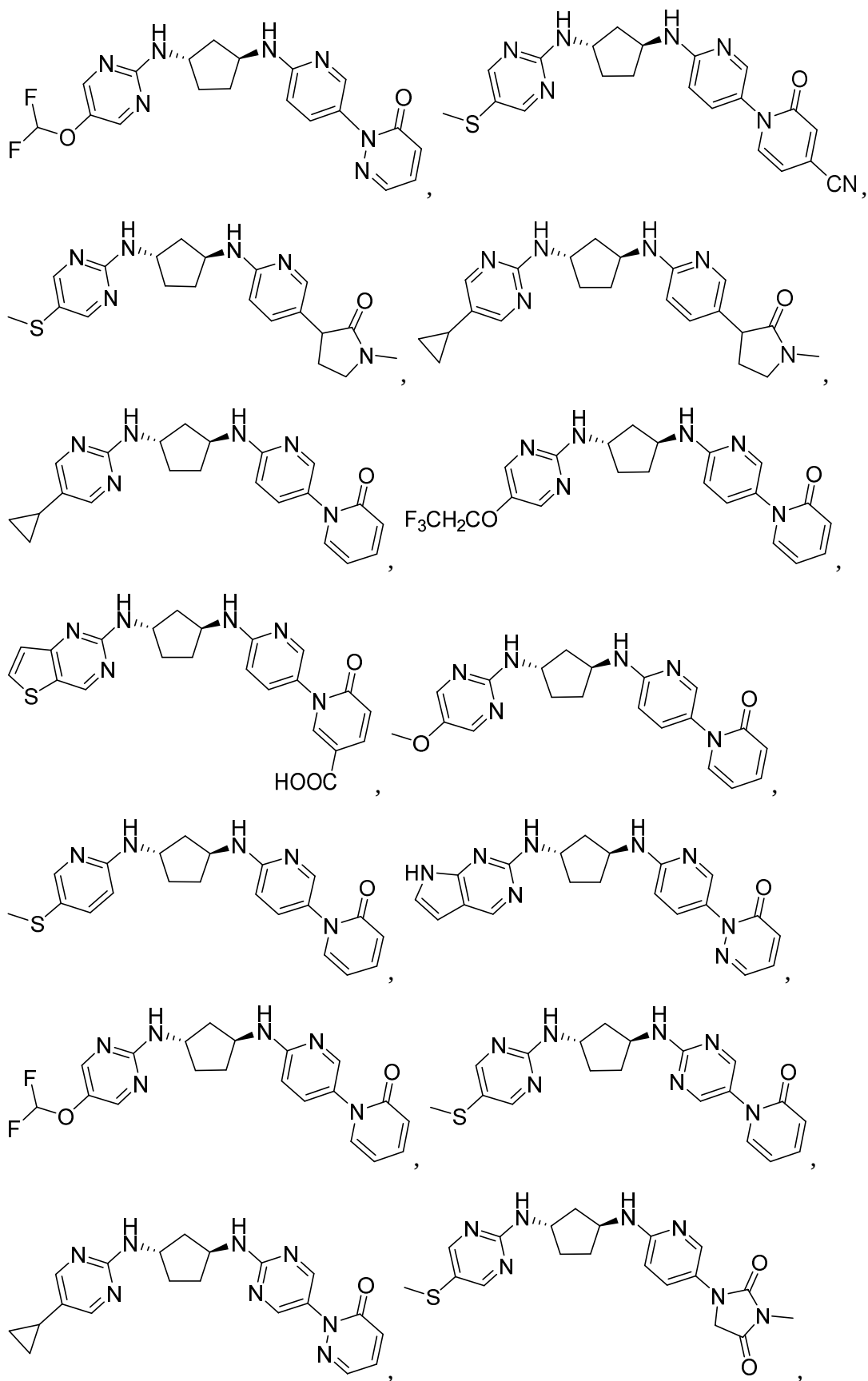


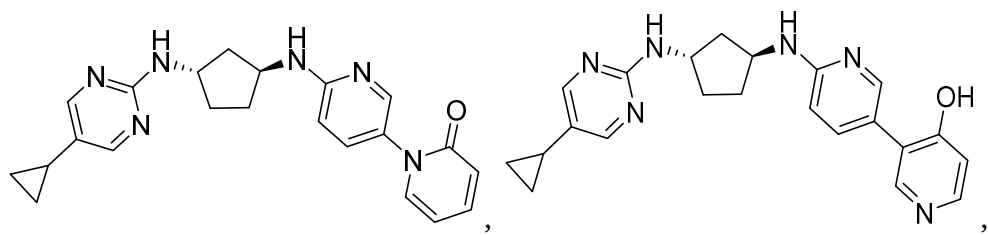
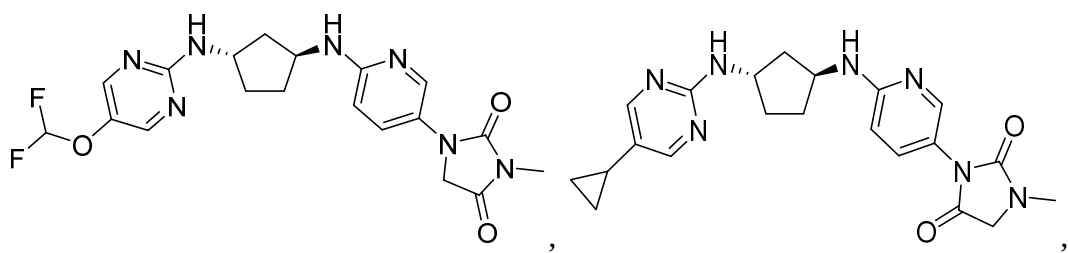
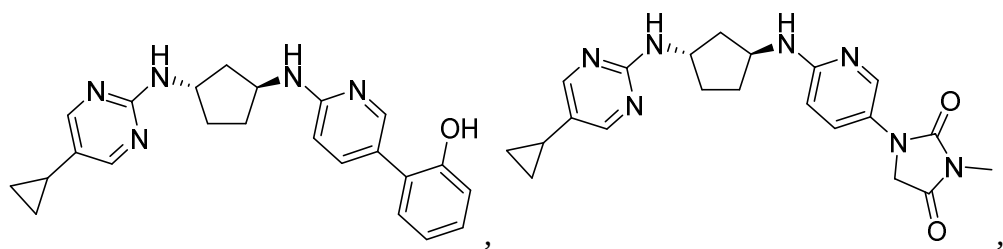
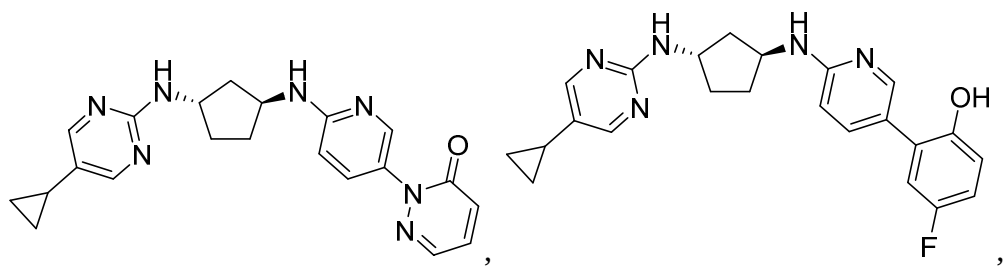
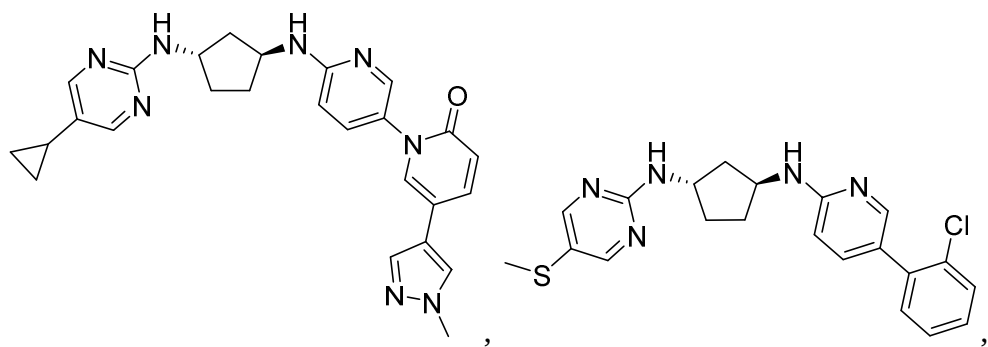
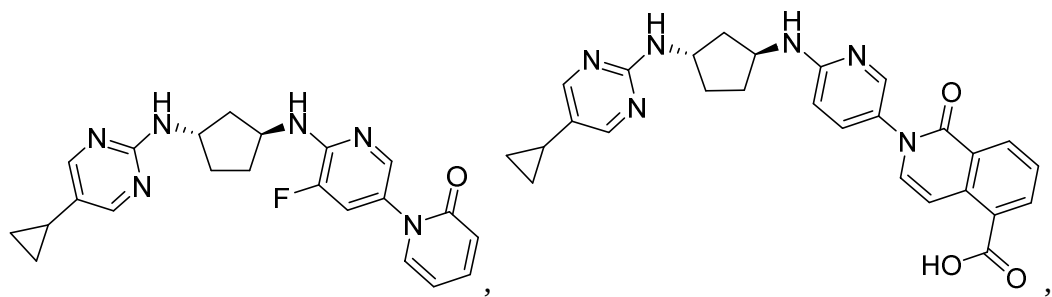


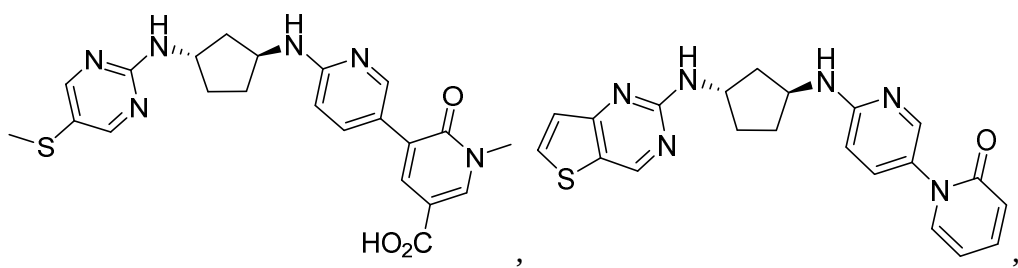
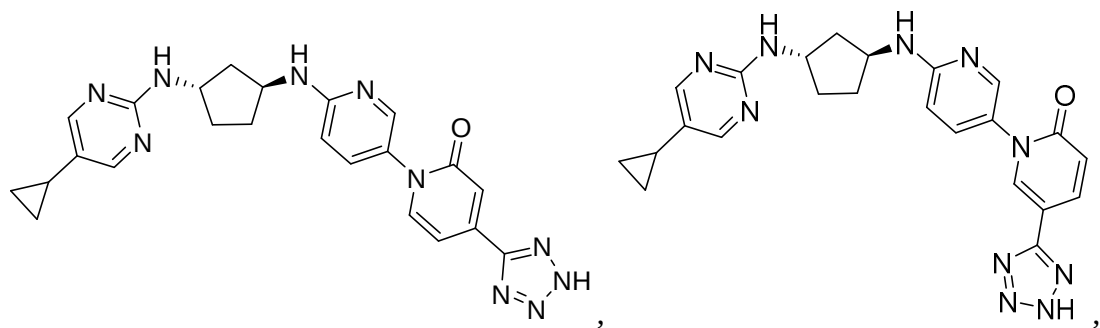
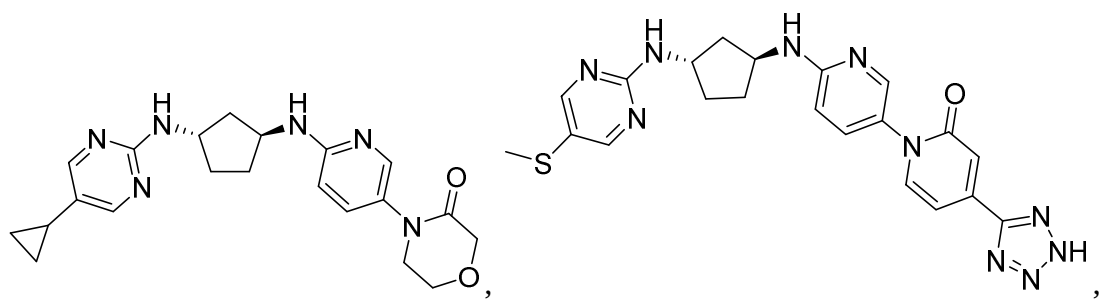
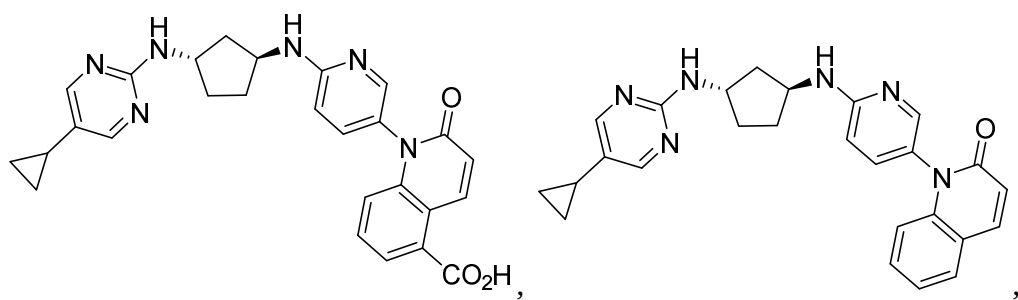
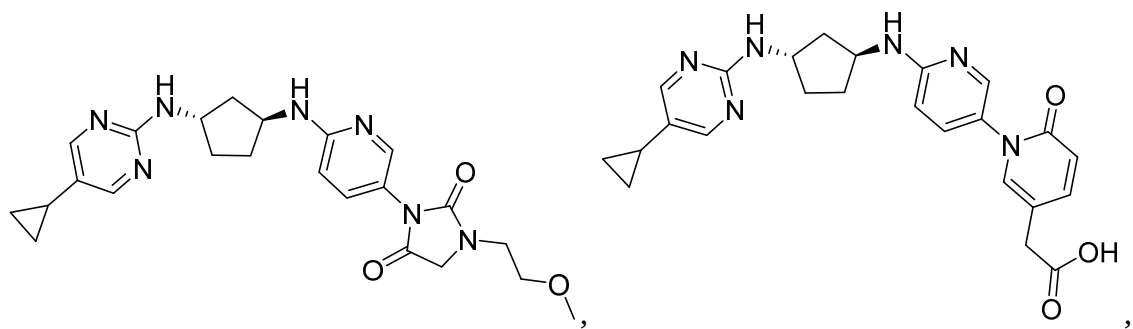


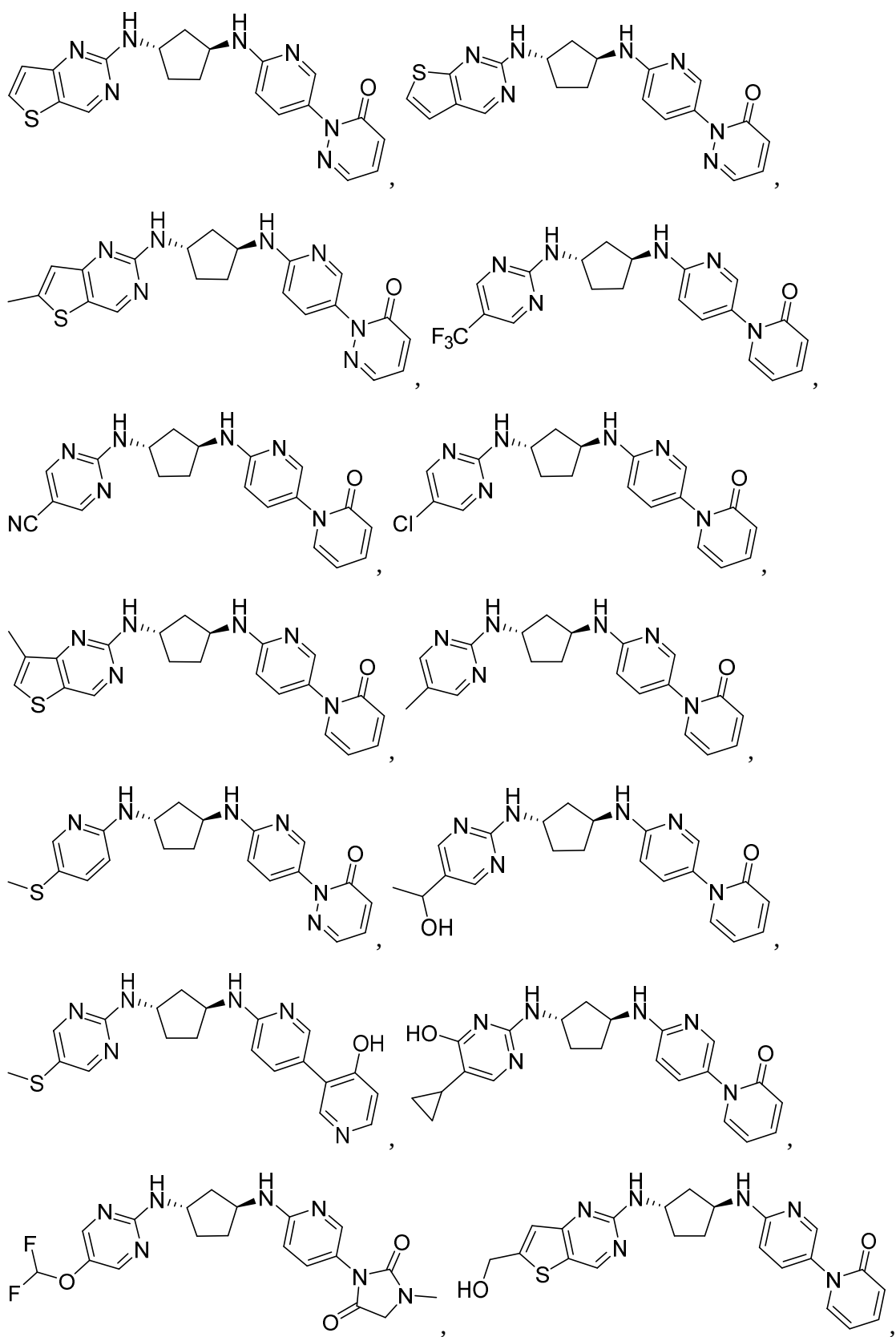


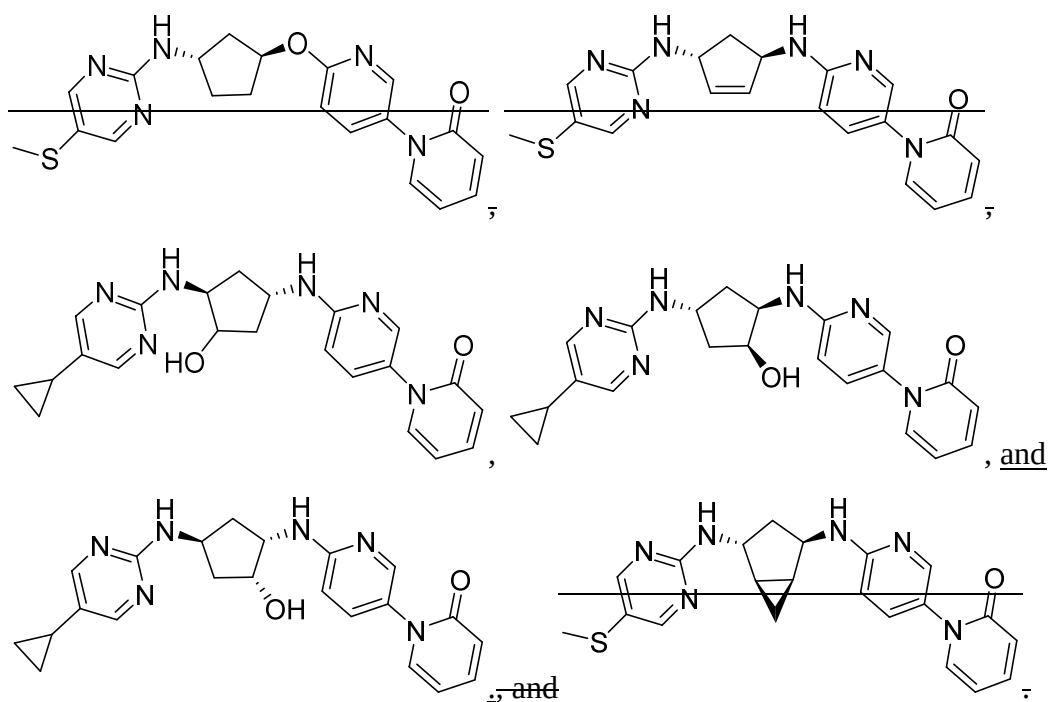




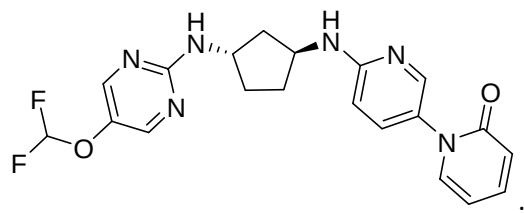




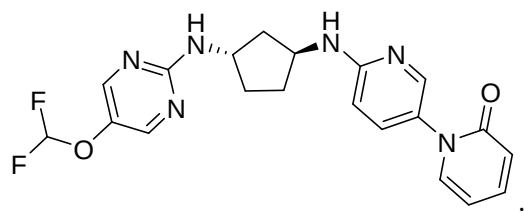




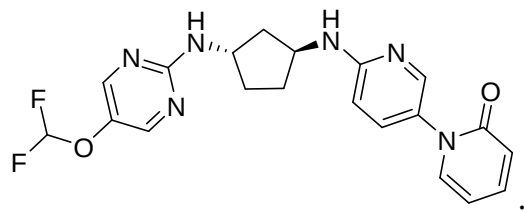
16. A compound, or a pharmaceutically acceptable salt thereof, which is



17. A compound which is



18. A compound which is a pharmaceutically acceptable salt of



~~20~~19. A pharmaceutical composition comprising a compound according to any one of claims ~~1-19~~18, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable excipients.

~~21~~20. A compound according to any one of claims ~~1-19~~18 for use in the treatment of cardiovascular disease.

~~22~~21. Use of a compound according to any one of claims ~~1-19~~18 in the manufacture of medicament for the treatment of cardiovascular disease.

~~23~~22. The use of claim ~~22~~21, wherein the cardiovascular disease is selected from hypercholesterolemia, hyperlipidemia, hyperlipoproteinemia, hypertriglyceridemia, dyslipidemia, dyslipoproteinemia, atherosclerosis, hepatic steatosis, metabolic syndrome and coronary artery disease.

~~24~~23. The use of claim ~~22-21~~21 or ~~23~~22, wherein the cardiovascular disease is familial hypercholesterolemia.

~~25~~24. The use of claim ~~22-21~~21 or ~~23~~22, wherein the cardiovascular disease is autosomal dominant hypercholesterolemia.

~~26~~25. The use of any one of claims ~~2221-25~~21-24, wherein the level of circulating serum cholesterol is decreased in the subject.

~~27~~26. The use of any one of claims ~~2221-26~~21-25, wherein the level of circulating serum LDL-cholesterol is decreased in the subject.

~~28~~27. The use of any one of claims ~~2221-27~~21-26, wherein the level of circulating serum VLDL-cholesterol is decreased in the subject.

~~29~~28. The use of any one of claims ~~2221-28~~21-27, wherein the level of circulating serum triglycerides is decreased in the subject.

~~30~~29. The use of any one of claims ~~2221-29~~221-28, wherein the level of circulating serum lipoprotein A is decreased in the subject.

~~31~~30. The use of any one of claims ~~2221-30~~221-29, wherein the subject has atherosclerosis.

~~32~~31. The use of any one of claims ~~2221-31~~221-30, wherein atherosclerotic plaque formation is decreased in the subject.

~~33. The use of any one of claims 22-32, wherein the subject has a gain-of-function mutation in PCSK9 gene.~~

~~34~~32. The use of any one of claims ~~2221-33~~221-31, further comprising conjointly administering one or more additional therapeutic agents.

~~35~~33. The use of claim ~~34~~32, wherein the one or more additional therapeutic agents are selected from alirocumab, evolocumab, bococizumab, RG7652, LY3015014, mAb316P, berberine, quercetin, ezetimibe, policosanol, BMS-962476, atorvastatin, cerivastatin, fluvastatin, lovastatin, mevastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin.

~~36~~34. The use of claim ~~34~~32, wherein the one or more additional therapeutic agents are selected from an HMG-CoA reductase inhibitor, an HMG-CoA synthase inhibitor, an HMG-CoA reductase gene expression inhibitor, an HMG-CoA synthase gene expression inhibitor, an MTP/Apo B secretion inhibitor, a CETP inhibitor, a bile acid absorption inhibitor, a cholesterol absorption inhibitor, a cholesterol synthesis inhibitor, a squalene synthetase inhibitor, a squalene epoxidase inhibitor, a squalene cyclase inhibitor, a combined squalene epoxidase/squalene cyclase inhibitor, a fibrate, niacin, a combination of niacin and lovastatin, an ion-exchange resin, an antioxidant, an ACAT inhibitor, a bile acid sequestrant, and a PCSK9 translation inhibitor.

35. The compound or a pharmaceutically acceptable salt thereof, for use in the treatment of cardiovascular disease according to claim 32, wherein the one or more additional therapeutic agents is a statin.

36. The compound or a pharmaceutically acceptable salt thereof, for use in the treatment of cardiovascular disease according to claim 32, wherein the one or more additional therapeutic agents are selected from atorvastatin, cerivastatin, fluvastatin, lovastatin, mevastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin.