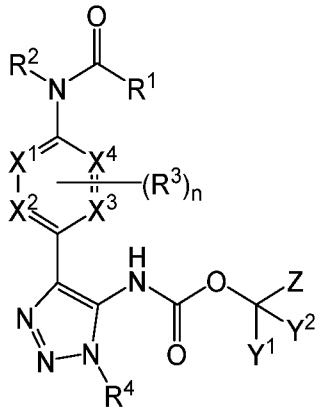
CLAIMS

1. A compound of Formula (I),



(I)

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, or 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, nitro, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, $-N(R^{1B1})(R^{1B2})$, $-O-R^{1B1}$, $-S-R^{1B1}$, $-C(O)N(R^{1B1})(R^{1B2})$, $-NR^{1B1}C(O)R^{1B2}$, $-NR^{1B1}C(O)N(R^{1B2})(R^{1B3})$, $-S(O)_{0-2}R^{1B1}$, $-S(O)_2N(R^{1B1})(R^{1B2})$, and $-NR^{1B1}S(O)_2R^{1B2}$, wherein each R^{1B1}, R^{1B2}, and R^{1B3} is independently hydrogen, C_{1-6} alkyl, or C_{3-6} cycloalkyl,

wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, $-O-R^{1D1}$, or

-N(R^{1D1})(R^{1D2}), wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl, and

wherein each R^{1B1}, R^{1B2}, and R^{1B3} alkyl and each R^{1B1}, R^{1B2}, and R^{1B3} cycloalkyl is optionally substituted with 1 to 3 halogens; or

R^1 is -O-R^{1D1} or -N(R^{1D1}) (R^{1D2}), wherein each R^{1D1} and R^{1D2} is independently hydrogen, C_{1-6} alkyl, or C_{3-6} cycloalkyl, wherein each C_{1-6} alkyl, or C_{3-6} cycloalkyl is optionally substituted with 1 to 4 R^{1E}, which can be the same or different, wherein each R^{1E} is independently selected from halogen, cyano, hydroxy, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, -O-R^{1F1}, –N(R^{1F1})(R^{1F2}), –C(O)N(R^{1F1}) (R^{1F2}), –NR^{1F1}C(O)R^{1F2}, –S(O)$_{0-2}$$R^{1F1}$, –S(O)$_2$N($R^{1F1}$)($R^{1F2}$), and –N$R^{1F1}$S(O)$_2$$R^{1F2}$, wherein each R^{1F1} and R^{1F2} is independently hydrogen or C_{1-6} alkyl, wherein each R^{1E} alkyl, cycloalkyl, aryl, and heteroaryl is optionally substituted with 1 to 3 R^{1G}, which can be the same or different, and wherein each R^{1G} is independently C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, halogen, or cyano;

R^2 is hydrogen or C_{1-6} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkoxy, and C_{3-10} cycloalkyl; or

R^2 is C_{3-6} cycloalkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkoxy, and C_{1-6} alkyl;

each R^3 is independently selected from deuterium, halogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, -O-R^{2A1}, and -N(R^{2A1})(R^{2A2}), wherein the C_{1-6} alkyl is optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from C_{1-4} alkoxy and halogen, and wherein each R^{2A1} and R^{2A2} is independently hydrogen or C_{1-3} alkyl optionally substituted with 1 to 3 halogens, which can be the same or different;

n is 0, 1, 2, 3, or 4;

R^4 is C_{1-6} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkoxy, -C(O)N(R^{4A1}), and

-N(R^{4A1})(R^{4A2}), wherein each R^{4A1} and R^{4A2} is independently hydrogen, C_{1-6} alkyl, or C_{3-10} cycloalkyl; or

R^4 is C_{3-6} cycloalkyl or 3 to 6 membered heterocyclyl having 1 or 2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein the cycloalkyl or heterocyclyl are optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkyl, and C_{1-4} alkoxy;

each of X^1, X^2, X^3, and X^4 is independently selected from CH and N;

each Y^1 and Y^2 is independently hydrogen, deuterium, or C_{1-6} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from deuterium, halogen, cyano, C_{2-3} alkynyl, C_{1-4} alkoxy, and -C(O)NH-($C_{1-4}H_{3-9}$); and

Z is C_{1-8} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{6-12} aryl, 3 to 12 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or 5 to 12 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein the alkyl, alkoxy, cycloalkyl, aryl, heterocyclyl, or heteroaryl are each optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, and C_{3-6} cycloalkyl, wherein the C_{1-4} alkyl is optionally substituted with 1 to 3 substituents, which can be the same or different, selected from C_{1-4} alkoxy and halogen; or

Y^1 and Z together with the carbon to which they are attached form C_{3-6} cycloalkyl, C_{6-12} aryl, 3 to 12 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or 5 to 12 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein the cycloalkyl, aryl, heterocyclyl, or heteroaryl are each optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from cyano, C_{1-4} alkyl, C_{1-4} alkoxy, C_{6-10} aryl, and halogen, wherein the C_{1-4} alkyl is optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from C_{1-4} alkoxy and halogen, and wherein the C_{6-10} aryl is optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from C_{1-4} alkyl, C_{1-4} alkoxy, and halogen, and Y^2 is hydrogen or deuterium.

2. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein:

R^1 is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, or 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, $-N(R^{1B1})(R^{1B2})$, $-O-R^{1B1}$, $-S-R^{1B1}$, $-C(O)N(R^{1B1})(R^{1B2})$, $-NR^{1B1}C(O)R^{1B2}$, $-NR^{1B1}C(O)N(R^{1B2})(R^{1B3})$, $-S(O)_{0-2}R^{1B1}$, $-S(O)_2N(R^{1B1})(R^{1B2})$, and $-NR^{1B1}S(O)_2R^{1B2}$, wherein each R^{1B1} , R^{1B2}, and R^{1B3} is independently hydrogen, or C_{1-6} alkyl,

wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, $-O-R^{1D1}$, or $-N(R^{1D1})(R^{1D2})$, wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl; or

R^1 is $-O-R^{1D1}$ or $-N(R^{1D1})(R^{1D2})$, wherein each R^{1D1} and R^{1D2} is independently hydrogen, C_{1-6} alkyl, or C_{3-6} cycloalkyl, wherein each C_{1-6} alkyl, or C_{3-6} cycloalkyl is optionally substituted with 1 to 4 R^{1E}, which can be the same or different, wherein each R^{1E} is independently selected from halogen, cyano, hydroxy, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, $-O-R^{1F1}$, $-N(R^{1F1})(R^{1F2})$, $-C(O)N(R^{1F1})(R^{1F2})$, $-NR^{1F1}C(O)R^{1F2}$, $-S(O)_{0-2}R^{1F1}$, $-S(O)_2N(R^{1F1})(R^{1F2})$, and $-NR^{1F1}S(O)_2R^{1F2}$, wherein each R^{1F1} and R^{1F2} is independently hydrogen or C_{1-6} alkyl, wherein each R^{1E} alkyl, cycloalkyl, aryl, and heteroaryl is optionally substituted with 1 to 3 R^{1G}, which can be the same or different,

and wherein each R^{1G} is independently C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, halogen, or cyano;

R^2 is hydrogen or C_{1-6} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkoxy, and C_{3-10} cycloalkyl; or

R^2 is C_{3-6} cycloalkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkoxy, and C_{1-6} alkyl;

each R^3 is independently selected from deuterium, halogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, -O-R^{2A1}, and -N(R^{2A1})(R^{2A2}), wherein the C_{1-6} alkyl is optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from C_{1-4} alkoxy and halogen, and wherein each R^{2A1} and R^{2A2} is independently hydrogen or C_{1-3} alkyl optionally substituted with 1 to 3 halogens, which can be the same or different;

n is 0, 1, 2, 3, or 4;

R^4 is C_{1-6} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkoxy, -C(O)N(R^{4A1}), and -N(R^{4A1})(R^{4A2}), wherein each R^{4A1} and R^{4A2} is independently hydrogen, C_{1-6} alkyl, or C_{3-10} cycloalkyl; or

R^4 is C_{3-6} cycloalkyl or 3 to 6 membered heterocyclyl having 1 or 2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein the cycloalkyl or heterocyclyl are optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkyl and C_{1-4} alkoxy;

each of X^1, X^2, X^3, and X^4 is independently selected from CH and N;

each Y^1 and Y^2 is independently hydrogen, deuterium, or C_{1-6} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from deuterium, halogen, cyano, C_{2-3} alkynyl, C_{1-4} alkoxy, and -C(O)NH-($C_{1-4}H_{3-9}$); and

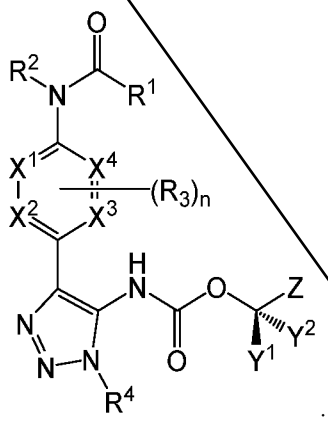
Z is C_{1-8} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{6-12} aryl, 3 to 12 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or 5 to 12 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein the alkyl, alkoxy, cycloalkyl, aryl, heterocyclyl, or heteroaryl are each optionally substituted with 1 to 3 substituents, which can be the

same or different, independently selected from halogen, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, and C_{3-6} cycloalkyl, wherein the C_{1-4} alkyl is optionally substituted with 1 to 3 substituents, which can be the same or different, selected from C_{1-4} alkoxy and halogen;

or

Y^1 and Z together with the carbon to which they are attached form C_{3-6} cycloalkyl, C_{6-12} aryl, 3 to 12 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or 5 to 12 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein the cycloalkyl, aryl, heterocyclyl, or heteroaryl are each optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from cyano, C_{1-4} alkyl, C_{1-4} alkoxy, C_{6-10} aryl, and halogen, wherein the C_{1-4} alkyl is optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from C_{1-4} alkoxy and halogen, and wherein the C_{6-10} aryl is optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from C_{1-4} alkyl, C_{1-4} alkoxy, and halogen, and Y^2 is hydrogen or deuterium.

3. The compound or pharmaceutically acceptable salt thereof of claim 1 or 2, wherein the compound is of Formula (Ia):



(Ia)

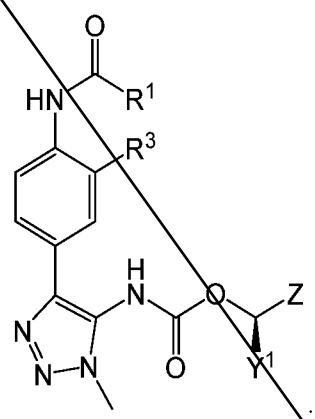
4. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein R^2 is hydrogen.

5. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-4, wherein R^4 is C_{1-3} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from -CN and -F.

6. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-5, wherein R^4 is $-CH_3$.

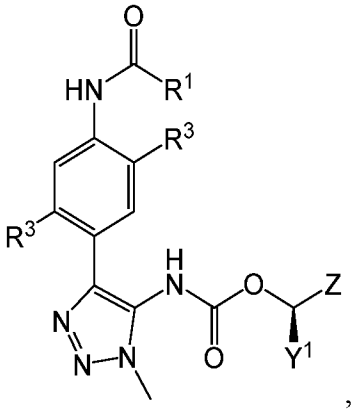
7. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-6, wherein Y^2 is hydrogen.

8. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIa):



(IIa)

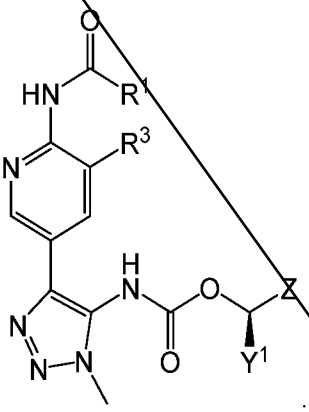
9. The compound or pharmaceutically acceptable salt thereof of any one of claim 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIb):



(IIb)

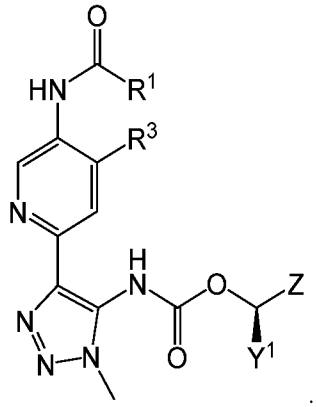
wherein each R^3 can be the same or different.

10. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIc):



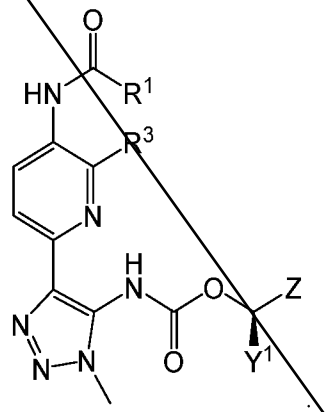
(IIc)

11. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IId):



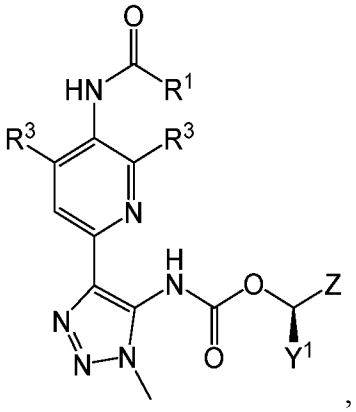
(IId)

12. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIe):



(IIe)

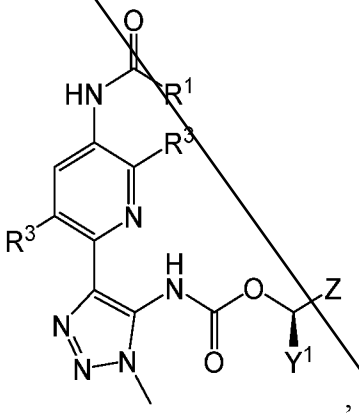
13. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIf):



(IIf)

wherein each R^3 can be the same or different.

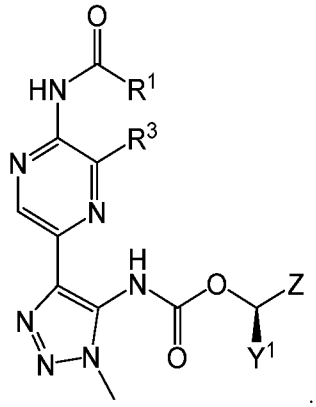
14. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIg):



(IIg)

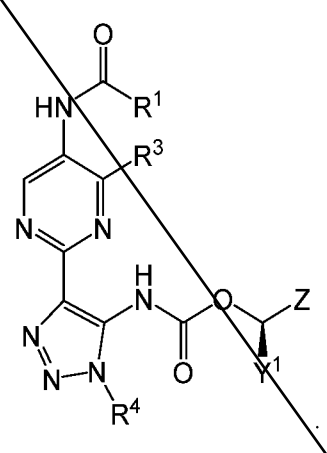
wherein each R^3 can be the same or different.

15. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIh):



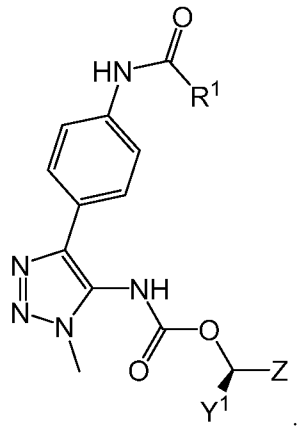
(IIh)

16. The compound or pharmaceutically acceptable salt thereof of claim 1 or 2, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIi):



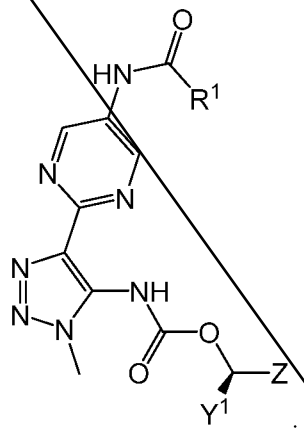
(IIi)

17. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIj):



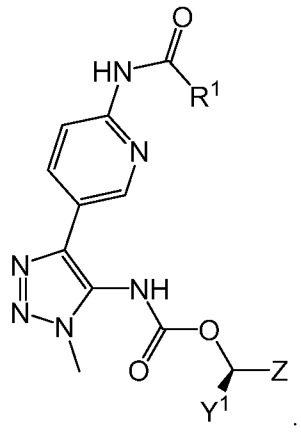
(IIj)

18. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIk):



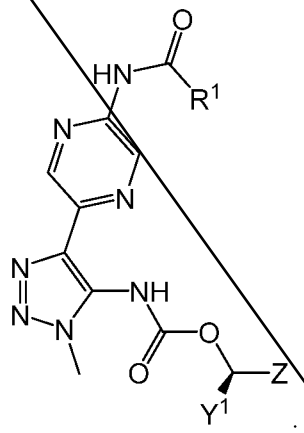
(IIk)

19. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIl):



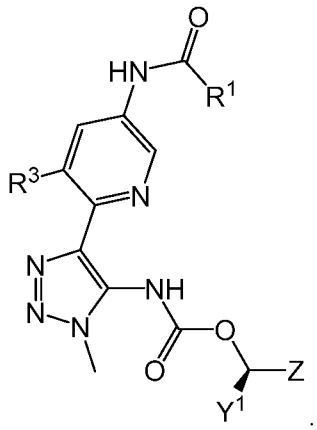
(IIl)

20. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIm):



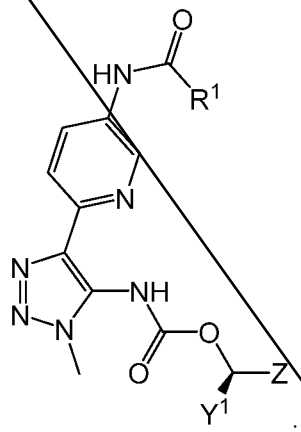
(IIm)

21. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIn):



(IIn)

22. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-3, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIo):



(IIo)

23. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22, wherein R^1 is hydrogen.

24. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22, wherein R^1 is C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, nitro, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and

sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, $–N(R^{1B1})(R^{1B2})$, $-O-R^{1B1}$, $-S-R^{1B1}$, $–C(O)N(R^{1B1})(R^{1B2})$, $–NR^{1B1}C(O)R^{1B2}$, $-NR^{1B1}C(O)N(R^{1B2})(R^{1B3})$, $–S(O)_{0-2}R^{1B1}$, $–S(O)_2N(R^{1B1})(R^{1B2})$, and $–NR^{1B1}S(O)_2R^{1B2}$, wherein each R^{1B1}, R^{1B2}, and R^{1B3} is independently hydrogen, C_{1-6} alkyl, or C_{3-6} cycloalkyl,

wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, $-O-R^{1D1}$, or $-N(R^{1D1})(R^{1D2})$, wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl, and

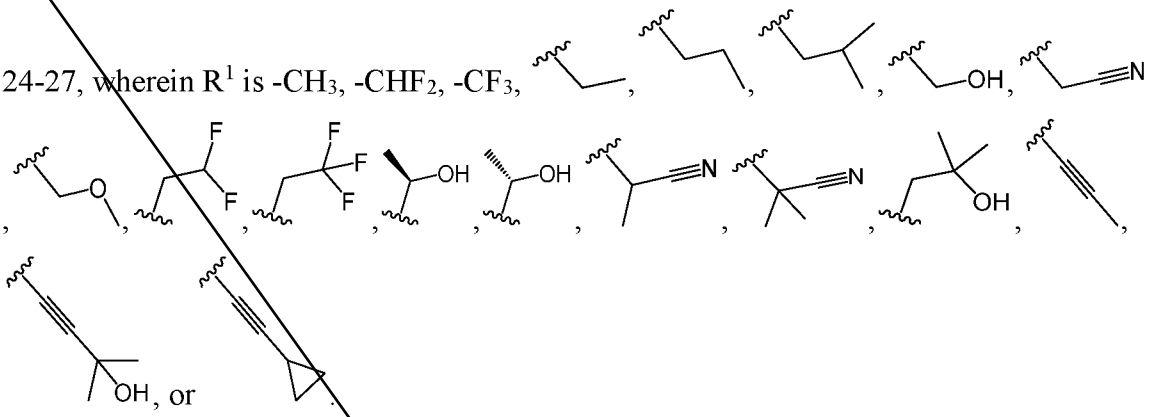
wherein each R^{1B1}, R^{1B2}, and R^{1B3} alkyl and each R^{1B1}, R^{1B2}, and R^{1B3} cycloalkyl is optionally substituted with 1 to 3 halogens.

25. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22, wherein R^1 is C_{1-6} alkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, $–N(R^{1B1})(R^{1B2})$, $-O-R^{1B1}$, $-S-R^{1B1}$, $–C(O)N(R^{1B1})(R^{1B2})$, $–NR^{1B1}C(O)R^{1B2}$, $-NR^{1B1}C(O)N(R^{1B2})(R^{1B3})$, $–S(O)_{0-2}R^{1B1}$, $–S(O)_2N(R^{1B1})(R^{1B2})$, and $–NR^{1B1}S(O)_2R^{1B2}$, wherein each R^{1B1}, R^{1B2}, and R^{1B3} is independently hydrogen or C_{1-6} alkyl,

wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, $-O-R^{1D1}$, or $-N(R^{1D1})(R^{1D2})$, wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl.

26. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22, 24 and 25, wherein R^1 is C_{1-6} alkyl or C_{2-6} alkynyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, hydroxy, C_{1-4} alkoxy, and C_{3-6} cycloalkyl.

27. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 24-26, wherein R^1 is C_{1-6} alkyl or C_{2-6} alkynyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from -F, -CN, -OH, $-OCH_3$, or cyclopropyl.

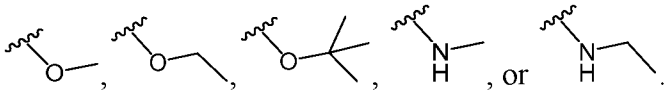
28. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 24-27, wherein R^1 is $-CH_3$, $-CHF_2$, $-CF_3$, , or .

29. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22, wherein R^1 is $-O-R^{1D1}$ or $-N(R^{1D1})(R^{1D2})$, wherein each R^{1D1} and R^{1D2} is independently hydrogen, C_{1-6} alkyl, or C_{3-6} cycloalkyl, wherein each C_{1-6} alkyl, or C_{3-6} cycloalkyl is optionally substituted with 1 to 4 R^{1E}, which can be the same or different, wherein each R^{1E} is independently selected from halogen, cyano, hydroxy, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, $-O-R^{1F1}$, $-N(R^{1F1})(R^{1F2})$, $-C(O)N(R^{1F1})(R^{1F2})$, $-NR^{1F1}C(O)R^{1F2}$, $-S(O)_{0-2}R^{1F1}$, $-S(O)_2N(R^{1F1})(R^{1F2})$, and $-NR^{1F1}S(O)_2R^{1F2}$, wherein each R^{1F1} and R^{1F2} is independently hydrogen or C_{1-6} alkyl, wherein each R^{1E} alkyl, cycloalkyl, aryl, and heteroaryl is optionally substituted with 1 to 3 R^{1G}, which can be the same or different, and wherein each R^{1G} is independently C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, halogen, or cyano.

30. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 29, wherein R^1 is $-O-R^{1D1}$ or $-N(R^{1D1})(R^{1D2})$, wherein each R^{1D1} and R^{1D2} is independently hydrogen, C_{1-6} alkyl, or C_{3-6} cycloalkyl, wherein each C_{1-6} alkyl, or C_{3-6} cycloalkyl is optionally substituted with 1 to 3 R^{1E}, which can be the same or different, wherein each

R^{1E} is independently selected from halogen and -C(O)N(R^{1F1})(R^{1F1}), wherein each R^{1F1} and R^{1F1} is independently hydrogen or C_{1-4} alkyl.

31. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 29-30, wherein R^1 is -O-R^{1D1} or -N(R^{1D1})(R^{1D2}), wherein each R^{1D} and R^{1D2} is independently -H, -CH_3, -C_2H_5, or -$C(CH_3)_3$.

32. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 29-31, wherein R^1 is .

33. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22, wherein R^1 is C_{3-10} cycloalkyl optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, nitro, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, –N(R^{1B1})(R^{1B2}), -O-R^{1B1}, -S-R^{1B1}, –C(O)N(R^{1B1})(R^{1B2}), –NR^{1B1}C(O)R^{1B2}, -NR^{1B1}C(O)N(R^{1B2})(R^{1B3}), –S(O)$_{0-2}$$R^{1B1}$, –S(O)$_2$N($R^{1B1}$)($R^{1B2}$), and –N$R^{1B1}$S(O)$_2$$R^{1B2}$, wherein each R^{1B1} , R^{1B2}, and R^{1B3} is independently hydrogen, C_{1-6} alkyl, or -C_{3-6} cycloalkyl,

wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, -O-R^{1D1}, or -N(R^{1D1})(R^{1D2}), wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl, and

wherein each R^{1B1} and R^{1B2} alkyl and each R^{1B1} and R^{1B2} cycloalkyl is optionally substituted with 1 to 3 halogens.

34. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 33, wherein R^1 is C_{3-10} cycloalkyl optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen and oxygen, –N(R^{1B1})(R^{1B2}),

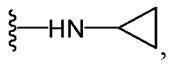
-O-R^{1B1}, –C(O)N(R^{1B1})(R^{1B2}), wherein each R^{1B1} and R^{1B2} is independently hydrogen, or C_{1-6} alkyl,

wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, -O-R^{1D1}, or -N(R^{1D1})(R^{1D2}), wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl.

35. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 33 or 34, wherein R^1 is C_{3-10} cycloalkyl optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, nitro, C_{1-4} alkyl, 3 to 6 membered heterocyclyl having 1 to 2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 5 or 6 membered heteroaryl having 1 or 2 heteroatoms independently selected from nitrogen or oxygen, –N(R^{1B1})(R^{1B2}), -OR^{1B1}, and –C(O)N(R^{1B1})(R^{1B2}), wherein each R^{1B1} and R^{1B2} is independently hydrogen, C_{1-4} alkyl, or C_{3-6} cycloalkyl, and wherein each R^{1A} C_{1-4} alkyl is optionally substituted with 1 to 3 halogens, and each heteroaryl in R^{1A} is optionally substituted with 1 to 3 C_{1-4} alkyl, wherein each R^{1B1} and R^{1B2} alkyl and each R^{1B1} and R^{1B2} cycloalkyl is optionally substituted with 1 to 3 halogens.

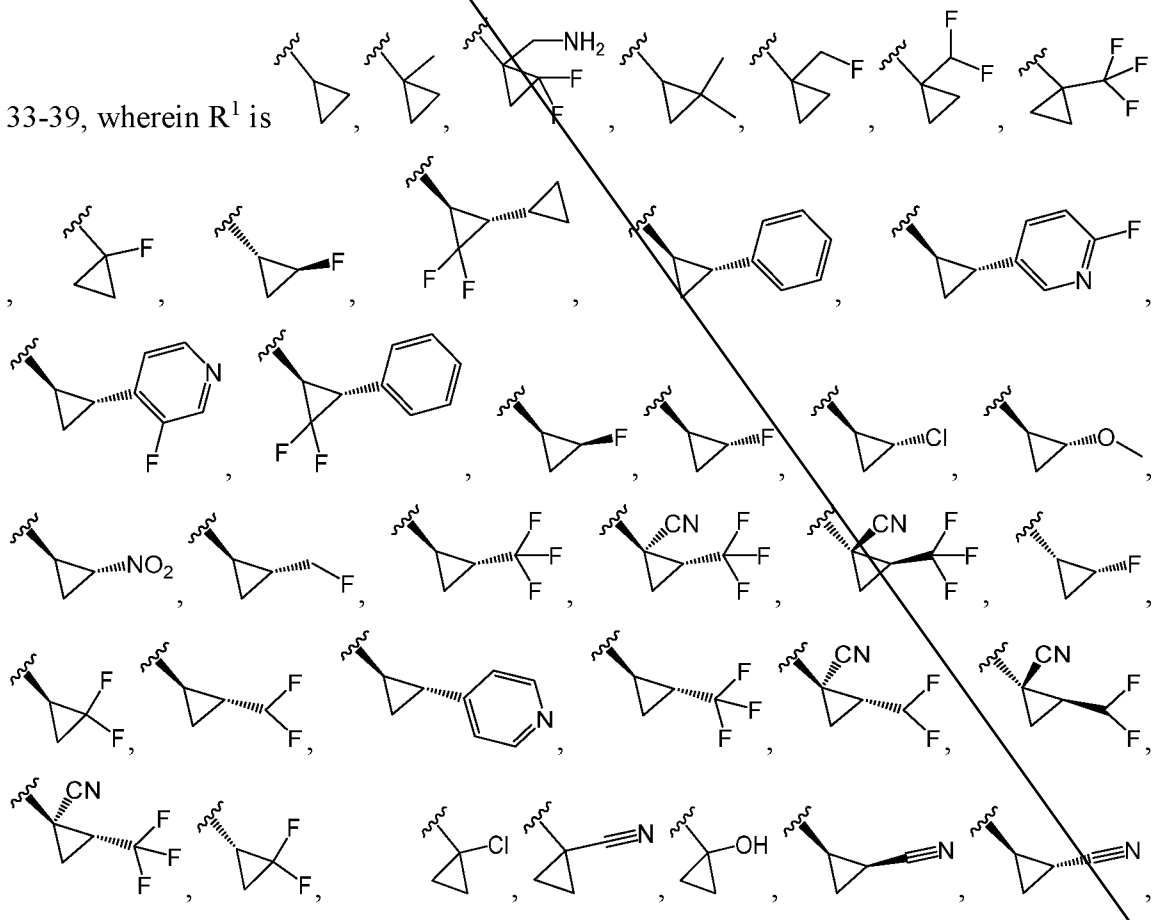
36. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 33-35, wherein R^1 is C_{3-10} cycloalkyl optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, C_{1-4} alkyl, 3 to 6 membered heterocyclyl having 1 to 2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 5 or 6 membered heteroaryl having 1 or 2 heteroatoms independently selected from nitrogen or oxygen, –N(R^{1B1})(R^{1B2}), -OR^{1B1}, and –C(O)N(R^{1B1})(R^{1B2}), wherein each R^{1B1} and R^{1B2} is independently hydrogen or C_{1-4} alkyl, and wherein each R^{1A} C_{1-4} alkyl is optionally substituted with 1 to 3 halogens, and each heteroaryl in R^{1A} is optionally substituted with 1 to 3 C_{1-4} alkyl.

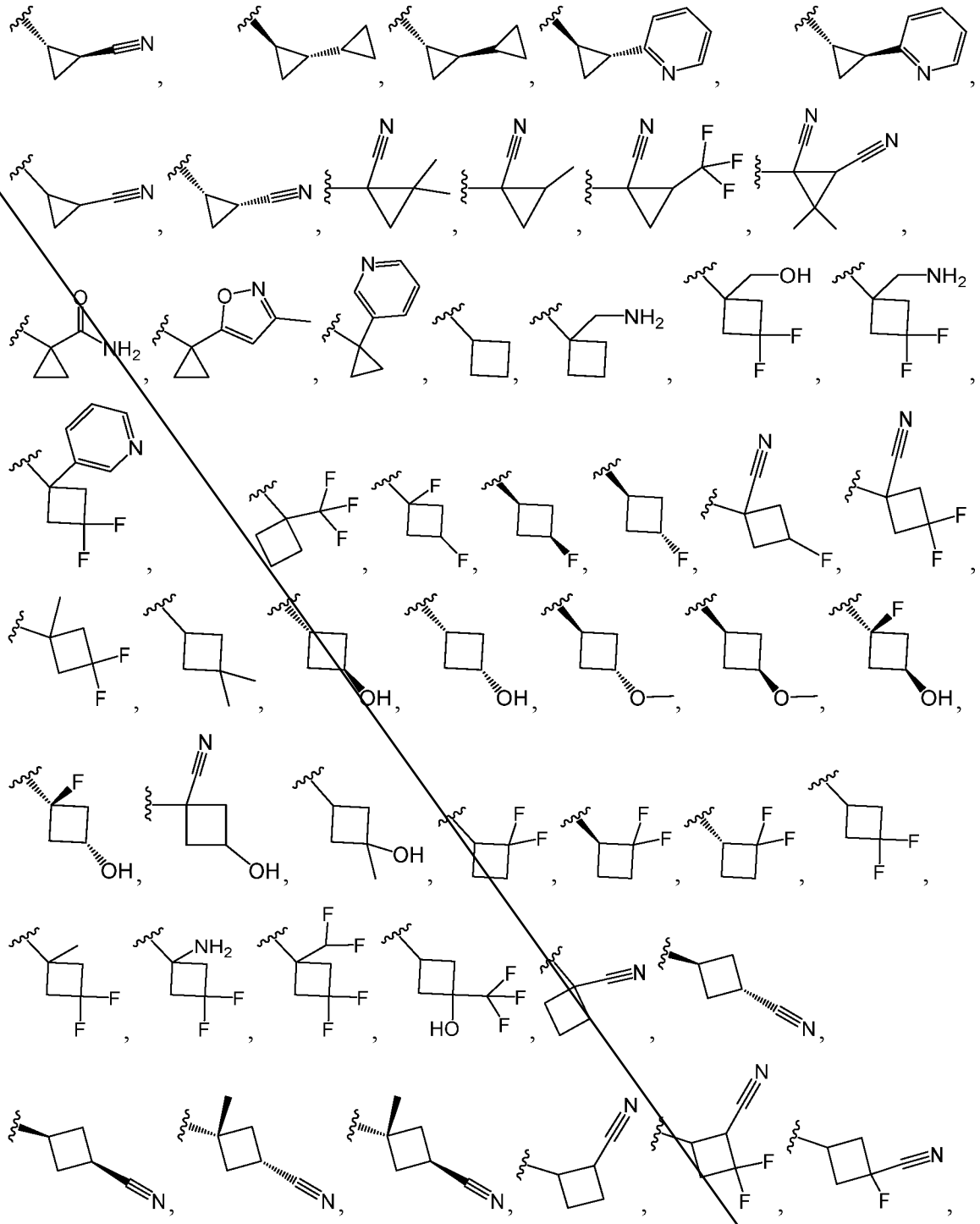
37. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 33-36, wherein R^1 is cyclopropyl or cyclobutyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, each independently selected from -F, -Cl, -CN, =O, -OH, -CH_3, -CH_2F, -CHF_2, -CF_3, -CH_2-OH, -CH_2-NH_2, -OCH_3, -NH_2, -NH-CH_2-CF_3,

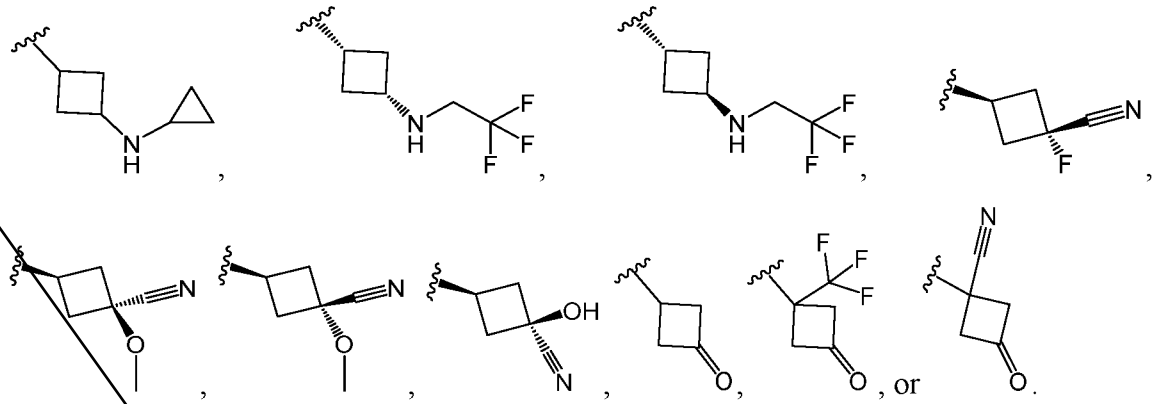
, $-NO_2$, cyclopropyl, isoxazyl, phenyl, pyridyl, and $-C(O)NH_2$, wherein each isoxazyl or pyridyl is optionally substituted with 1 to 2 -F or $-CH_3$.

38. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 33-37, wherein R^1 is cyclopropyl or cyclobutyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, each independently selected from -F, -Cl, -CN, =O, -OH, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-CH_2$-OH, $-CH_2-NH_2$, $-OCH_3$, $-NH_2$, cyclopropyl, isoxazyl, phenyl, pyridyl, and $-C(O)NH_2$, wherein each isoxazyl or pyridyl is optionally substituted with 1 to 2 -F or $-CH_3$.

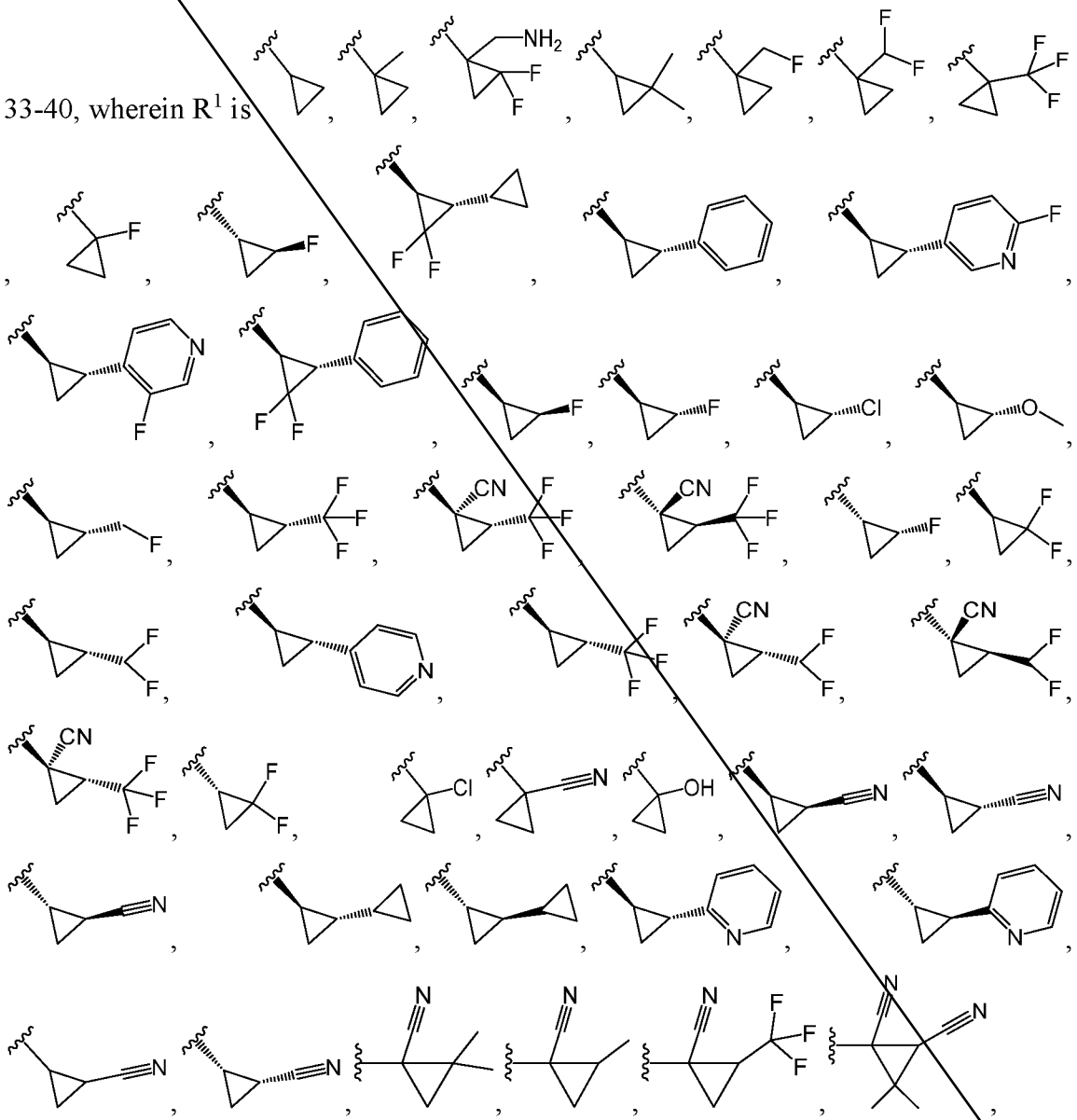
39. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 33-37, wherein R^1 is cyclopropyl or cyclobutyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, each independently selected from -F, -Cl, -CN, =O, -OH, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-OCH_3$, isoxazyl, pyridyl, and $-C(O)NH_2$, wherein each isoxazyl or pyridyl is optionally substituted with 1 to 2 $-CH_3$.

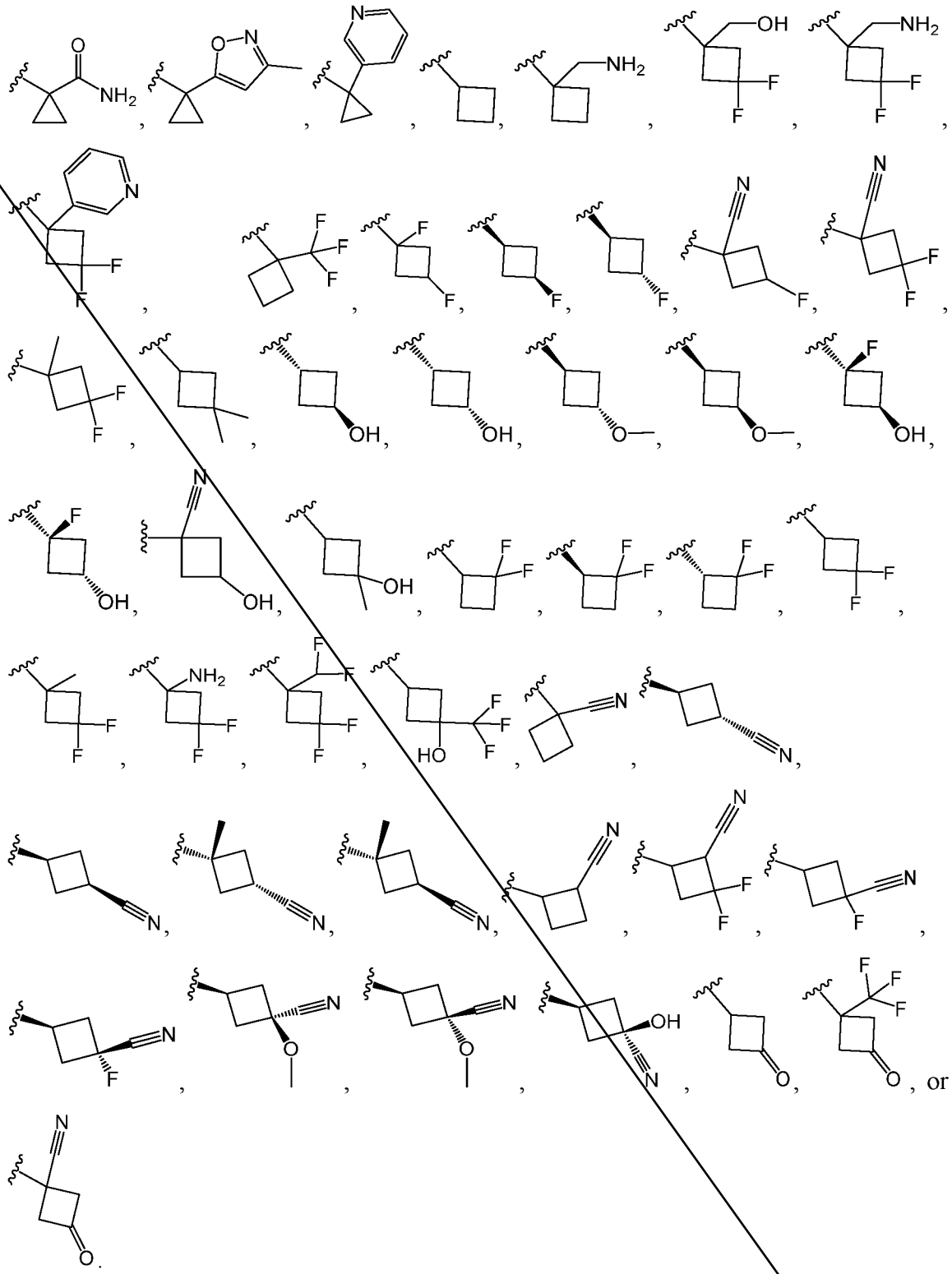
40. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 33-39, wherein R^1 is 

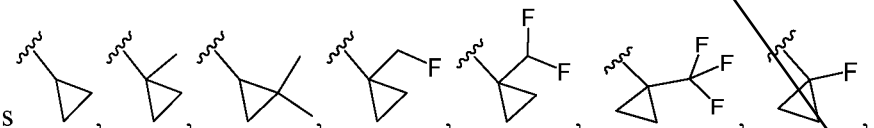


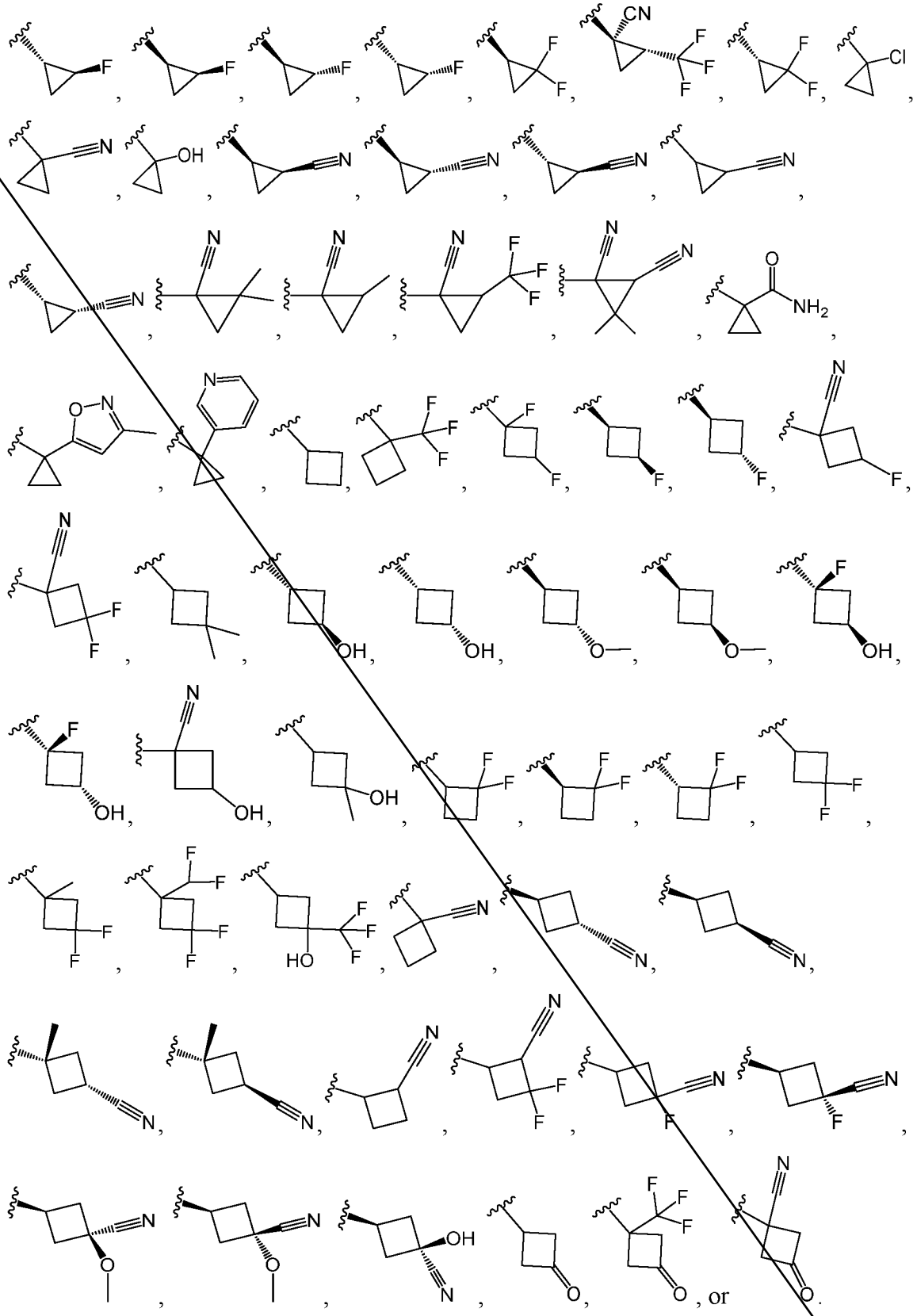


41. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 33-40, wherein R^1 is





42. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 33-36, wherein R^1 is ,

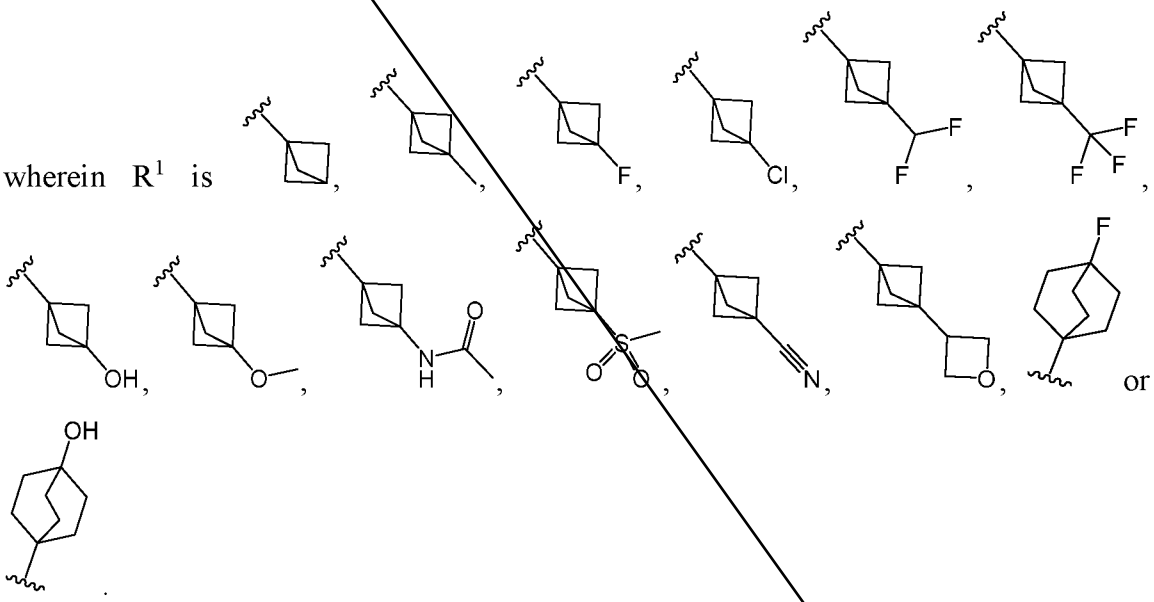


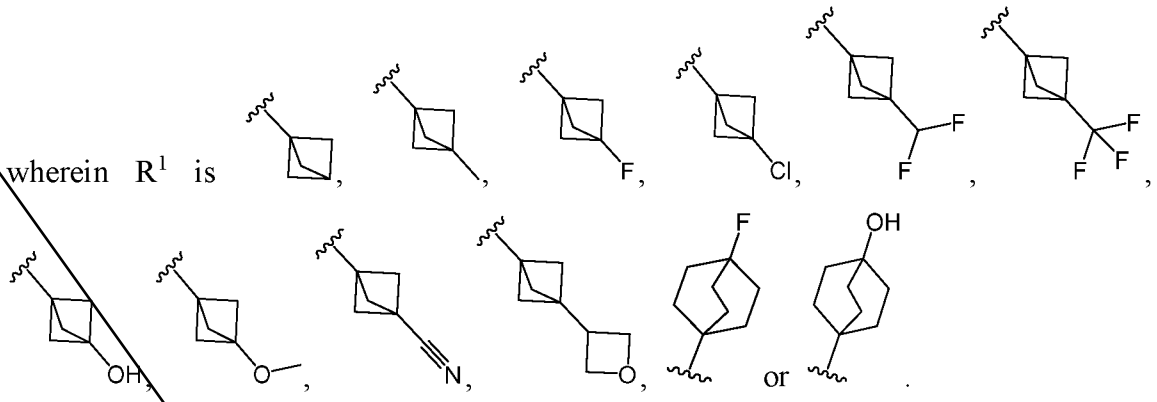
43. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 22 and 33-36, wherein the C_{3-10} cycloalkyl is a C_{5-10} bicyclic cycloalkyl.

44. The compound or pharmaceutically acceptable salt thereof of claim 43, wherein the C_{5-10} bicyclic cycloalkyl is a C_{5-8} bridged bicyclic cycloalkyl.

45. The compound or pharmaceutically acceptable salt thereof of claim 44, wherein the C_{5-8} bridged bicyclic cycloalkyl is bicyclopentanyl or bicyclooctanyl, each optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from -F, -Cl, -OH, -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-O-CH_3$, $-NH-CO-CH_3$, $-SO_2-CH_3$, and oxetanyl.

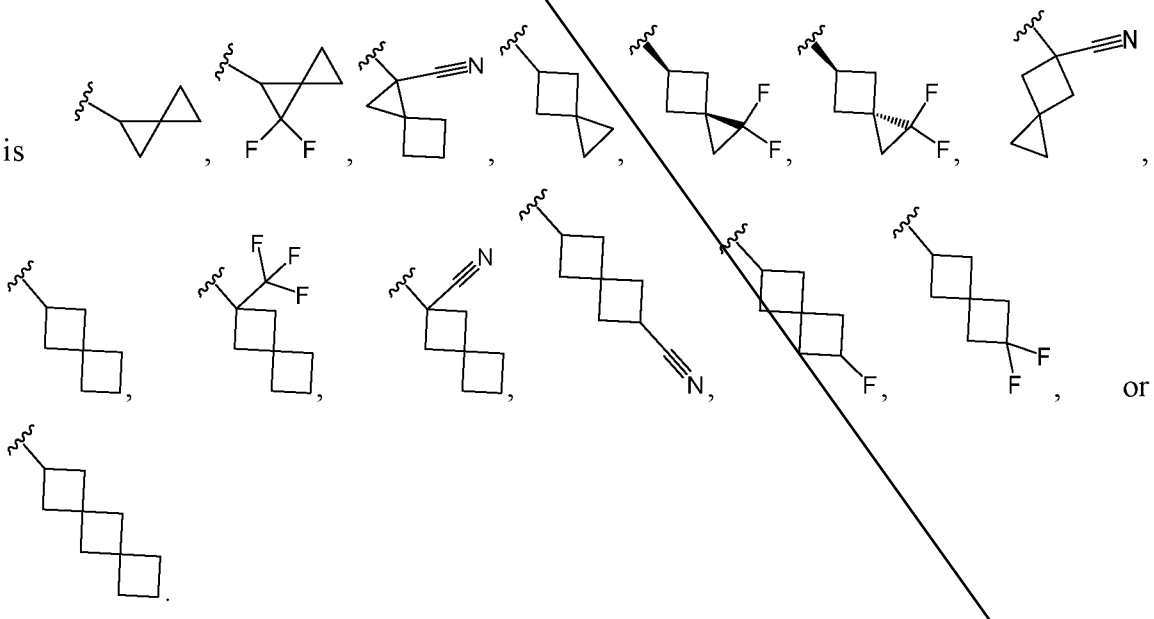
46. The compound or pharmaceutically acceptable salt thereof of claim 44 or 45, wherein the C_{5-8} bridged bicyclic cycloalkyl is bicyclopentanyl or bicyclooctanyl, each optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from -F, -Cl, -OH, -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-O-CH_3$, and oxetanyl.

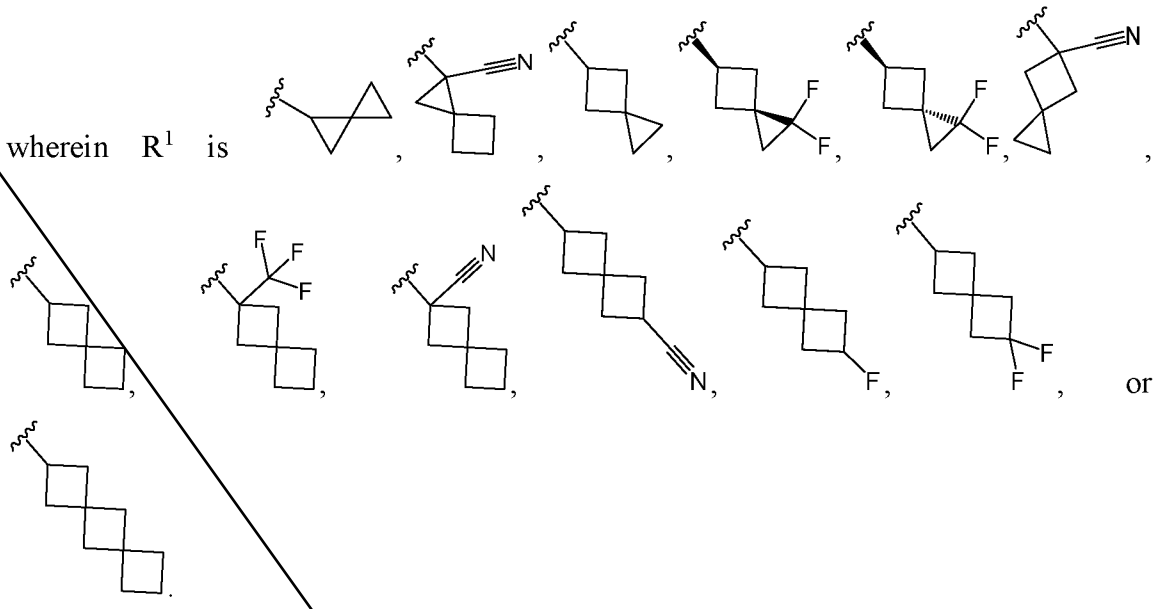
47. The compound or pharmaceutically acceptable salt thereof of any one of claims 44-46, wherein R^1 is .

48. The compound or pharmaceutically acceptable salt thereof of any one of claims 44-47, wherein R^1 is .

49. The compound or pharmaceutically acceptable salt thereof of claim 43, wherein the C_{5-10} bicyclic cycloalkyl is a C_{5-10} spiro bicyclic cycloalkyl.

50. The compound or pharmaceutically acceptable salt thereof of claim 49, wherein the C_{5-10} spiro bicyclic cycloalkyl is spiropentanyl, spirohexanyl, spiroheptanyl, or spirodecanyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is each independently selected from -F, -Cl, -OH, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, -CN, and $-O-CH_3$.

51. The compound or pharmaceutically acceptable salt thereof of claim 49 or 50, wherein R^1 is .

52. The compound or pharmaceutically acceptable salt thereof of any one of claims 49-50, wherein R^1 is .

53. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22, wherein R^1 is 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, nitro, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, $–N(R^{1B1})(R^{1B2})$, $-O-R^{1B1}$, $-S-R^{1B1}$, $–C(O)N(R^{1B1})(R^{1B2})$, $–NR^{1B1}C(O)R^{1B2}$, $-NR^{1B1}C(O)N(R^{1B2})(R^{1B3})$, $–S(O)_{0-2}R^{1B1}$, $–S(O)_2N(R^{1B1})(R^{1B2})$, and $–NR^{1B1}S(O)_2R^{1B2}$, wherein each R^{1B1}, R^{1B2}, and R^{1B3} is independently hydrogen, C_{1-6} alkyl or $-C_{3-6}$ cycloalkyl,

wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, $-O-R^{1D1}$, or $-N(R^{1D1})(R^{1D2})$, wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl,

wherein each R^{1B1} and R^{1B2} alkyl and each R^{1B1} and R^{1B2} cycloalkyl is optionally substituted with 1 to 3 halogens.

54. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22, wherein R^1 is 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, $-N(R^{1B1})(R^{1B2})$, $-O-R^{1B1}$, $-S-R^{1B1}$, $-C(O)N(R^{1B1})(R^{1B2})$, $-NR^{1B1}C(O)R^{1B2}$, $-NR^{1B1}C(O)N(R^{1B2})(R^{1B3})$, $-S(O)_{0-2}R^{1B1}$, $-S(O)_2N(R^{1B1})(R^{1B2})$, and $-NR^{1B1}S(O)_2R^{1B2}$, wherein each R^{1B1} , R^{1B2}, and R^{1B3} is independently hydrogen or C_{1-6} alkyl,

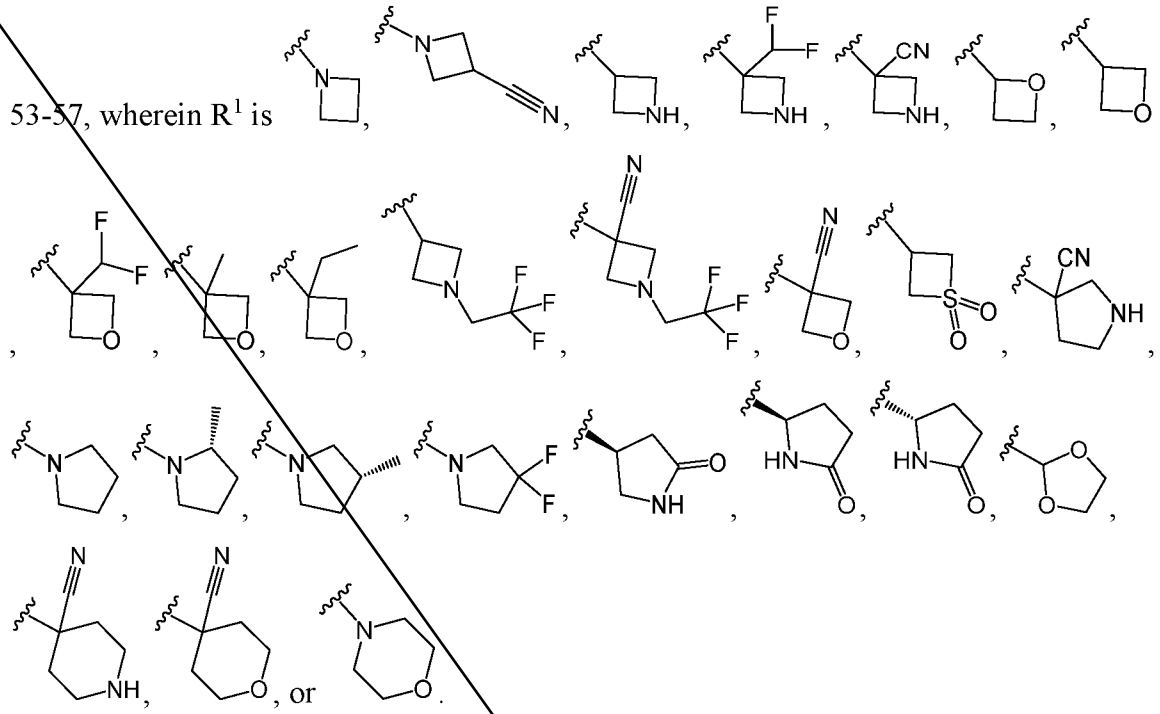
wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, $-O-R^{1D1}$, or $-N(R^{1D1})(R^{1D2})$, wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl.

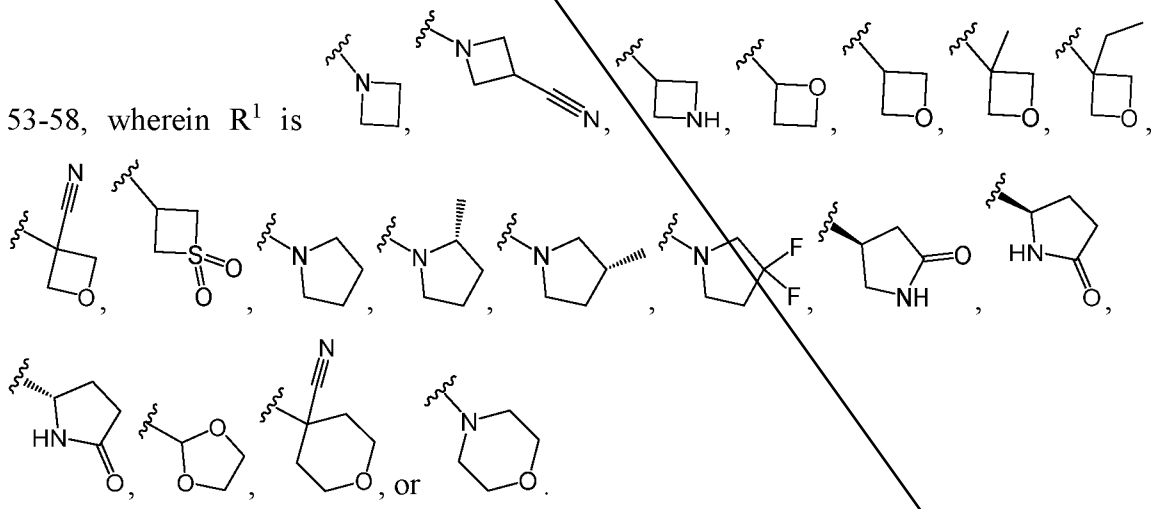
55. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 53-54, wherein R^1 is 3 to 8 membered heterocyclyl having 1 to 2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, optionally substituted with 1 to 4 R^{1A}, which can be the same or different, each independently selected from halogen, cyano, oxo, or C_{1-4} alkyl, wherein each R^{1A} C_{1-4} alkyl is optionally substituted with 1 to 3 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkoxy, halogen, or cyano.

56. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 53-55, wherein R^1 is azetidinyl, oxetyl, thietanyl, pyrrolidinyl, dioxolanyl, tetrahydropyranyl, piperidinyl, or morpholinyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, each independently selected from -F, -Cl, -OH, -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-C_2H_5$, $-CH_2-CF_3$, and $-O-CH_3$.

57. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 53-56, wherein R^1 is azetidinyl, oxetyl, thietanyl, pyrrolidinyl, dioxolanyl, tetrahydropyranyl, or morpholinyl, each optionally substituted with 1 to 4 R^{1A}, which can

be the same or different, each independently selected from -F, -Cl, -OH, -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, and $-O-CH_3$.

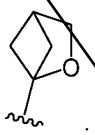
58. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 53-57, wherein R^1 is , or .

59. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 53-58, wherein R^1 is , or .

60. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 22 and 53-55, wherein the 3 to 10 membered heterocyclyl forms a bicyclic heterocyclyl.

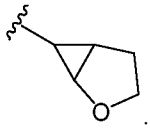
61. The compound or pharmaceutically acceptable salt thereof of claim 60, wherein the bicyclic heterocyclyl is a bridged bicyclic heterocyclyl.

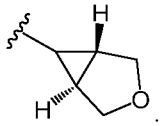
62. The compound or pharmaceutically acceptable salt thereof of claim 61, wherein the bridged bicyclic heterocyclyl is an oxabicyclohexanyl optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from -F, -Cl, -OH, -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, and $-O-CH_3$.

63. The compound or pharmaceutically acceptable salt thereof of claim 52, wherein R^1 is .

64. The compound or pharmaceutically acceptable salt thereof of claim 60, wherein the bicyclic heterocyclyl is a fused bicyclic heterocyclyl.

65. The compound or pharmaceutically acceptable salt thereof of claim 64, wherein the fused bicyclic heterocyclyl is an oxabicyclohexanyl optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from -F, -Cl, -OH, -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, and $-O-CH_3$.

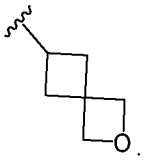
66. The compound or pharmaceutically acceptable salt thereof of claim 65, wherein R^1 is .

67. The compound or pharmaceutically acceptable salt thereof of claim 65 or 66, wherein R^1 is .

68. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 60, wherein the 3 to 10 membered heterocyclyl is a spiro bicyclic heterocyclyl.

69. The compound or pharmaceutically acceptable salt thereof of claim 68, wherein the spiro bicyclic heterocyclyl is an oxaspiroheptane optionally substituted with 1 to 4 substituents, which can be the same or different, each independently selected from -F, -Cl, -OH, -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, and $-O-CH_3$.

70. The compound or pharmaceutically acceptable salt thereof of claim 69, wherein R^1 is



71. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22, wherein R^1 is 6 to 10 membered aryl optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, nitro, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, $-N(R^{1B1})(R^{1B2})$, $-O-R^{1B1}$, $-S-R^{1B1}$, $-C(O)N(R^{1B1})(R^{1B2})$, $-NR^{1B1}C(O)R^{1B2}$, $-NR^{1B1}C(O)N(R^{1B2})(R^{1B3})$, $-S(O)_{0-2}R^{1B1}$, $-S(O)_2N(R^{1B1})(R^{1B2})$, and $-NR^{1B1}S(O)_2R^{1B2}$, wherein each R^{1B1}, R^{1B2}, and R^{1B3} is independently hydrogen, C_{1-6} alkyl, or $-C_{3-6}$ cycloalkyl,

wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, $-O-R^{1D1}$, or $-N(R^{1D1})(R^{1D2})$, wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl,

wherein each R^{1B1} and R^{1B2} alkyl and each R^{1B1} and R^{1B2} cycloalkyl is optionally substituted with 1 to 3 halogens.

72. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22, wherein R^1 is 6 to 10 membered aryl optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, $-N(R^{1B1})(R^{1B2})$, $-O-R^{1B1}$, $-S-R^{1B1}$, $-C(O)N(R^{1B1})(R^{1B2})$, $-NR^{1B1}C(O)R^{1B2}$, $-NR^{1B1}C(O)N(R^{1B2})(R^{1B3})$, $-S(O)_{0-2}R^{1B1}$, $-S(O)_2N(R^{1B1})(R^{1B2})$, and $-NR^{1B1}S(O)_2R^{1B2}$, wherein each R^{1B1} , R^{1B2}, and R^{1B3} is independently hydrogen or C_{1-6} alkyl,

wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, -O-R^{1D1}, or -N(R^{1D1})(R^{1D2}), wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl.

73. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 71-72, wherein R^1 is phenyl optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, C_{1-3} alkyl, or C_{1-4} alkoxy.

74. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 71-73, wherein R^1 is phenyl optionally substituted with 1 to 3 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from -F, -Cl, -CN, or -CH_3.

75. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22, wherein R^1 is 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, nitro, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, –N(R^{1B1})(R^{1B2}), -O-R^{1B1}, -S-R^{1B1}, –C(O)N(R^{1B1})(R^{1B2}), –NR^{1B1}C(O)R^{1B2}, -NR^{1B1}C(O)N(R^{1B2})(R^{1B3}), –S(O)$_{0-2}$$R^{1B1}$, –S(O)$_2$N($R^{1B1}$)($R^{1B2}$), and –N$R^{1B1}$S(O)$_2$$R^{1B2}$, wherein each R^{1B1}, R^{1B2}, and R^{1B3} is independently hydrogen, C_{1-6} alkyl or -C_{3-6} cycloalkyl,

wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, -O-R^{1D1}, or -N(R^{1D1})(R^{1D2}), wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl,

wherein each R^{1B1} and R^{1B2} alkyl and each R^{1B1} and R^{1B2} alkyl cycloalkyl is optionally substituted with 1 to 3 halogens.

76. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22, wherein R^1 is 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, $-N(R^{1B1})(R^{1B2})$, $-O-R^{1B1}$, $-S-R^{1B1}$, $-C(O)N(R^{1B1})(R^{1B2})$, $-NR^{1B1}C(O)R^{1B2}$, $-NR^{1B1}C(O)N(R^{1B2})(R^{1B3})$, $-S(O)_{0-2}R^{1B1}$, $-S(O)_2N(R^{1B1})(R^{1B2})$, and $-NR^{1B1}S(O)_2R^{1B2}$, wherein each R^{1B1} , R^{1B2}, and R^{1B3} is independently hydrogen or C_{1-6} alkyl,

wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, $-O-R^{1D1}$, or $-N(R^{1D1})(R^{1D2})$, wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl.

77. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 75-76, wherein R^1 is imidazolyl, pyrazolyl, pyridinyl, oxazolyl, isoxazolyl, oxadiazolyl, pyridinonyl, pyrimidinyl, pyridazinyl, benzoisoxazolyl, pyrazolopyridinyl, imidazopyridinyl, or benzoimidazolyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen and oxygen, $-N(R^{1B1})(R^{1B2})$, $-O-R^{1B1}$, and $-S(O)_{0-2}R^{1B1}$, wherein each R^{1B1} and R^{1B2} is independently hydrogen or C_{1-6} alkyl,

wherein each R^{1A} alkyl, cycloalkyl, and heterocyclyl, is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, or cyano.

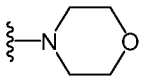
78. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 75-77, wherein R^1 is imidazolyl, pyrazolyl, pyridinyl, oxazolyl, isoxazolyl, oxadiazolyl, pyridinonyl, pyrimidinyl, pyridazinyl, benzoisoxazolyl, pyrazolopyridinyl, imidazopyridinyl, or benzoimidazolyl, each optionally substituted with 1 to 4 R^{1A}, which

can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, oxo, methyl, cyclopropyl, morpholinyl, $-N(R^{1B1})(R^{1B2})$, $-O-R^{1B1}$, and $-S(O)_{0-2}R^{1B1}$, wherein each R^{1B1} and R^{1B2} is independently hydrogen or methyl,

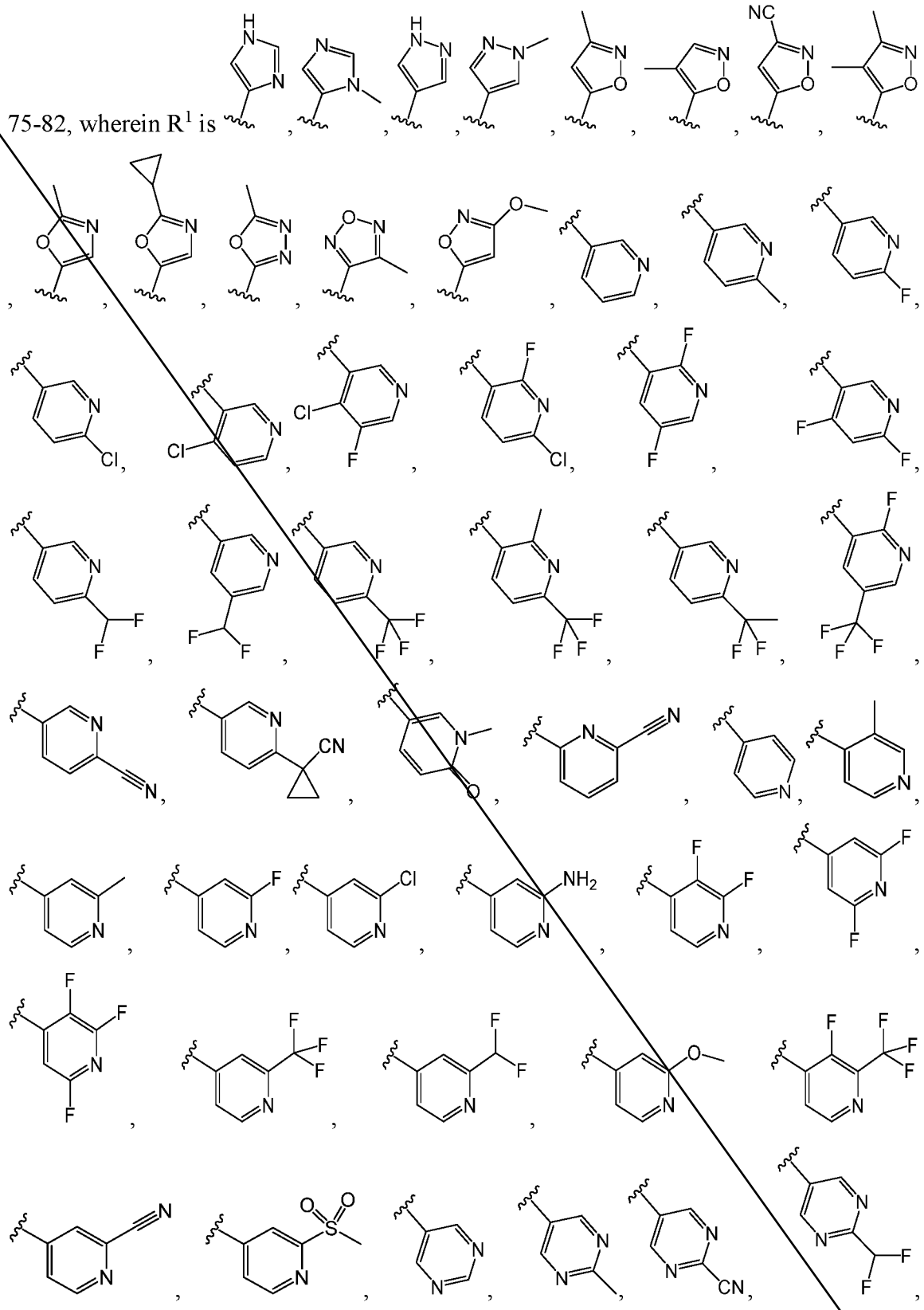
wherein each R^{1A} methyl, cyclopropyl, and morpholinyl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently methyl, halogen, or cyano.

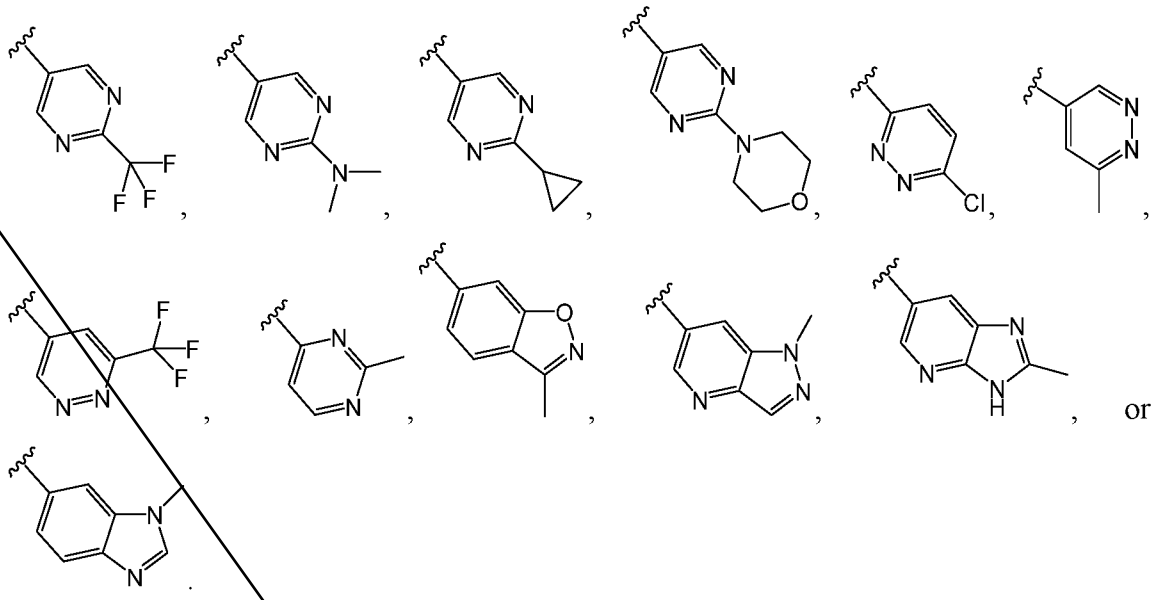
79. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 75-78, wherein R^1 is imidazolyl, pyrazolyl, pyridinyl, oxazolyl, isoxazolyl, oxadiazolyl, pyridinonyl, pyrimidinyl, pyridazinyl, benzoisoxazolyl, pyrazolopyridinyl, imidazopyridinyl, or benzoimidazolyl, each optionally substituted with 1 to 4 substituents, which can be the same or different, each independently selected from halogen, cyano, C_{1-4} alkyl, or C_{1-4} alkoxy.

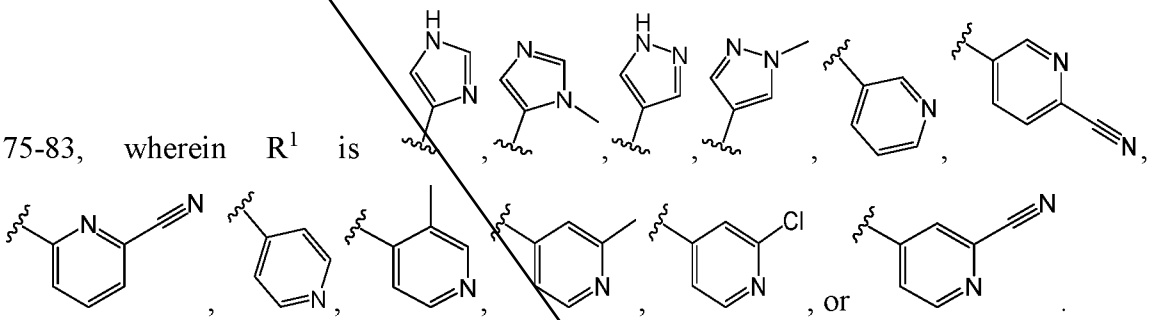
80. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 75-79, wherein R^1 is imidazolyl, pyrazolyl, or pyridinyl, each optionally substituted with 1 to 4 substituents, which can be the same or different, each independently selected from halogen, cyano, C_{1-4} alkyl, or C_{1-4} alkoxy.

81. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 75-80, wherein R^1 is imidazolyl, pyrazolyl, pyridinyl, oxazolyl, isoxazolyl, oxadiazolyl, pyridinonyl, pyrimidinyl, pyridazinyl, benzoisoxazolyl, pyrazolopyridinyl, imidazopyridinyl, or benzoimidazolyl, each optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from -F, -Cl, -CN, $-CH_3$, $-CHF_2$, $-CF_3$, $-OCH_3$, $-NH_2$, $-N(CH_3)_2$, $-SO_2-CH_3$, , , or .

82. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 75-81, wherein R^1 is imidazolyl, pyrazolyl, or pyridinyl, each optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from -F, -Cl, -CN, or $-CH_3$.

83. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 75-82, wherein R^1 is 



84. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-22 and 75-83, wherein R^1 is 

85. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-84, wherein each R^3 is independently selected from deuterium, halogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, -O-R^{2A1}, and -N(R^{2A1})(R^{2A2}), wherein the C_{1-6} alkyl is optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from C_{1-4} alkoxy and halogen, and wherein each R^{2A1} and R^{2A2} is independently hydrogen or C_{1-4} alkyl optionally substituted with 1 to 3 halogens, which can be the same or different.

86. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-85, wherein each R^3 is independently selected from C_{1-6} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkoxy, and C_{3-10} cycloalkyl.

87. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-86, wherein R^3 is $-CH_3$.

88. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-85, wherein R^3 is halogen.

89. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-85, wherein R^3 is -F.

90. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein n is 0, 1, or 2.

91. The compound or pharmaceutically acceptable salt thereof of claim 90, wherein n is 0.

92. The compound or pharmaceutically acceptable salt thereof of claim 90, wherein n is 1.

93. The compound or pharmaceutically acceptable salt thereof of claim 90, wherein n is 2.

94. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is CH, X^2 is CH, X^3 is CH, and X^4 is CH.

95. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is $C(R^3)$, X^2 is CH, X^3 is CH, and X^4 is CH.

96. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is $C(R^3)$, X^2 is CH, X^3 is $C(R^3)$, and X^4 is CH.

97. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is N, X^2 is CH, X^3 is CH, and X^4 is $C(R^3)$.

98. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is CH, X^2 is N, X^3 is CH, and X^4 is $C(R^3)$.

99. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is $C(R^3)$, X^2 is N, X^3 is CH, and X^4 is CH.

100. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is $C(R^3)$, X^2 is N, X^3 is CH, and X^4 is $C(R^3)$.

101. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is $C(R^3)$, X^2 is CH, X^3 is $C(R^3)$, and X^4 is CH.

102. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is N, X^2 is CH, X^3 is N, and X^4 is $C(R^3)$.

103. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is $C(R^3)$, X^2 is N, X^3 is N, and X^4 is CH.

104. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is CH, X^2 is N, X^3 is N, and X^4 is CH.

105. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is N, X^2 is CH, X^3 is CH, and X^4 is CH.

106. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is N, X^2 is CH, X^3 is N, and X^4 is CH.

107. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is CH, X^2 is N, X^3 is $C(R^3)$, and X^4 is CH.

108. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-7 and 23-89, wherein X^1 is CH, X^2 is N, X^3 is CH, and X^4 is CH.

109. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-6 and 23-108, wherein each Y^1 and Y^2 is independently hydrogen, deuterium, or C_{1-6} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{2-3} alkynyl, C_{1-4} alkoxy, and $-C(O)NH-(C_{1-4}H_{3-9})$.

110. The compound or pharmaceutically acceptable salt thereof of claim 109, wherein Y_1 is C_{1-4} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from halogen, cyano, and C_{1-4} alkoxy, and Y_2 is hydrogen.

111. The compound or pharmaceutically acceptable salt thereof of claim 110, wherein Y_1 is methyl optionally substituted with 1 to 3 susbstituents, which can be the same or different, each independently selected from -F, -Cl, -CN, and $-O-CH_3$.

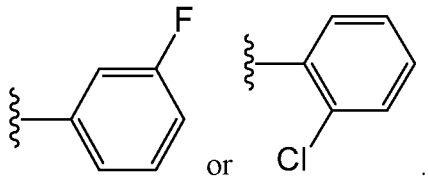
112. The compound or pharmaceutically acceptable salt thereof of claim 110 or 111, wherein Y_1 is $-CH_3$ or $-CH_2F$.

113. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-112, wherein Z is C_{6-12} aryl, optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from halogen, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, and C_{3-6} cycloalkyl, wherein the C_{1-4} alkyl is optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from C_{1-4} alkoxy and halogen.

114. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-113, wherein Z is phenyl, optionally substituted with 1 to 3 sustituents, which can be the same or different, each independently selected from halogen and C_{1-4} alkyl.

115. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-114, wherein Z is phenyl, optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from -F and -Cl.

116. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-115, wherein Z is

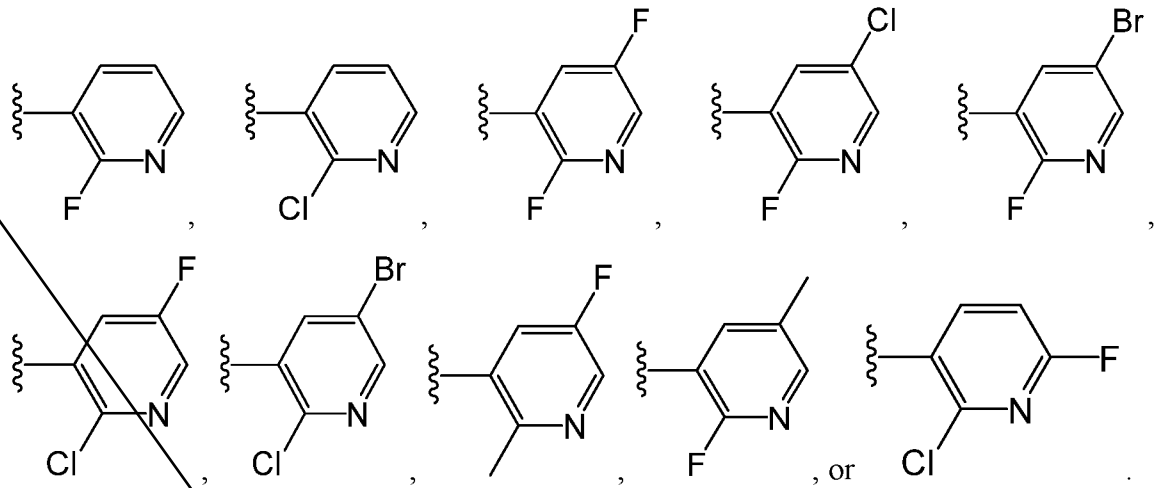


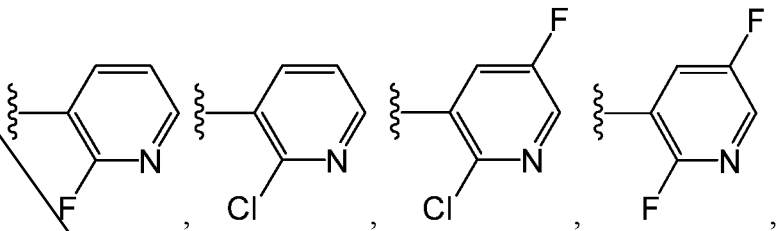
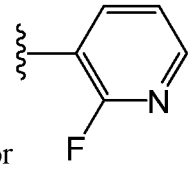
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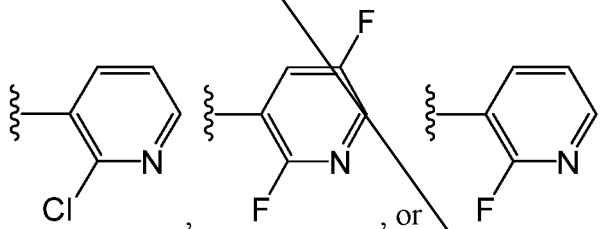
117. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-116, wherein Z is 5 or 6 membered heteroaryl having 1-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein the heteroaryl is optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from halogen and C_{1-4} alkyl.

118. The compound or pharmaceutically acceptable salt thereof of claim 117, wherein Z is pyridyl, optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from -F, -Cl, -Br, and $-CH_3$.

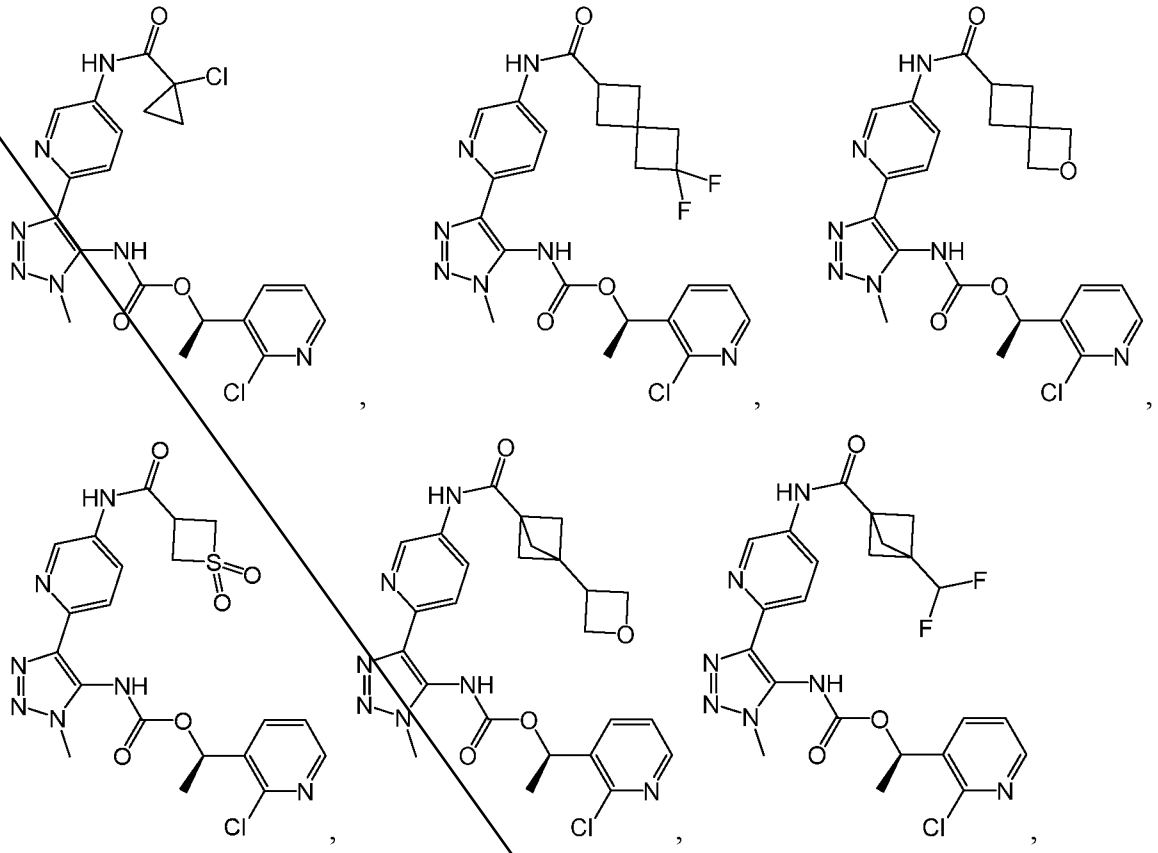
119. The compound or pharmaceutically acceptable salt thereof of claim 116 or 117, wherein Z is

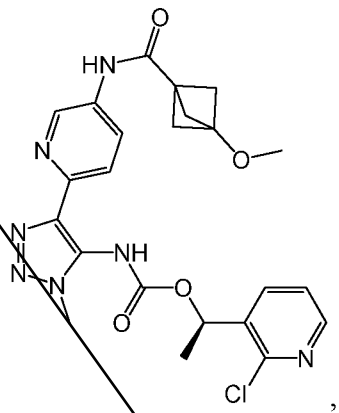
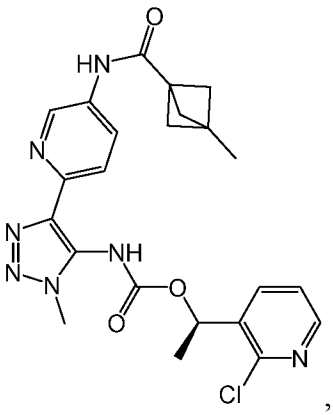
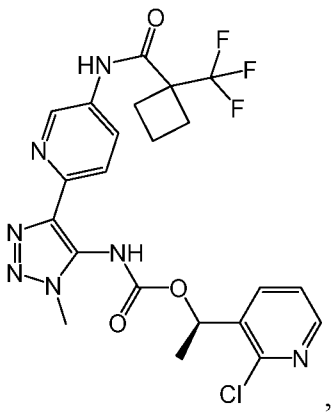
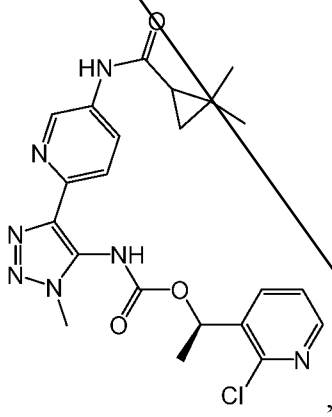
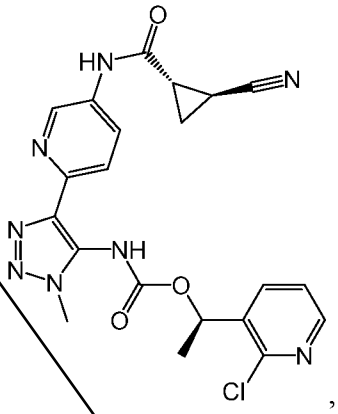
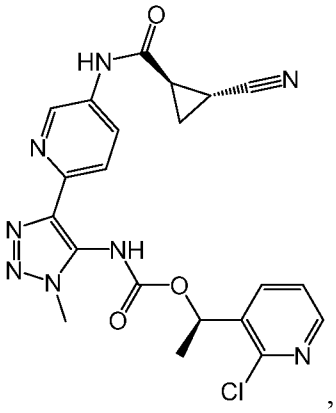
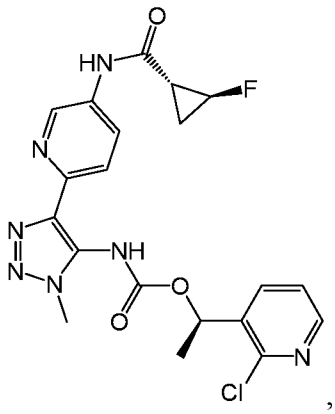
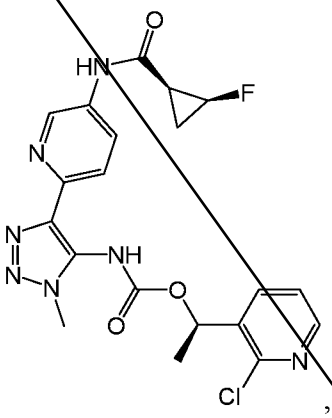
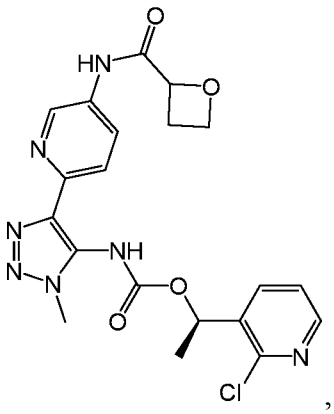
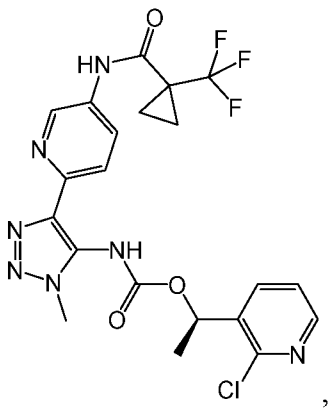
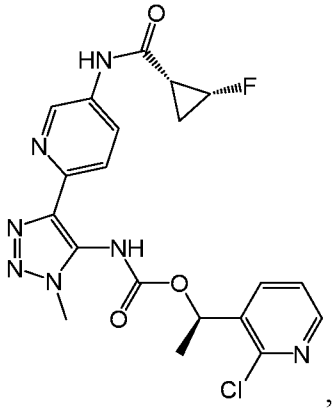
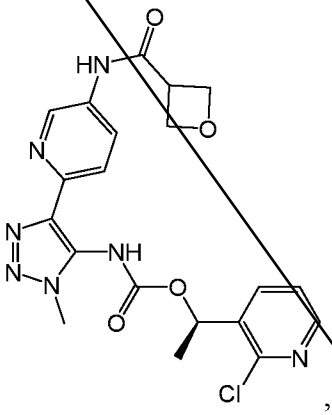


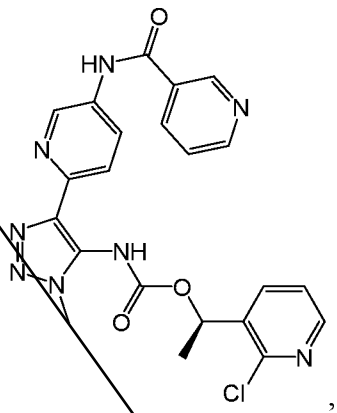
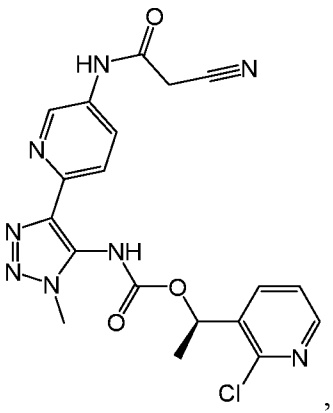
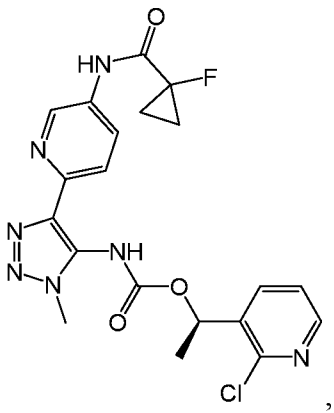
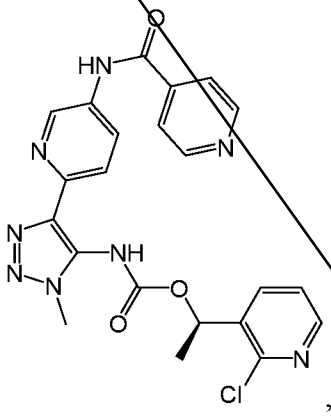
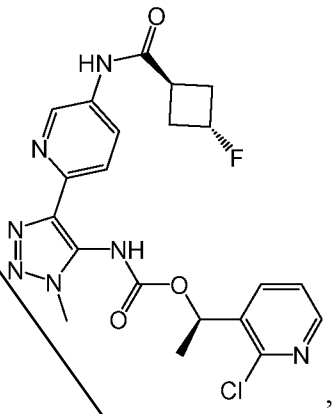
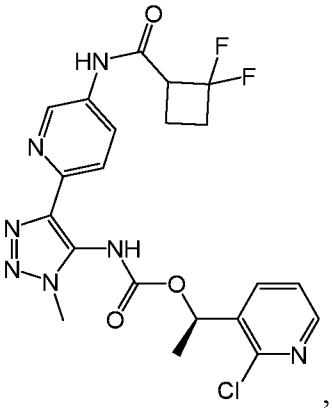
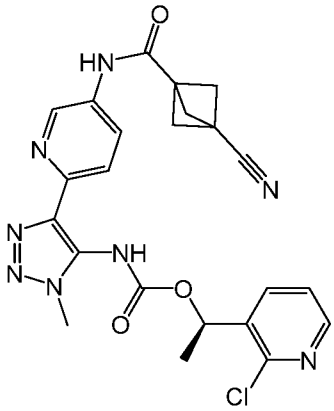
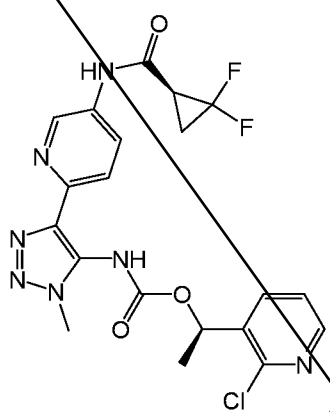
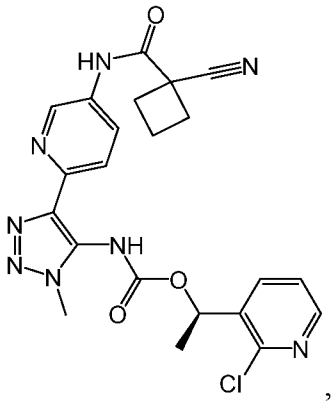
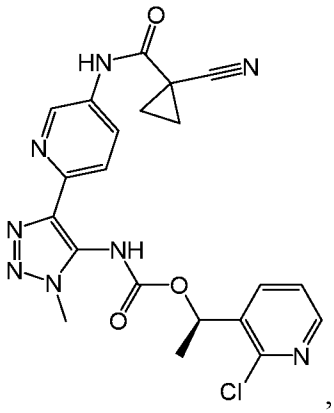
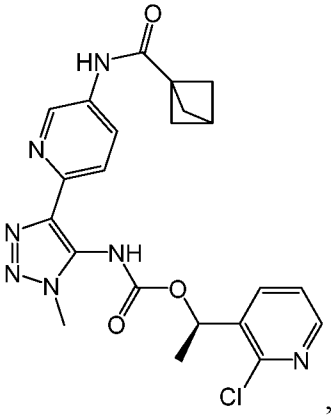
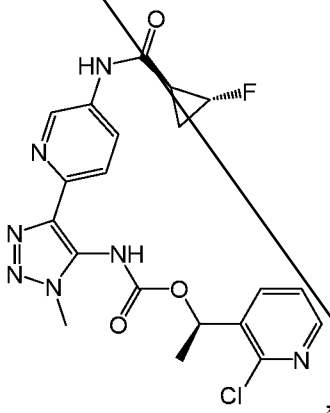
120. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-119, wherein Y_1 is $-CH_3$ and Z is  or .

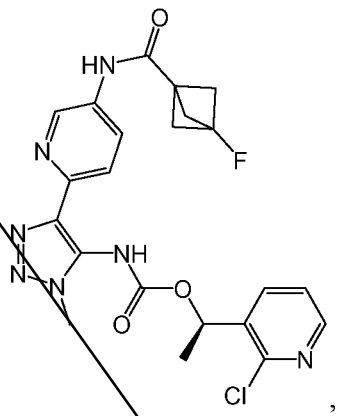
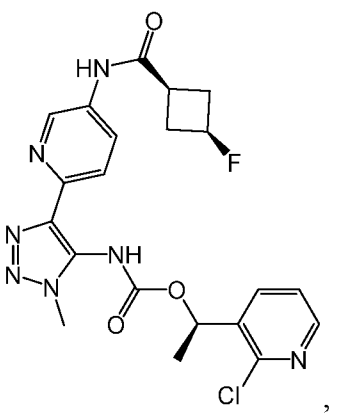
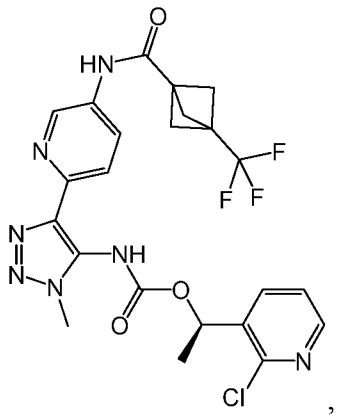
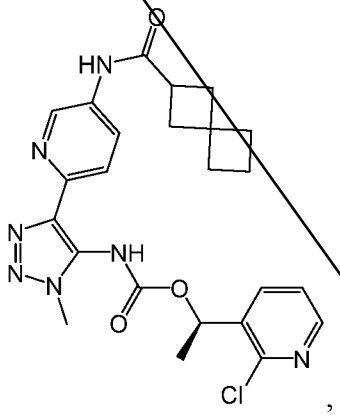
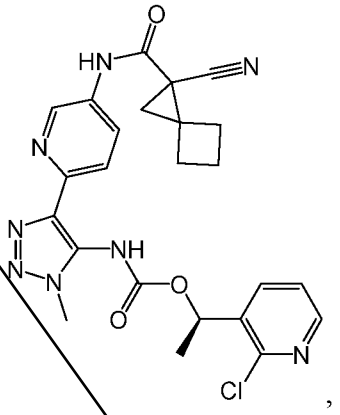
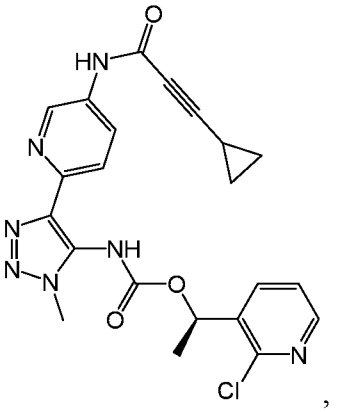
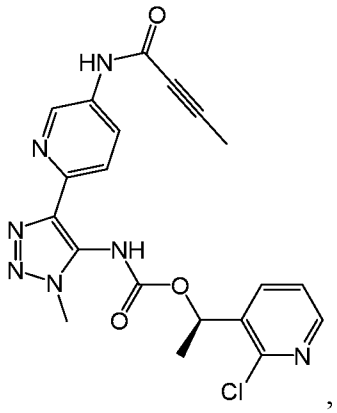
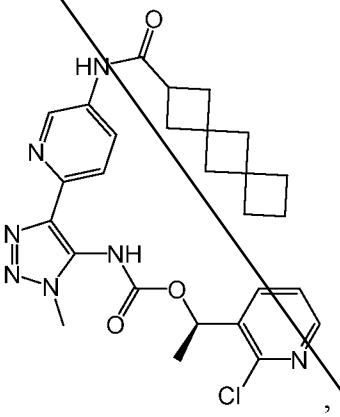
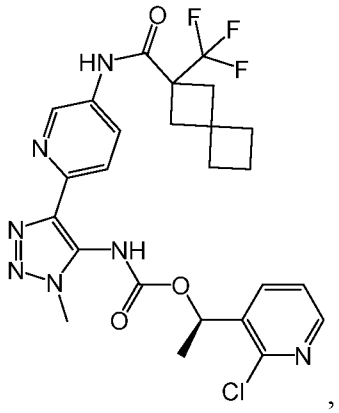
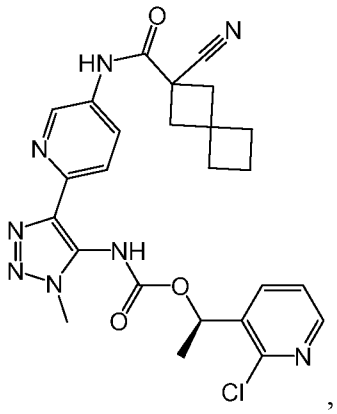
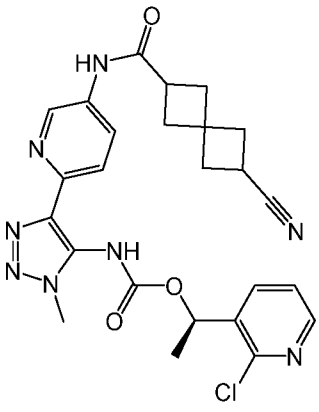
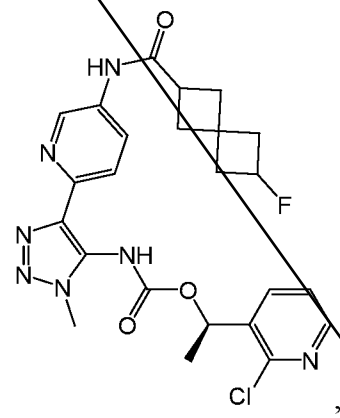
121. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-120, wherein Y_1 is $-CH_3$ and Z is .

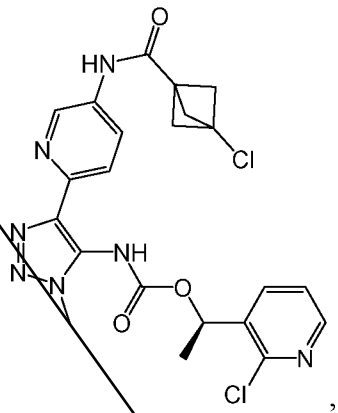
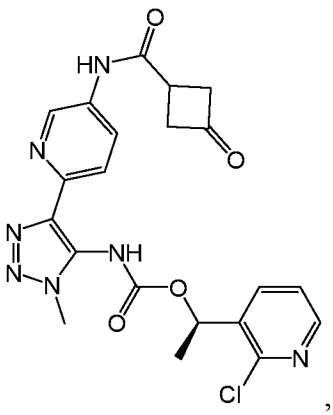
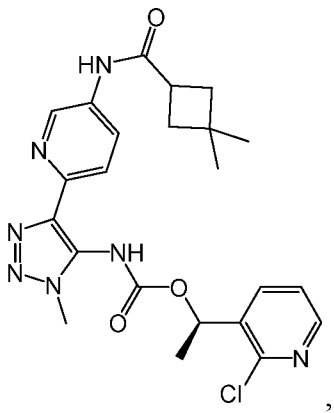
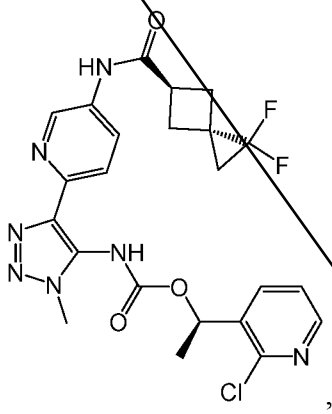
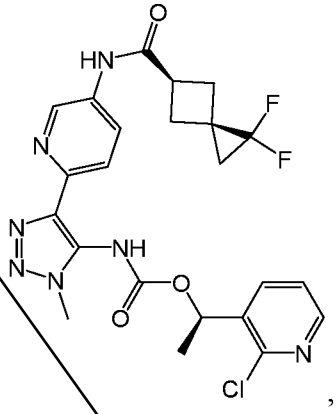
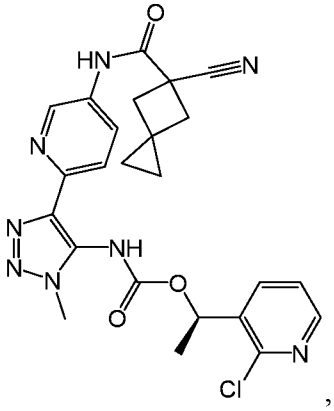
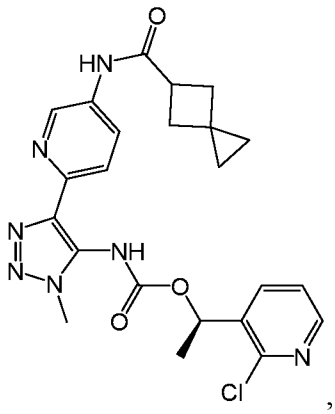
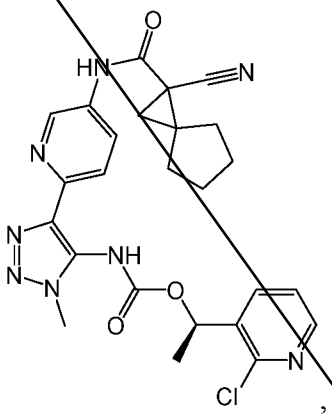
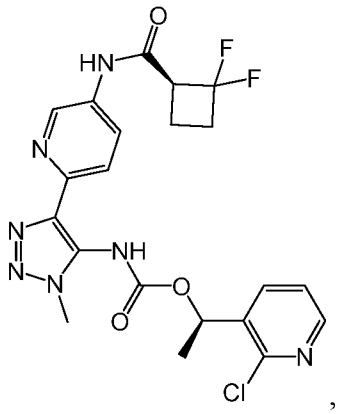
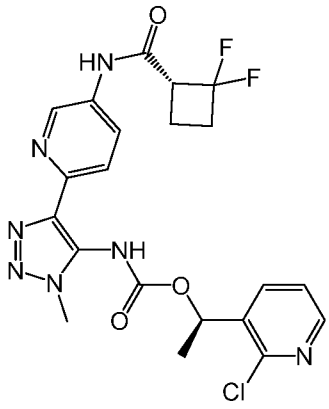
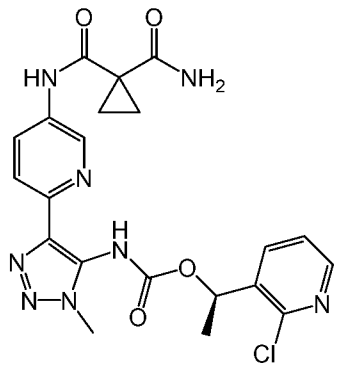
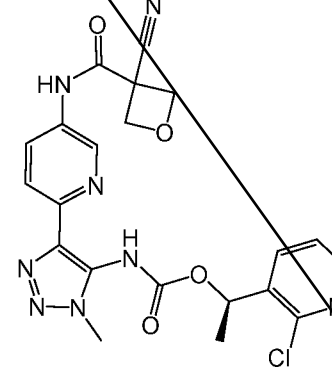
122. A compound selected from the group consisting of:




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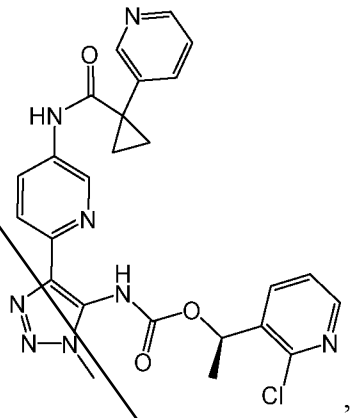
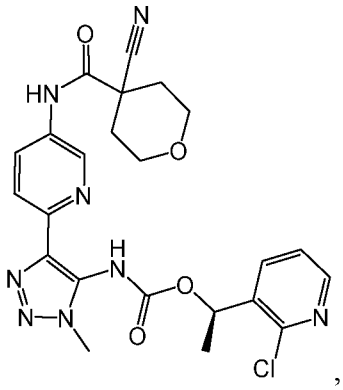
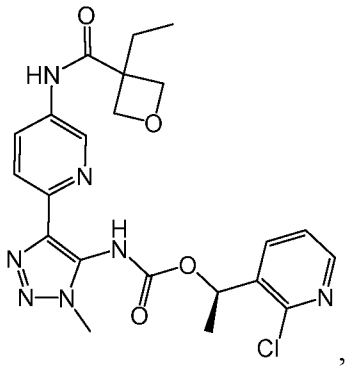
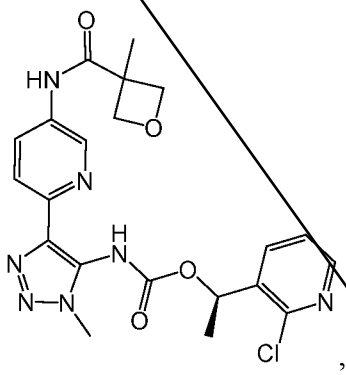
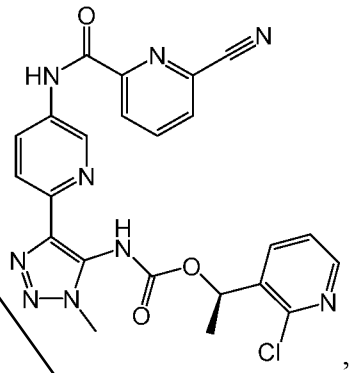
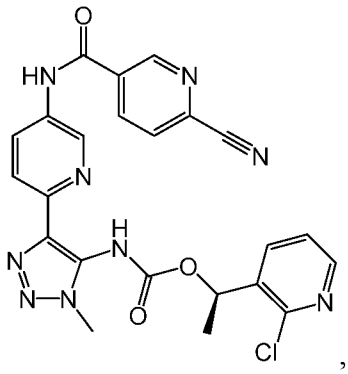
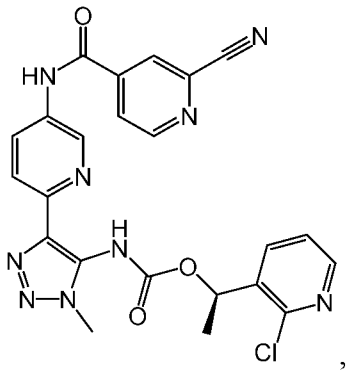
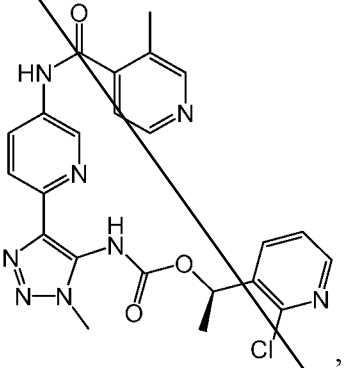
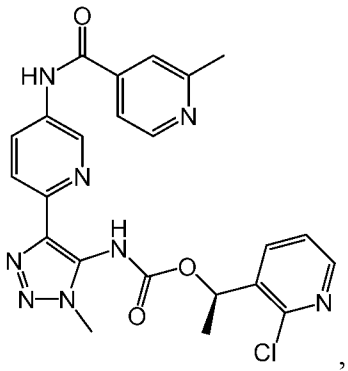
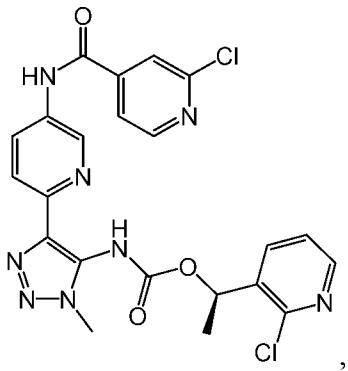
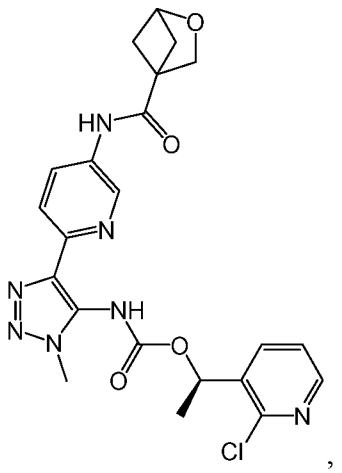
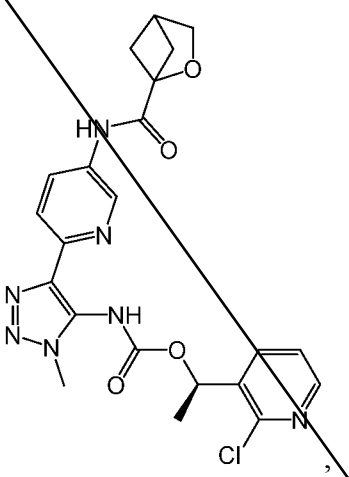

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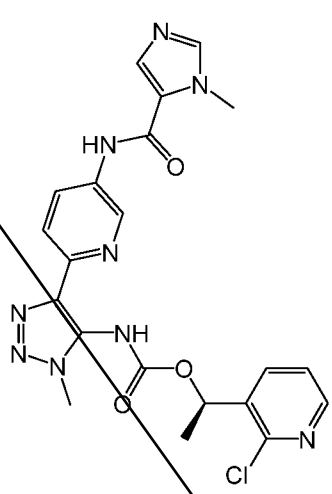
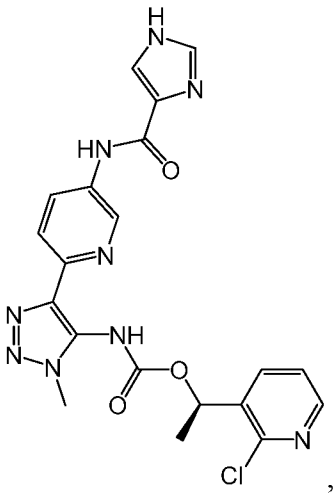
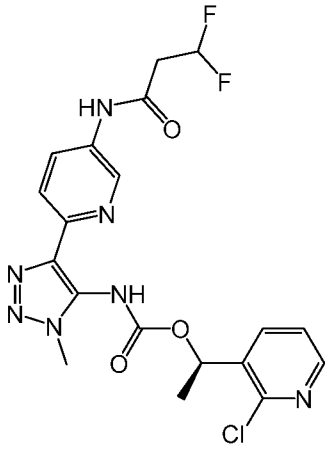
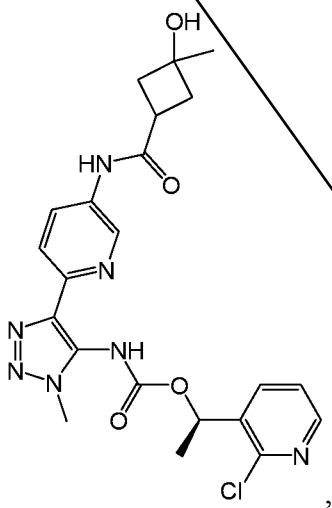
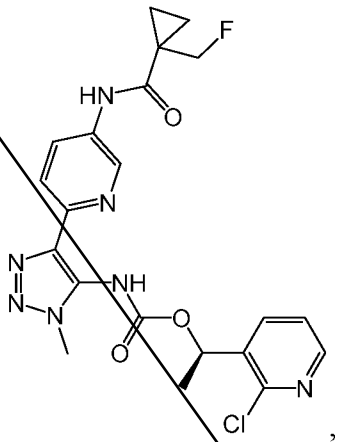
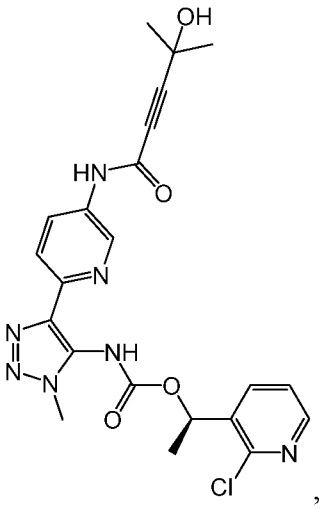

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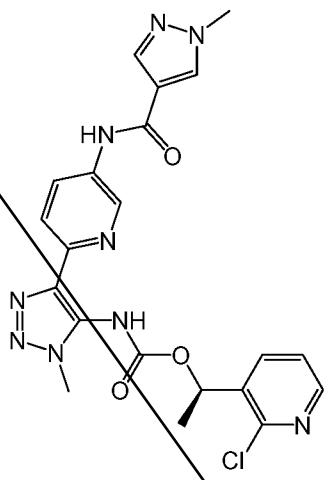
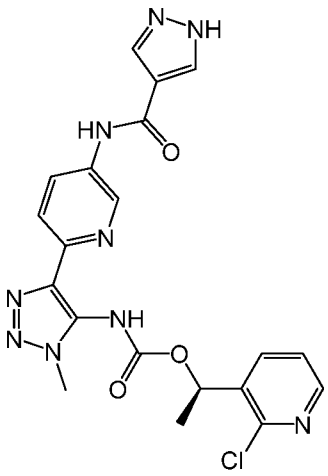
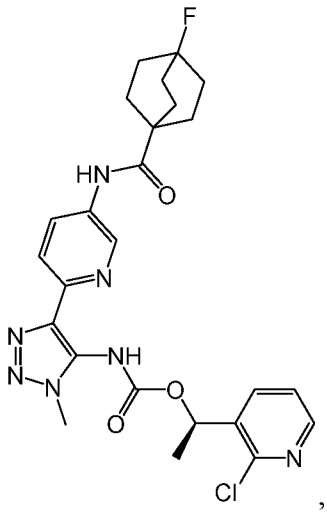
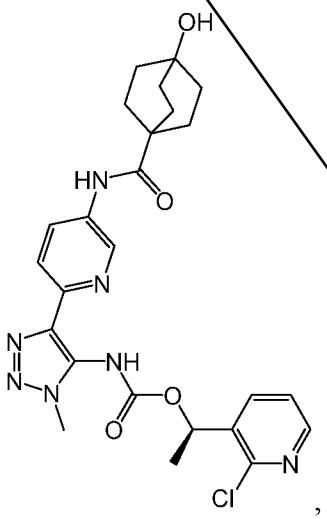
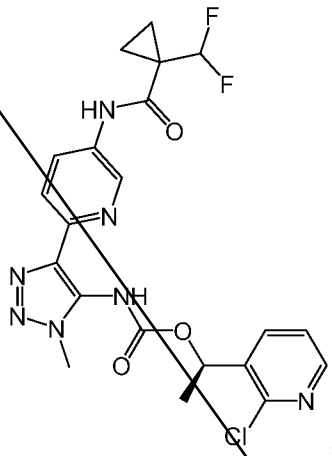
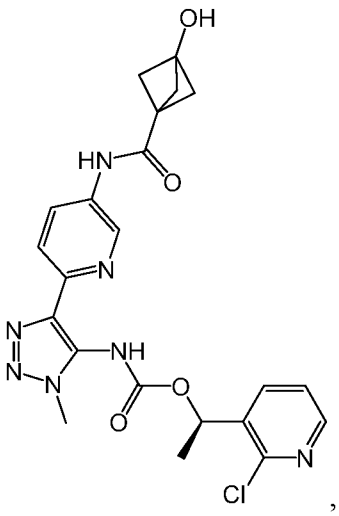
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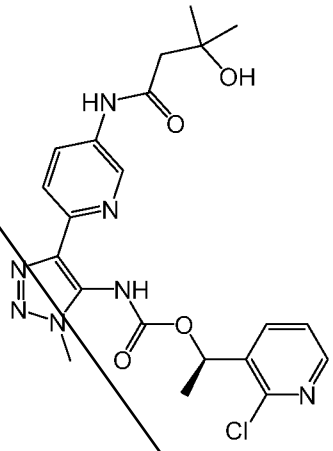
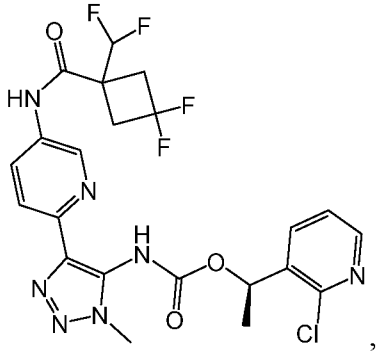
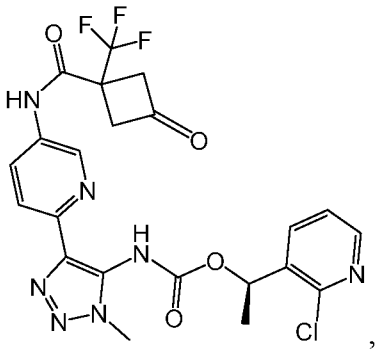
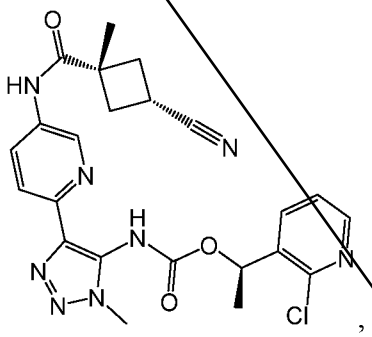
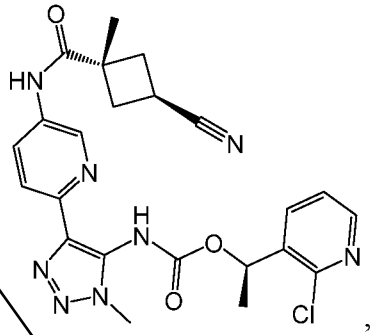
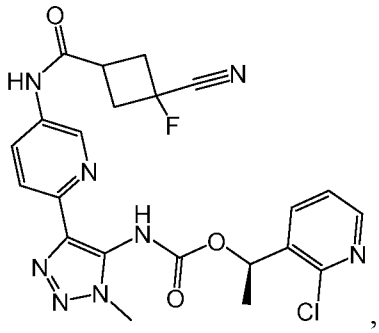
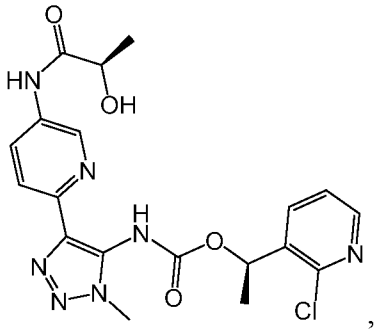
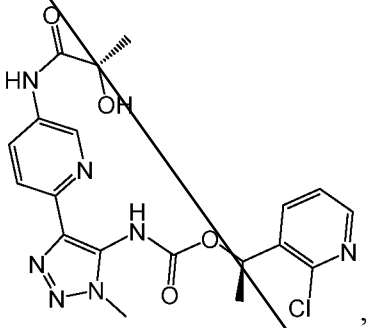
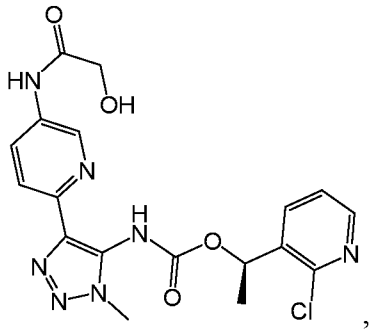
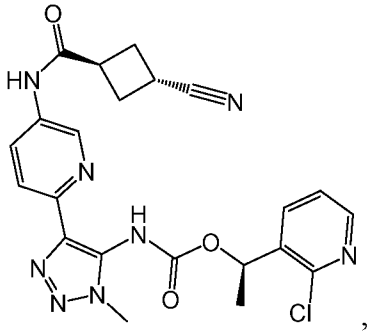
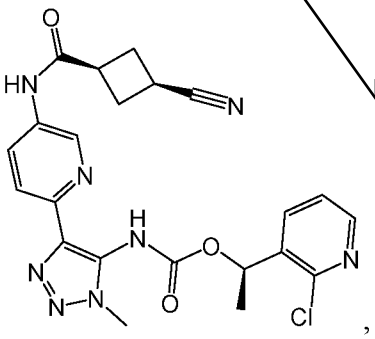
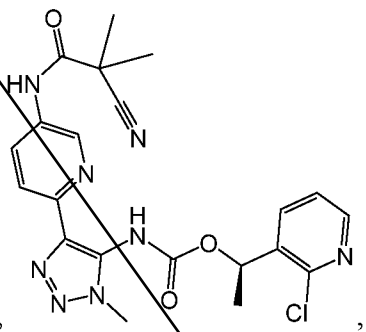
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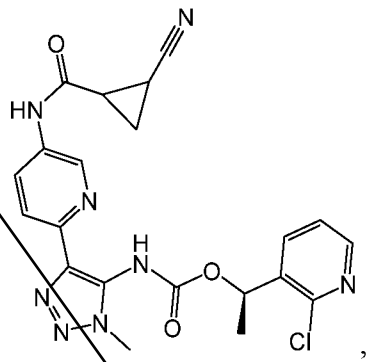
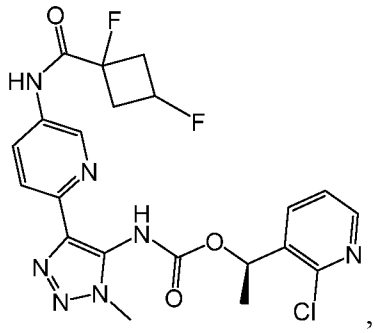
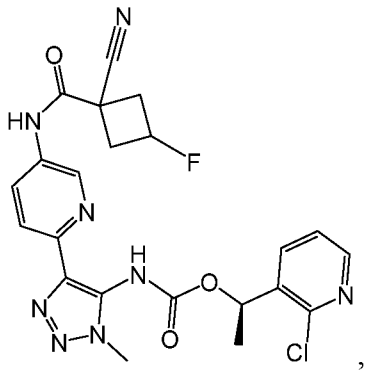
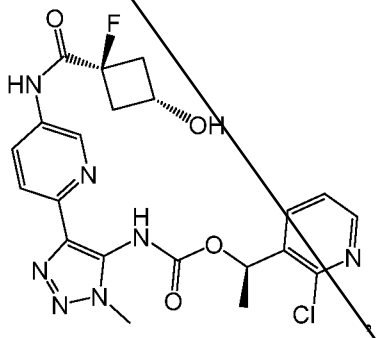
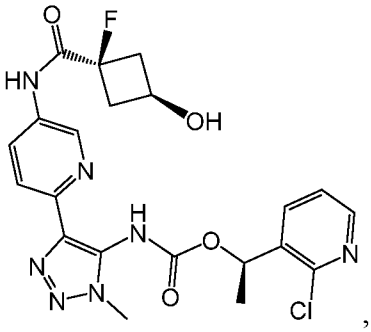
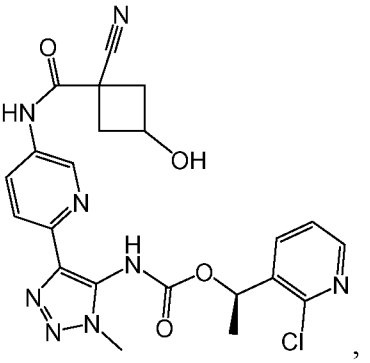
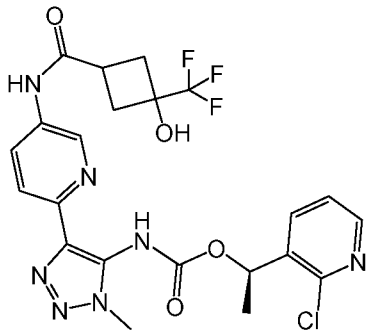
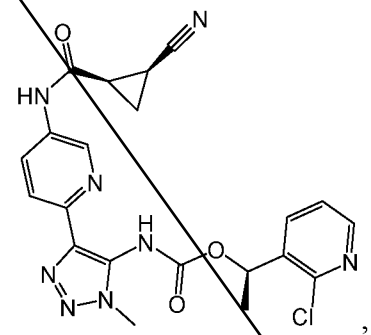
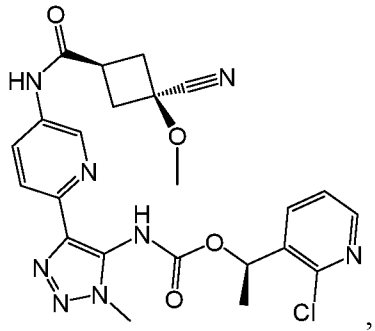
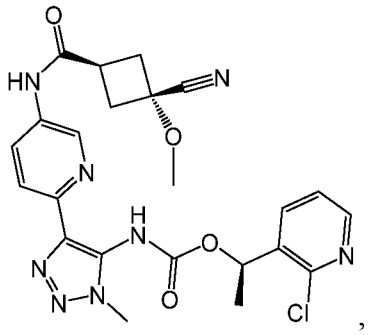
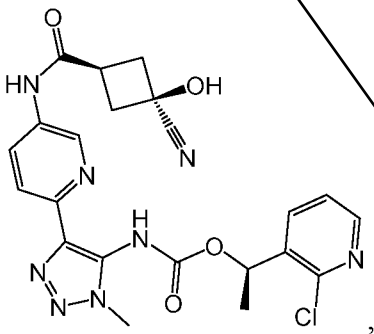
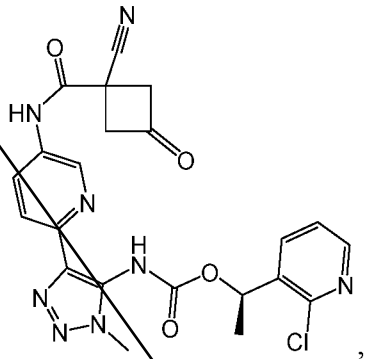
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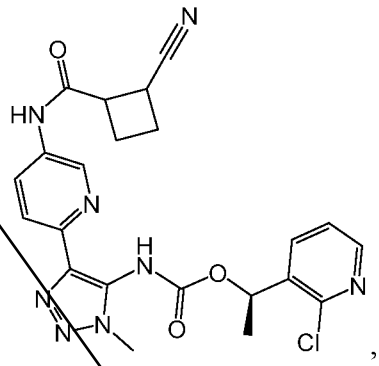
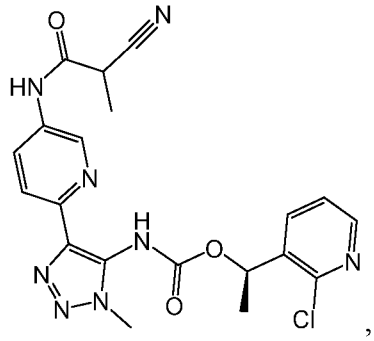
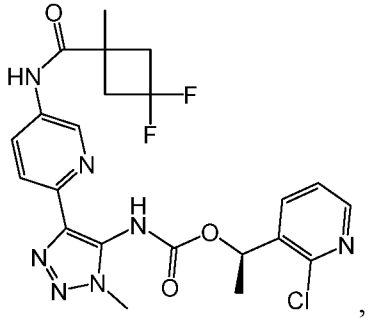
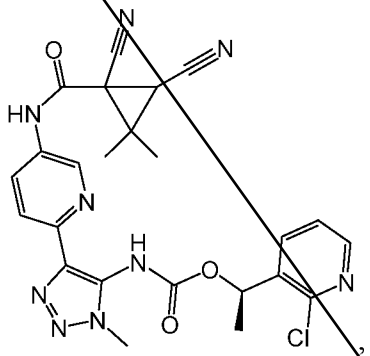
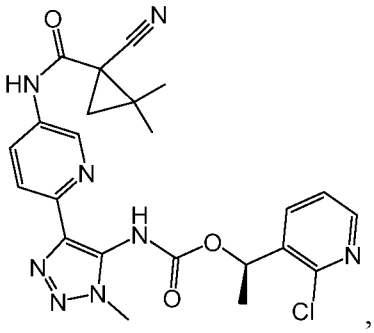
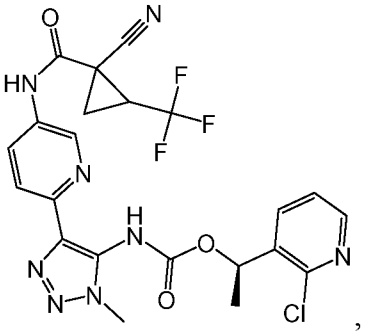
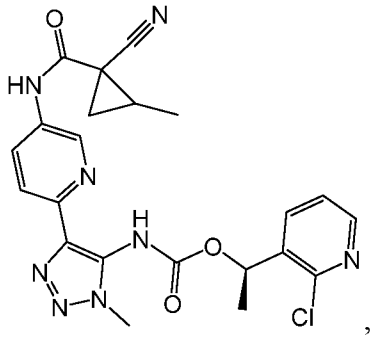
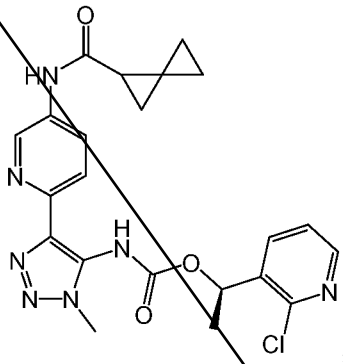
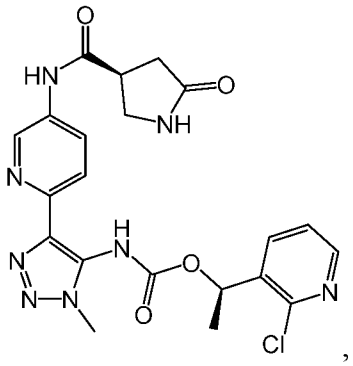
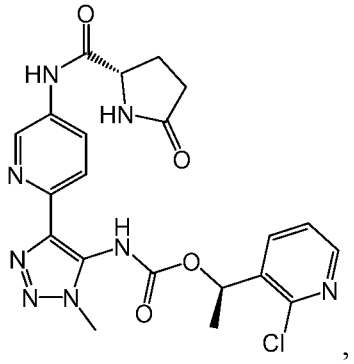
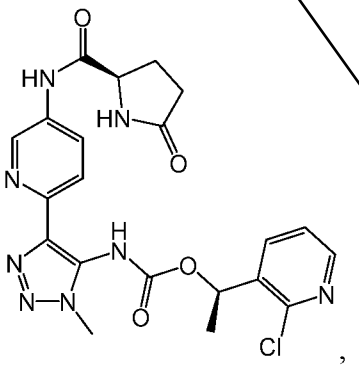
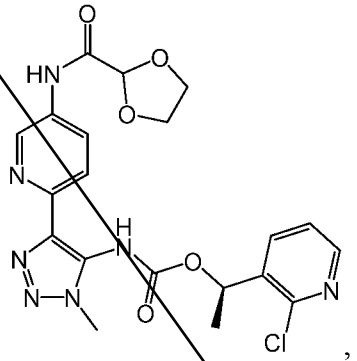

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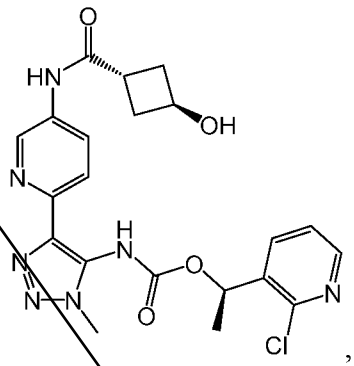
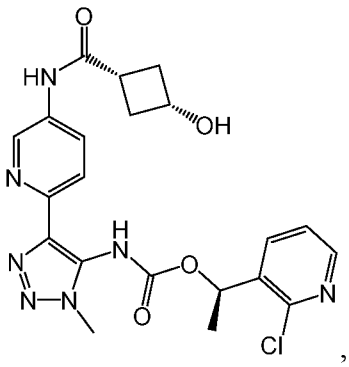
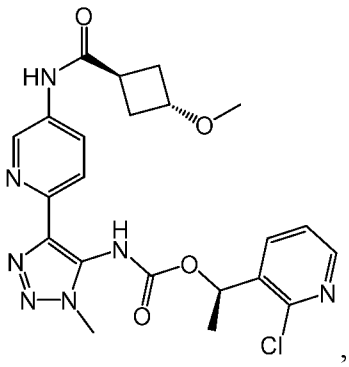
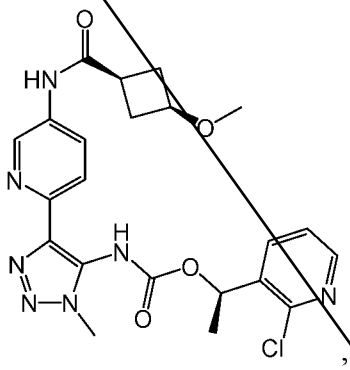
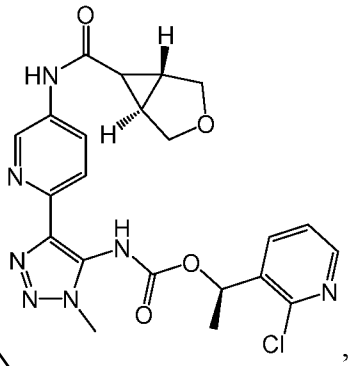
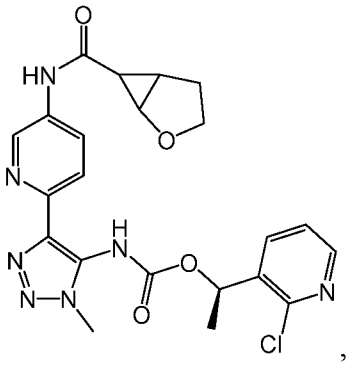
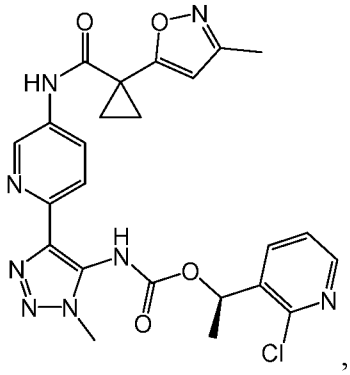
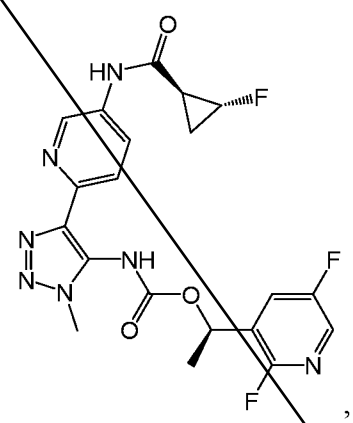
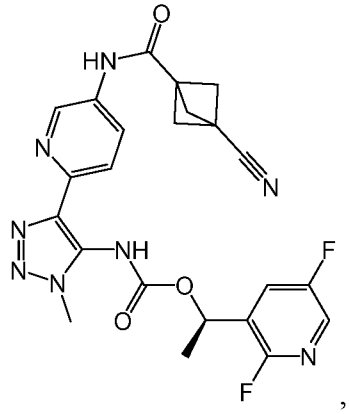
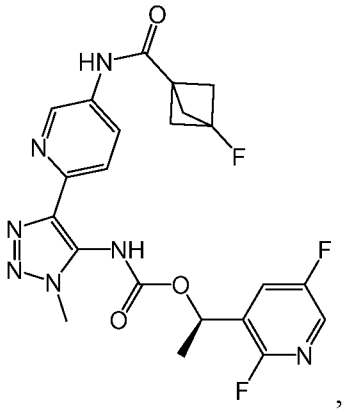
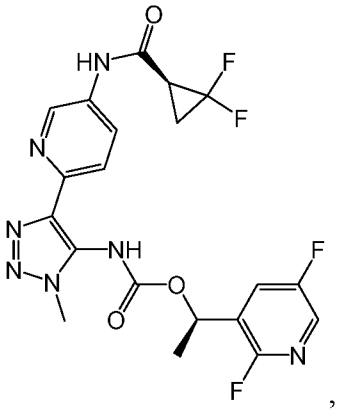
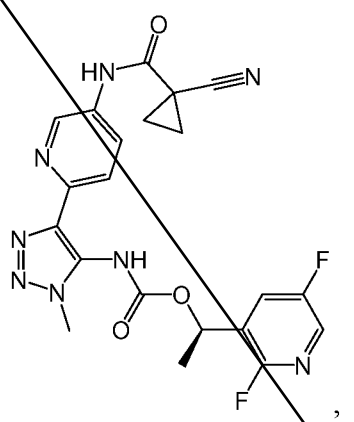

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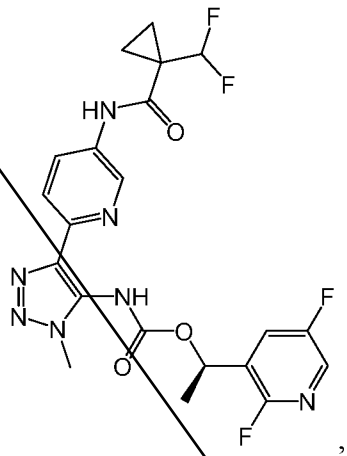
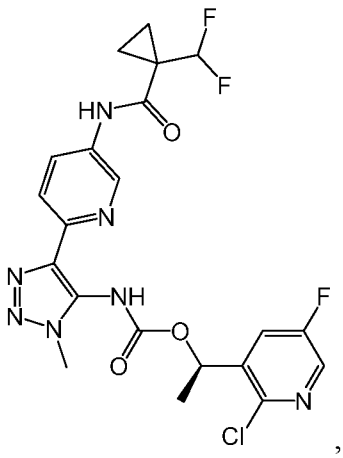
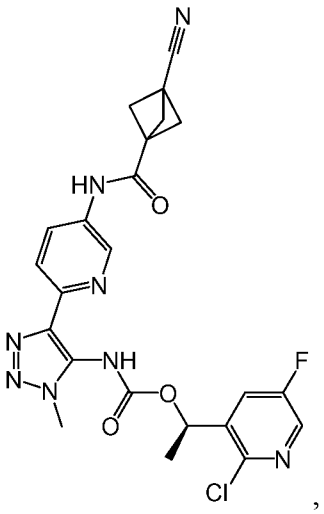
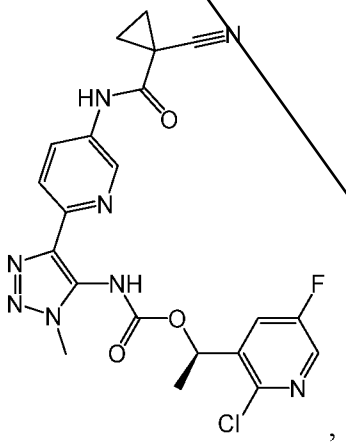
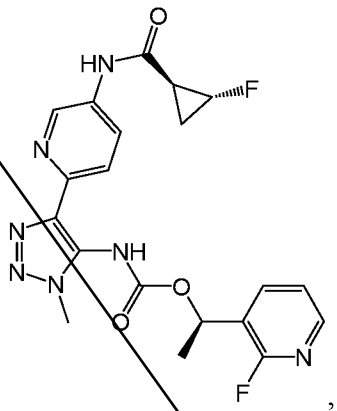
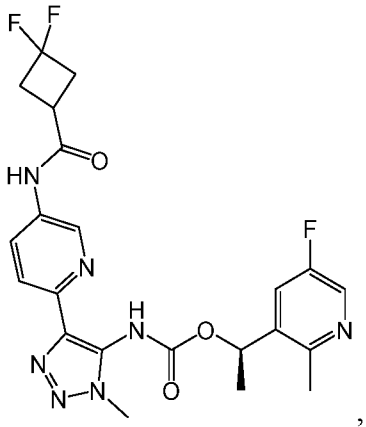

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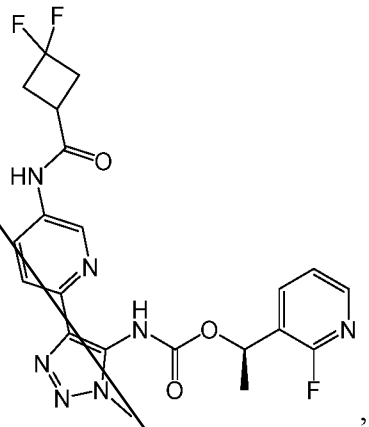
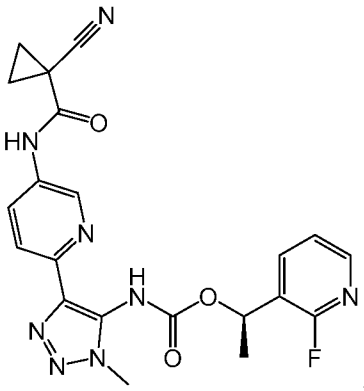
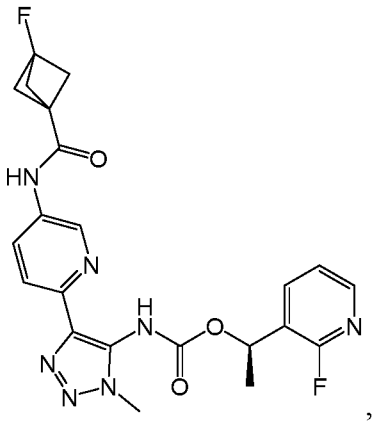
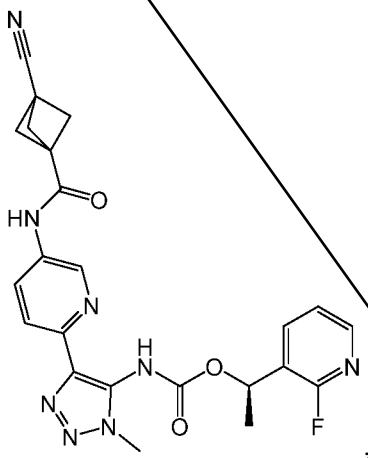
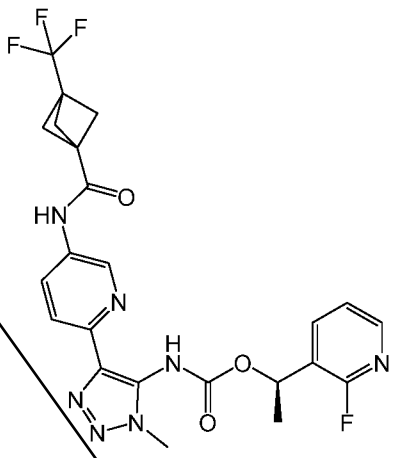
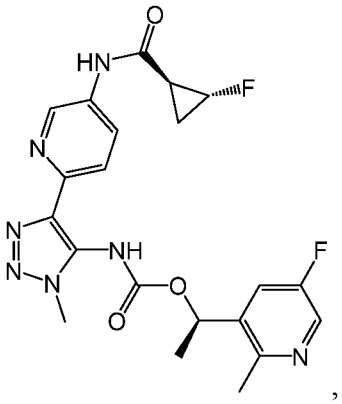

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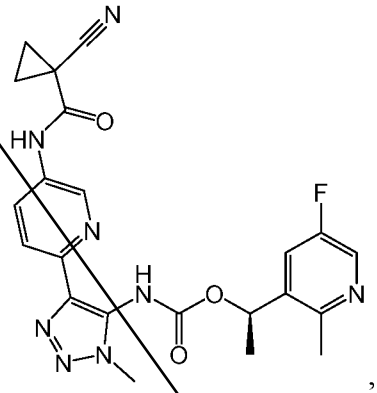
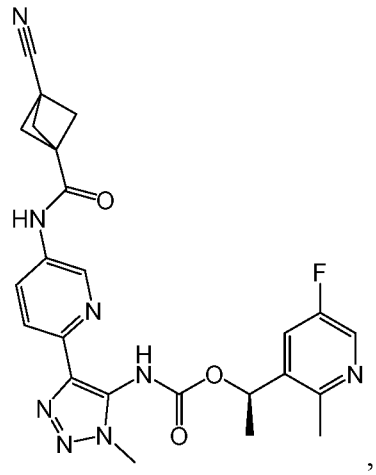
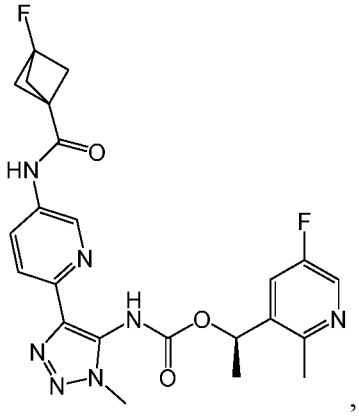
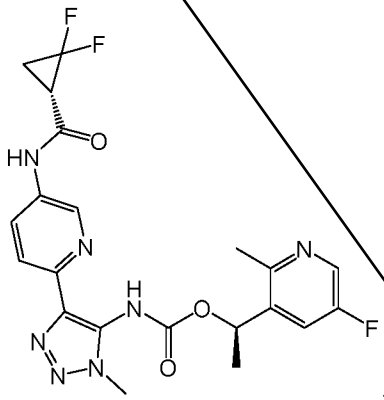
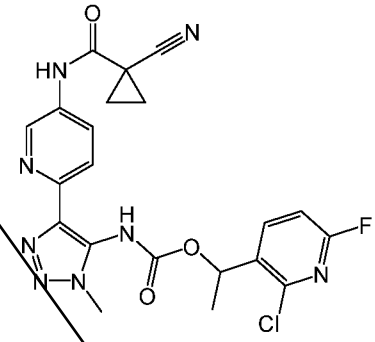
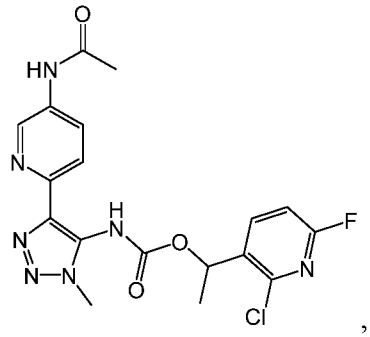
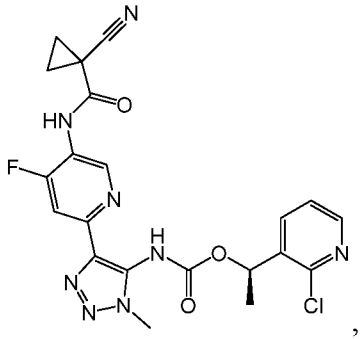
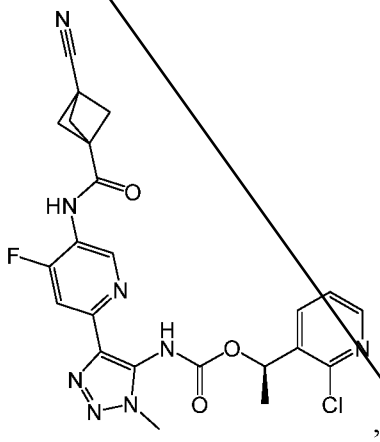
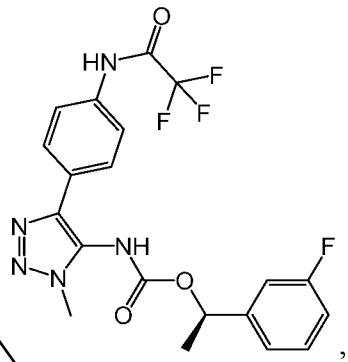
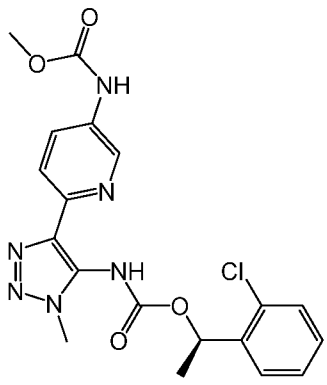
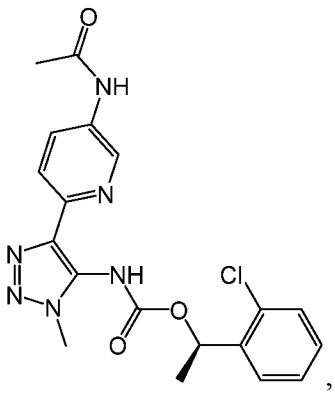
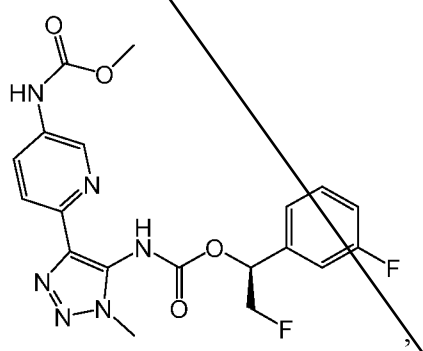

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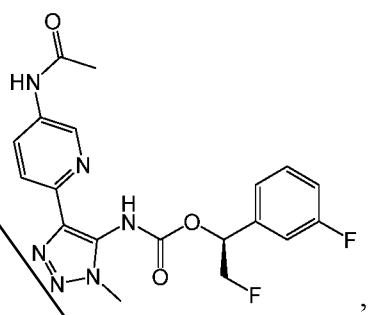
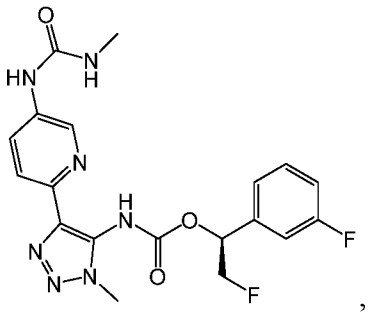
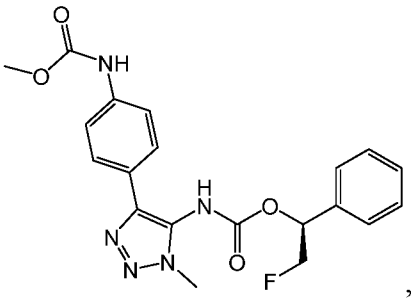
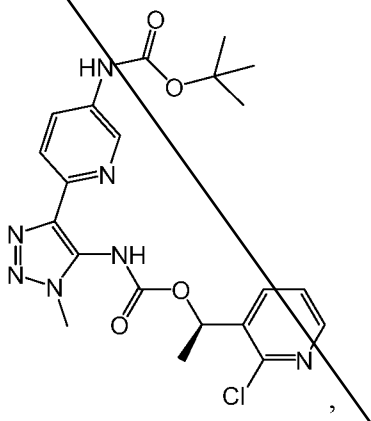
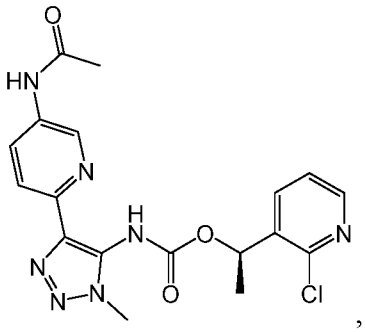
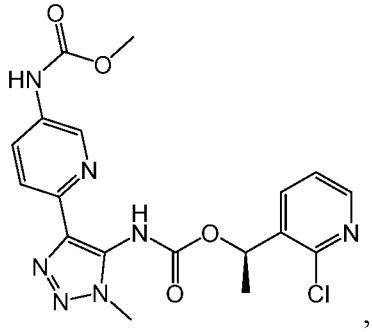
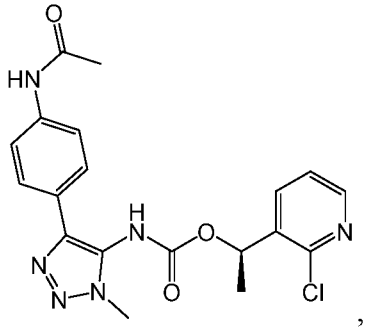
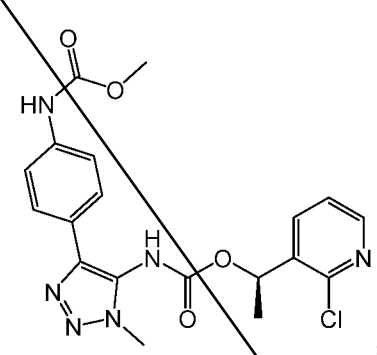
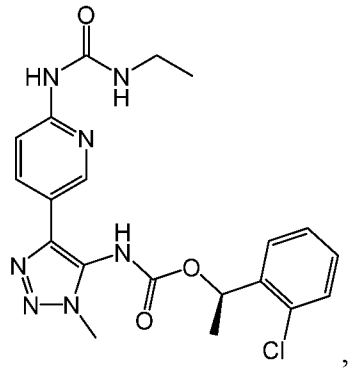
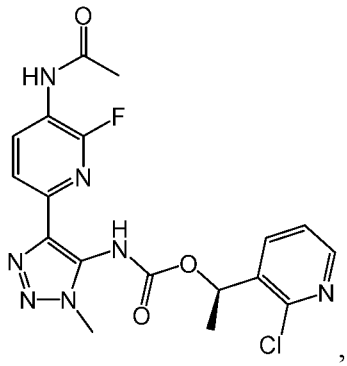
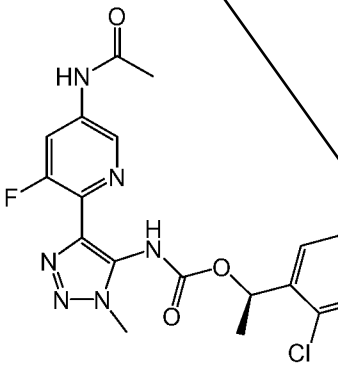
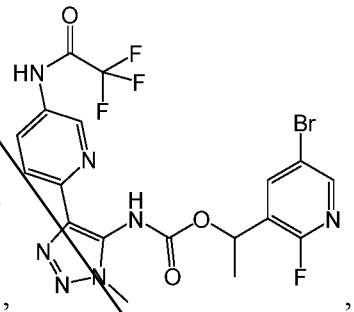

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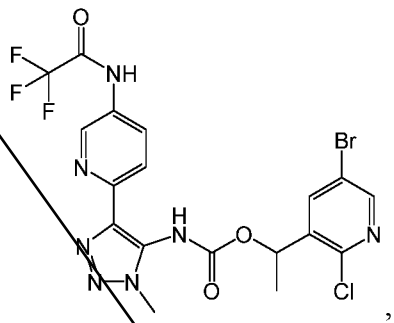
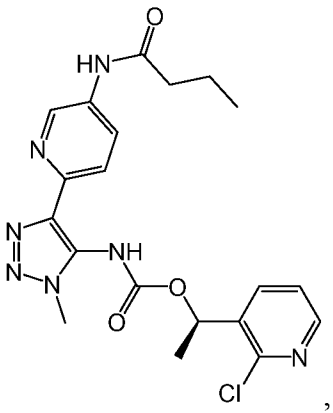
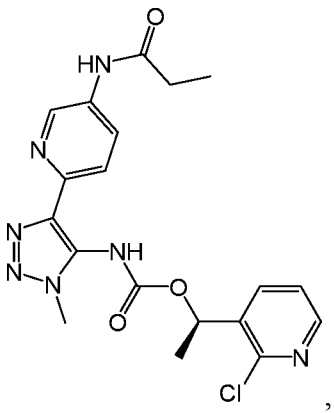
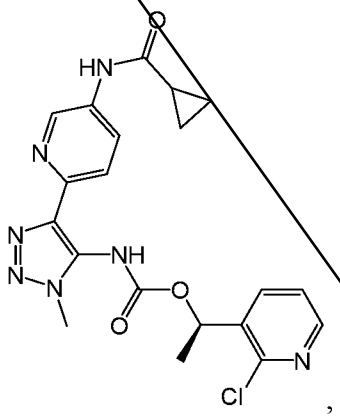
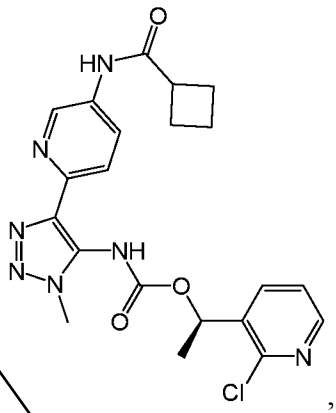
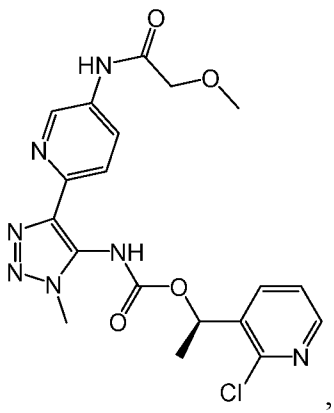
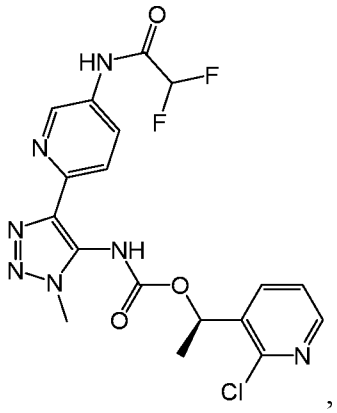
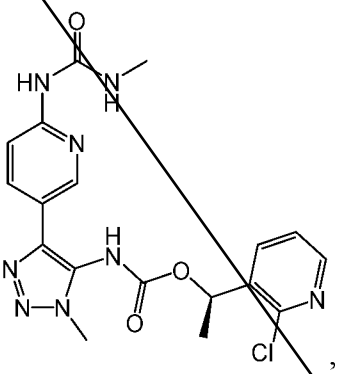
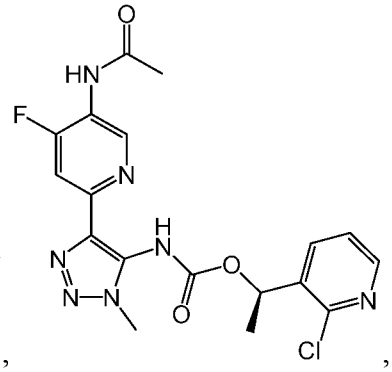
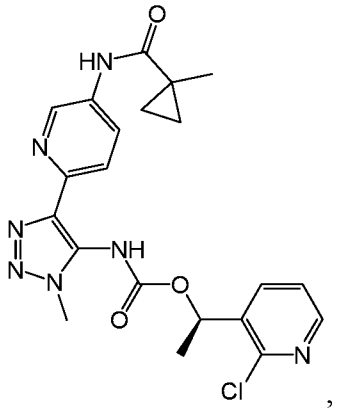
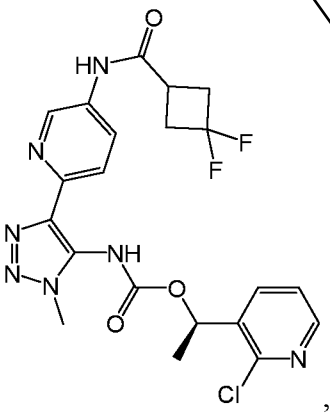
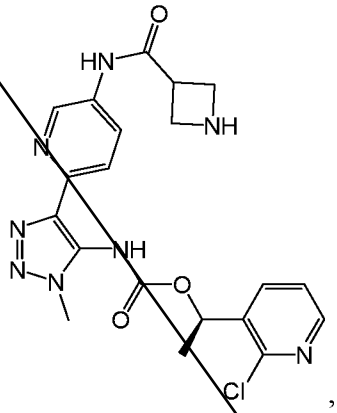

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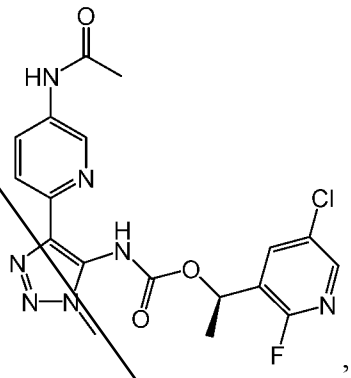
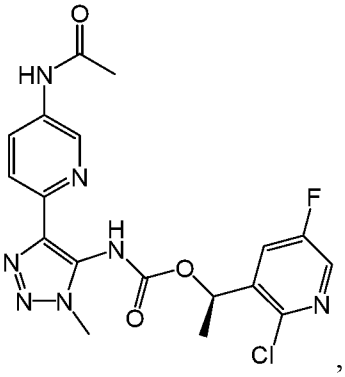
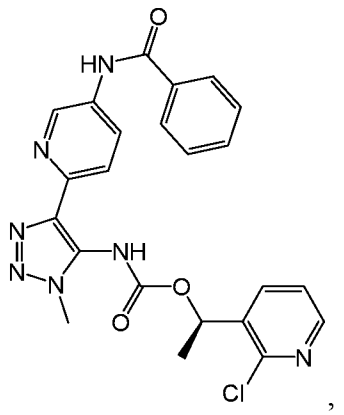
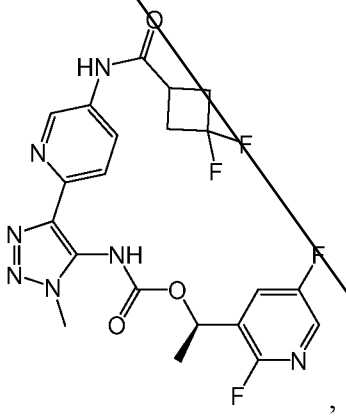
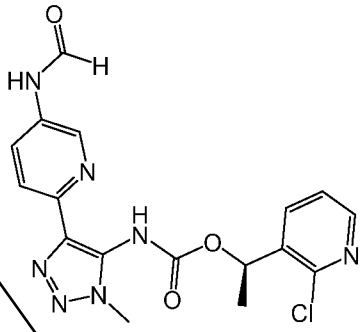
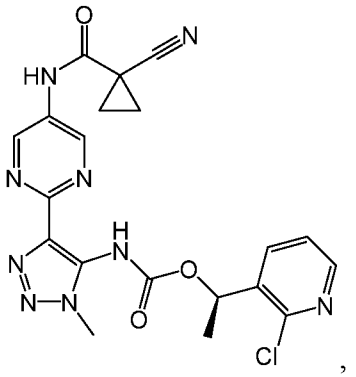
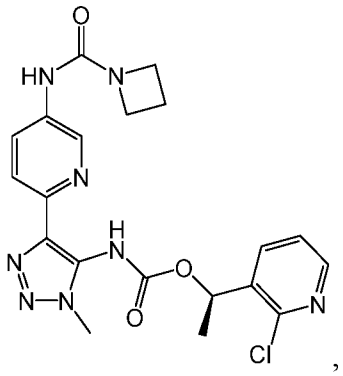
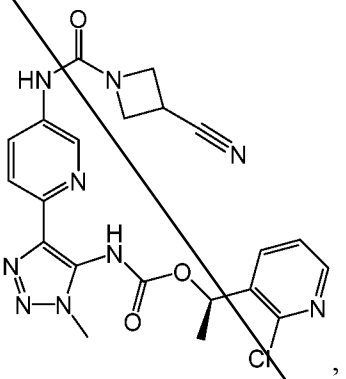
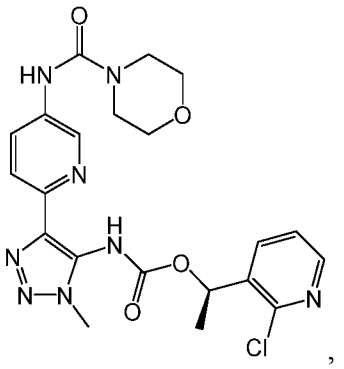
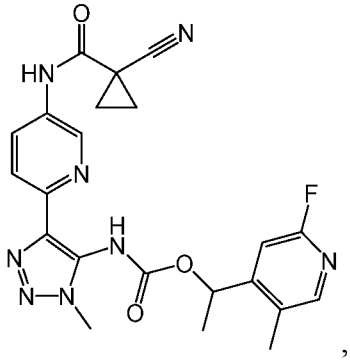
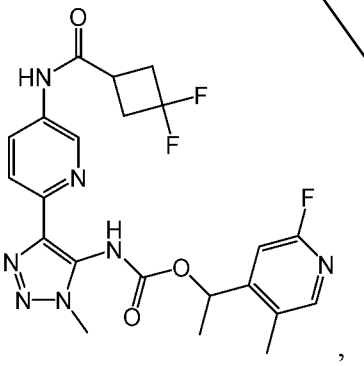
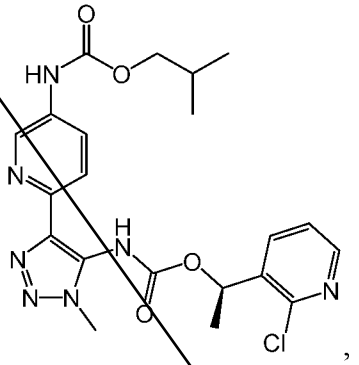

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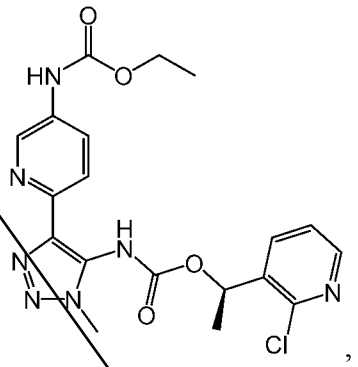
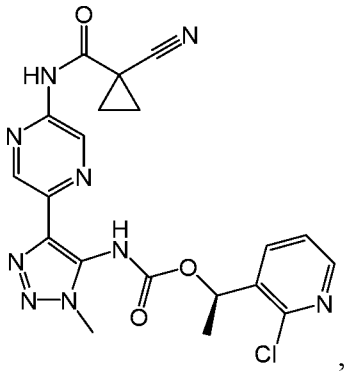
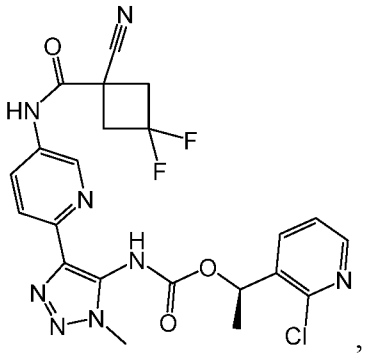
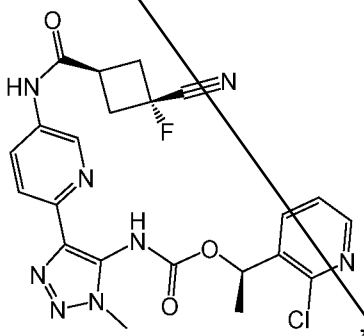
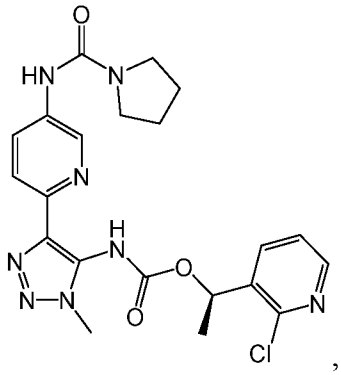
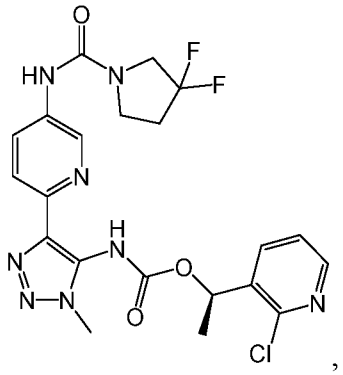
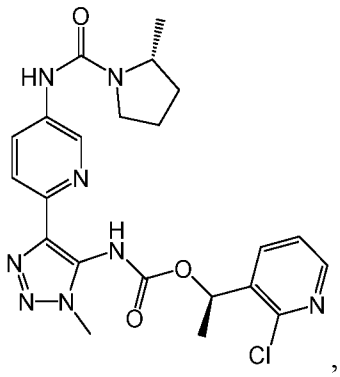
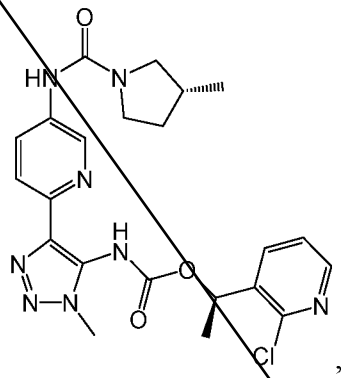

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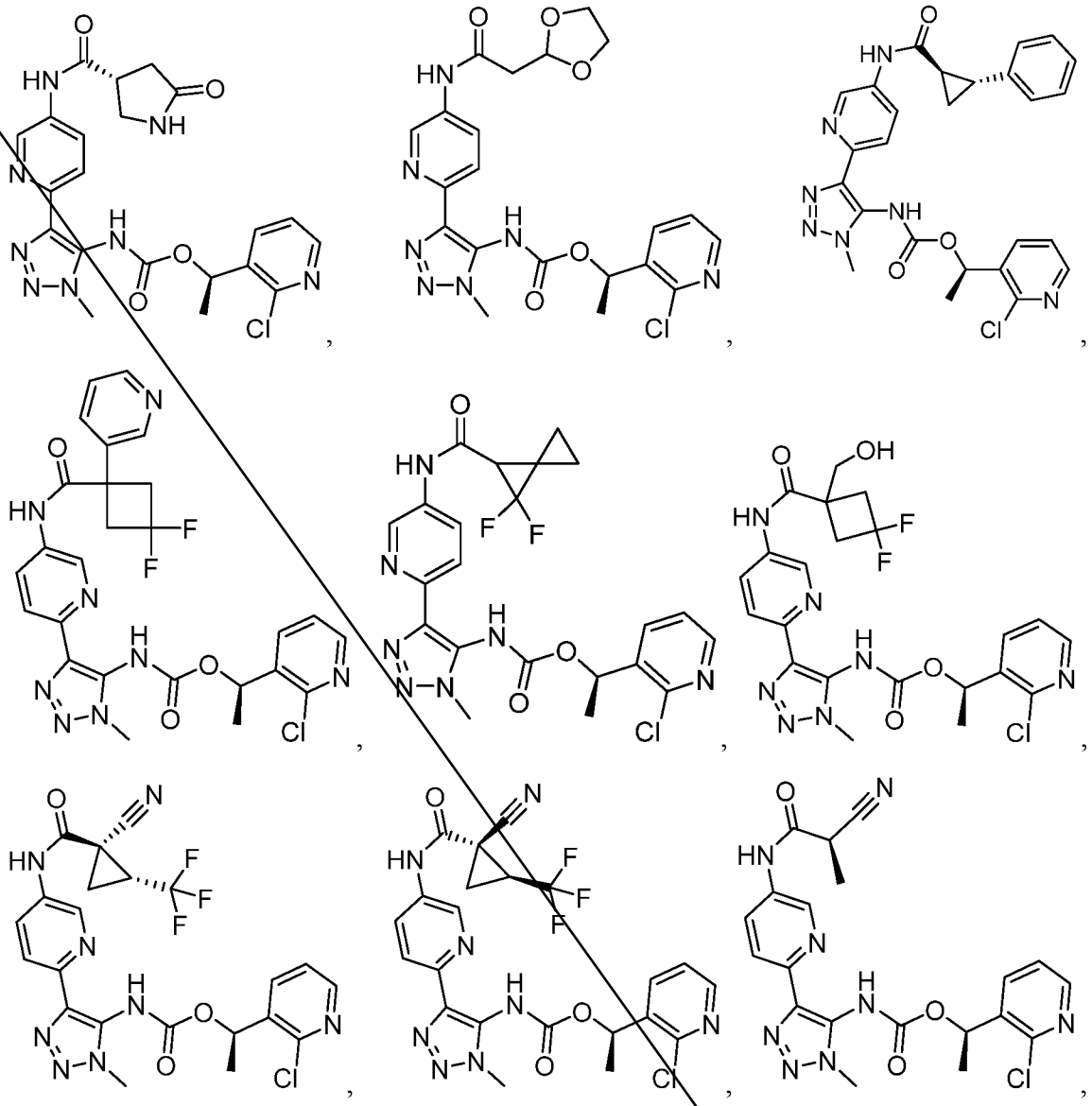

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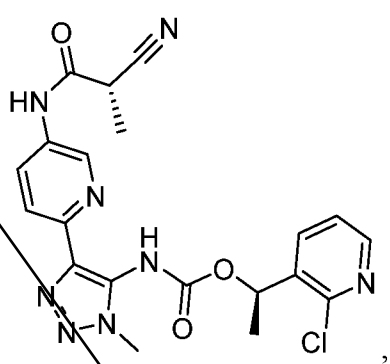
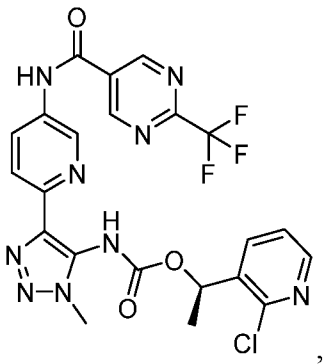
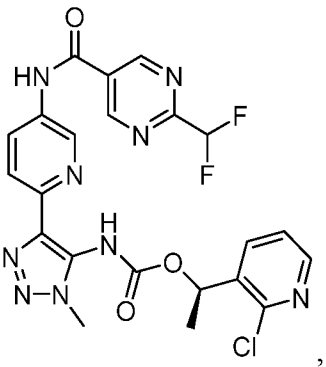
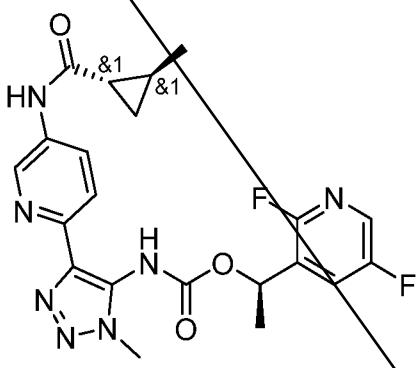
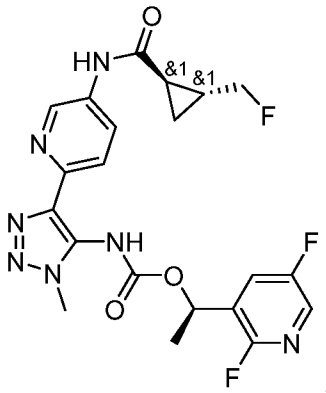
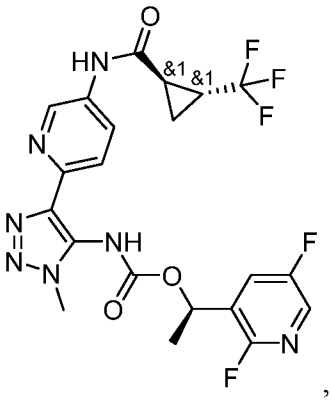
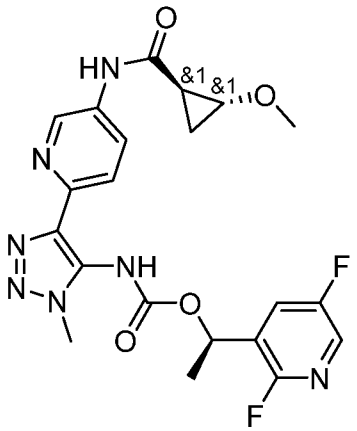
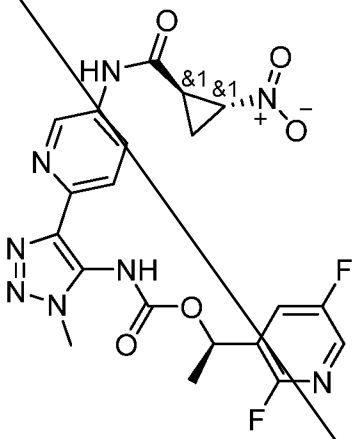
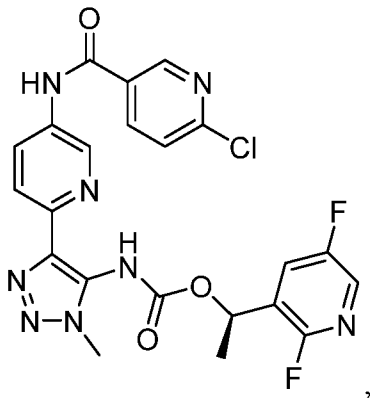
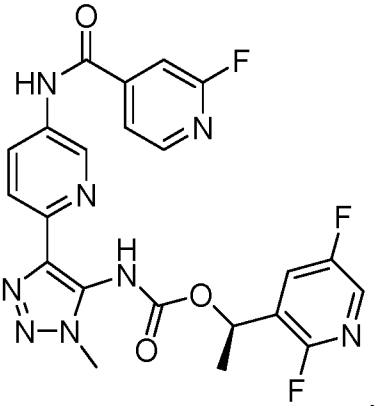
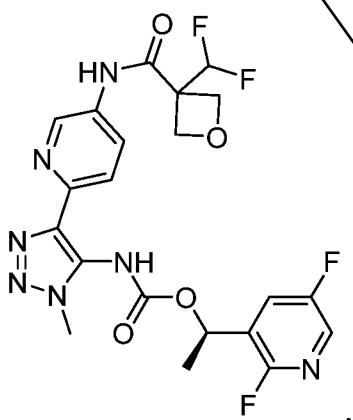
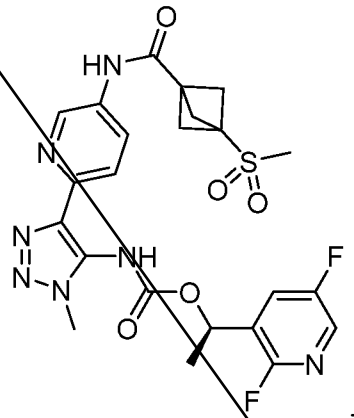

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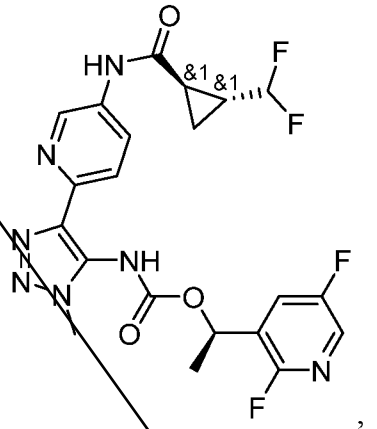
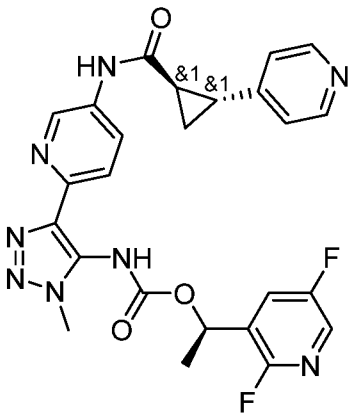
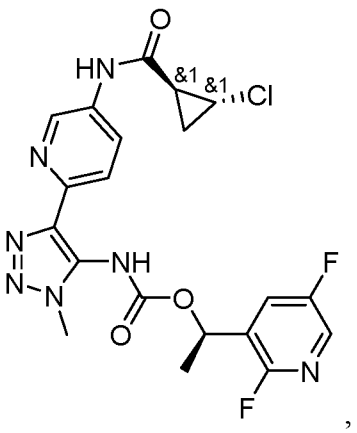
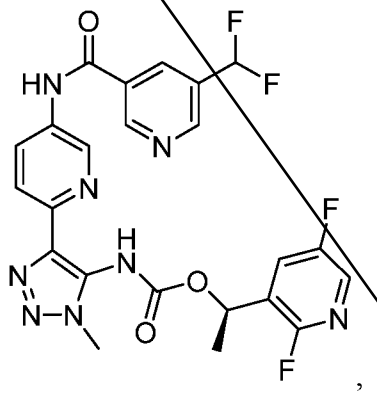
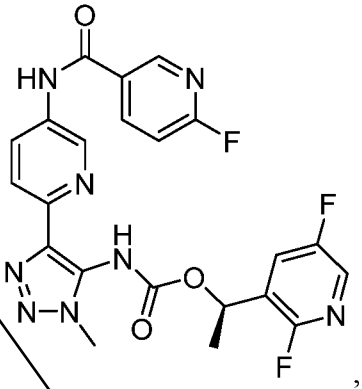
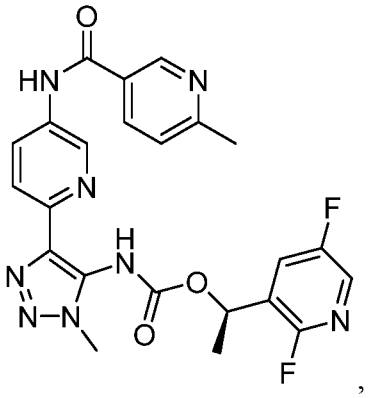
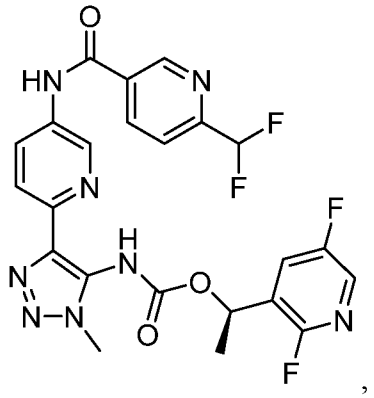
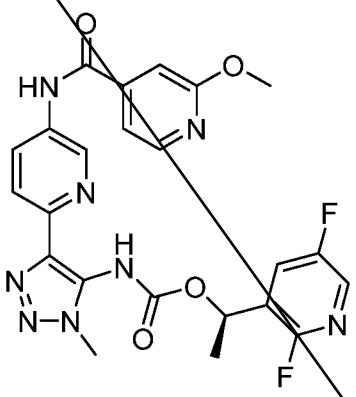
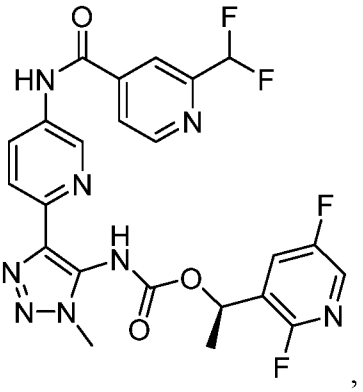
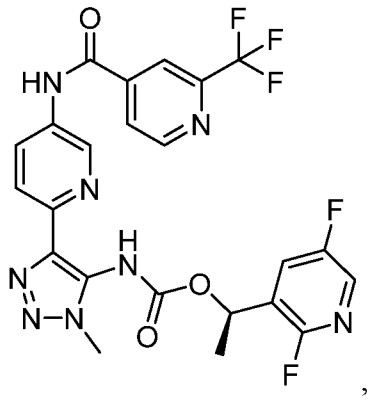
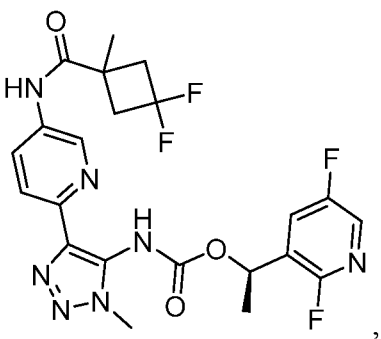
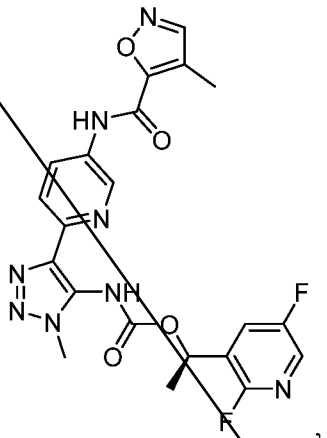

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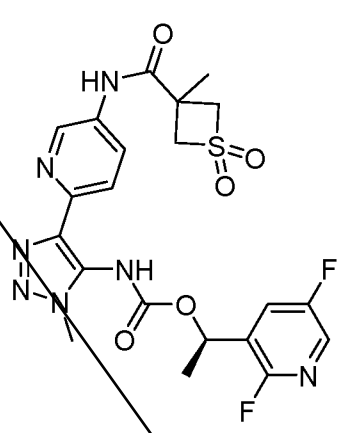
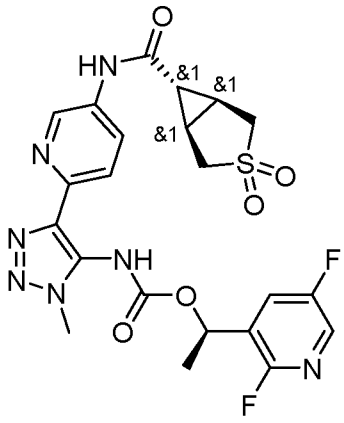
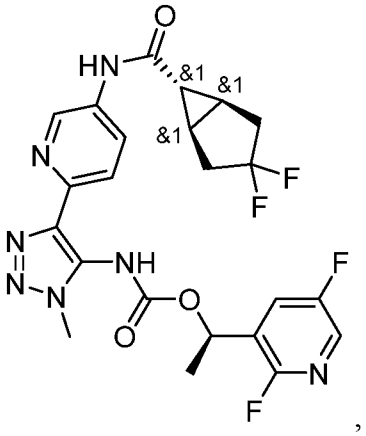
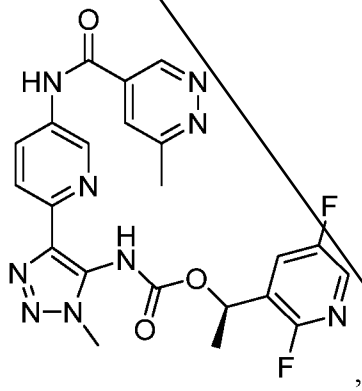
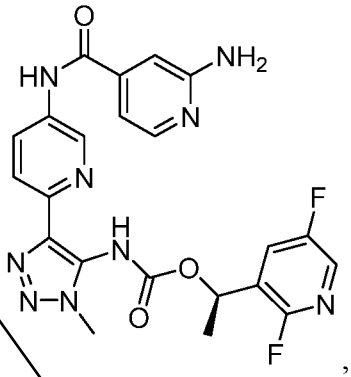
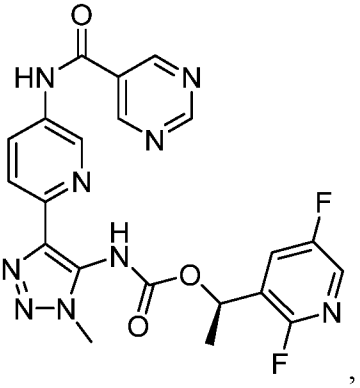
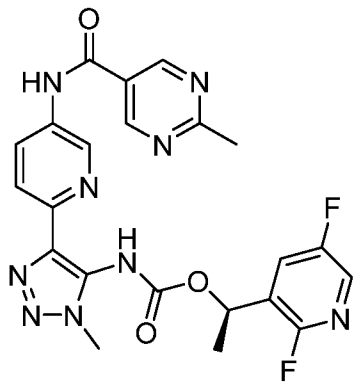
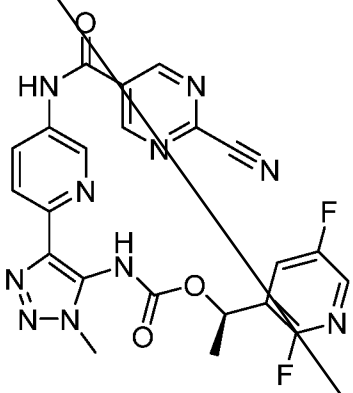
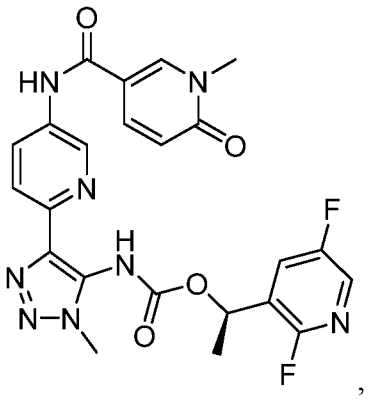
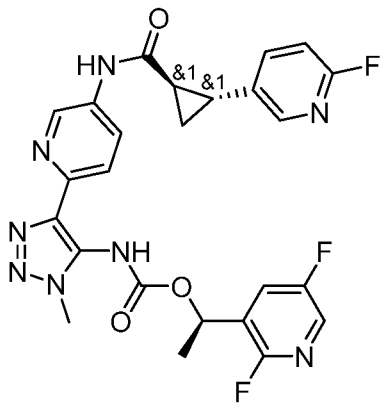
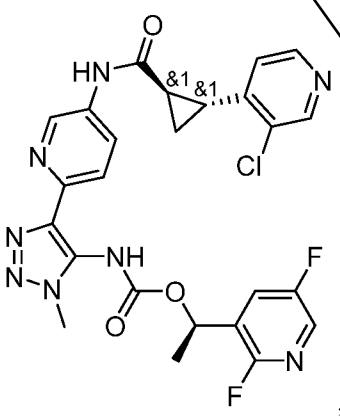
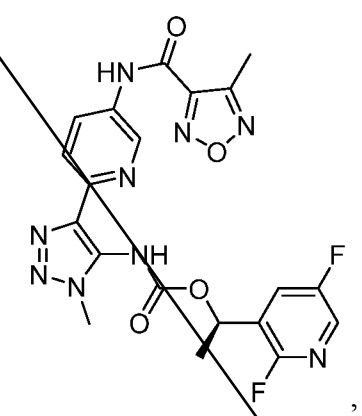
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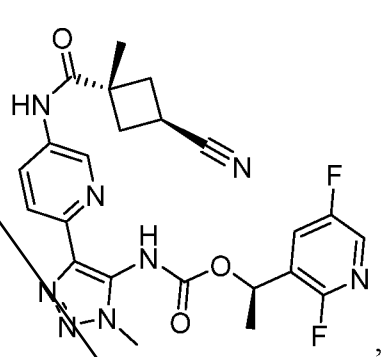
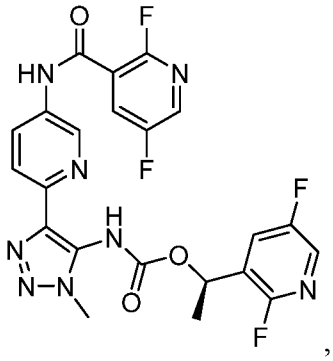
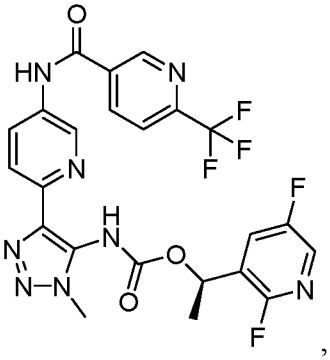
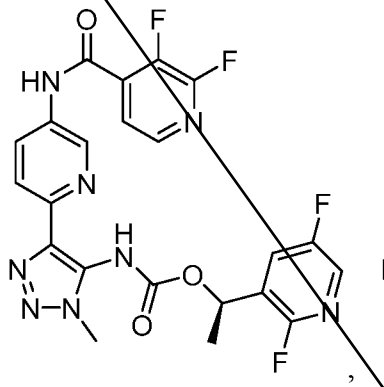
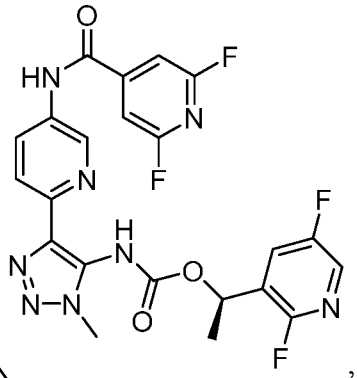
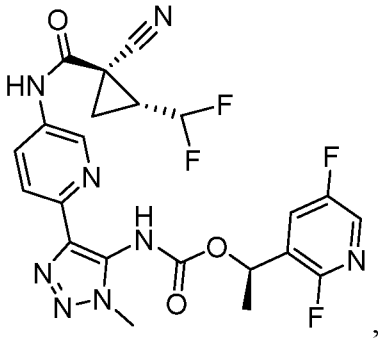
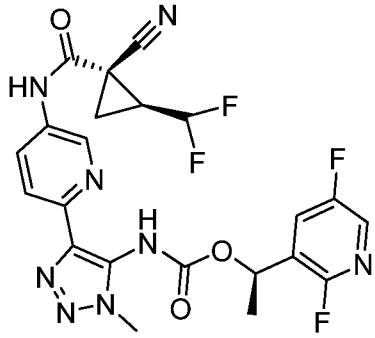
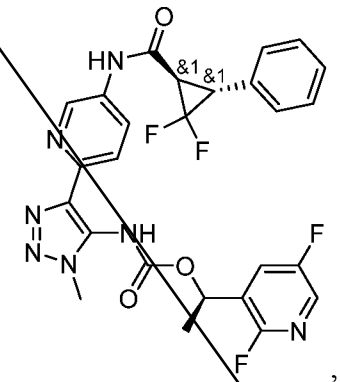
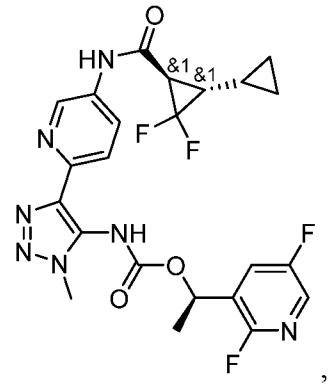
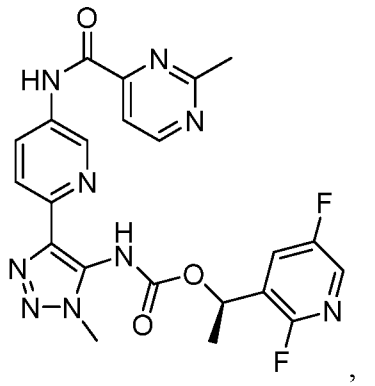
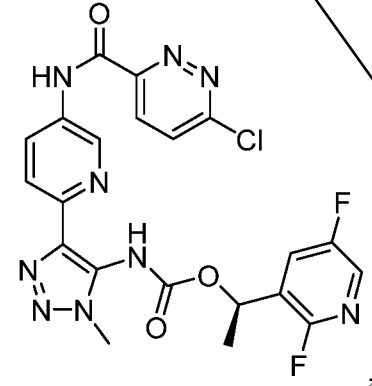
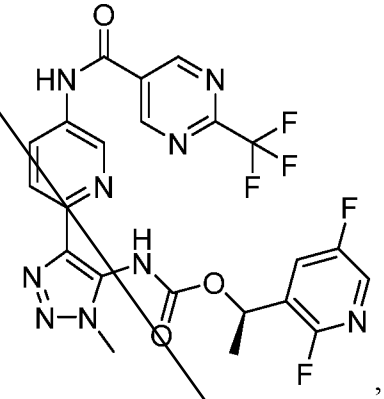
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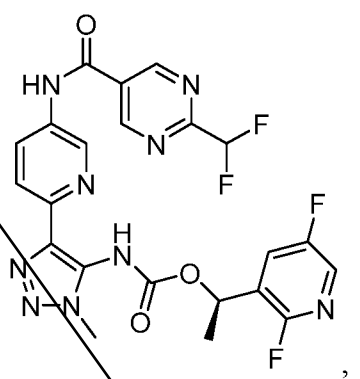
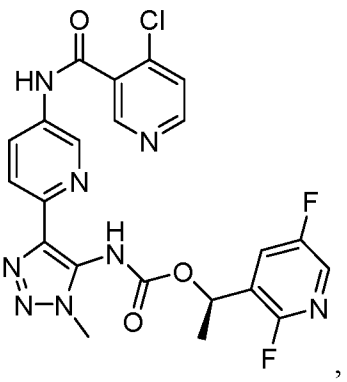
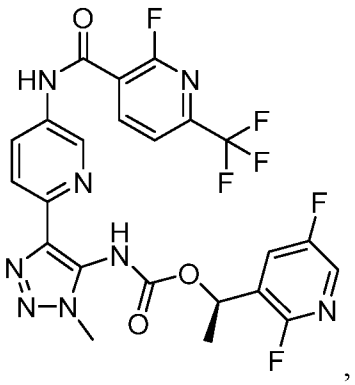
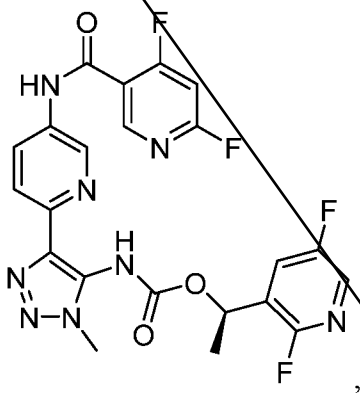
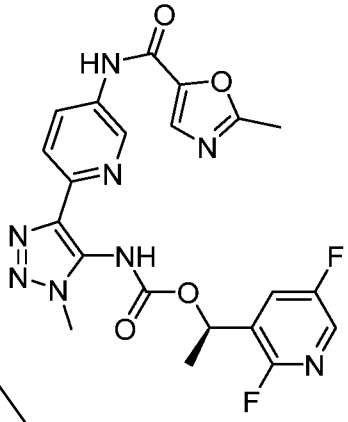
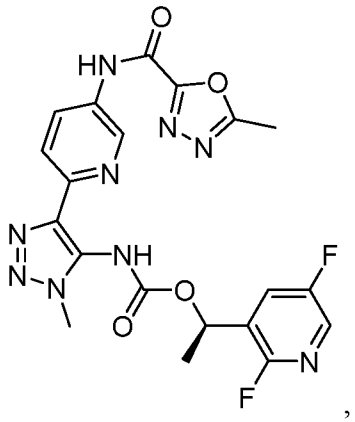
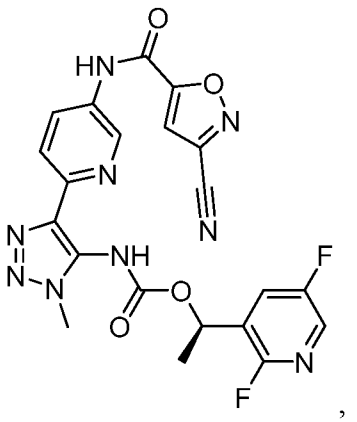
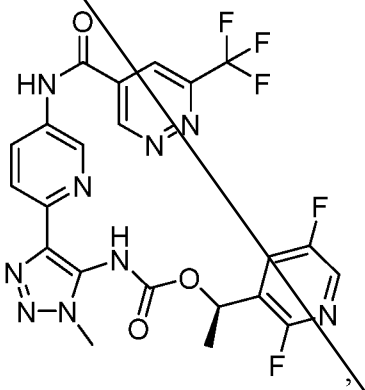
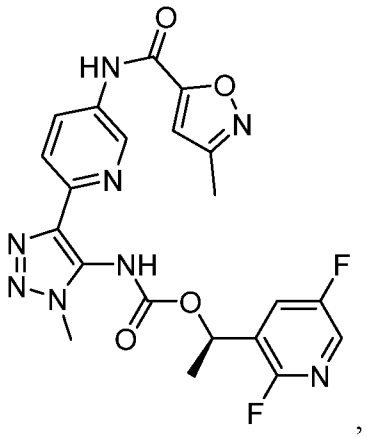
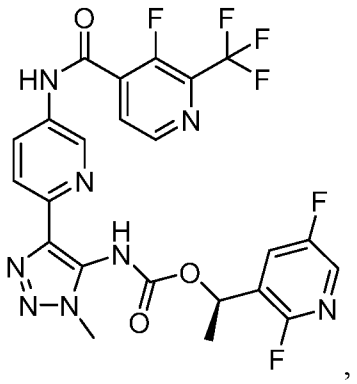
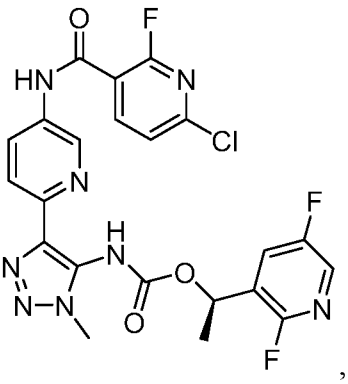
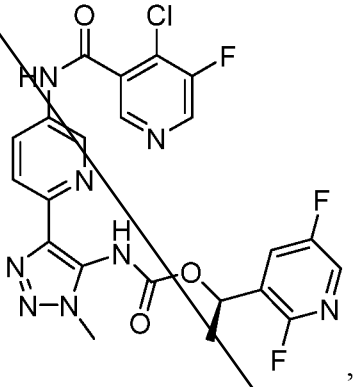


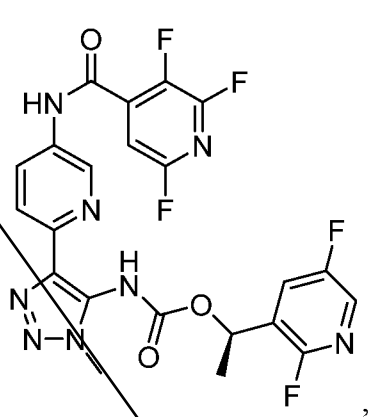
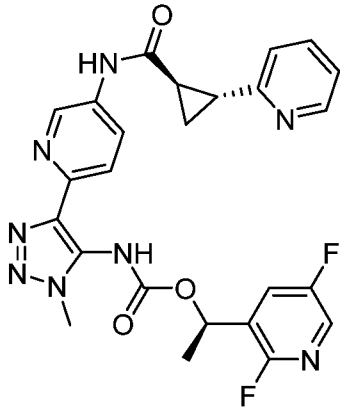
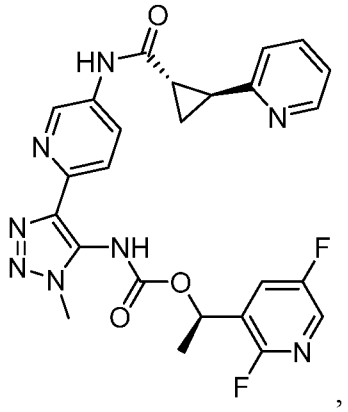
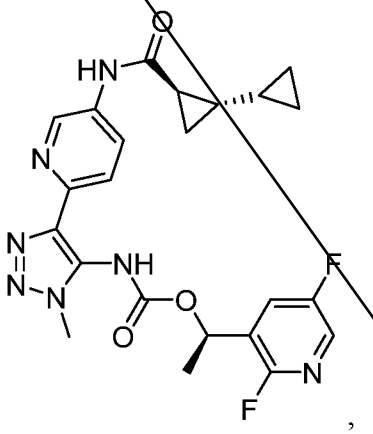
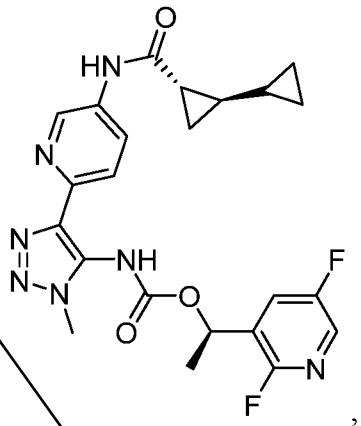
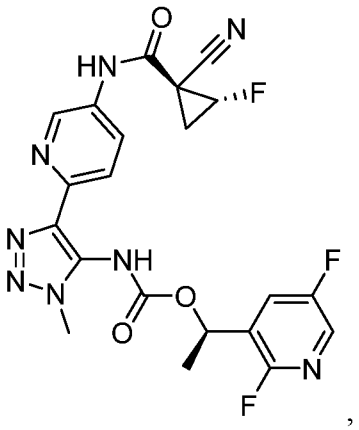
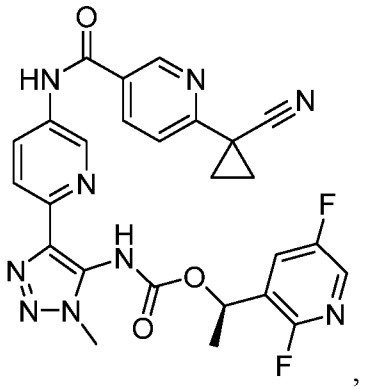
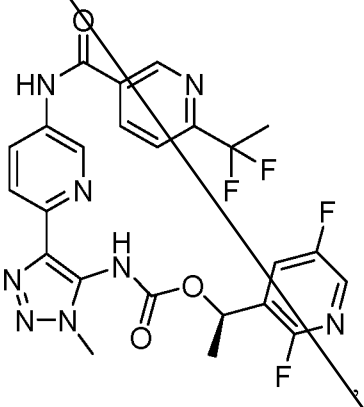
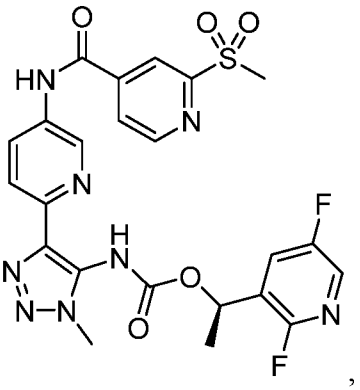
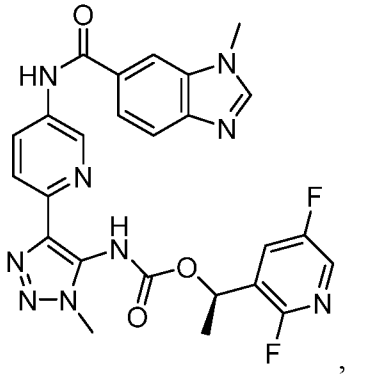
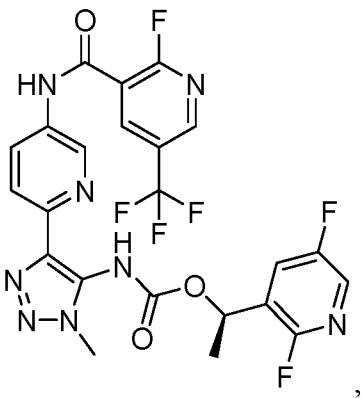
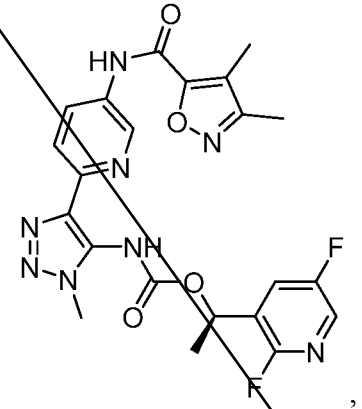

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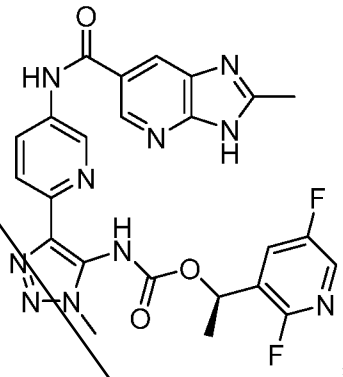
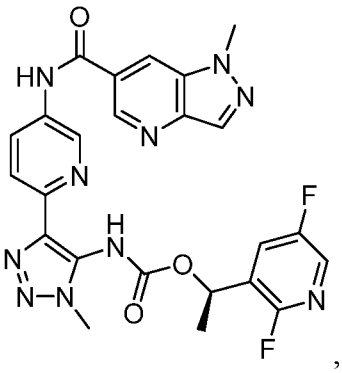
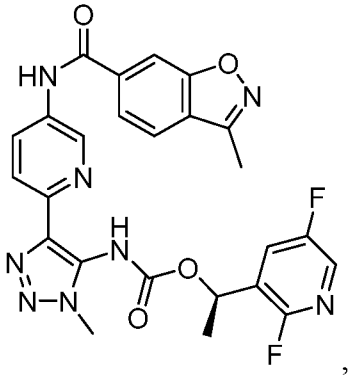
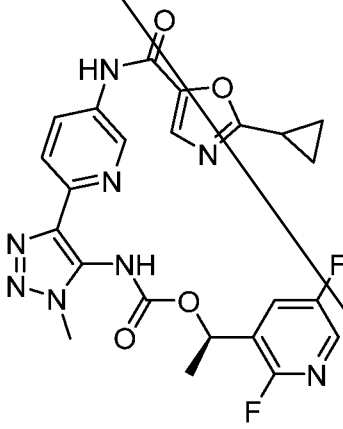
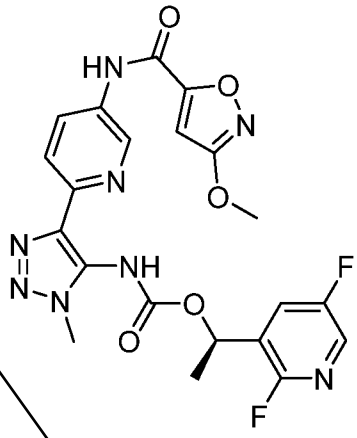
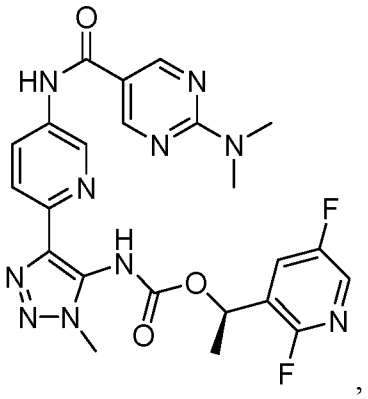
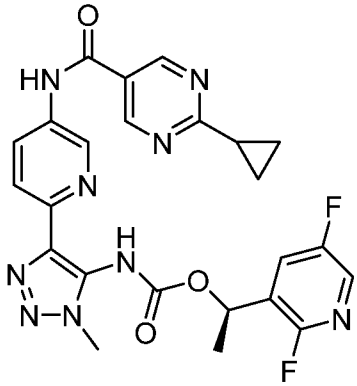
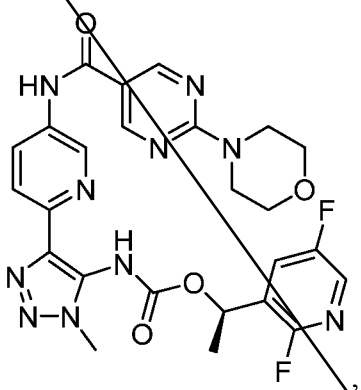
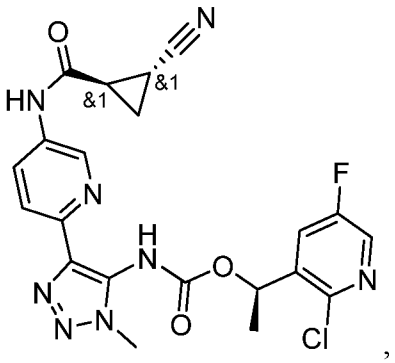
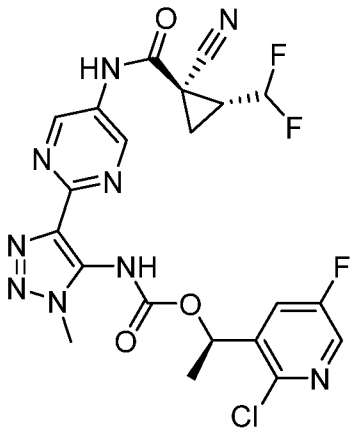
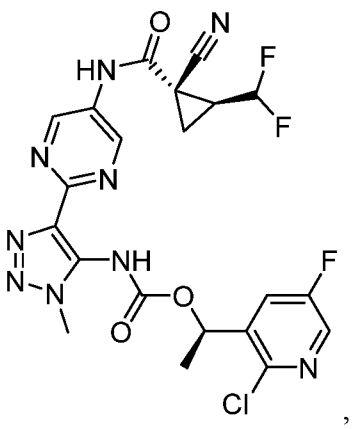
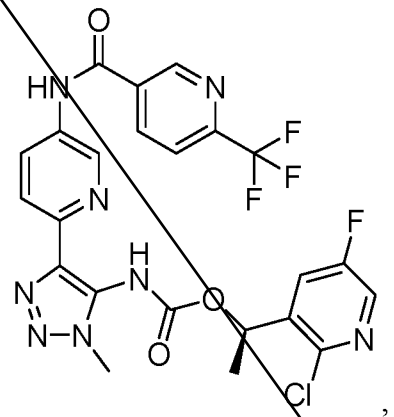

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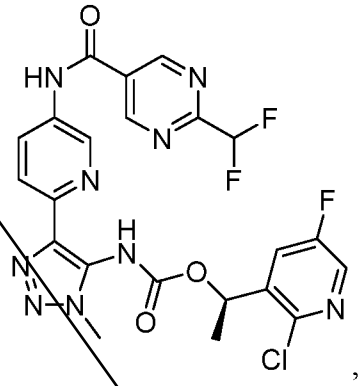
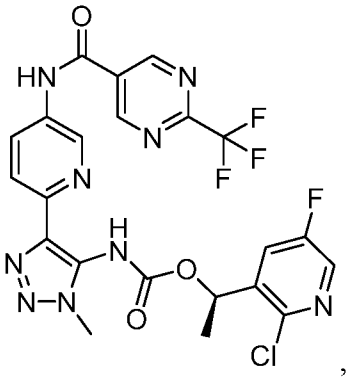
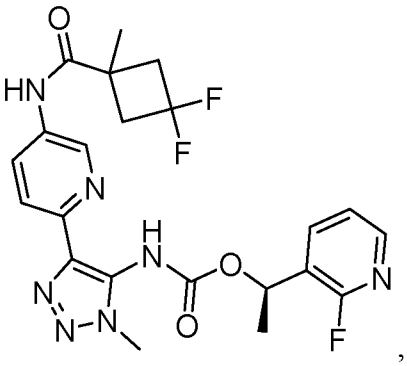
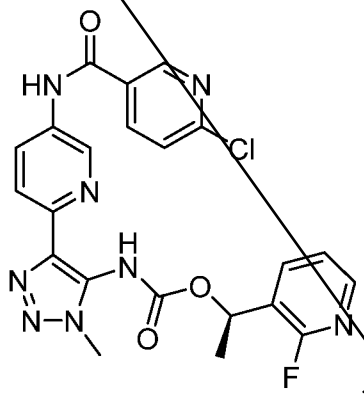
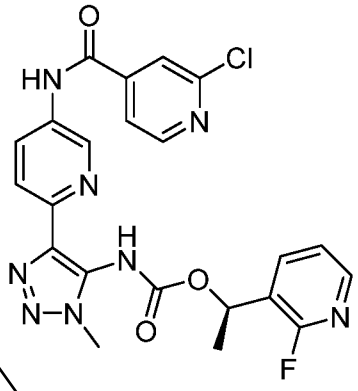
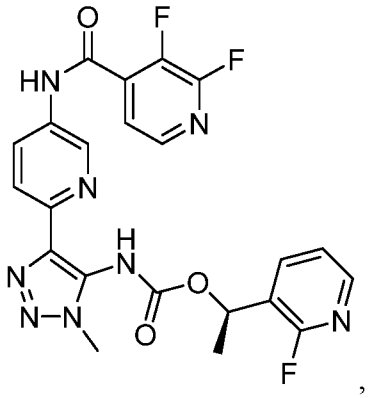
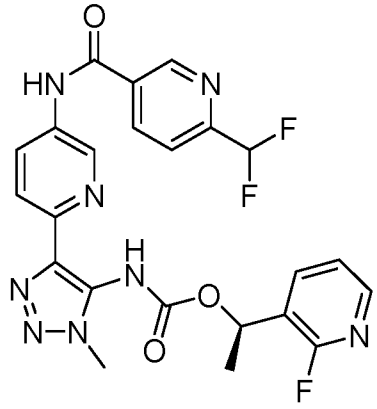
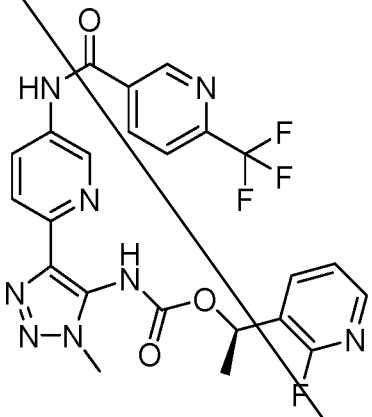
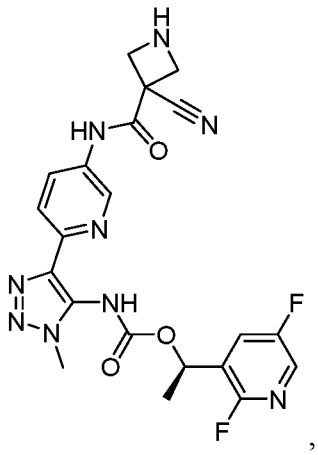

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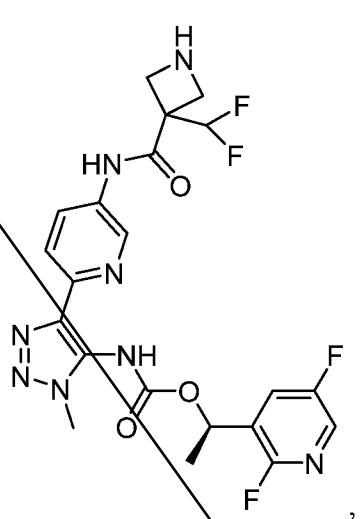
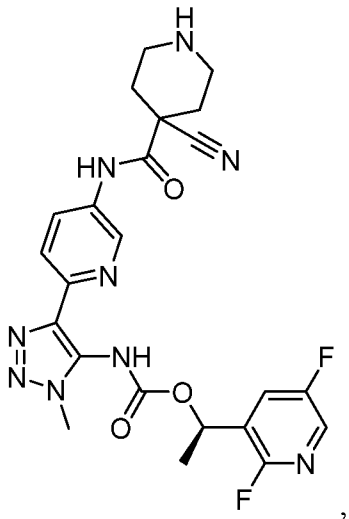
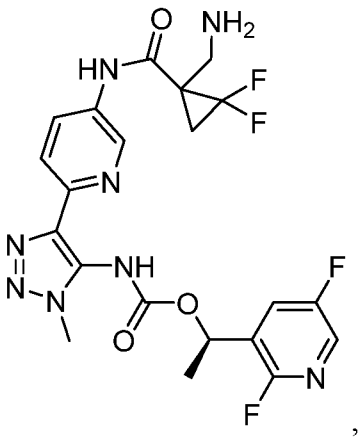
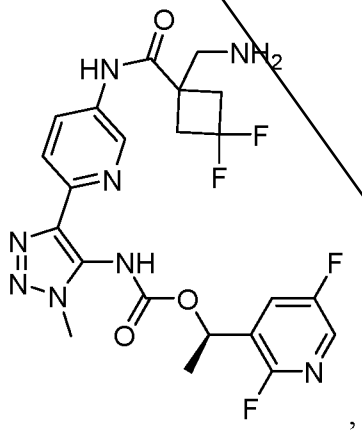
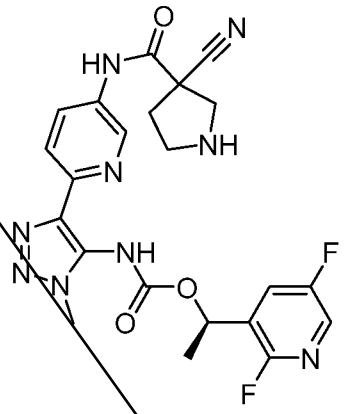
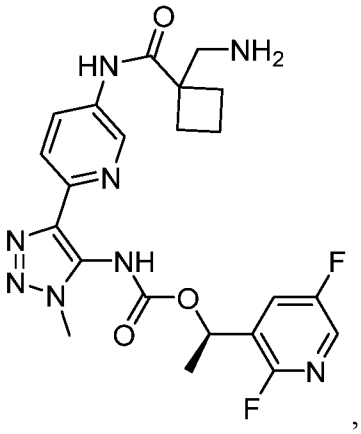
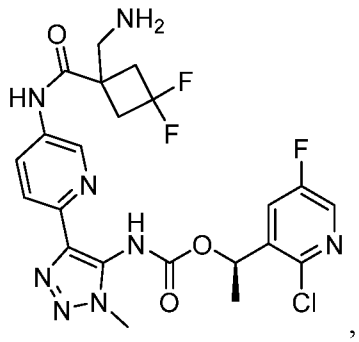
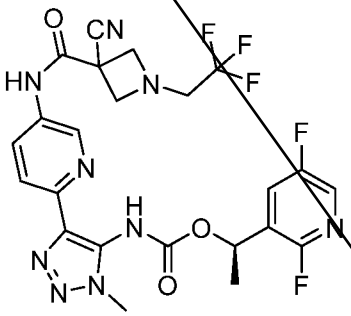
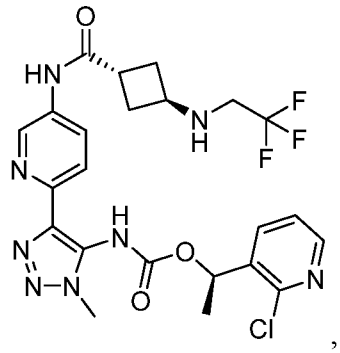
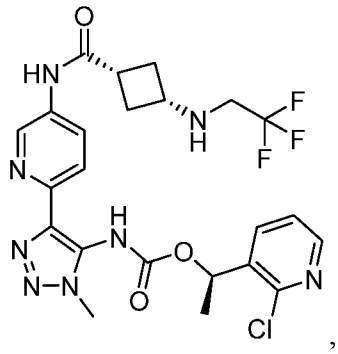
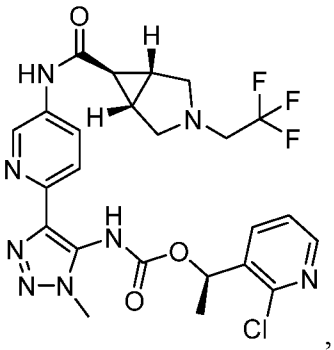
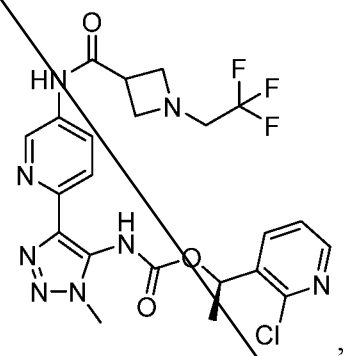

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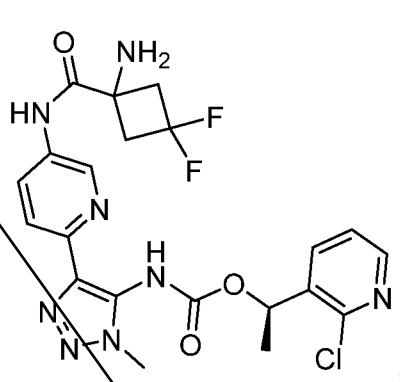
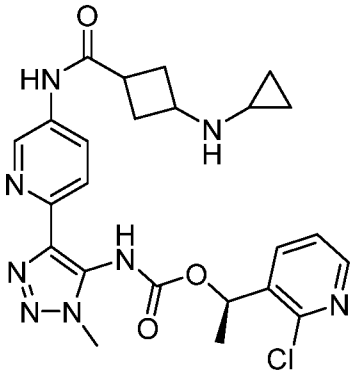
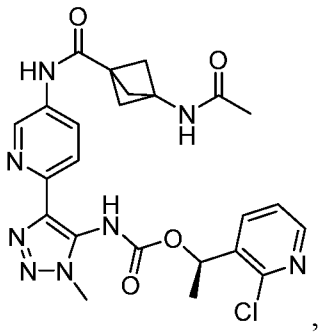
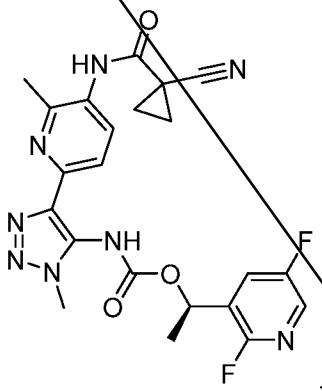
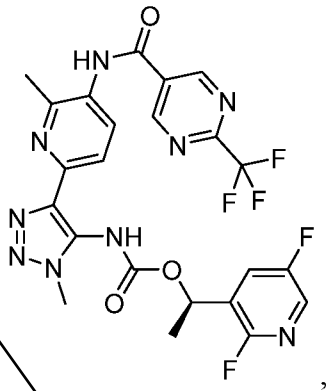
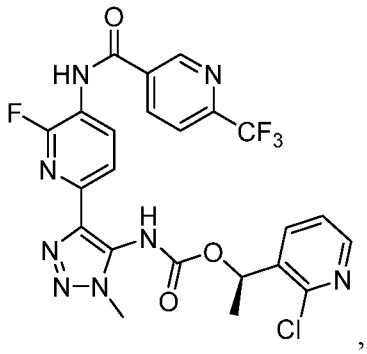
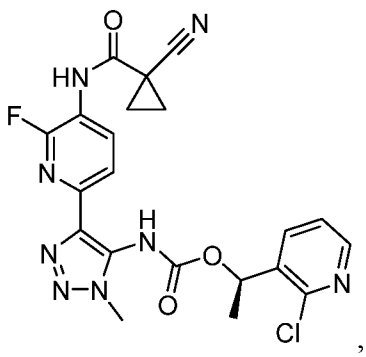
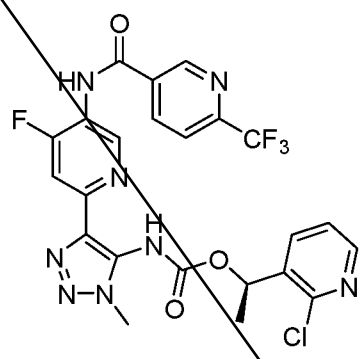
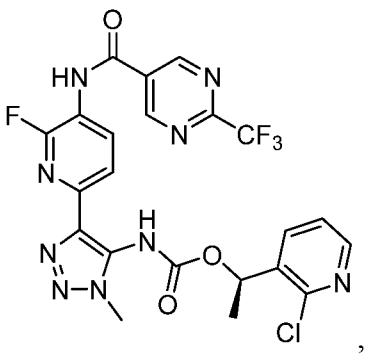
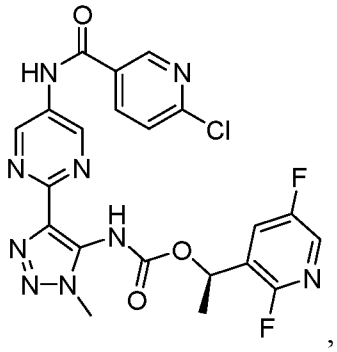
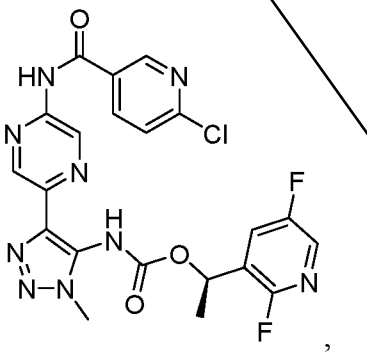
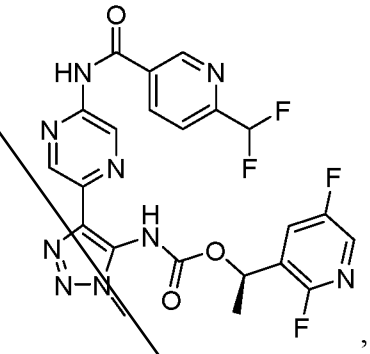

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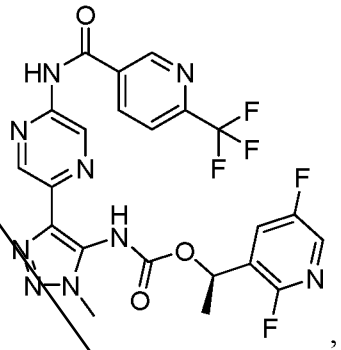
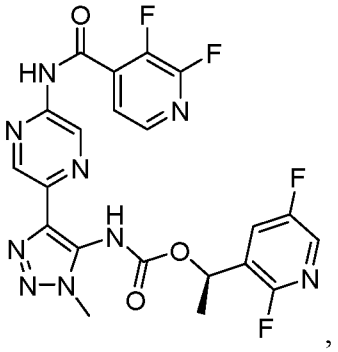
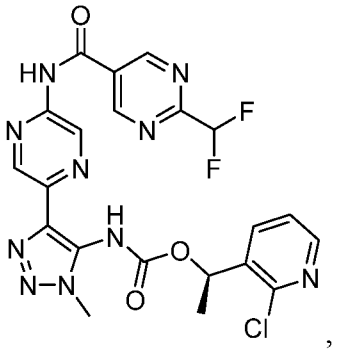
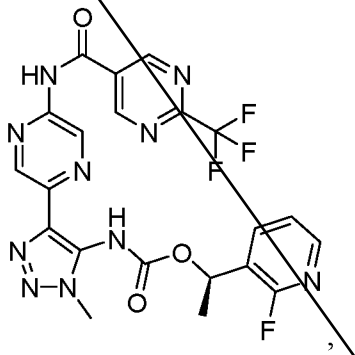
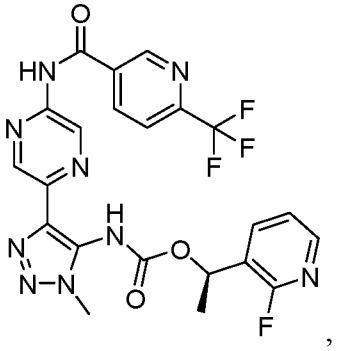
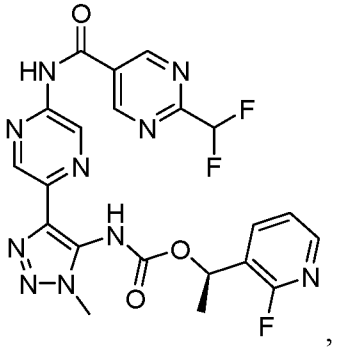
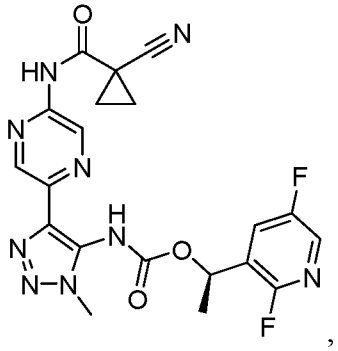
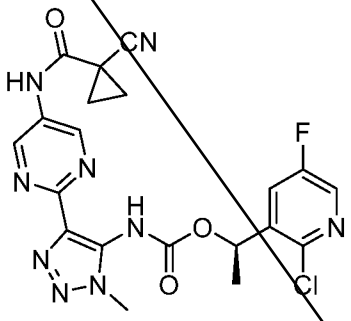
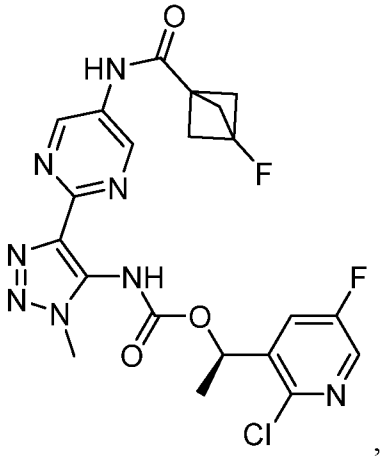
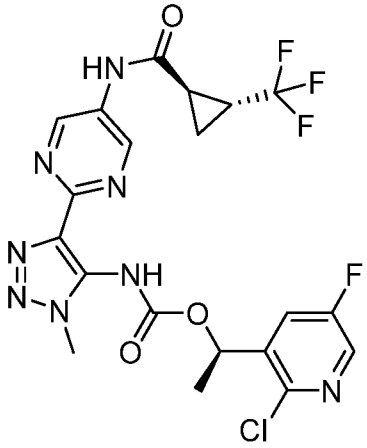
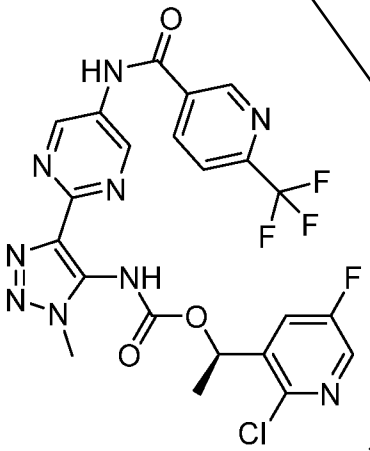
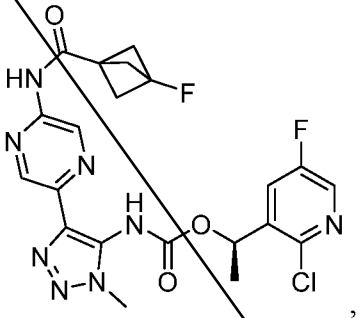

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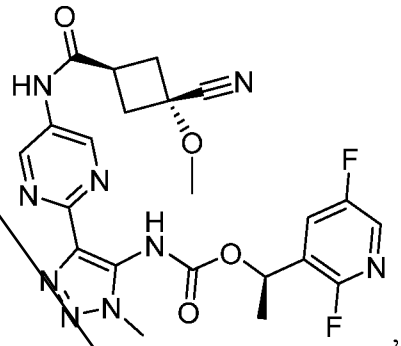
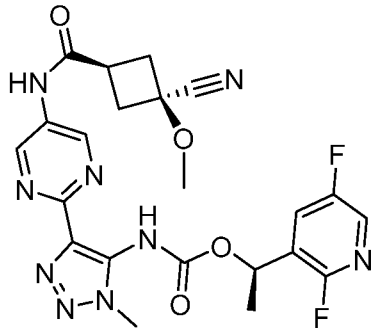
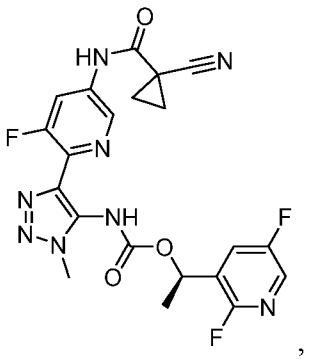
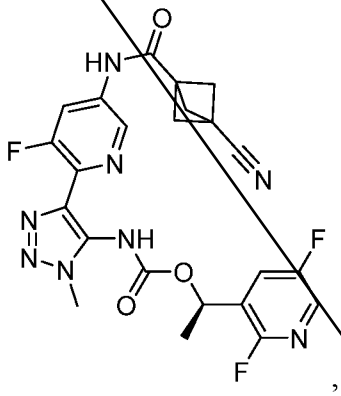
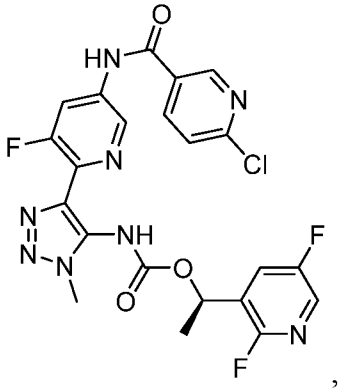

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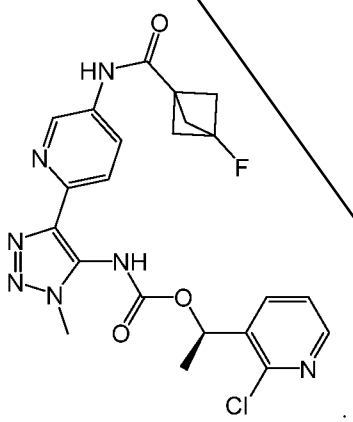

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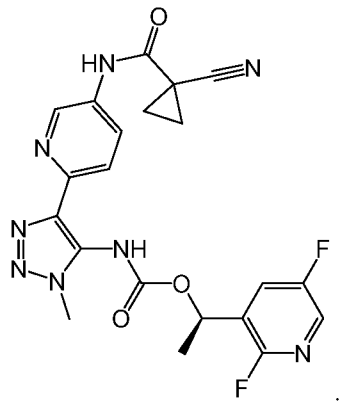

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or a pharmaceutically acceptable salt thereof.

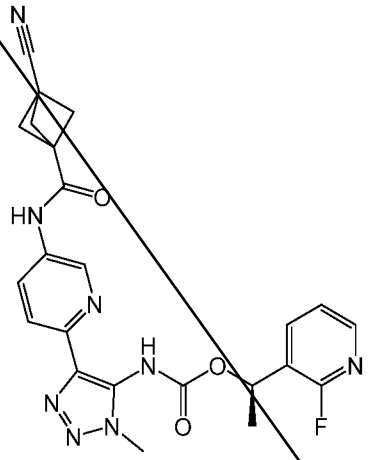
124. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is


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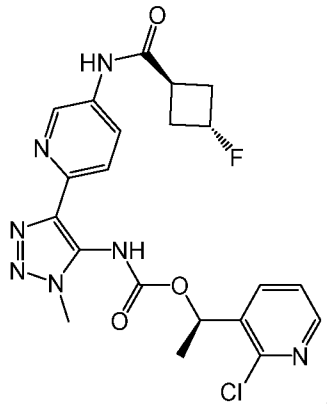
125. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



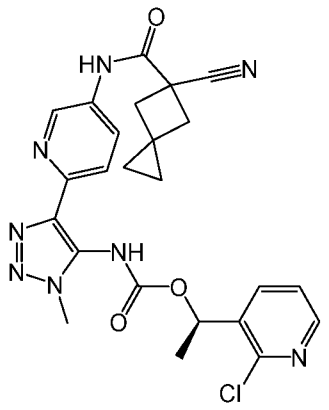
126. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



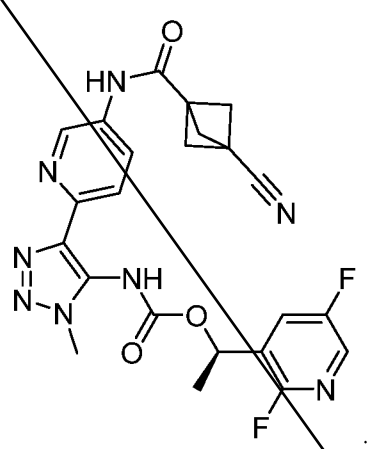
127. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



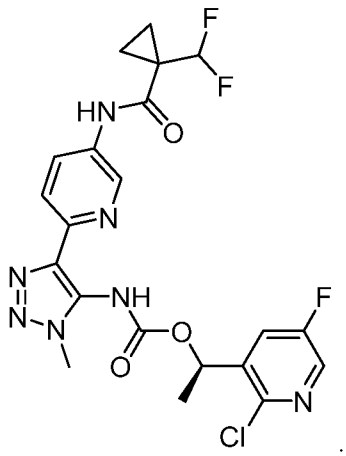
128. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



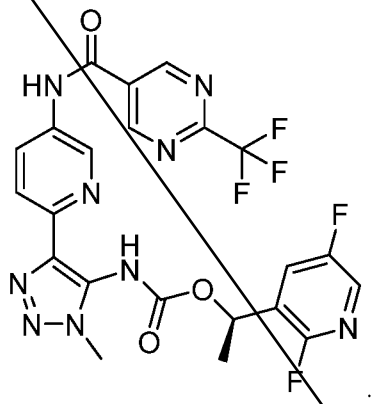
129. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



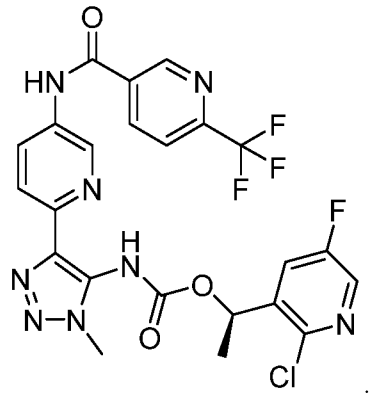
130. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



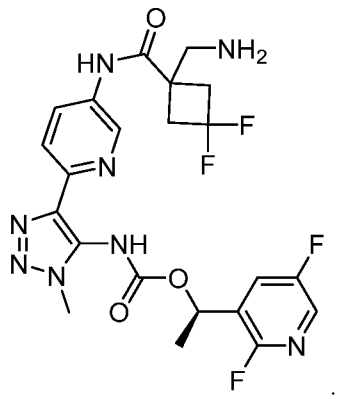
131. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



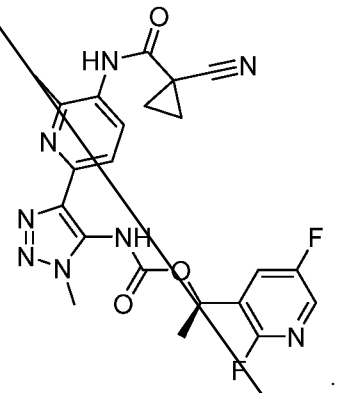
132. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



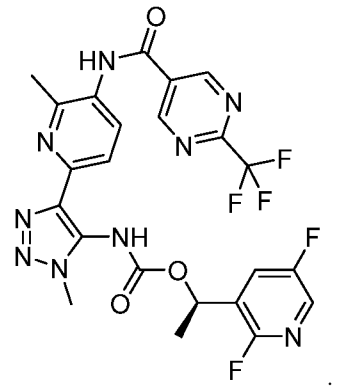
133. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



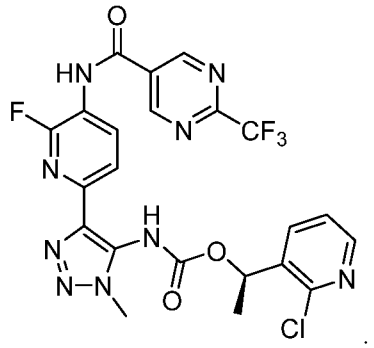
134. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



135. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



136. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



137. A pharmaceutical composition comprising a therapeutically effective amount of a compound, or pharmaceutically acceptable salt thereof, of any one of claims 1 to 136, and a pharmaceutically acceptable excipient.

138. The pharmaceutical composition of claim 137, further comprising an additional therapeutic agent.

139. A method of treating, stabilizing, or lessening the severity or progression of an LPAR1 mediated disease or condition comprising administering to a patient in need thereof a therapeutically effective amount of a compound of any one of claims 1 to 136, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claims 137 or 138.

140. The method of claim 139, wherein the LPAR1 mediated disease or condition is selected from the group consisting of wound healing, cancer, pain, respiratory disorder, allergic disorder, nervous system disorder, cardiovascular disorder, and inflammatory disorder.

141. The method of claim 139, wherein the LPAR1 mediated disease or condition is an interstitial lung disease (ILD).

142. The method of claim 141, wherein the interstitial lung disease (ILD) is nonspecific interstitial pneumonitis (NSIP), sarcoidosis, asbestosis, an ILD related to an occupational exposure, progressive fibrosing ILD, idiopathic interstitial pneumonia (IIP), connective tissue disease-associated interstitial lung disease (CTD-ILD), rheumatoid arthritis-associated ILD, scleroderma-associated ILD, or extrinsic alveolar alveolitis.

143. The method of claim 139, wherein the LPAR1 mediated disease or condition is a chronic kidney disease (CKD).

144. The method of claim 143, wherein the CKD is complement glomerulopathy, membranous glomerulopathy, polycystic kidney disease, IgA nephropathy, focal segmental glomerulosclerosis (FSGS), or Alport Syndrome.

145. The method of claim 139 or 140, wherein the LPAR1 mediated disease or condition comprises fibrosis.

146. The method of claim 145, wherein fibrosis is pulmonary fibrosis, renal fibrosis, hepatic fibrosis, ocular fibrosis, cardiac fibrosis, or systemic sclerosis.

147. The method of claim 146, wherein pulmonary fibrosis is idiopathic pulmonary fibrosis (IPF) or Progressive Fibrotic interstitial lung disease (PF-ILD).

148. The method of claim 147, wherein the pulmonary fibrosis is secondary to a systemic inflammatory disease.

149. The method of claim 148, wherein the systemic inflammatory disease is rheumatoid arthritis, scleroderma, lupus, cryptogenic fibrosing alveolitis, radiation induced fibrosis, chronic obstructive pulmonary disease (COPD), scleroderma, chronic asthma, silicosis, asbestos induced pulmonary or pleural fibrosis, acute lung injury or acute respiratory distress.

150. The method of claim 149, wherein the renal fibrosis is associated with diabetic kidney disease.

151. The method of claim 139, wherein the LPAR1 mediated disease or condition is a liver disease.

152. The method of claim 151, wherein the liver disease comprises liver fibrosis.

153. The method of claim 151 or 152, wherein the liver disease comprises non-alcoholic fatty liver disease (NAFLD).

154. The method of any one of claims 151-153, wherein the liver disease comprises steatosis.

155. The method of any one of claims 151-154, wherein the liver disease comprises non-alcoholic steatoheptitis (NASH).

156. The method of any one of claims 151-155, wherein the liver disease comprises liver cirrhosis.

157. The method of claim 156, wherein the liver cirrhosis is compensated liver cirrhosis.

158. The method of claim 156, wherein the liver cirrhosis is decompensated liver cirrhosis.

159. The method of any one of claims 151-158, wherein the liver disease comprises hepatocellular carcinoma (HCC).

160. The method of any one of claims 151-158, wherein the liver disease comprises Primary Biliary Cirrhosis (PBC) or Primary Sclerosing Choleangitis (PSC).

161. The method of any one of claims 151-158, wherein the liver disease comprises portal hypertension.

162. The method of any one of claims 139-161, wherein the compound or pharmaceutically acceptable salt thereof is administered in combination with an additional therapeutic agent.

163. The pharmaceutical composition of claim 137 or the method of claim 162, wherein the additional therapeutic agent is one, two, three, or four additional therapeutic agents.

164. The pharmaceutical composition of claim 137, or the method of claim 162 or 163, wherein the additional therapeutic agent comprises an acetyl-CoA carboxylase (ACC) inhibitor, an apoptotic signal-regulating kinase (ASK-1) inhibitor, a farnesoid X receptor (FXR) agonist, fish oil, a glucagon-like peptide-1 receptor agonist, a peroxisome proliferator-activated receptor alpha (PPARα) agonist, or a TGFβ antagonist.

165. The pharmaceutical composition or method of claim 164, wherein the the ACC inhibitor is firsocostat.

166. The pharmaceutical composition or method of claim 164, wherein the the ASK1 inhibitor is selonsertib.

167. The pharmaceutical composition or method of claims 164, wherein the the FXR agonist is cilofexor.

168. The pharmaceutical composition or method of claim 164, wherein the PPARα agonist is a fibrate.

169. The pharmaceutical composition or method of claim 164, wherein the fish oil is icosapent ethyl.

170. The pharmaceutical composition or method of claim 164, wherein the GLP-1 receptor agonist is liraglutide or semaglutide.

171. The pharmaceutical composition or method of claim 164, wherein the TGFβ antagonist is an anti-TGFβ1 specific antibody.

172. The pharmaceutical composition or method of claim 164, wherein the TGFβ antagonist is a TGFβ receptor.

173. The pharmaceutical composition or method of claim 164, wherein the additional therapeutic agent comprises firsocostat and cilofexor.

174. The pharmaceutical composition or method of claim 164, wherein the additional therapeutic agents comprise firsocostat and liraglutide or semaglutide.

175. The pharmaceutical composition or method of claim 164 or 165, wherein the additional therapeutic agents comprise a fibrate or icosapent ethyl.

176. The pharmaceutical composition or method of claim 164, wherein the additional therapeutic agent comprises cilofexor and liraglutide or semaglutide.

177. The pharmaceutical composition of claim 137, or the method of claim 162 or 163, wherein the additional therapeutic agent comprises a VEGFR inhibitor, a FGFR inhibitor, a PDGFR inhibitor, an autaxin inhibitor, a GPR84 agonist, a PASK inhibitor, a CFTR agonist, a JAK1 inhibitor, an ADAMTS5 inhibitor, a TOL2/3 inhibitor, a CTGF inhibitor, a soluble PTX2, an anti-galectin-3 antibody, an integrin-α_V-β_6/α_V-β_1 antagonist, a JNK1 inhibitor, a mineralocorticoid receptor antagonist, a Nrf2 activator, a chymase inhibitor, a

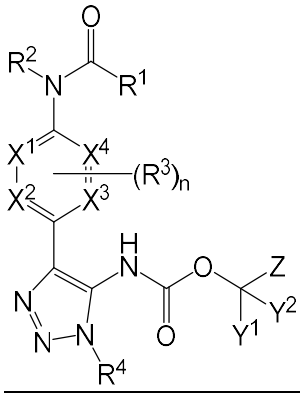
PDE inhibitor, a NOX1/4 inhibitor, a leukotriene/thromboxane receptor antagonist, SLC22A12 inhibitor, an sGC inhibitor, or a xanthine oxidase inhibitor.

178. The pharmaceutical composition of claim 137, or the method of claim 162 or 163, wherein the additional therapeutic agent is selected from the group consisting of nintedanib, pirfenidone, pamrevlumab, PRM-151, GB-0139, PLN-74809, CC-90001, finerenone, BAY1142524, PCS-499, setanaxib, SER150, RDEA3170, praliciguat, TMX-049, GLPG1690, GLPG1205, GLPG1972, GLPG4059, GLPG2737, GLPG3970, and filgotinib.

179. Use of a compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 136 for the manufacture of a medicament for the treatment of an LPAR1 mediated disease or condition.

CLAIMS

1. A compound of Formula (I),



(I)

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, or 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, nitro, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, $-N(R^{1B1})(R^{1B2})$, $-O-R^{1B1}$, $-S-R^{1B1}$, $-C(O)N(R^{1B1})(R^{1B2})$, $-NR^{1B1}C(O)R^{1B2}$, $-NR^{1B1}C(O)N(R^{1B2})(R^{1B3})$, $-S(O)_{0-2}R^{1B1}$, $-S(O)_2N(R^{1B1})(R^{1B2})$, and $-NR^{1B1}S(O)_2R^{1B2}$, wherein each R^{1B1}, R^{1B2}, and R^{1B3} is independently hydrogen, C_{1-6} alkyl, or C_{3-6} cycloalkyl,

wherein each R^{1A} alkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1 to 4 R^{1C}, which can be the same or different, and wherein each R^{1C} is independently C_{1-4} alkyl, halogen, cyano, $-O-R^{1D1}$, or

-N(R^{1D1})(R^{1D2}), wherein each R^{1D1} and R^{1D2} is independently hydrogen or C_{1-6} alkyl, and

wherein each R^{1B1}, R^{1B2}, and R^{1B3} alkyl and each R^{1B1}, R^{1B2}, and R^{1B3} cycloalkyl is optionally substituted with 1 to 3 halogens; or

R^1 is -O-R^{1D1} or -N(R^{1D1}) (R^{1D2}), wherein each R^{1D1} and R^{1D2} is independently hydrogen, C_{1-6} alkyl, or C_{3-6} cycloalkyl, wherein each C_{1-6} alkyl, or C_{3-6} cycloalkyl is optionally substituted with 1 to 4 R^{1E}, which can be the same or different, wherein each R^{1E} is independently selected from halogen, cyano, hydroxy, oxo, C_{1-4} alkyl, C_{3-10} cycloalkyl, 3 to 10 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, 6 to 10 membered aryl, 5 to 10 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, -O-R^{1F1}, –N(R^{1F1})(R^{1F2}), –C(O)N(R^{1F1}) (R^{1F2}), –NR^{1F1}C(O)R^{1F2}, –S(O)$_{0-2}$$R^{1F1}$, –S(O)$_2$N($R^{1F1}$)($R^{1F2}$), and –N$R^{1F1}$S(O)$_2$$R^{1F2}$, wherein each R^{1F1} and R^{1F2} is independently hydrogen or C_{1-6} alkyl, wherein each R^{1E} alkyl, cycloalkyl, aryl, and heteroaryl is optionally substituted with 1 to 3 R^{1G}, which can be the same or different, and wherein each R^{1G} is independently C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy, halogen, or cyano;

R^2 is hydrogen or C_{1-6} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkoxy, and C_{3-10} cycloalkyl; or

R^2 is C_{3-6} cycloalkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkoxy, and C_{1-6} alkyl;

each R^3 is independently selected from deuterium, halogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, -O-R^{2A1}, and -N(R^{2A1})(R^{2A2}), wherein the C_{1-6} alkyl is optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from C_{1-4} alkoxy and halogen, and wherein each R^{2A1} and R^{2A2} is independently hydrogen or C_{1-3} alkyl optionally substituted with 1 to 3 halogens, which can be the same or different;

n is 0, 1, 2, 3, or 4;

R^4 is C_{1-6} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkoxy, -C(O)N(R^{4A1}), and

-N(R^{4A1})(R^{4A2}), wherein each R^{4A1} and R^{4A2} is independently hydrogen, C_{1-6} alkyl, or C_{3-10} cycloalkyl; or

R^4 is C_{3-6} cycloalkyl or 3 to 6 membered heterocyclyl having 1 or 2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein the cycloalkyl or heterocyclyl are optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkyl, and C_{1-4} alkoxy;

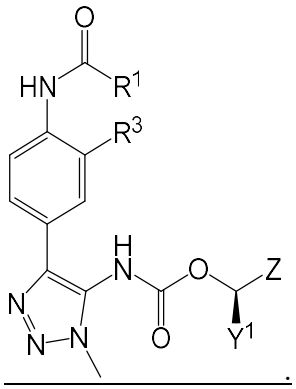
each of X^1, X^2, X^3, and X^4 is independently selected from CH and N;

each Y^1 and Y^2 is independently hydrogen, deuterium, or C_{1-6} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from deuterium, halogen, cyano, C_{2-3} alkynyl, C_{1-4} alkoxy, and -C(O)NH-($C_{1-4}H_{3-9}$); and

Z is C_{1-8} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{6-12} aryl, 3 to 12 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or 5 to 12 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein the alkyl, alkoxy, cycloalkyl, aryl, heterocyclyl, or heteroaryl are each optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from halogen, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, and C_{3-6} cycloalkyl, wherein the C_{1-4} alkyl is optionally substituted with 1 to 3 substituents, which can be the same or different, selected from C_{1-4} alkoxy and halogen; or

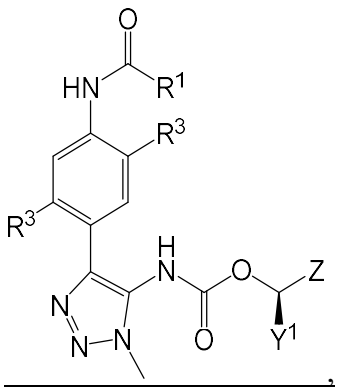
Y^1 and Z together with the carbon to which they are attached form C_{3-6} cycloalkyl, C_{6-12} aryl, 3 to 12 membered heterocyclyl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or 5 to 12 membered heteroaryl having 1 to 4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein the cycloalkyl, aryl, heterocyclyl, or heteroaryl are each optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from cyano, C_{1-4} alkyl, C_{1-4} alkoxy, C_{6-10} aryl, and halogen, wherein the C_{1-4} alkyl is optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from C_{1-4} alkoxy and halogen, and wherein the C_{6-10} aryl is optionally substituted with 1 to 3 substituents, which can be the same or different, independently selected from C_{1-4} alkyl, C_{1-4} alkoxy, and halogen, and Y^2 is hydrogen or deuterium.

2. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIa):



(IIa)

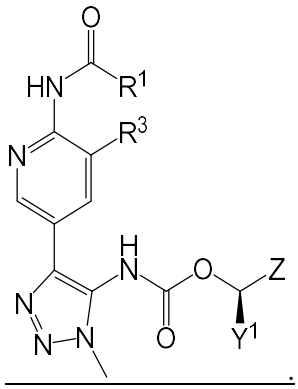
3. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIb):



(IIb)

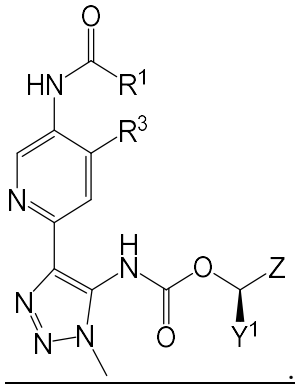
wherein each R^3 can be the same or different.

4. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIc):



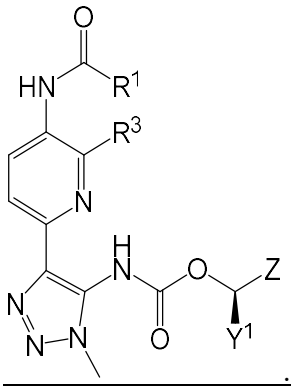
(IIc)

5. The compound or pharmaceutically acceptable salt thereof of claims 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IId):



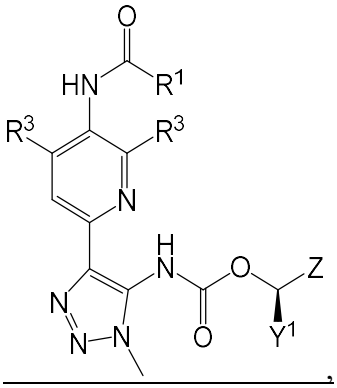
(IId)

6. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIe):



(IIe)

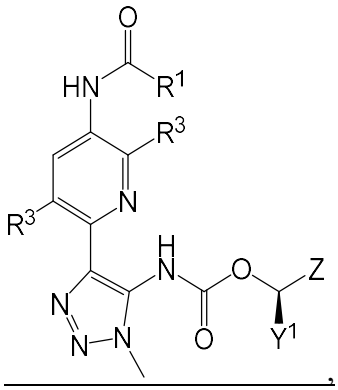
7. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIf):



(IIf)

wherein each R^3 can be the same or different.

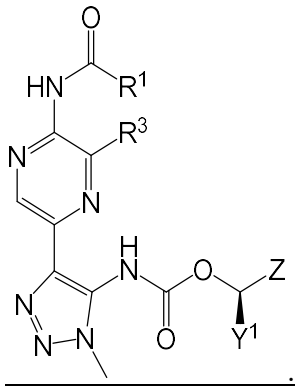
8. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIg):



(IIg)

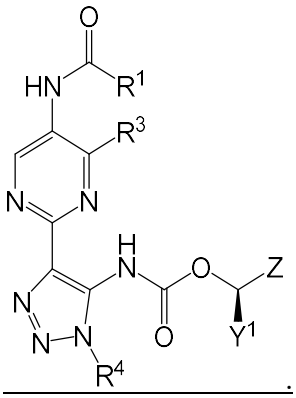
wherein each R^3 can be the same or different.

9. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIh):



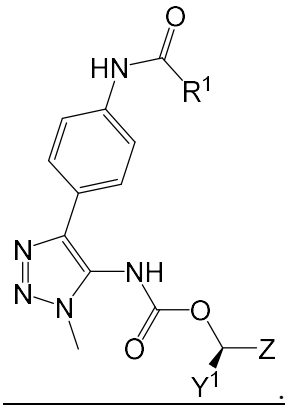
(IIh)

10. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIi):



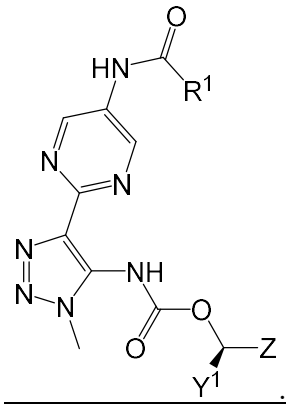
(IIi)

11. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIj):



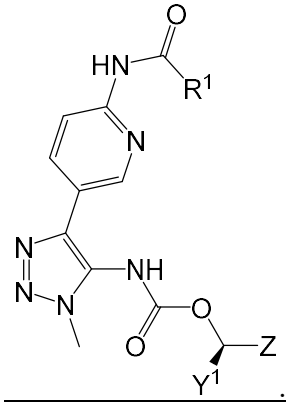
(IIj)

12. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIk):



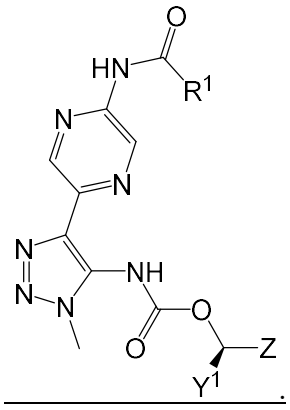
(IIk)

13. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (III):



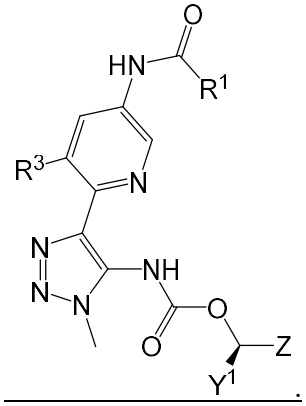
(III)

14. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIm):



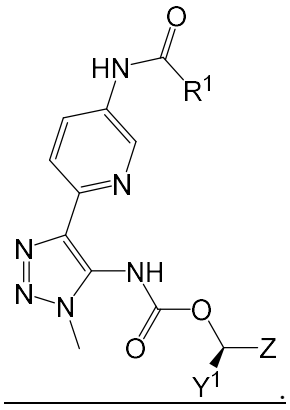
(IIm)

15. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIn):



(IIn)

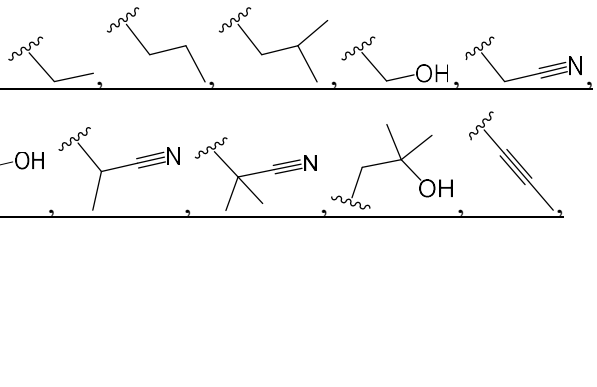
16. The compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound of Formula (I) or Formula (Ia) is of Formula (IIo):



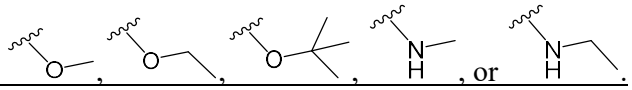
(IIo)

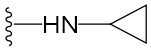
17. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-17, wherein R^1 is hydrogen.

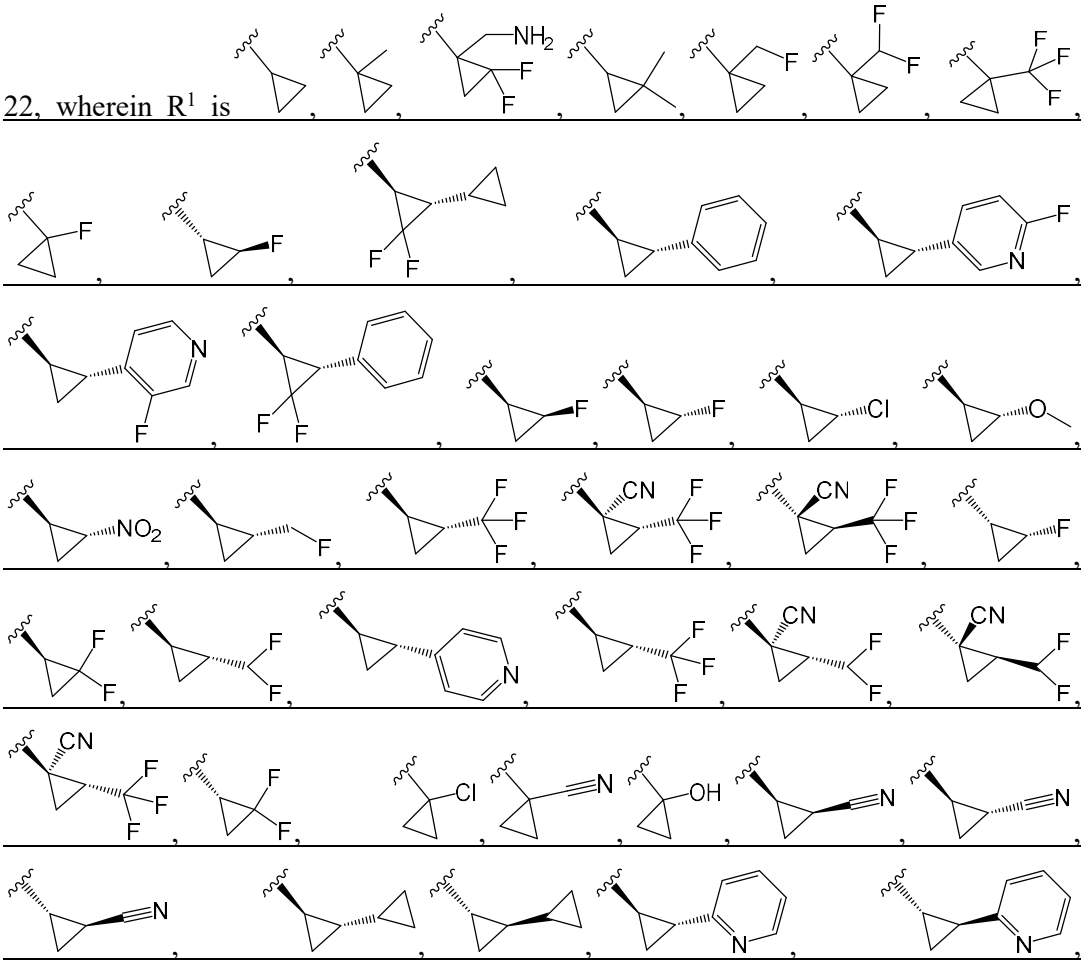
18. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-17, wherein R^1 is C_{1-6} alkyl or C_{2-6} alkynyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from halogen, cyano, hydroxy, C_{1-4} alkoxy, and C_{3-6} cycloalkyl.

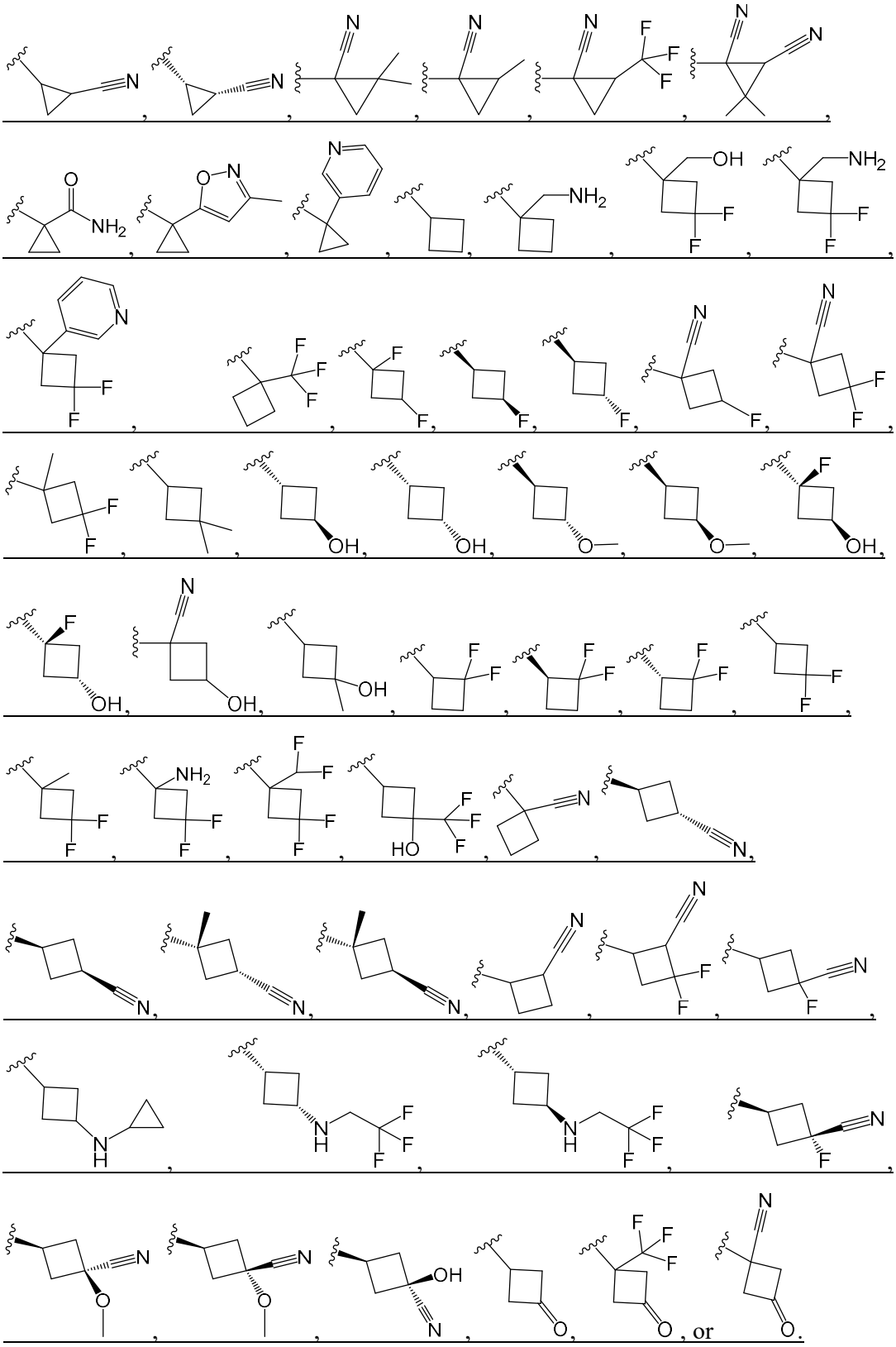
19. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-17 and 18, wherein R^1 is $-CH_3$, $-CHF_2$, $-CF_3$, 

20. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-17, wherein R^1 is $-O-R^{1D1}$ or $-N(R^{1D1})(R^{1D2})$, wherein each R^{1D} and R^{1D2} is independently -H, $-CH_3$, $-C_2H_5$, or $-C(CH_3)_3$.

21. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-17 and 20, wherein R^1 is .

22. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-17, wherein R^1 is cyclopropyl or cyclobutyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, each independently selected from -F, -Cl, -CN, =O, -OH, -CH_3, -CH_2F, -CHF_2, -CF_3, -CH_2-OH, -CH_2-NH_2, -OCH_3, -NH_2, -NH-CH_2-CF_3, , -NO_2, cyclopropyl, isoxazyl, phenyl, pyridyl, and –C(O)NH_2, wherein each isoxazyl or pyridyl is optionally substituted with 1 to 2 -F or -CH_3.

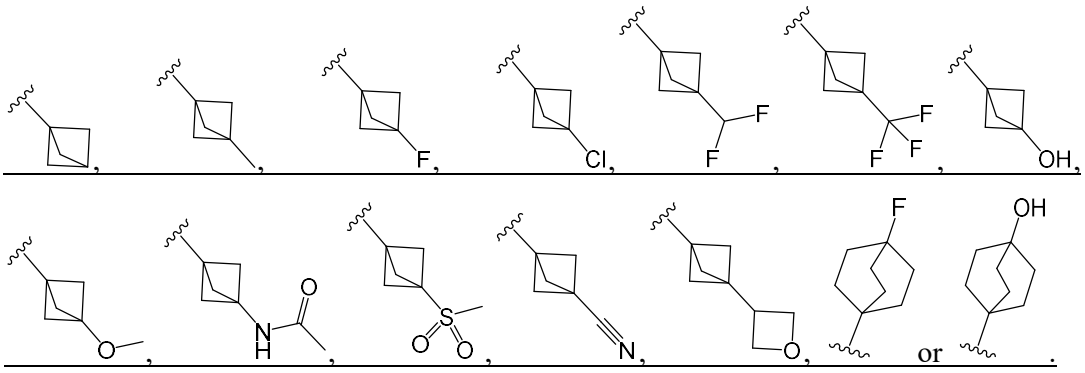
23. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-17 and 22, wherein R^1 is .



, or

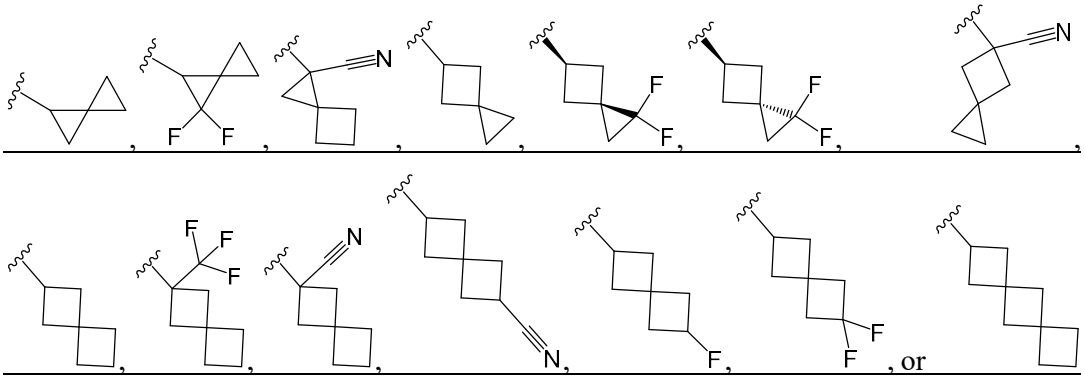
24. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 17, wherein the C_{5-8} bridged bicyclic cycloalkyl is bicyclopentanyl or bicyclooctanyl, each optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from -F, -Cl, -OH, -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-O-CH_3$, and oxetanyl.

25. The compound or pharmaceutically acceptable salt thereof of claim 24, wherein R^1 is



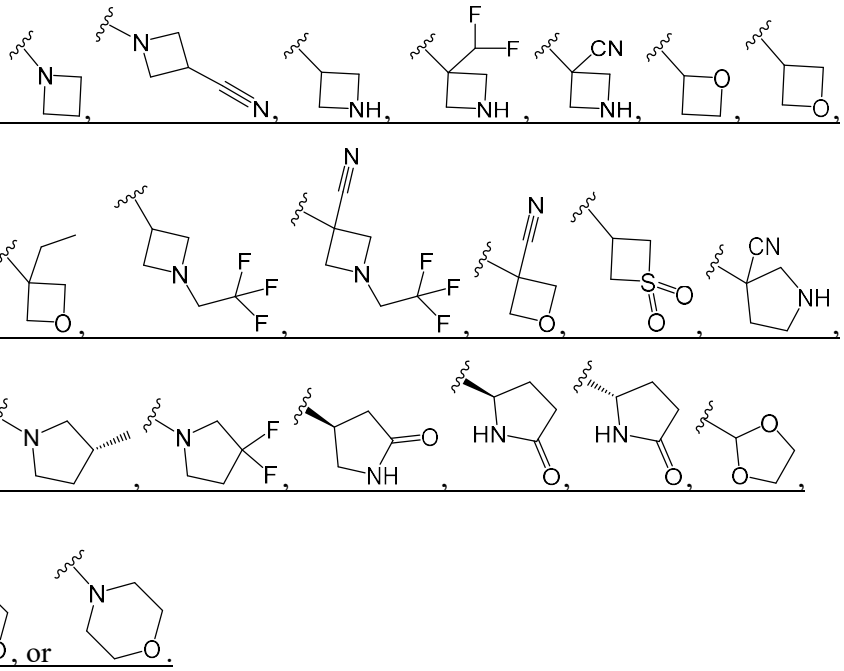
26. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 17, wherein the C_{5-10} spiro bicyclic cycloalkyl is spiropentanyl, spirohexanyl, spiroheptanyl, or spirodecanyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is each independently selected from -F, -Cl, -OH, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, -CN, and $-O-CH_3$.

27. The compound or pharmaceutically acceptable salt thereof of claim 26, wherein R^1 is

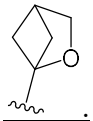


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28. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-17, wherein R^1 is azetidinyl, oxetyl, thietanyl, pyrrolidinyl, dioxolanyl, tetrahydropyranyl, piperidinyl, or morpholinyl, each optionally substituted with 1 to 4 R^{1A}, which can be the same or different, each independently selected from -F, -Cl, -OH, -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, $-C_2H_5$, $-CH_2-CF_3$, and $-O-CH_3$.

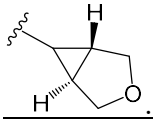
29. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-17 and 28, wherein R^1 is , or .

30. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 17, wherein the bridged bicyclic heterocyclyl is an oxabicyclohexanyl optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from -F, -Cl, -OH, -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, and $-O-CH_3$.

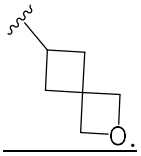
31. The compound or pharmaceutically acceptable salt thereof of claim 30, wherein R^1 is .

32. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 17, wherein the fused bicyclic heterocyclyl is an oxabicyclohexanyl optionally substituted with 1 to 4 R^{1A}, which can be the same or different, wherein each R^{1A} is independently

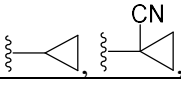
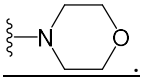
selected from -F, -Cl, -OH, -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, and $-O-CH_3$.

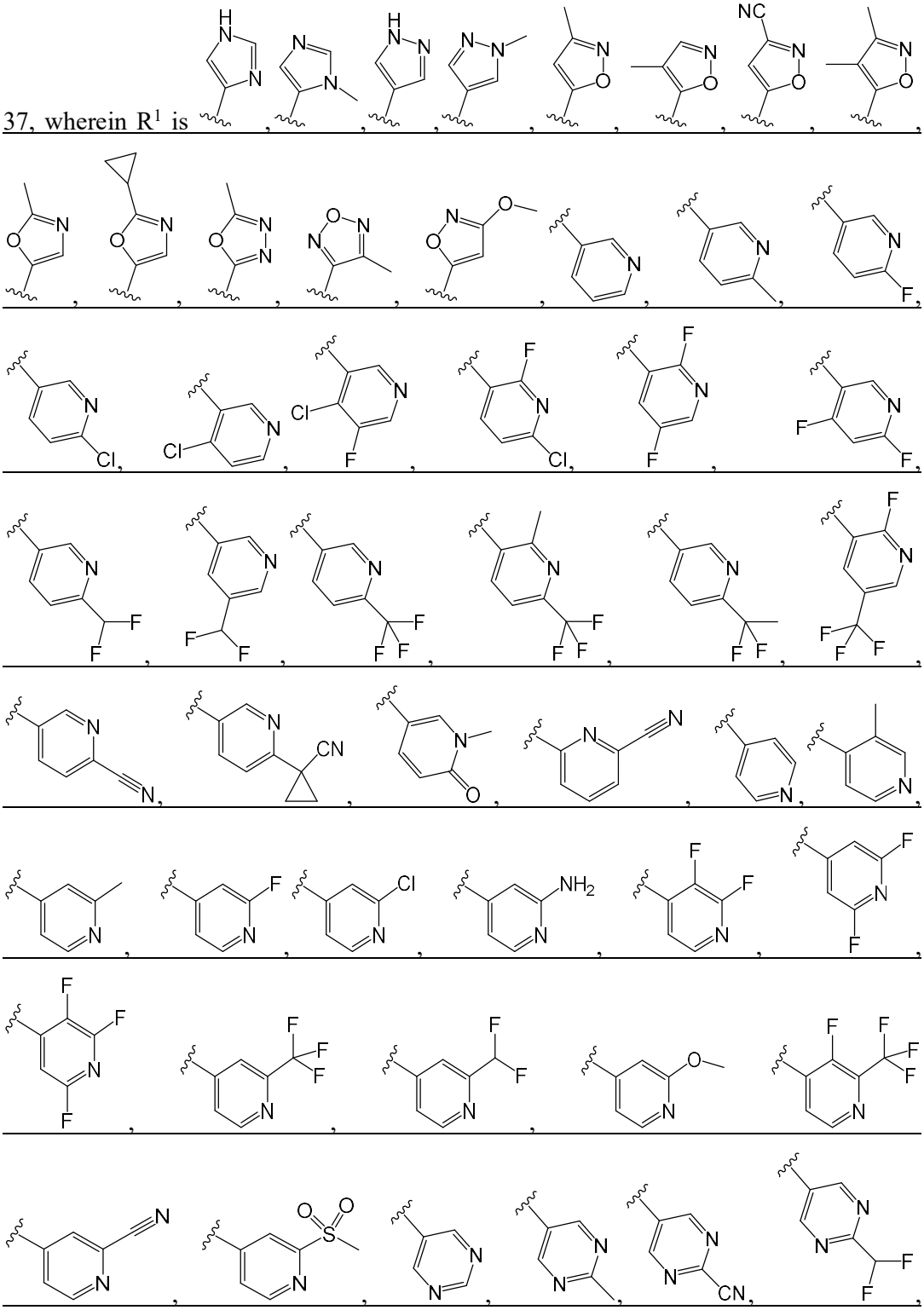
33. The compound or pharmaceutically acceptable salt thereof of claim 32, wherein R^1 is .

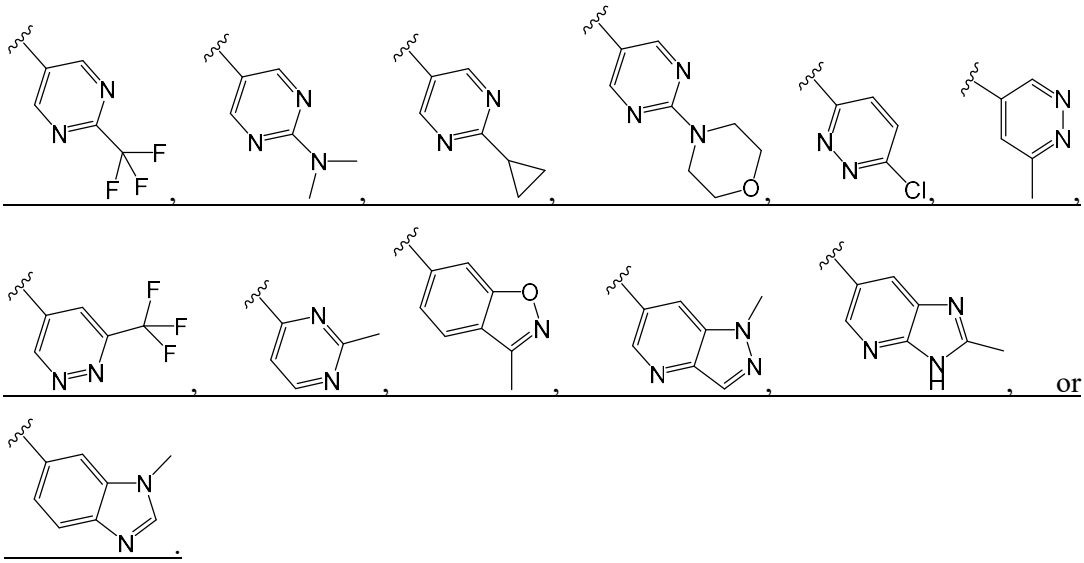
34. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 17, wherein the spiro bicyclic heterocyclyl is an oxaspiroheptane optionally substituted with 1 to 4 substituents, which can be the same or different, each independently selected from -F, -Cl, -OH, -CN, $-CH_3$, $-CH_2F$, $-CHF_2$, $-CF_3$, and $-O-CH_3$.

35. The compound or pharmaceutically acceptable salt thereof of claim 34, wherein R^1 is .

36. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-17, wherein R^1 is phenyl optionally substituted with 1 to 3 R^{1A}, which can be the same or different, wherein each R^{1A} is independently selected from -F, -Cl, -CN, or $-CH_3$.

37. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-17, wherein R^1 is imidazolyl, pyrazolyl, pyridinyl, oxazolyl, isoxazolyl, oxadiazolyl, pyridinonyl, pyrimidinyl, pyridazinyl, benzoisoxazolyl, pyrazolopyridinyl, imidazopyridinyl, or benzoimidazolyl, each optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from -F, -Cl, -CN, $-CH_3$, $-CHF_2$, $-CF_3$, $-OCH_3$, $-NH_2$, $-N(CH_3)_2$, $-SO_2-CH_3$, , or .

38. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-17 and 37, wherein R^1 is 



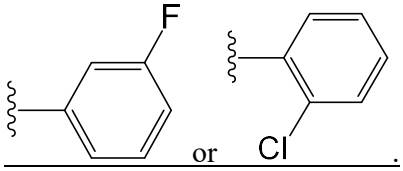
39. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-38, wherein R^3 is $–CH_3$.

40. The compound or pharmaceutically acceptable salt thereof of claim 1 and 17-39, wherein Y_1 is C_{1-4} alkyl optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from halogen, cyano, and C_{1-4} alkoxy, and Y_2 is hydrogen.

41. The compound or pharmaceutically acceptable salt thereof of claim 40, wherein Y_1 is $-CH_3$ or $-CH_2F$.

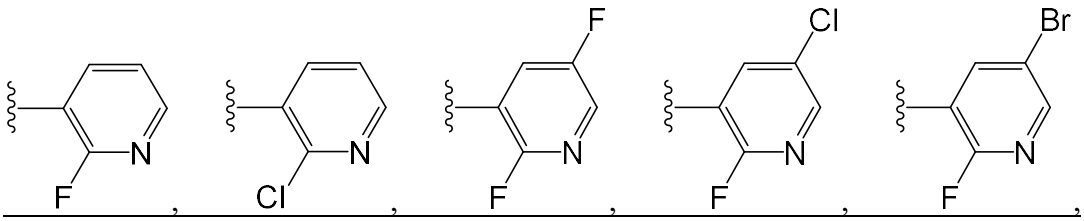
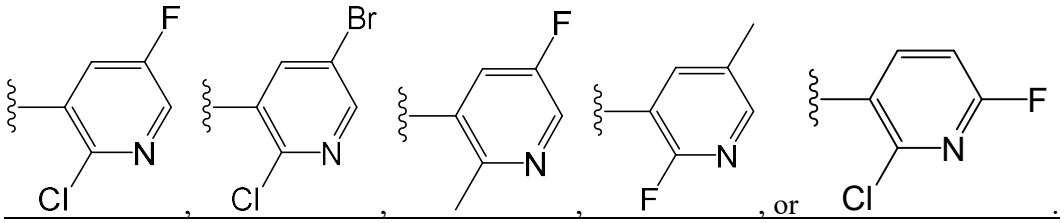
42. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-41, wherein Z is phenyl, optionally substituted with 1 to 3 sustituents, which can be the same or different, each independently selected from halogen and C_{1-4} alkyl.

43. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-42, wherein Z is

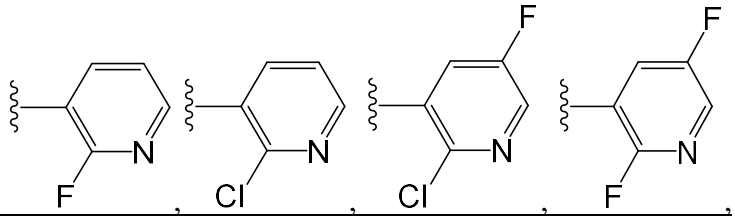
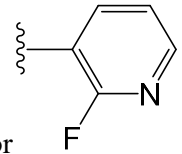


44. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 43, wherein Z is pyridyl, optionally substituted with 1 to 3 substituents, which can be the same or different, each independently selected from -F, -Cl, -Br, and -CH_3.

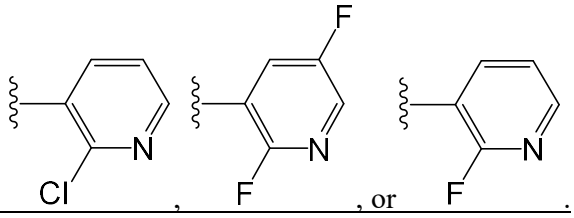
45. The compound or pharmaceutically acceptable salt thereof of claim 43, wherein Z is

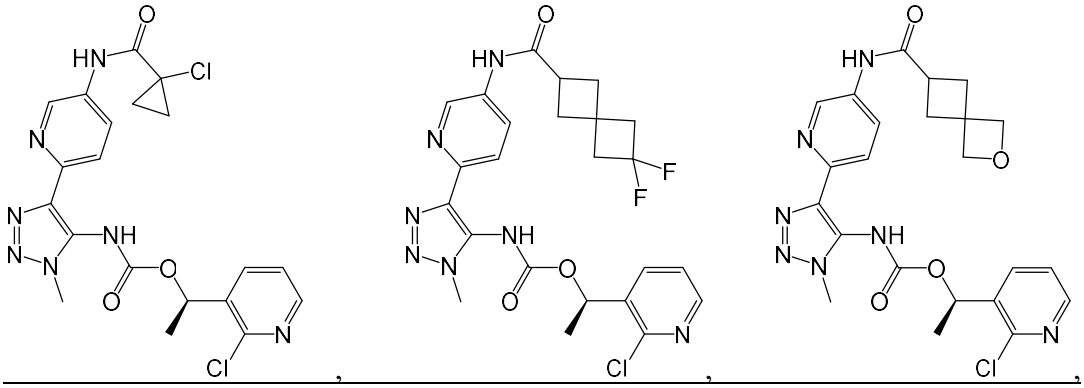
46. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-45, wherein Y_1 is -CH_3 and Z is

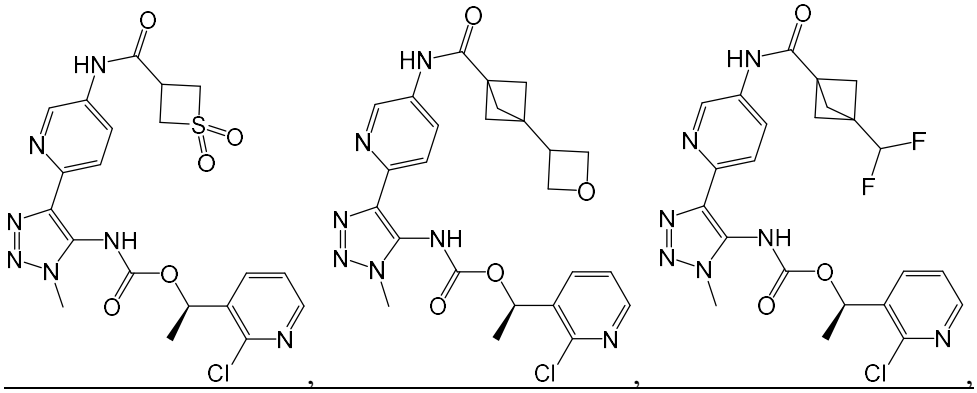



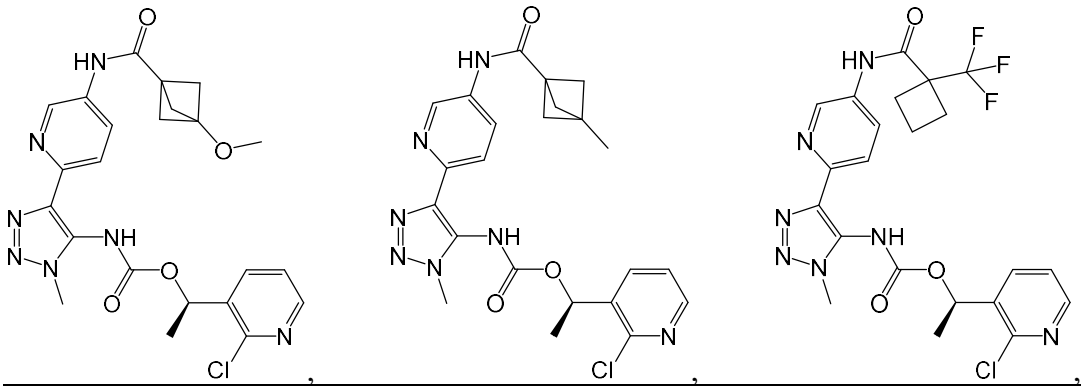
47. The compound or pharmaceutically acceptable salt thereof of any one of claims 1-46, wherein Y_1 is -CH_3 and Z is

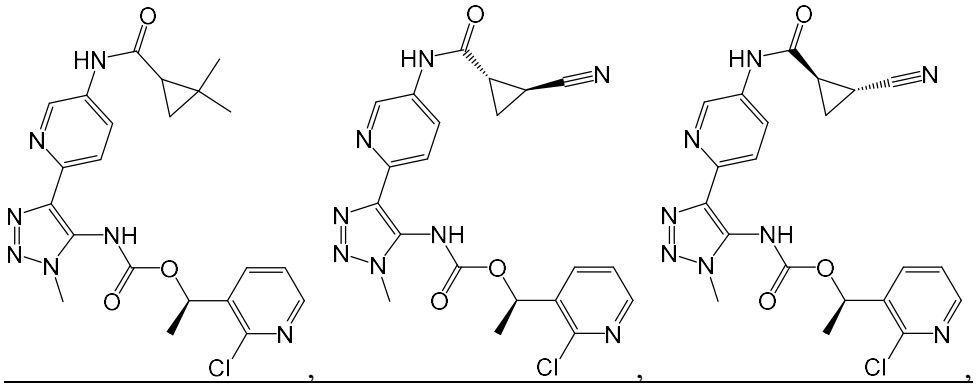


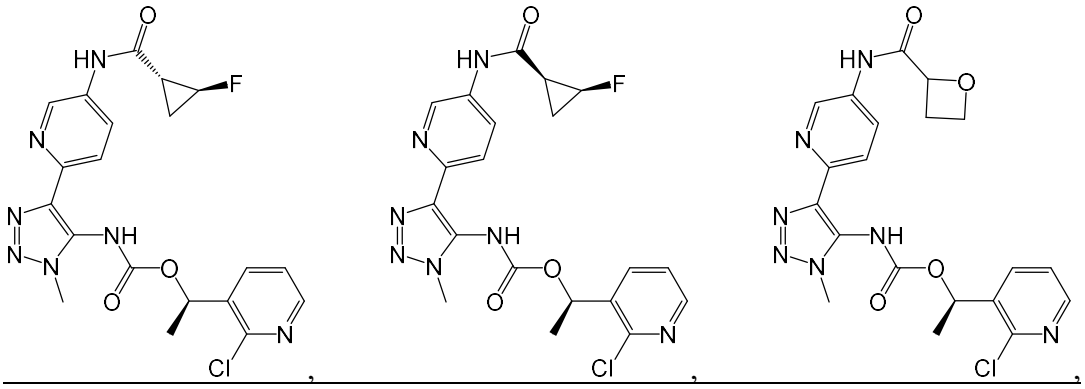
48. A compound selected from the group consisting of:

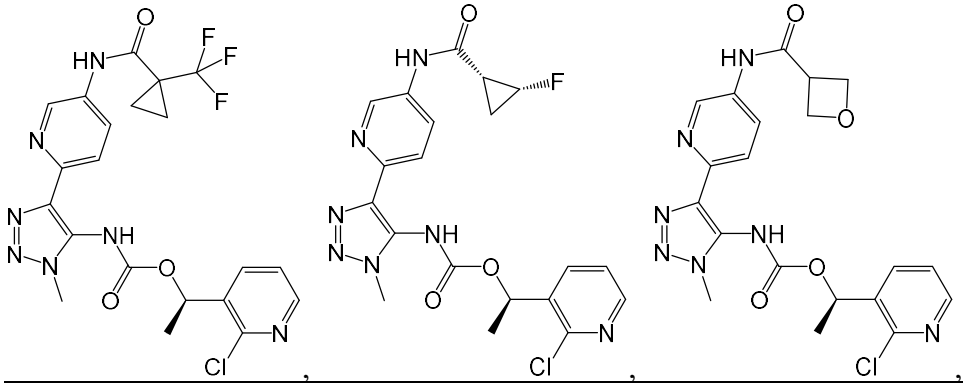


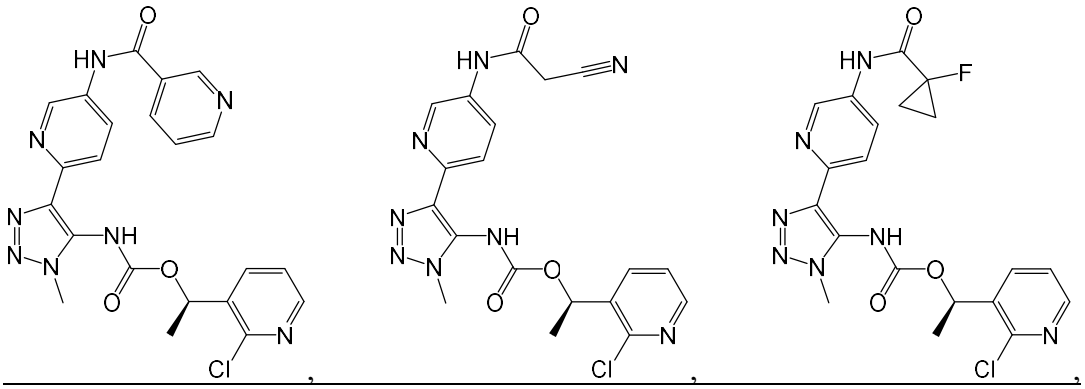


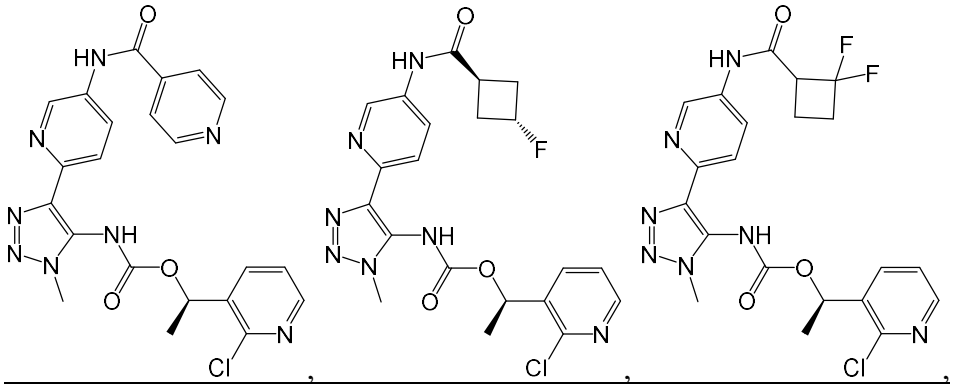


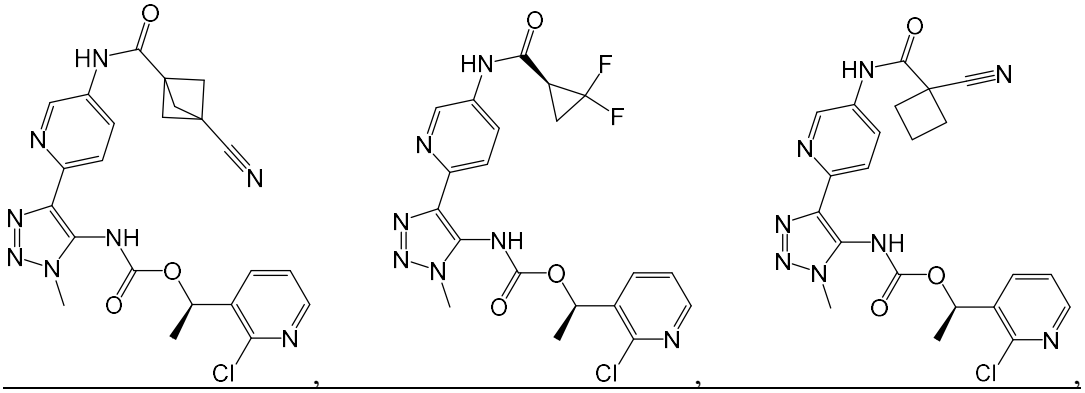


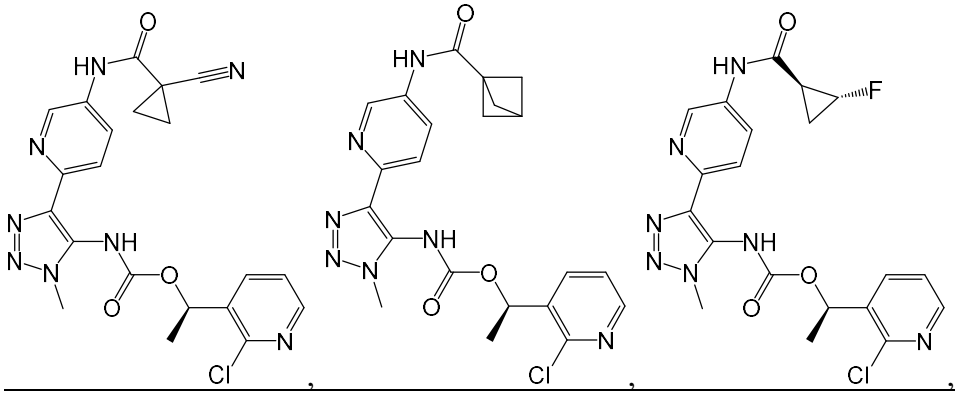


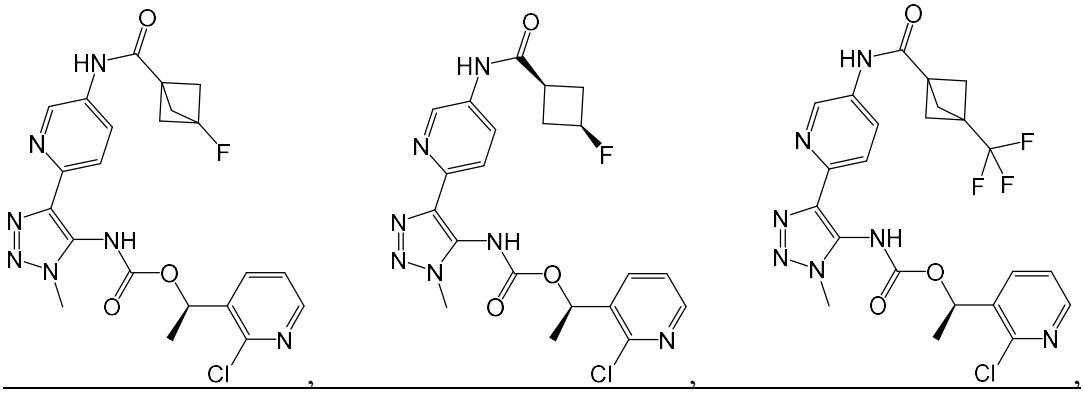


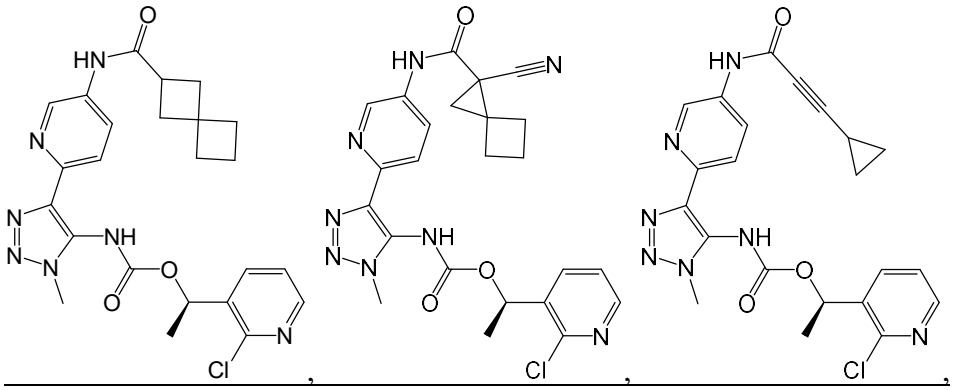


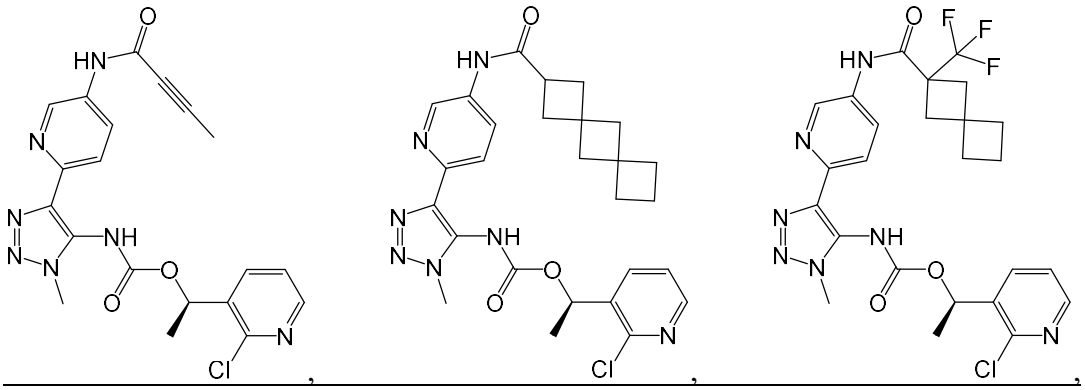


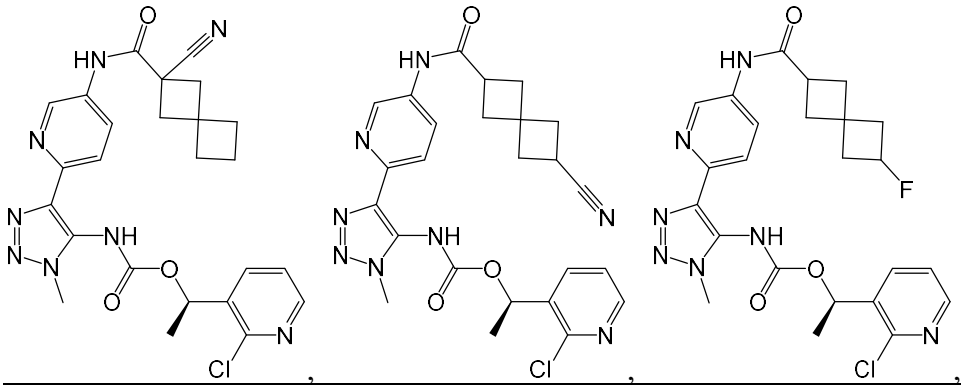


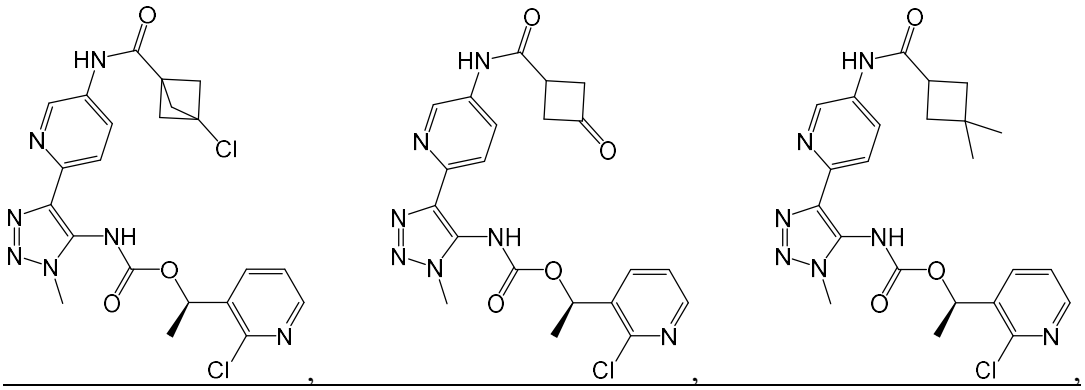


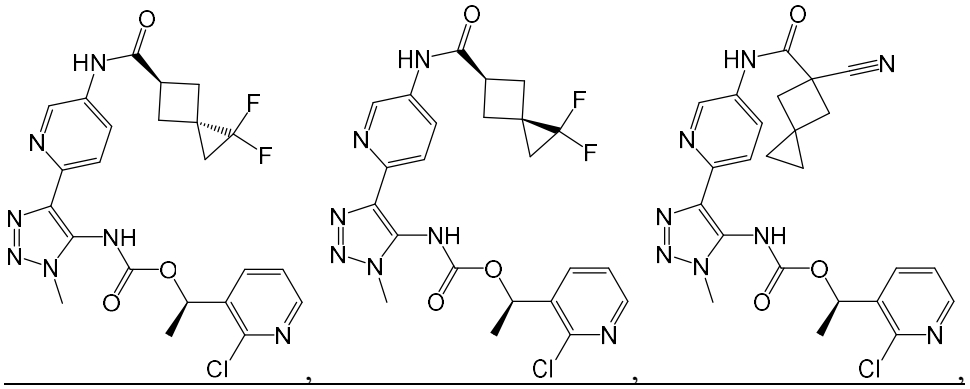


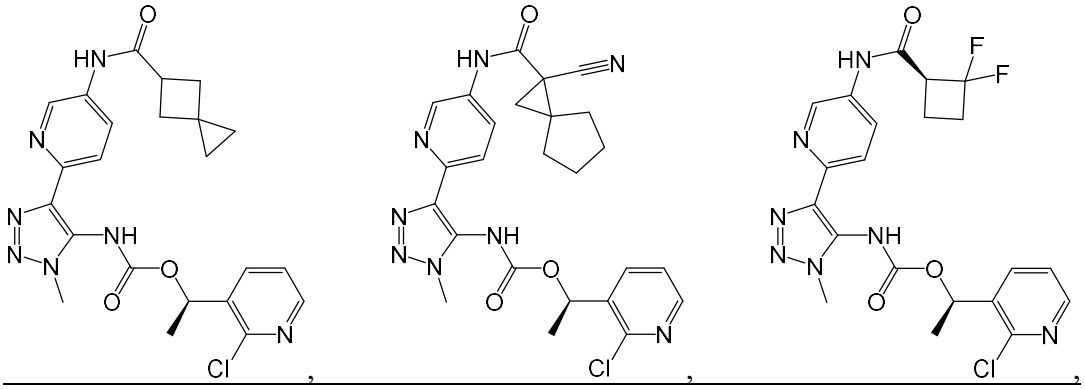


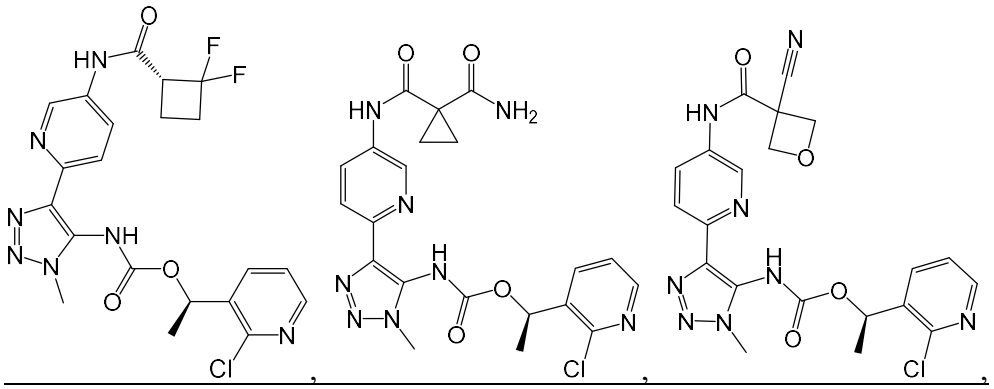


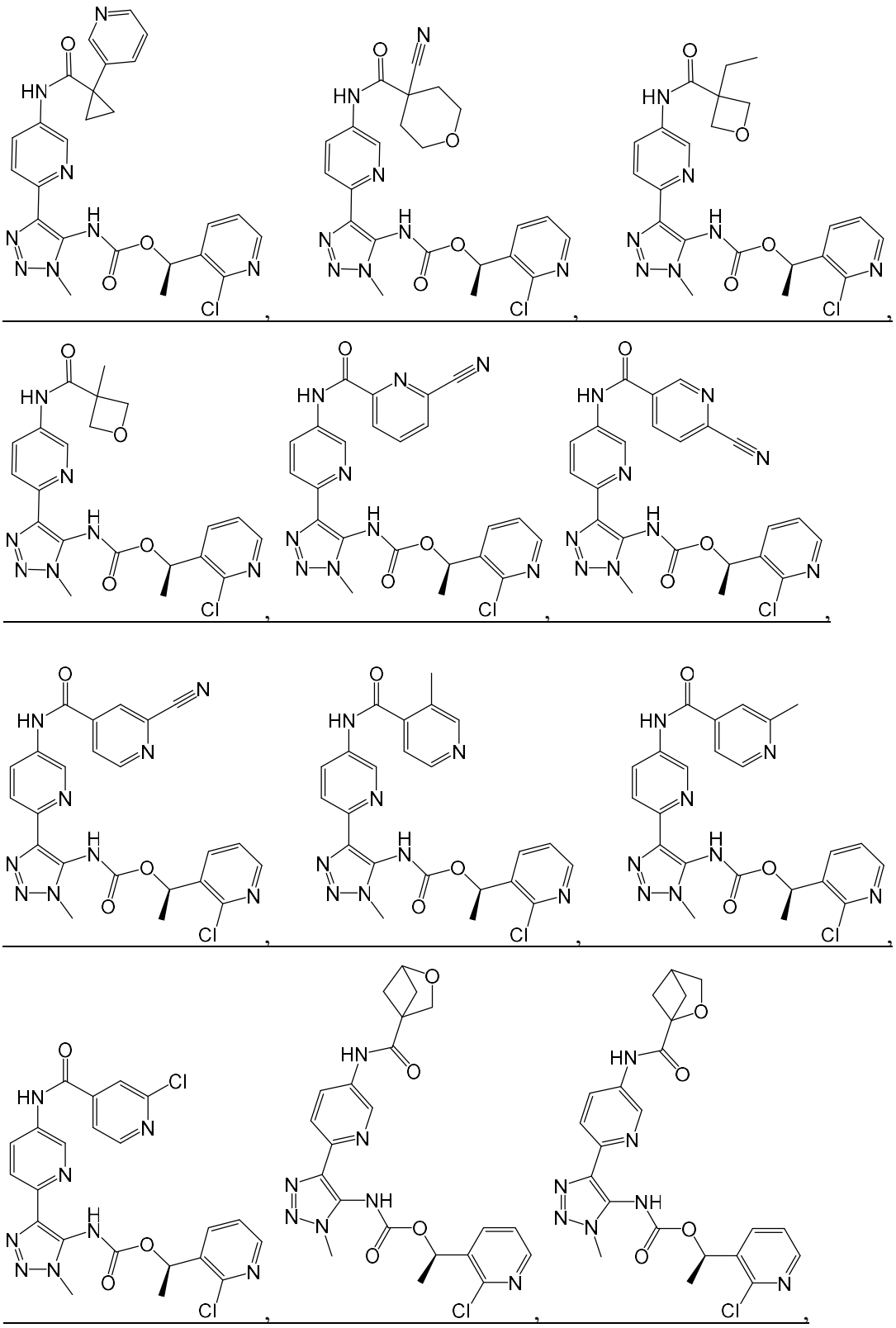


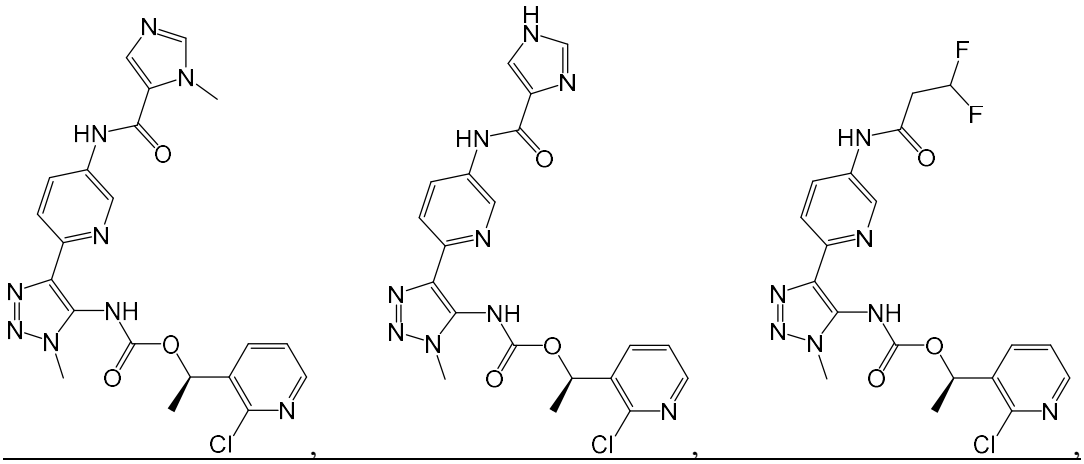


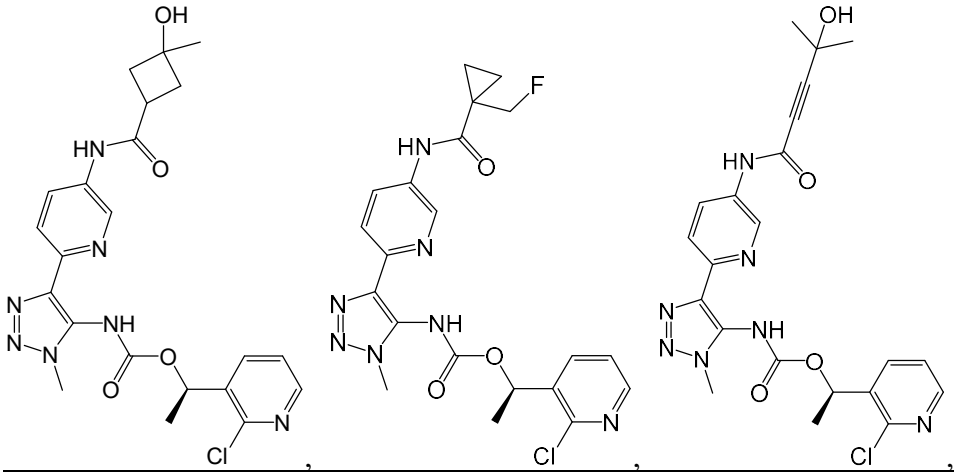


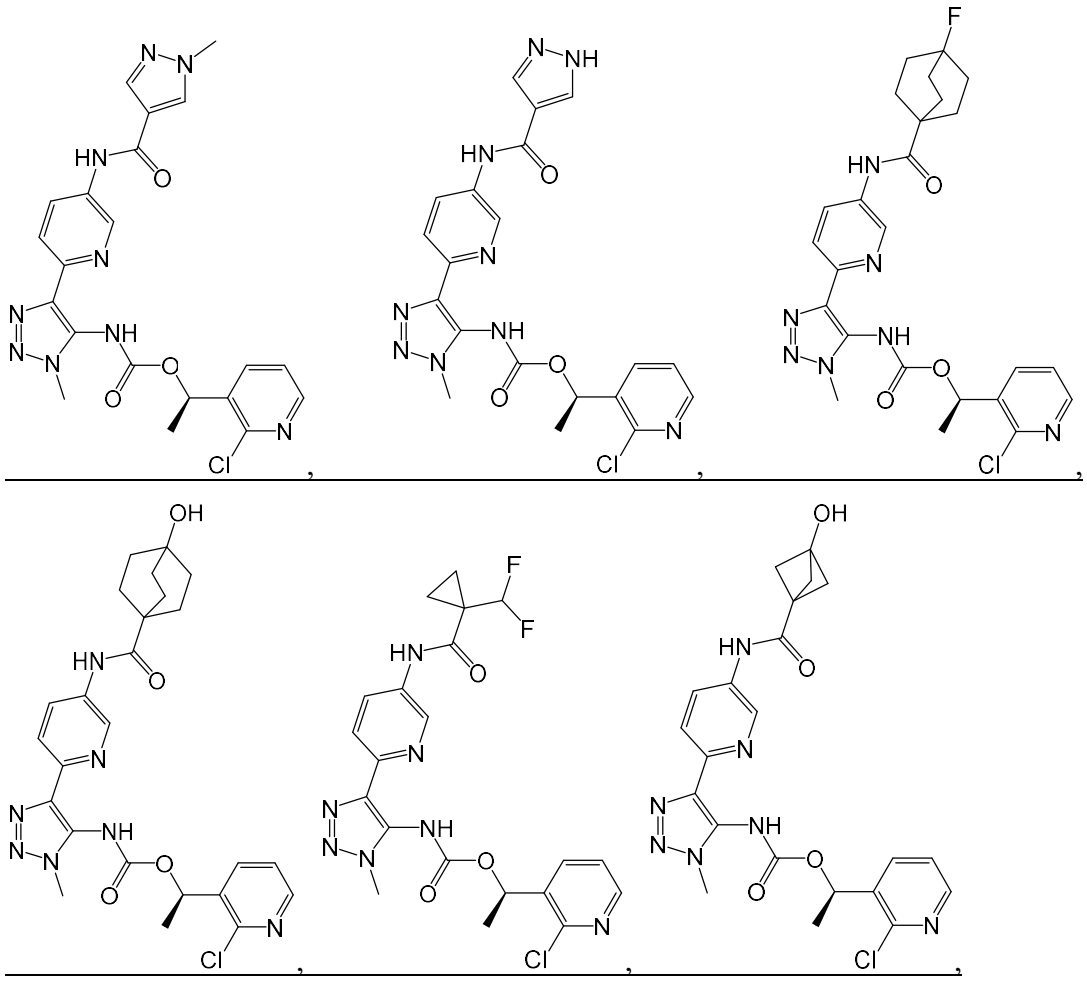


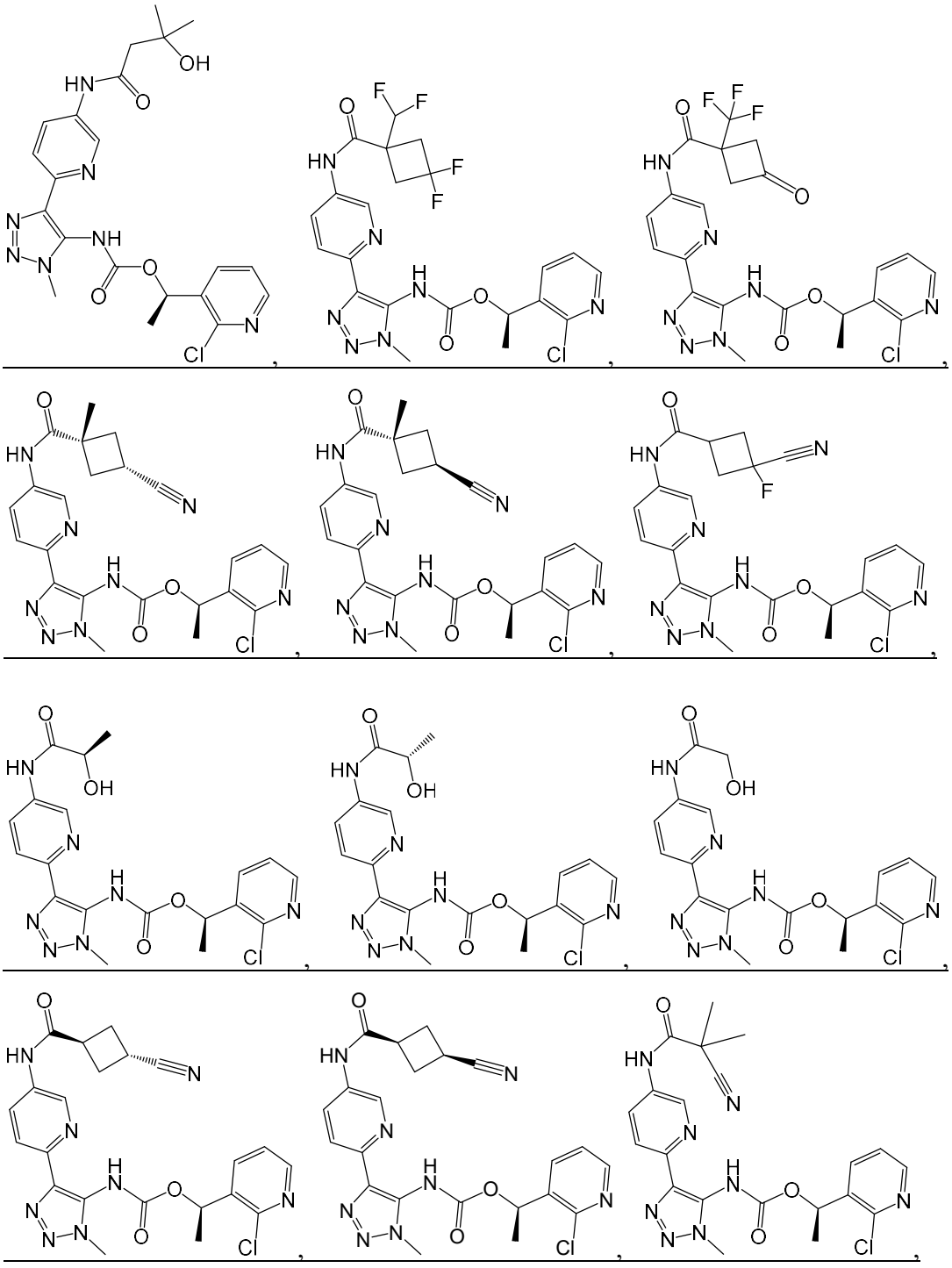


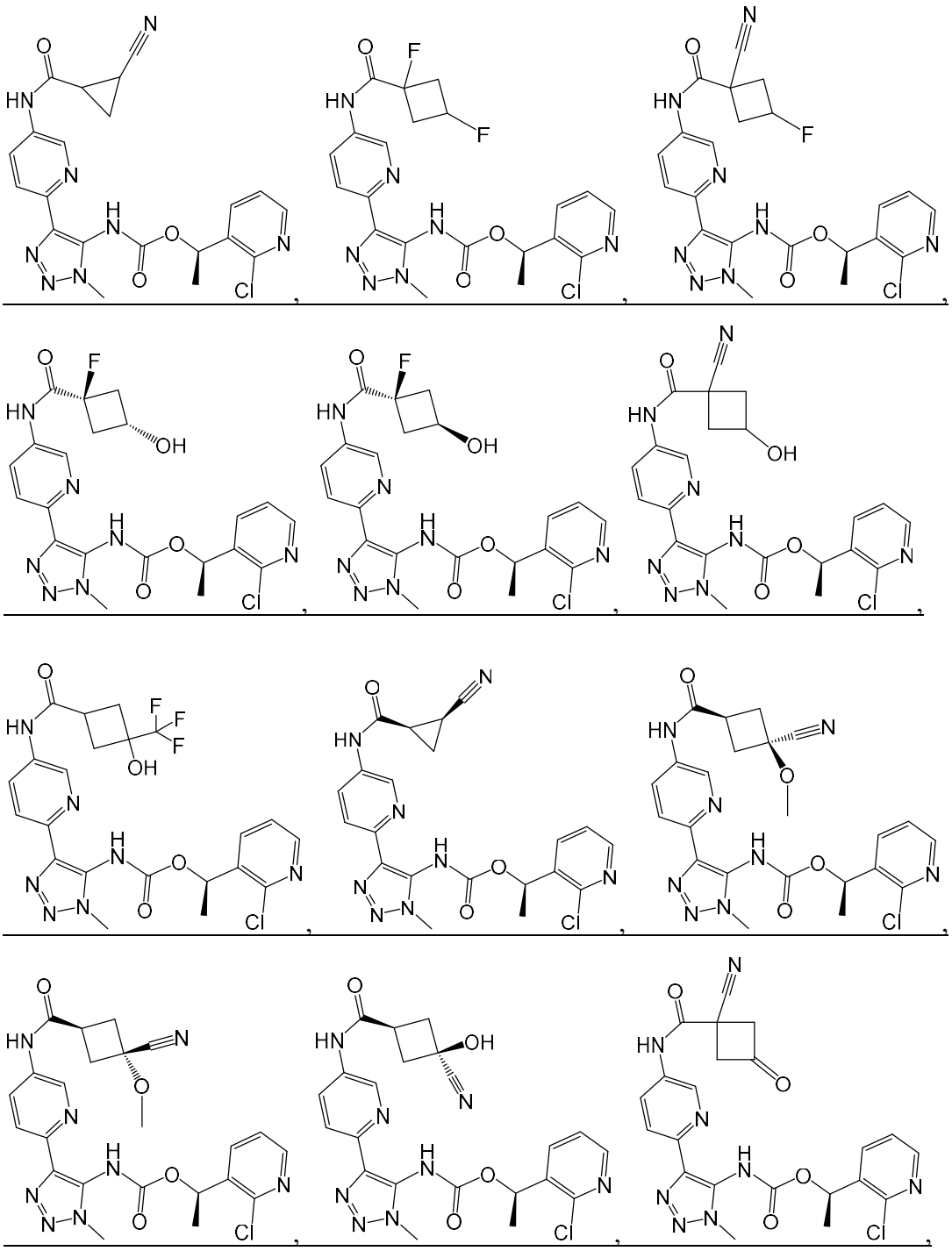


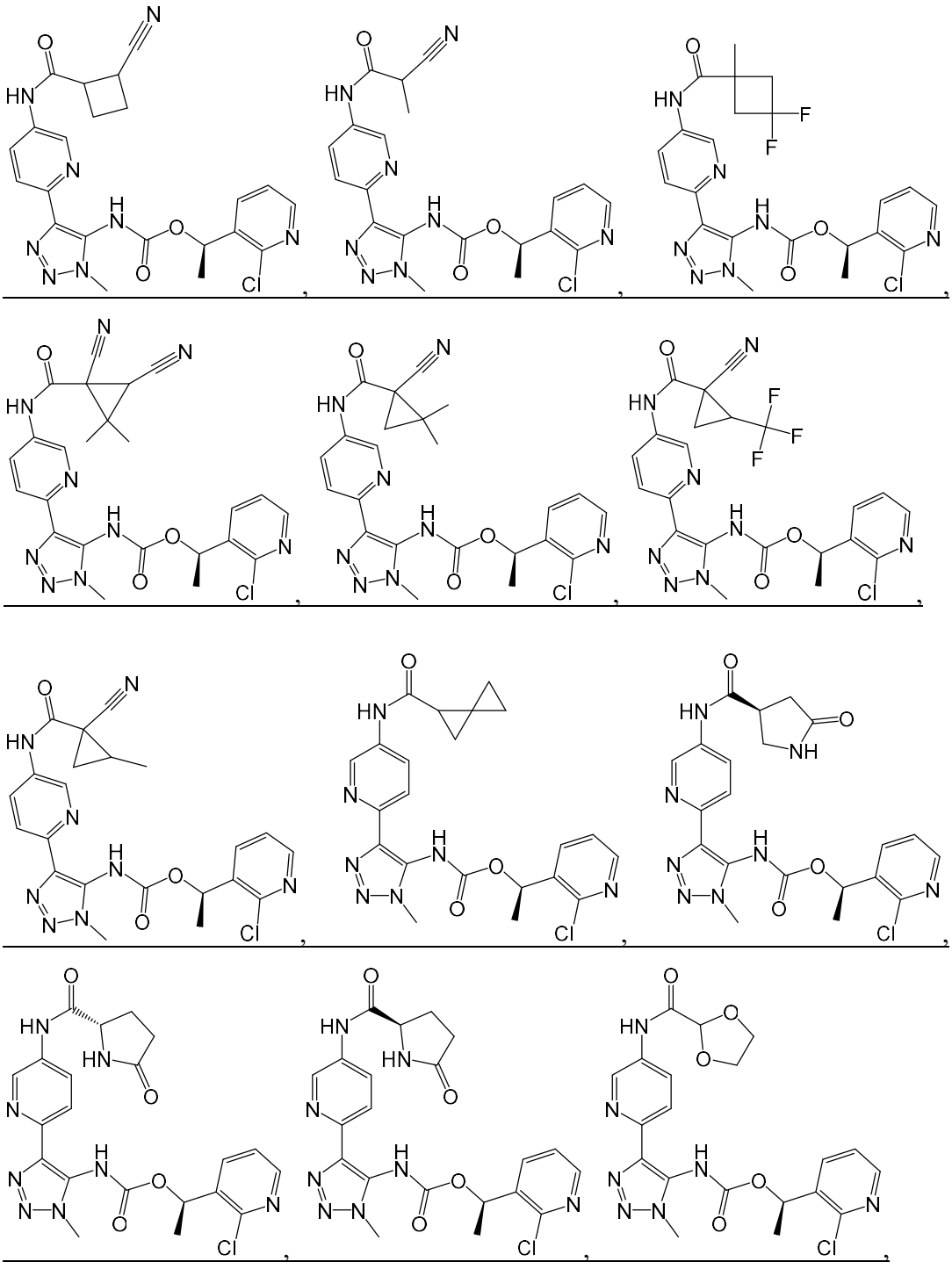


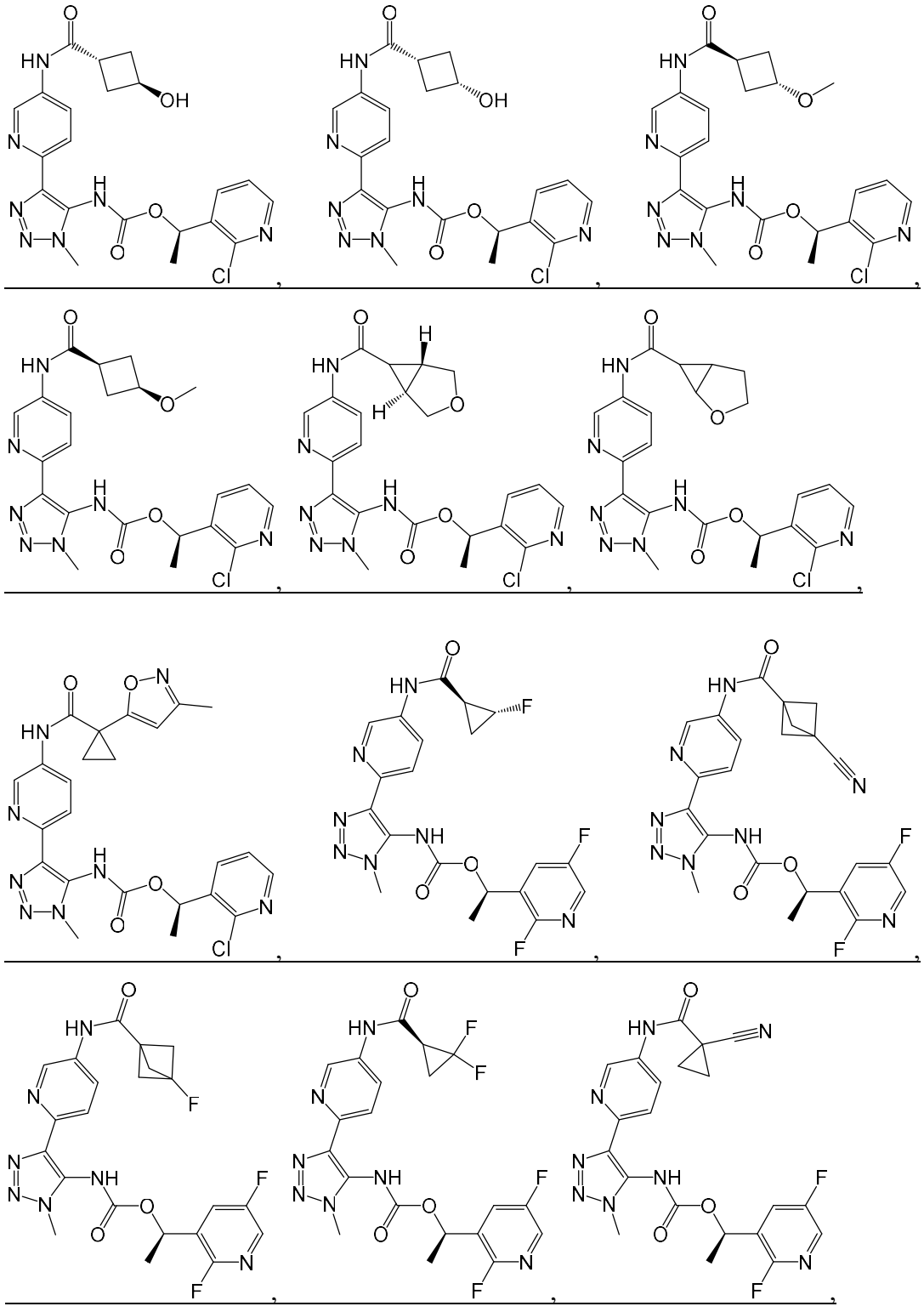


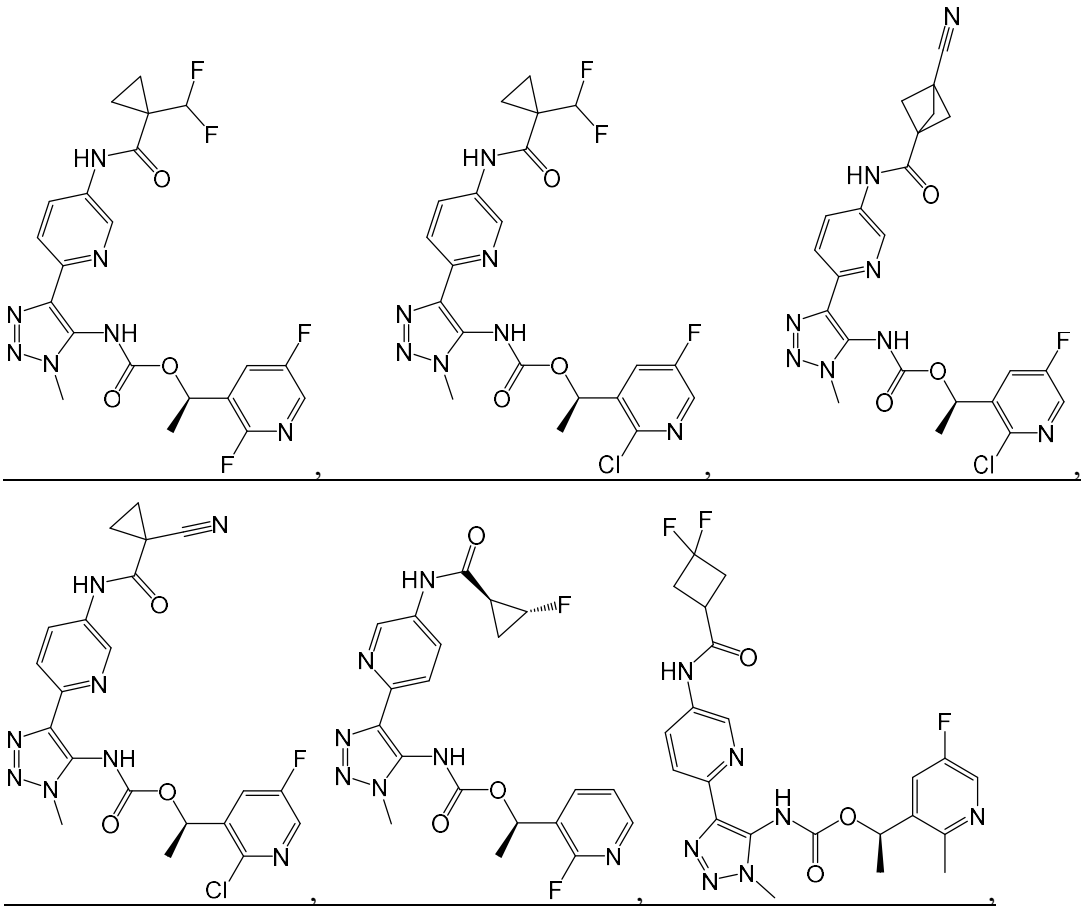


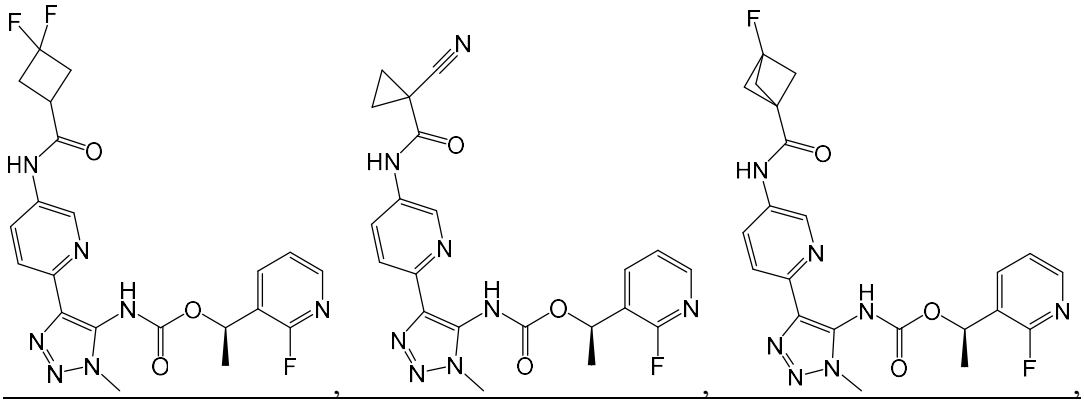


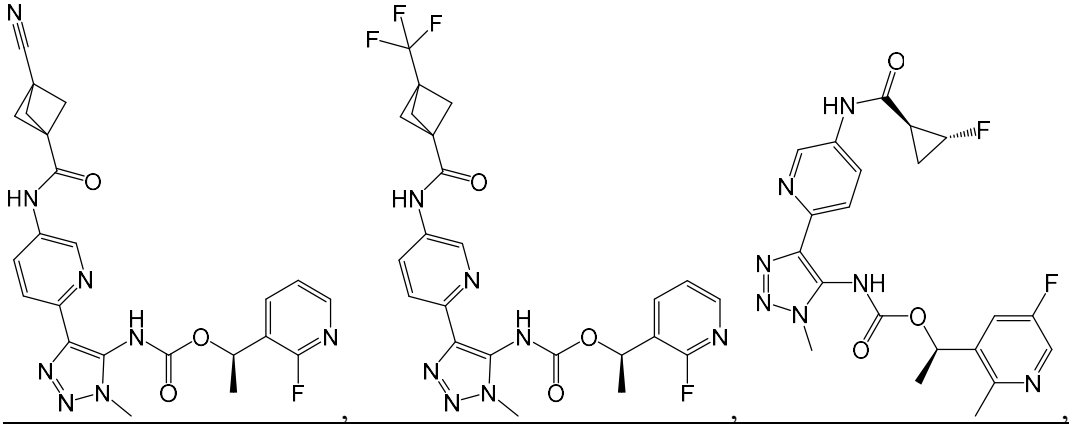


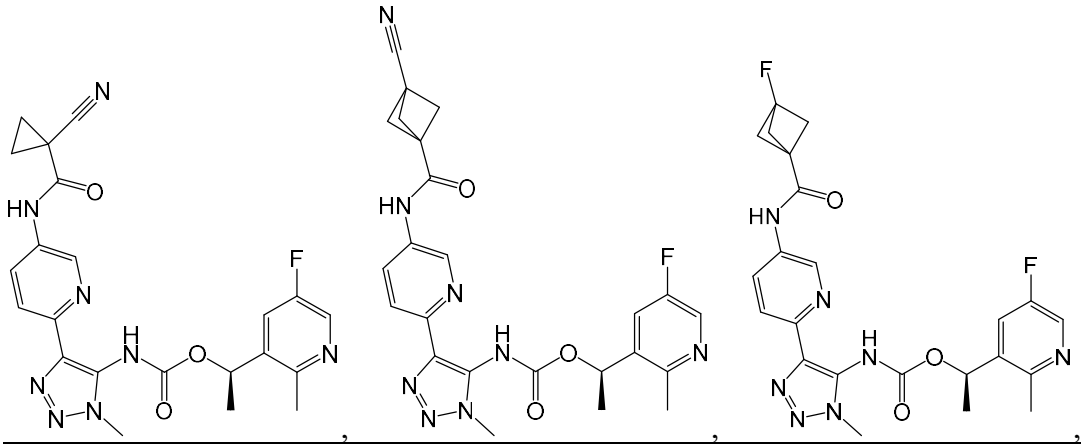


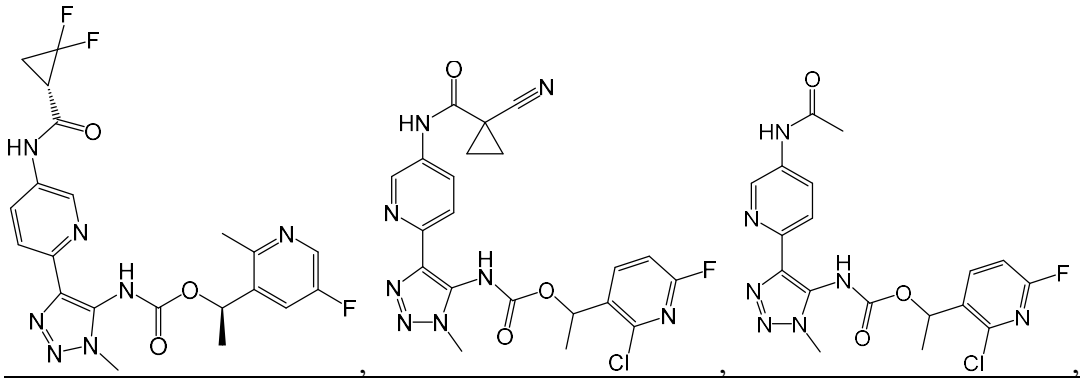


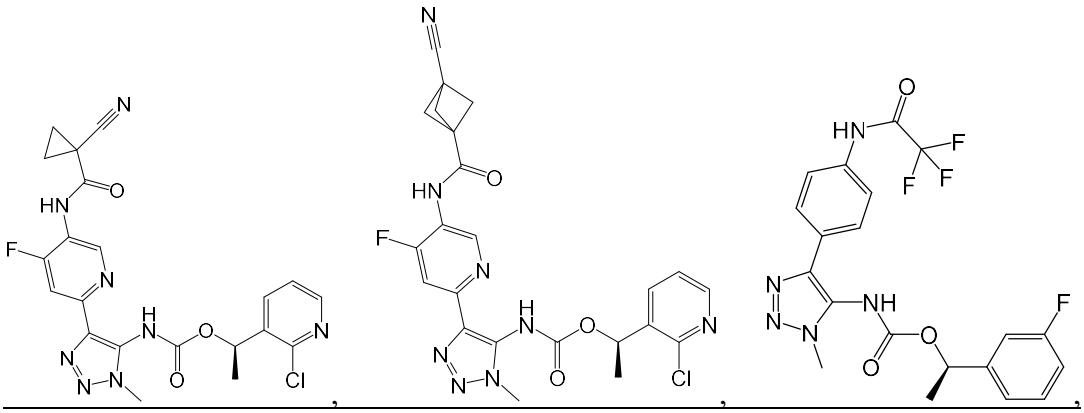


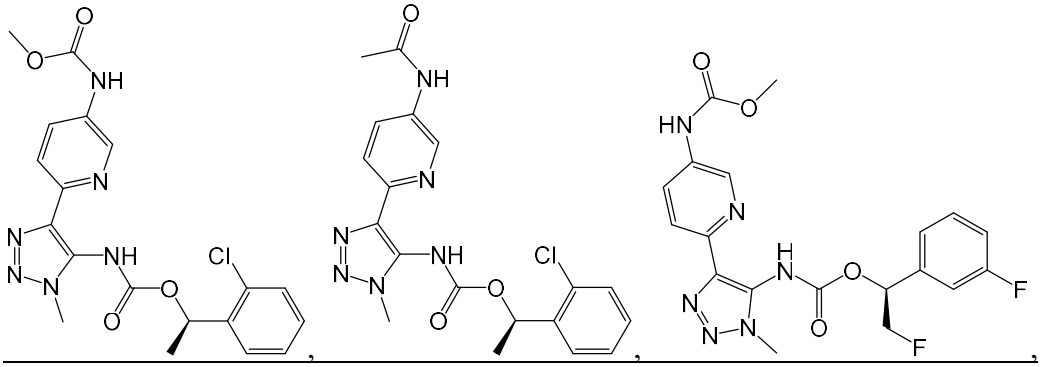


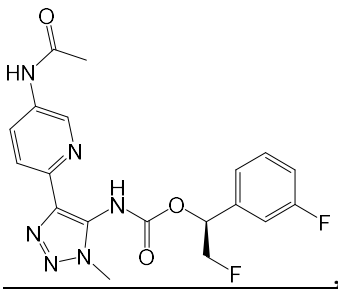
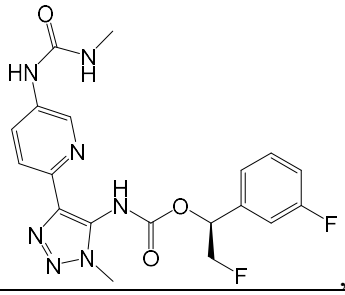
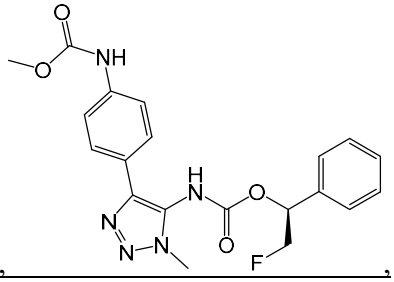
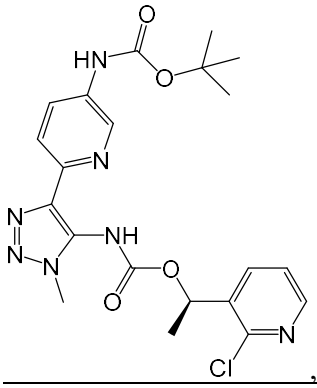
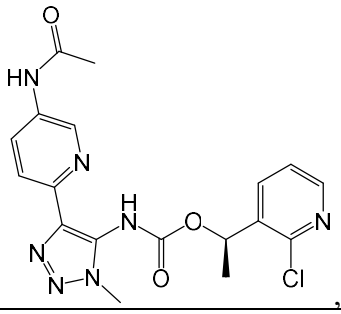
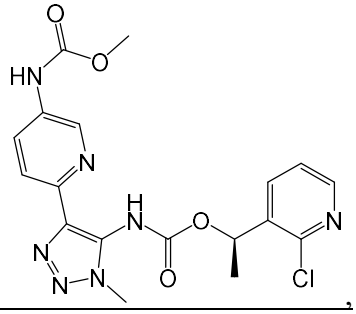
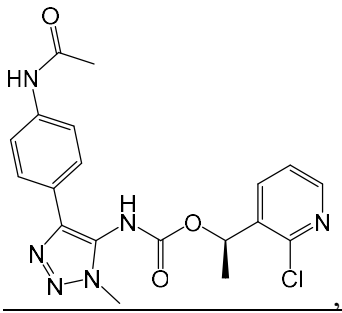
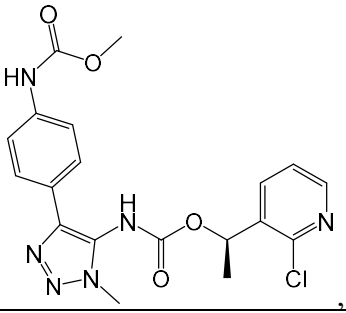
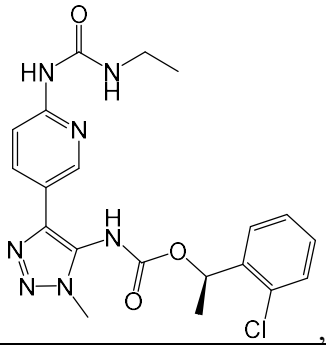
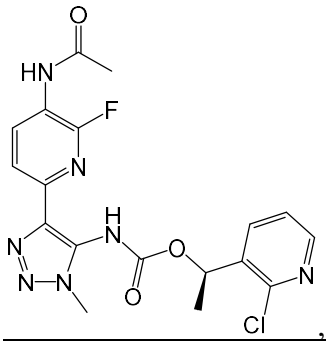
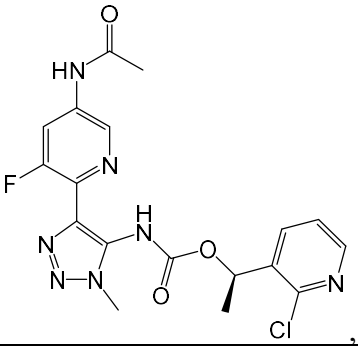
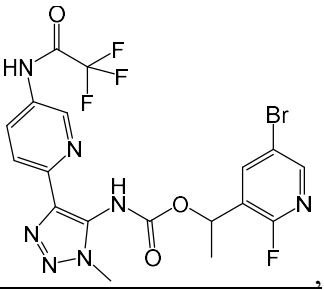


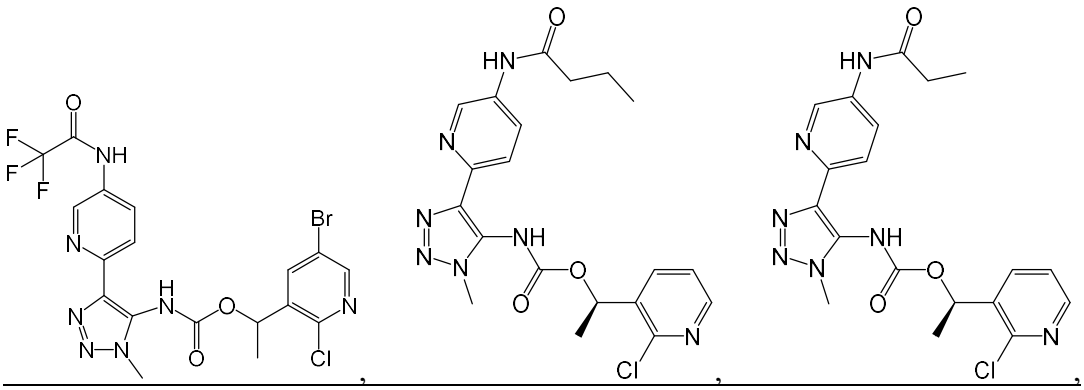


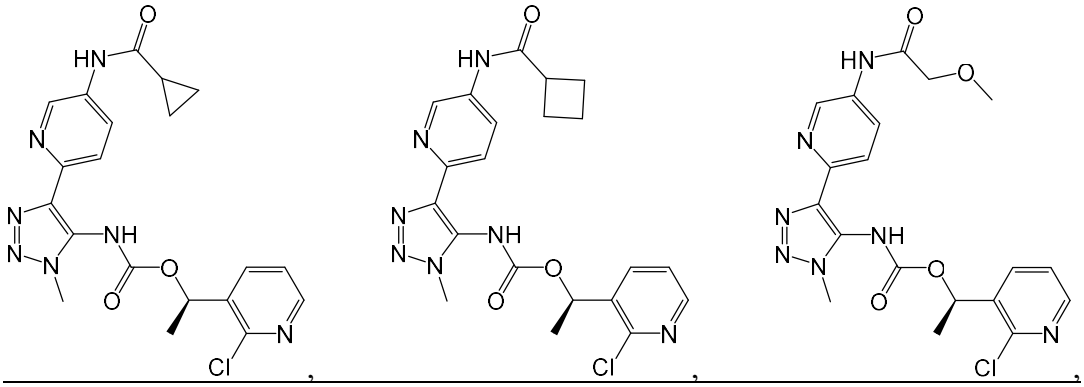


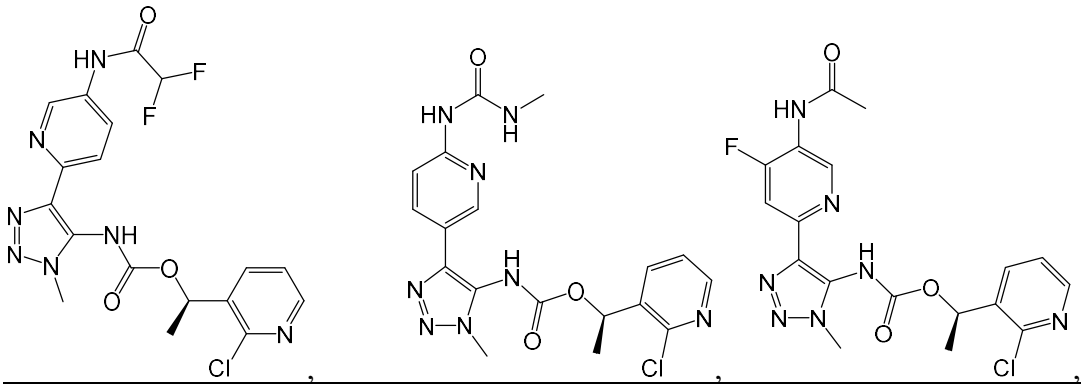


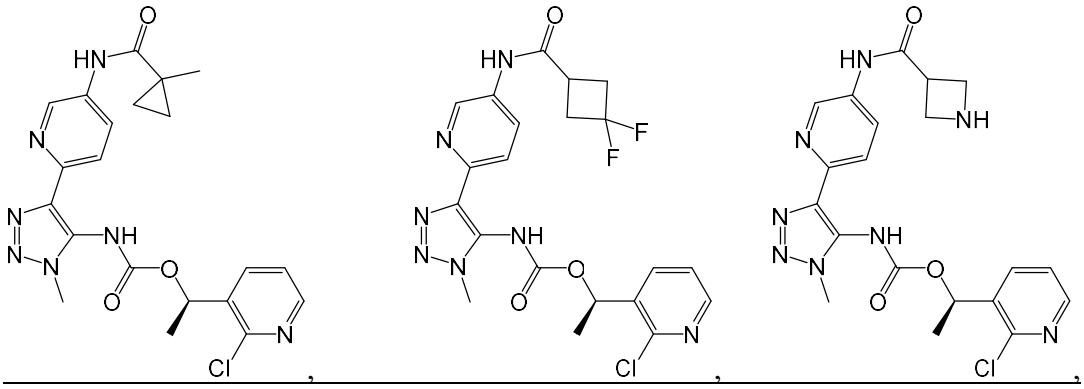


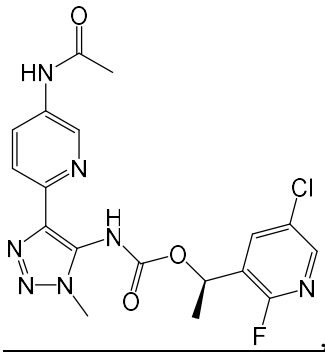
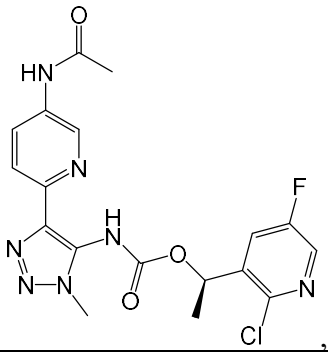
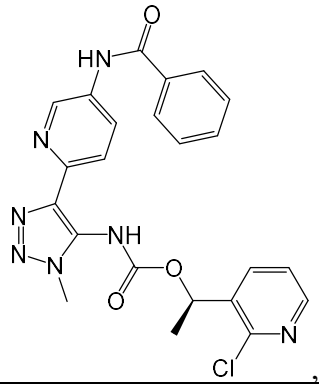
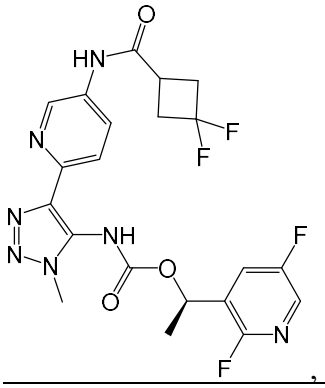
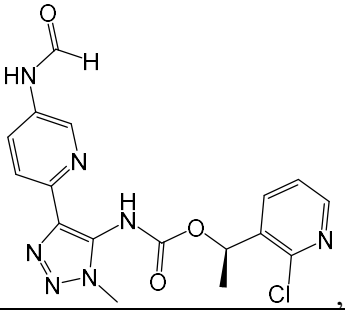
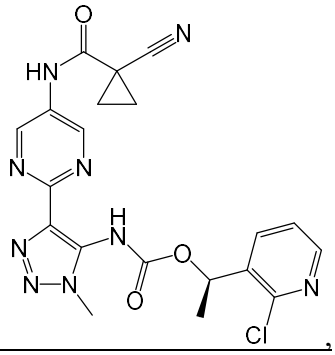
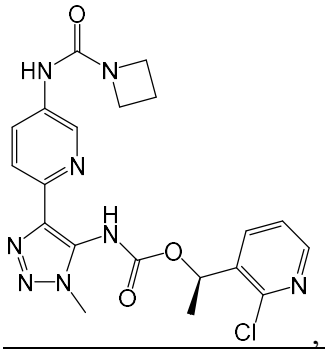
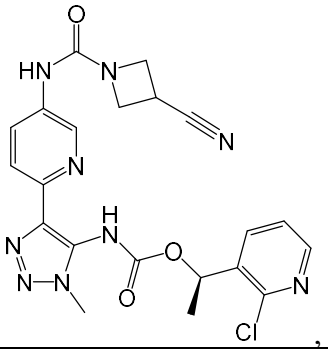
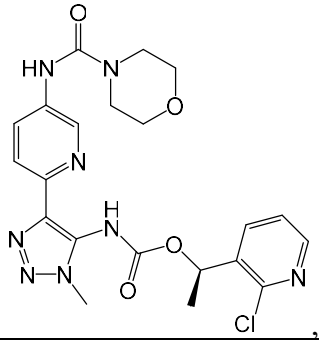
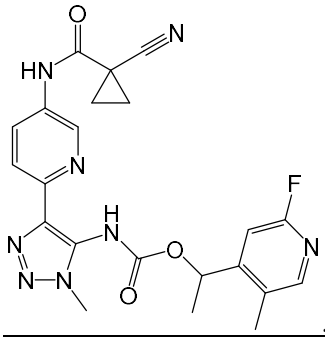
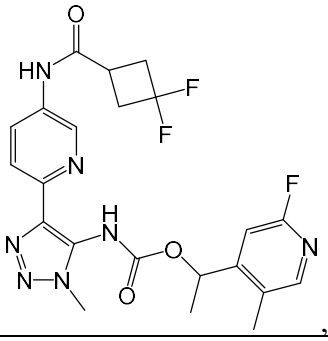
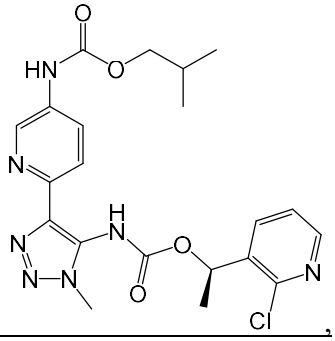

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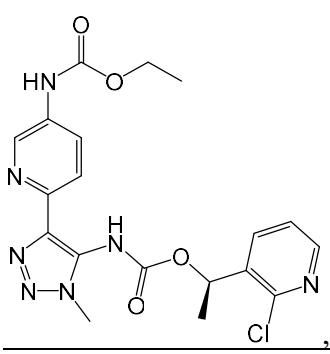
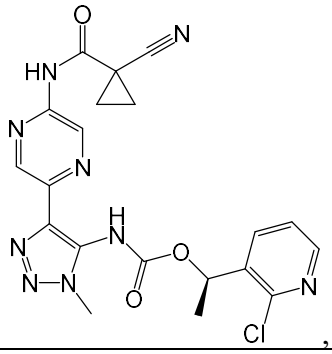
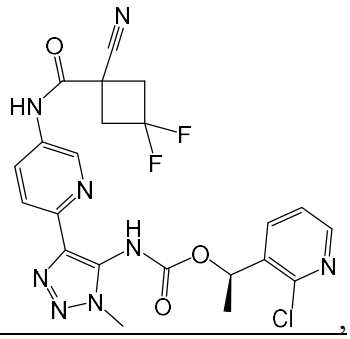


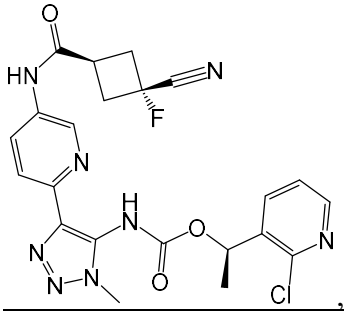
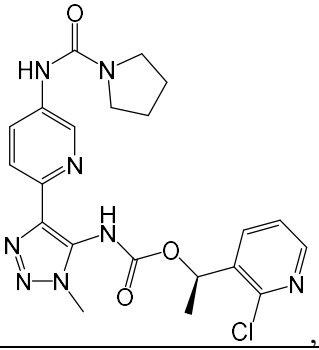
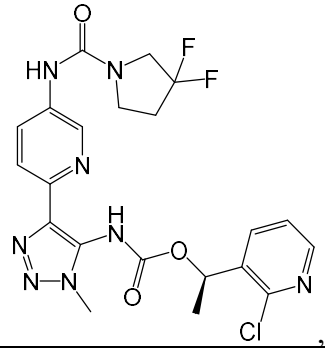


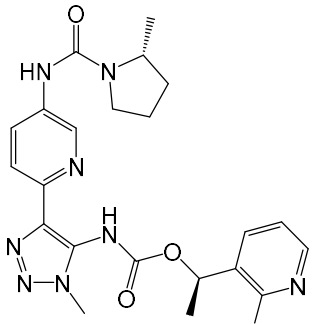
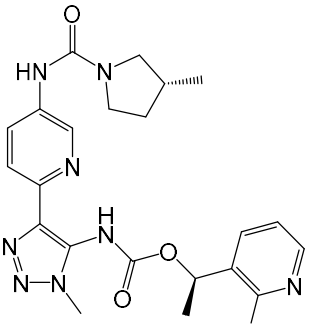





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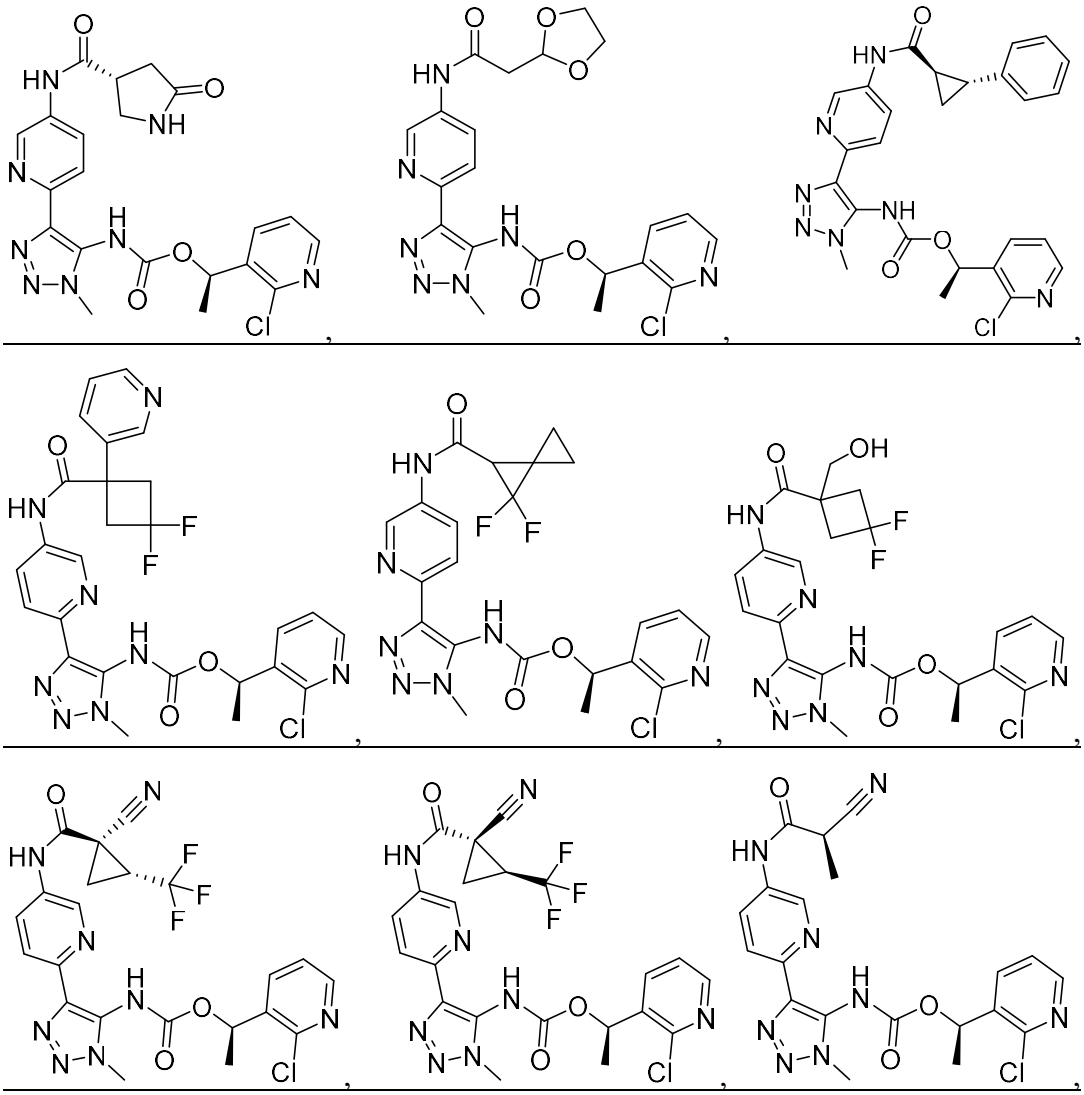
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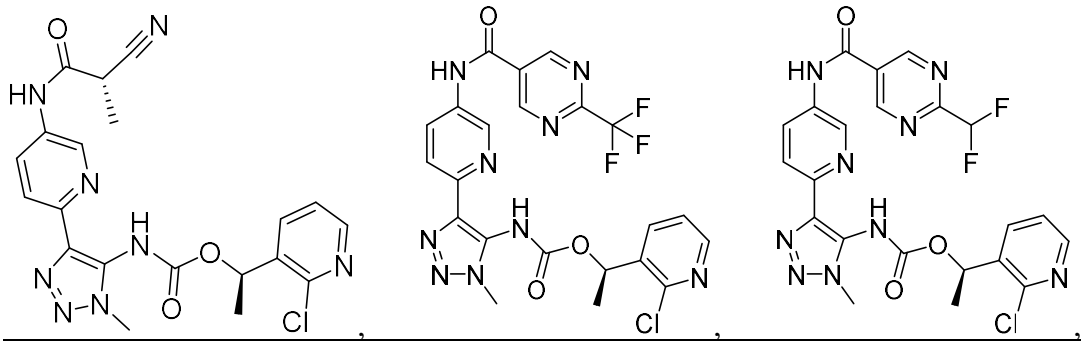
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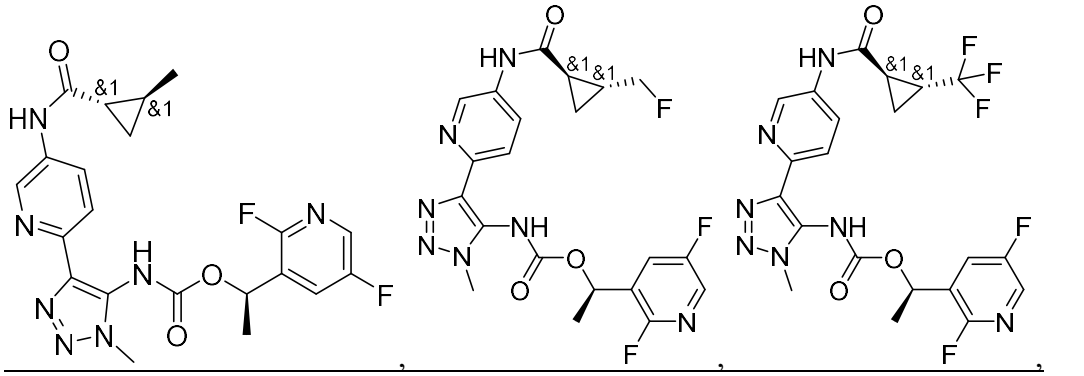
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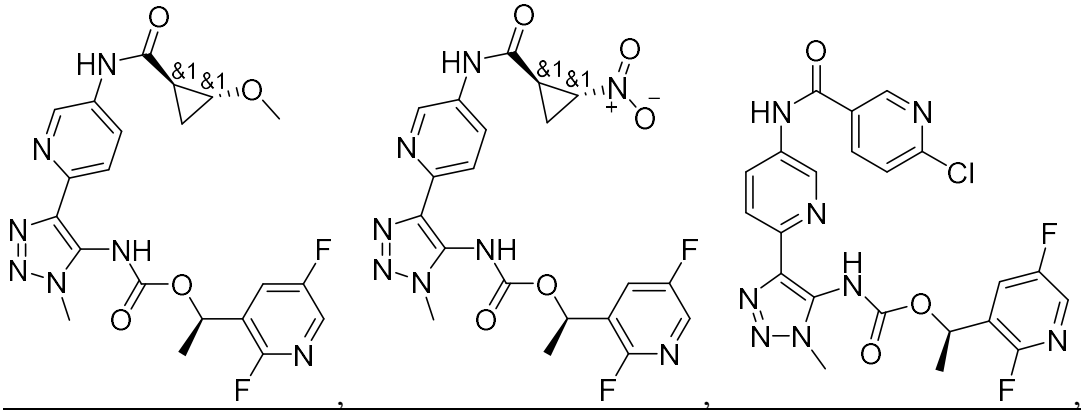
or a pharmaceutically acceptable salt thereof.

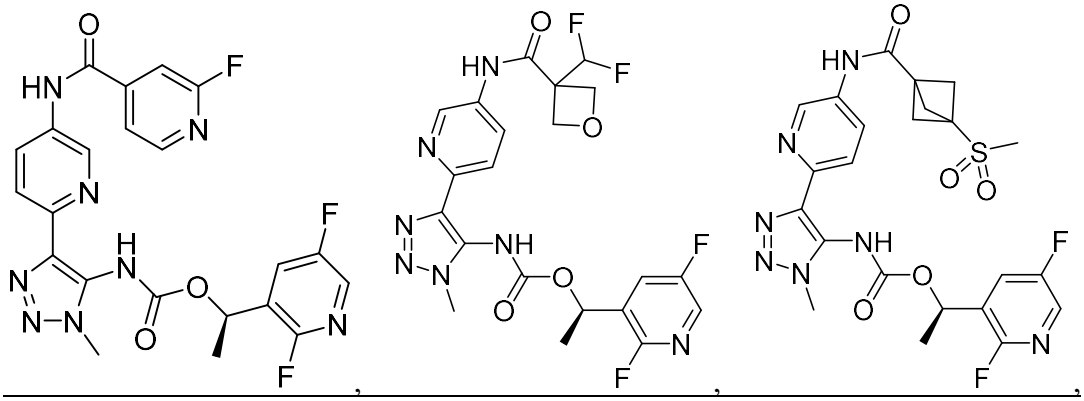
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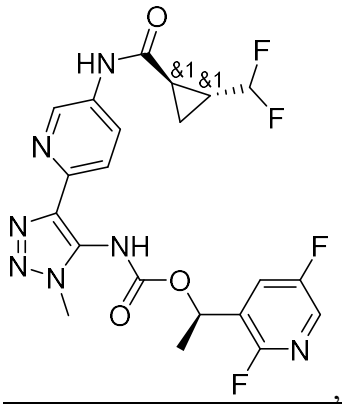
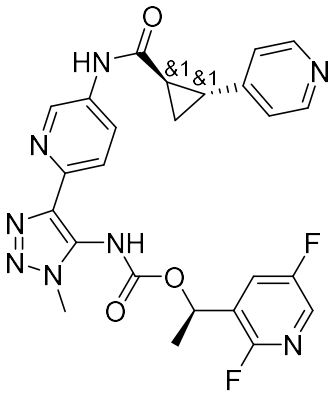
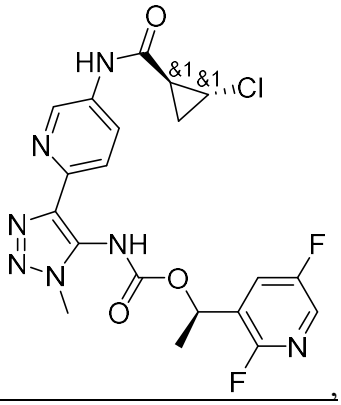


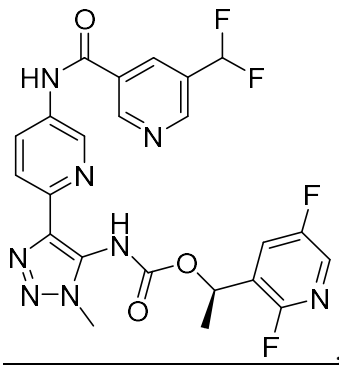
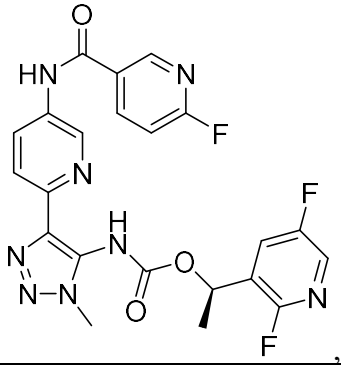
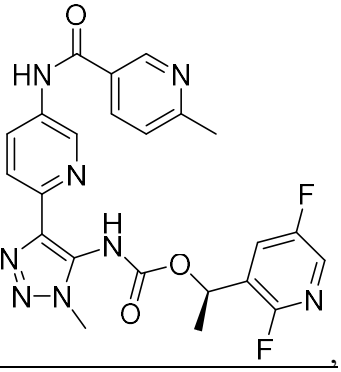


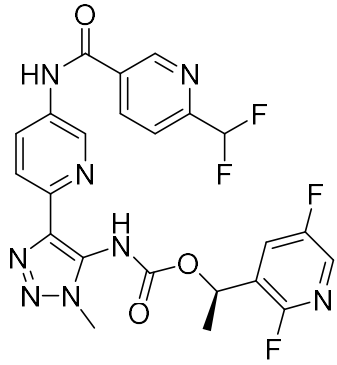
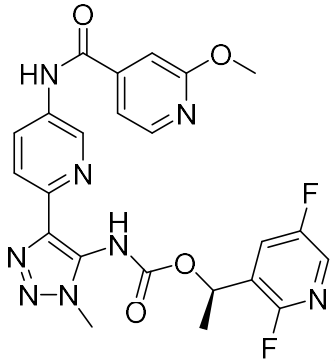
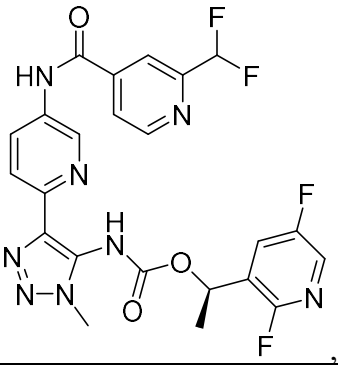


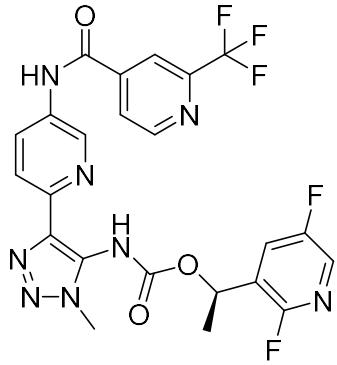
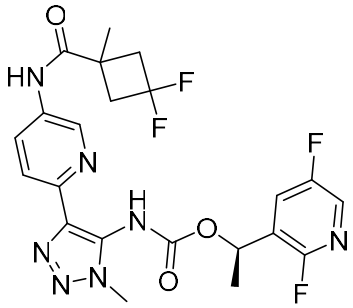
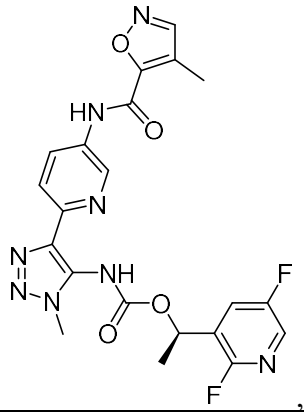


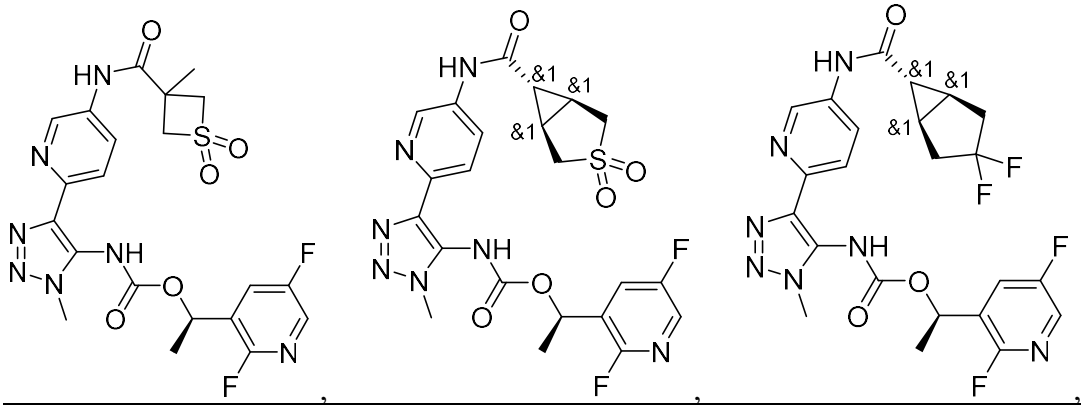


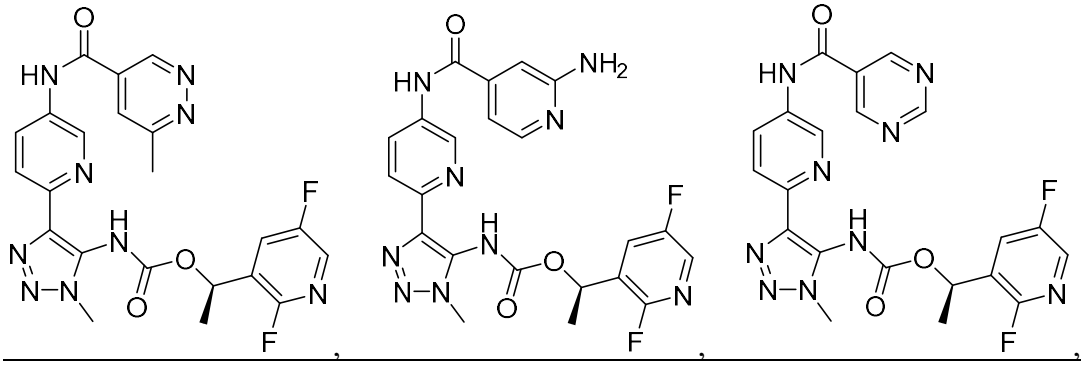

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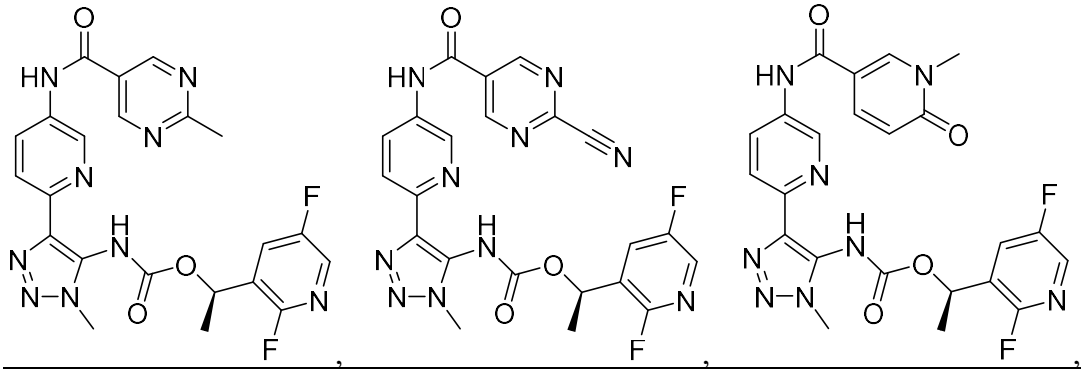

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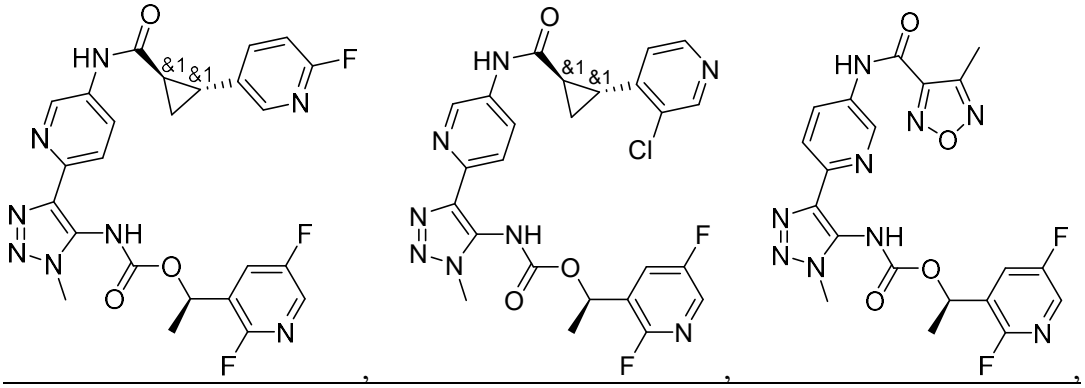

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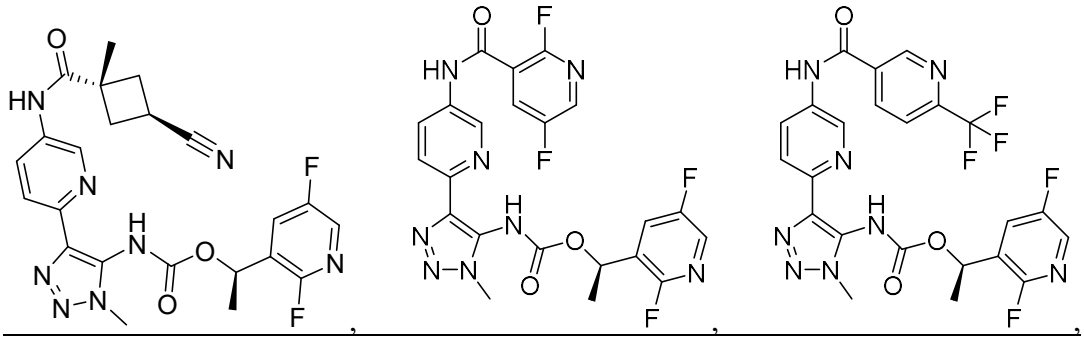

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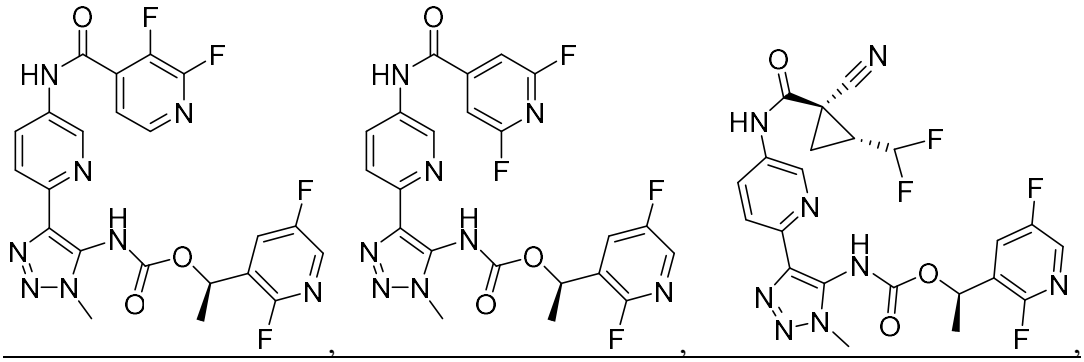


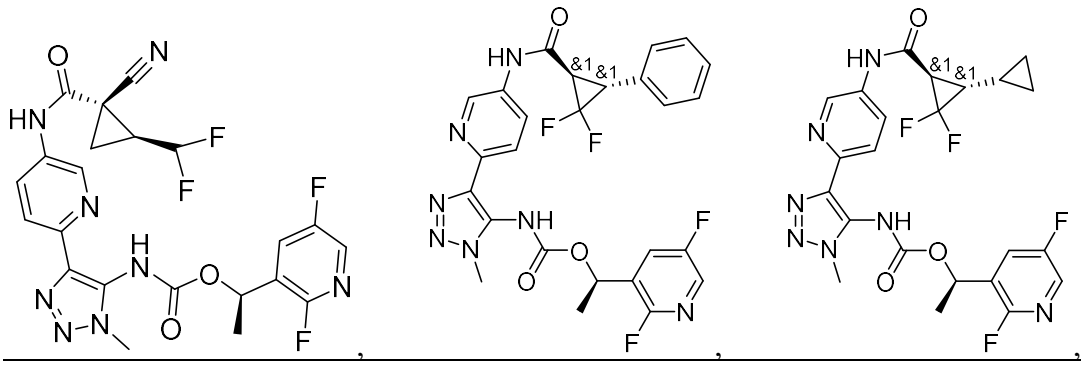


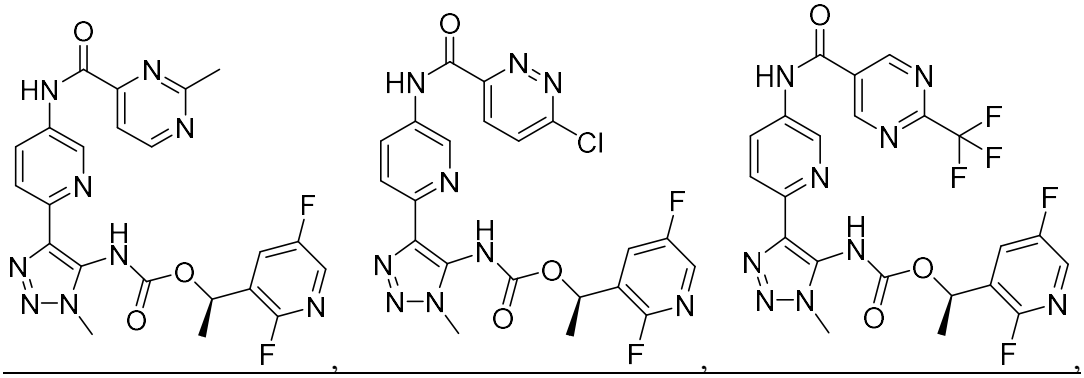


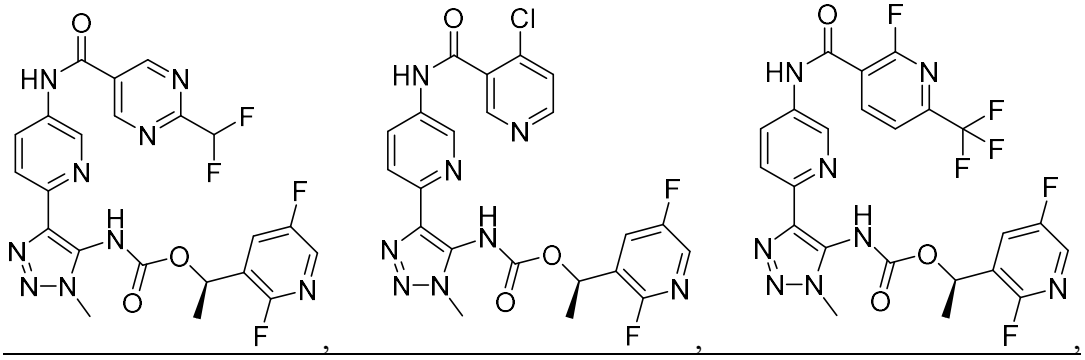


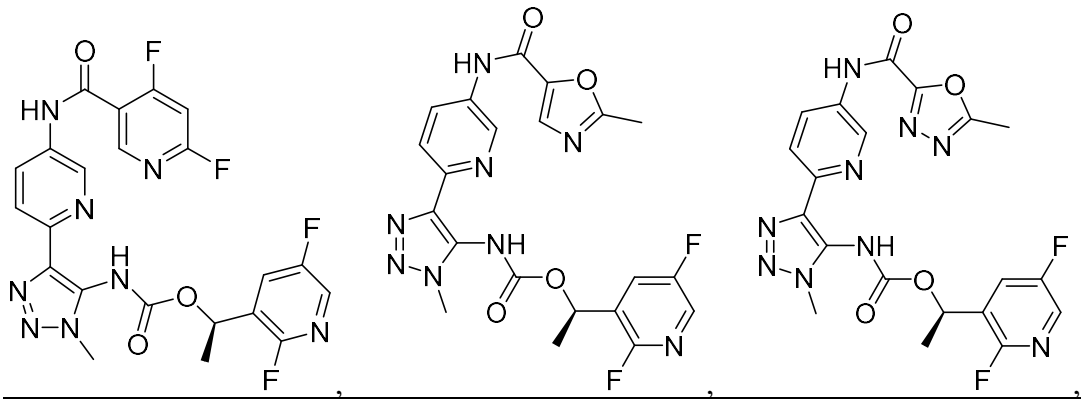


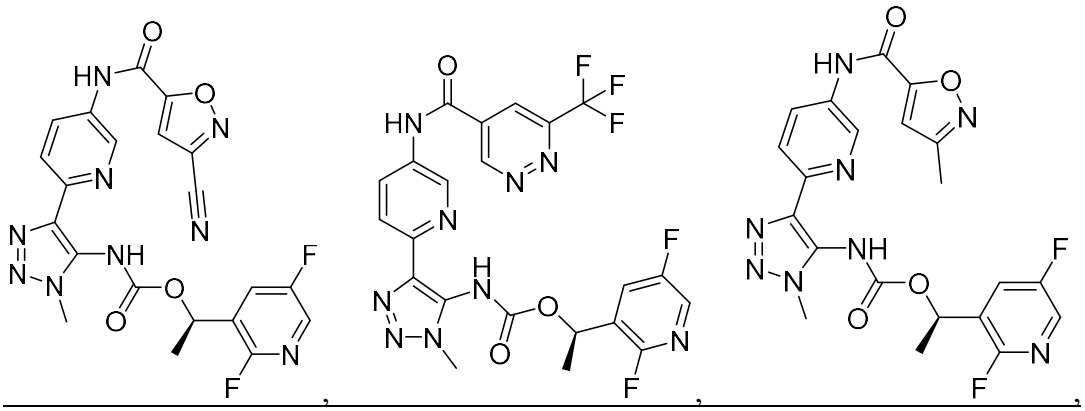


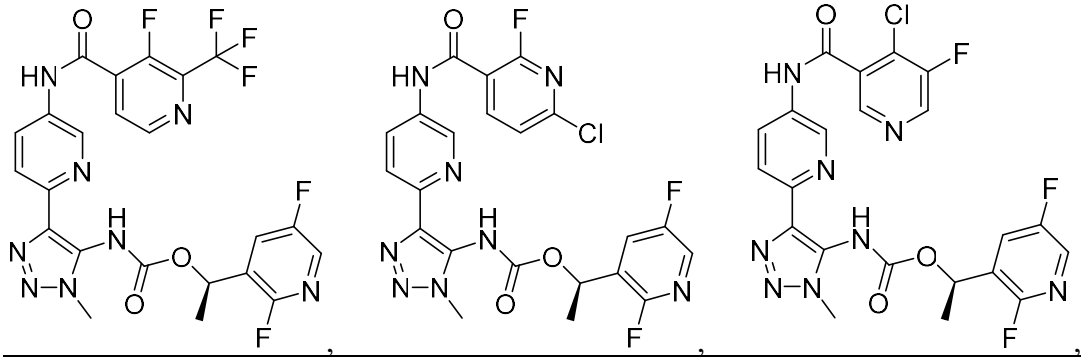


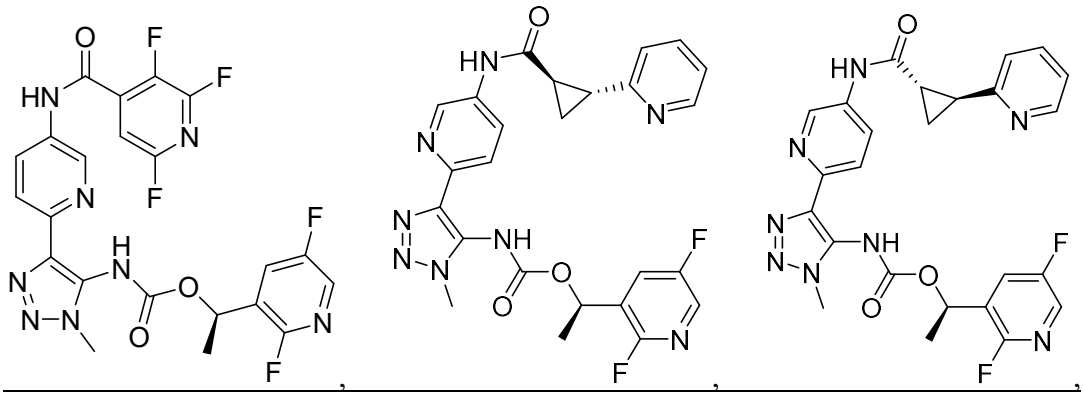


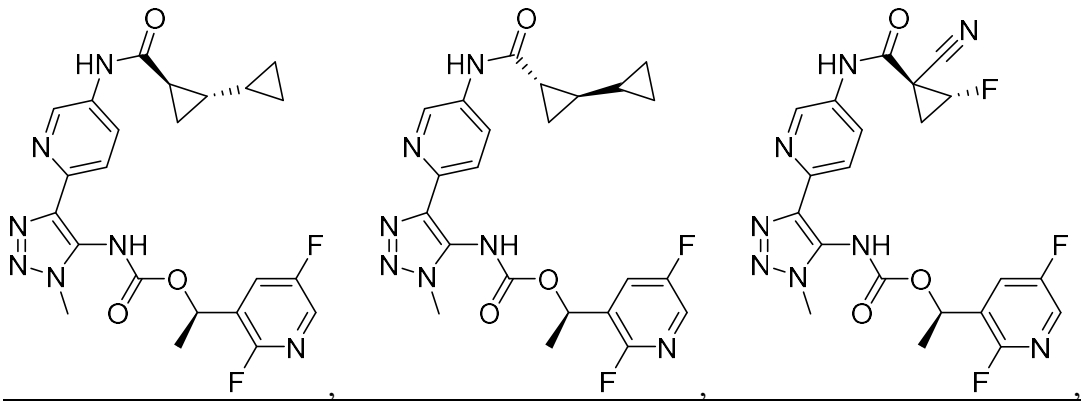


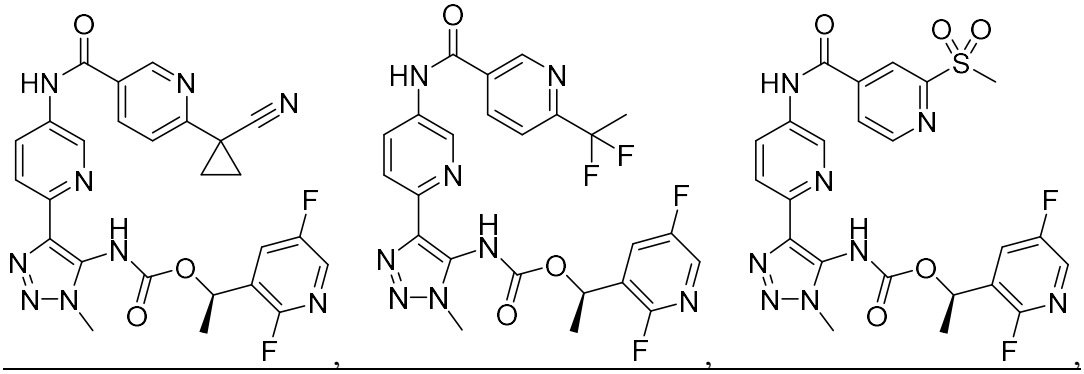


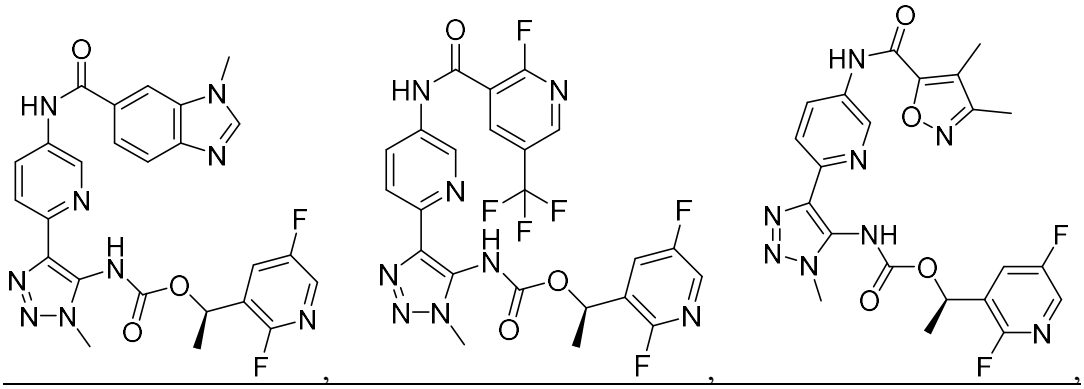


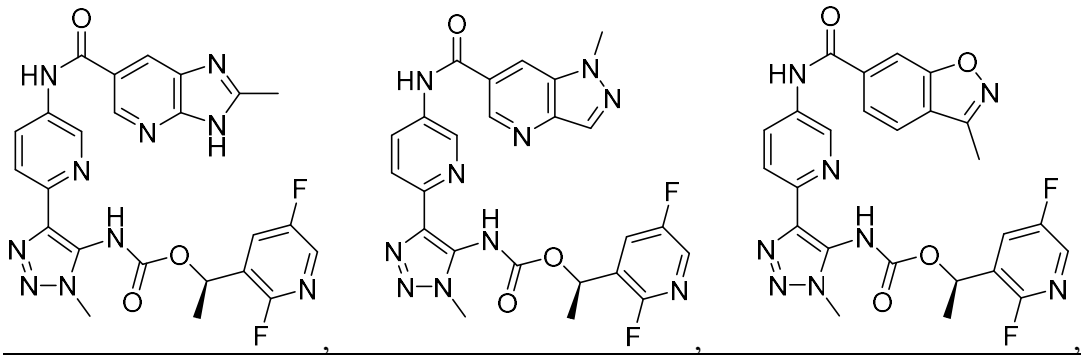


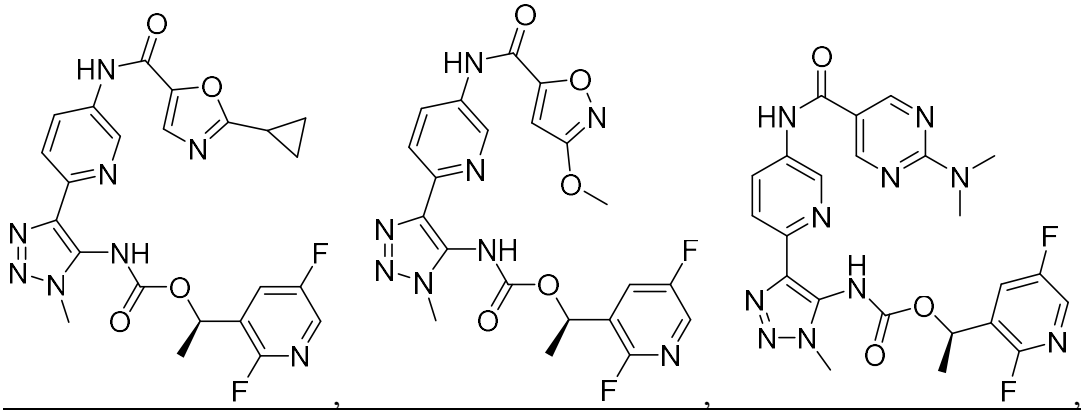


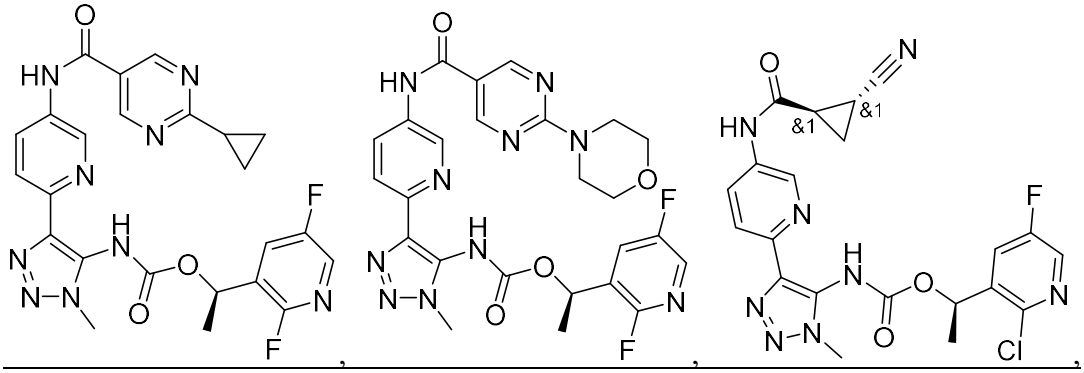


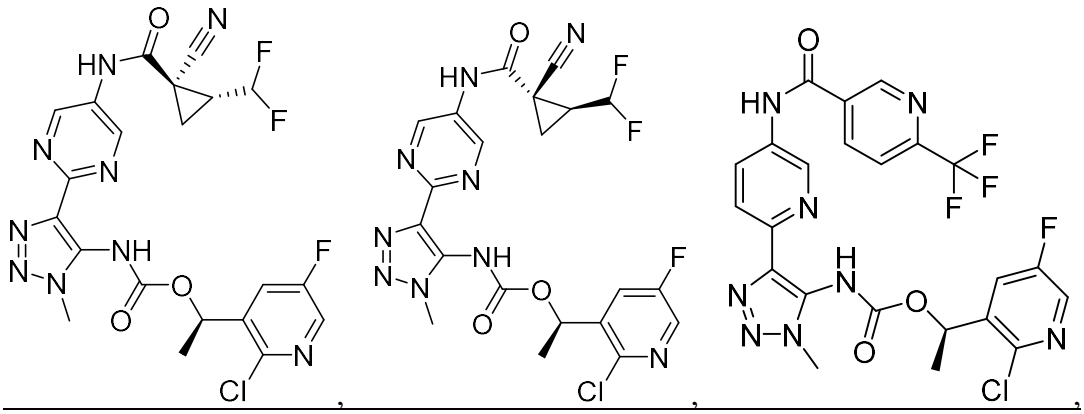


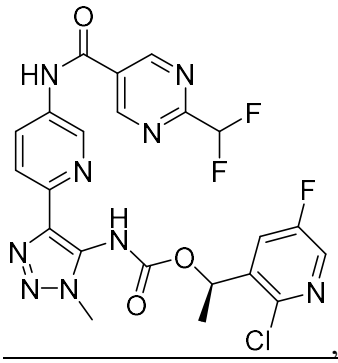
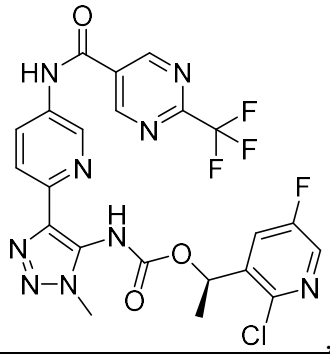
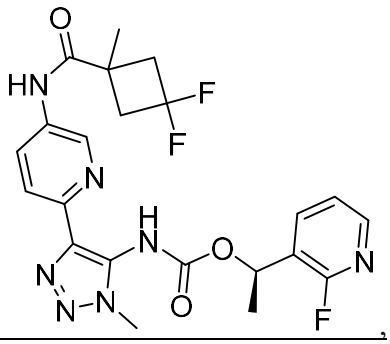


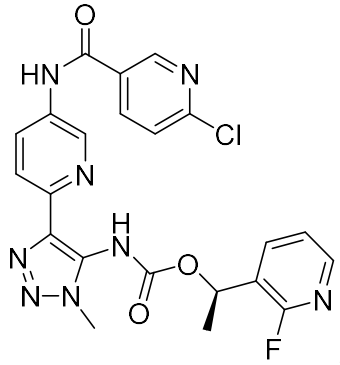
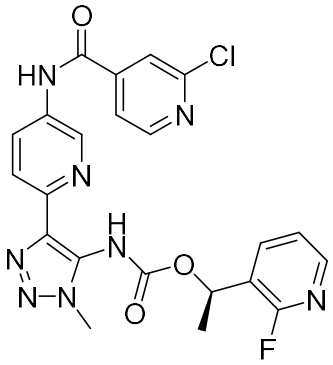
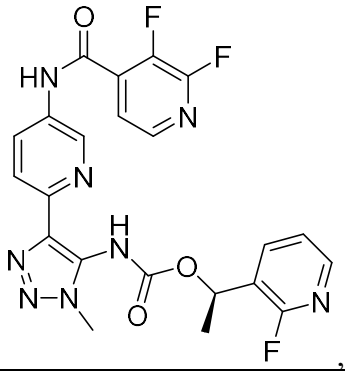


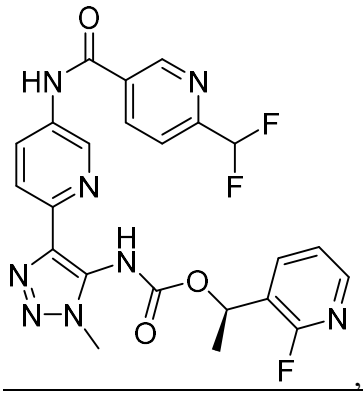
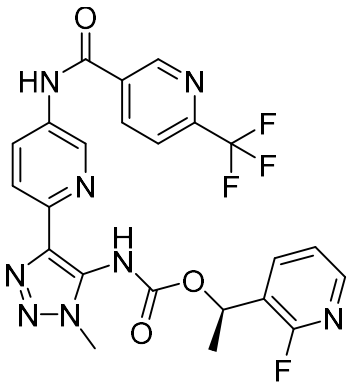
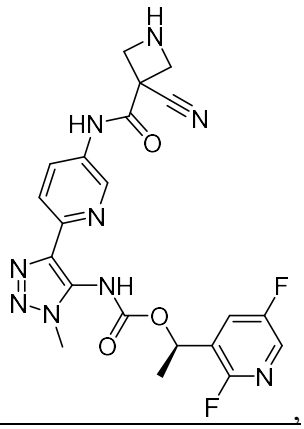


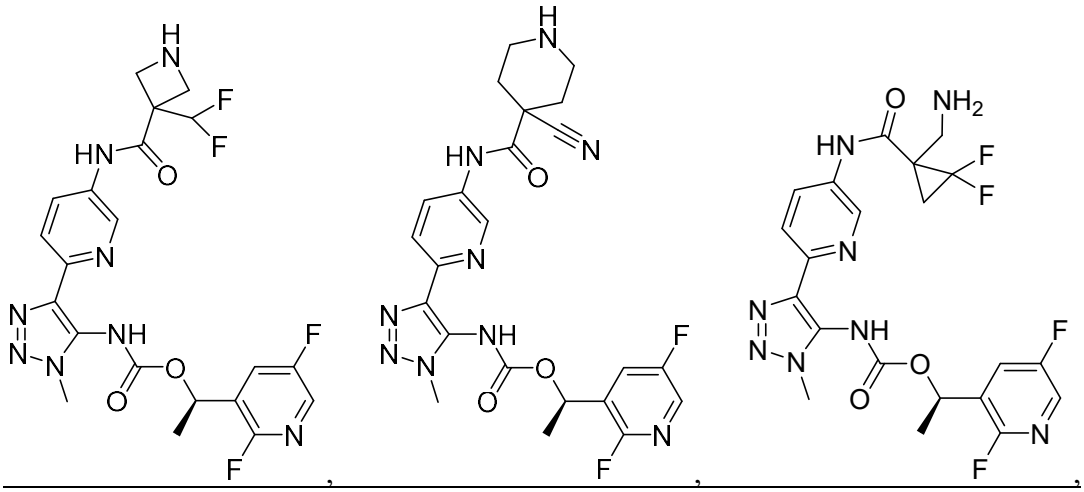


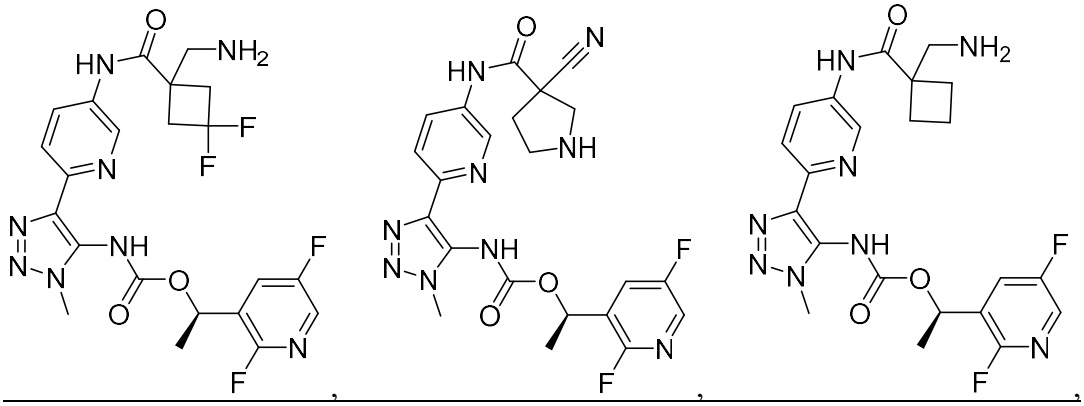


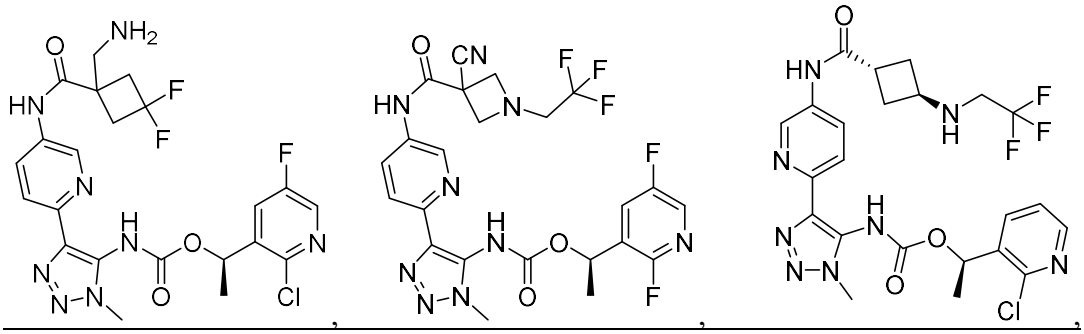

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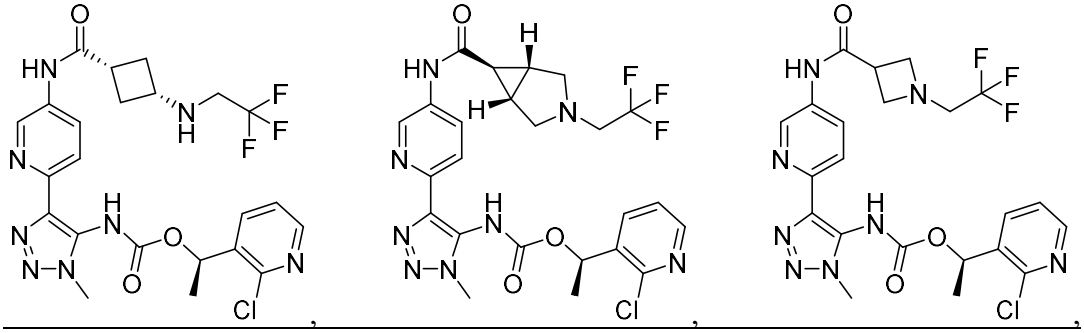

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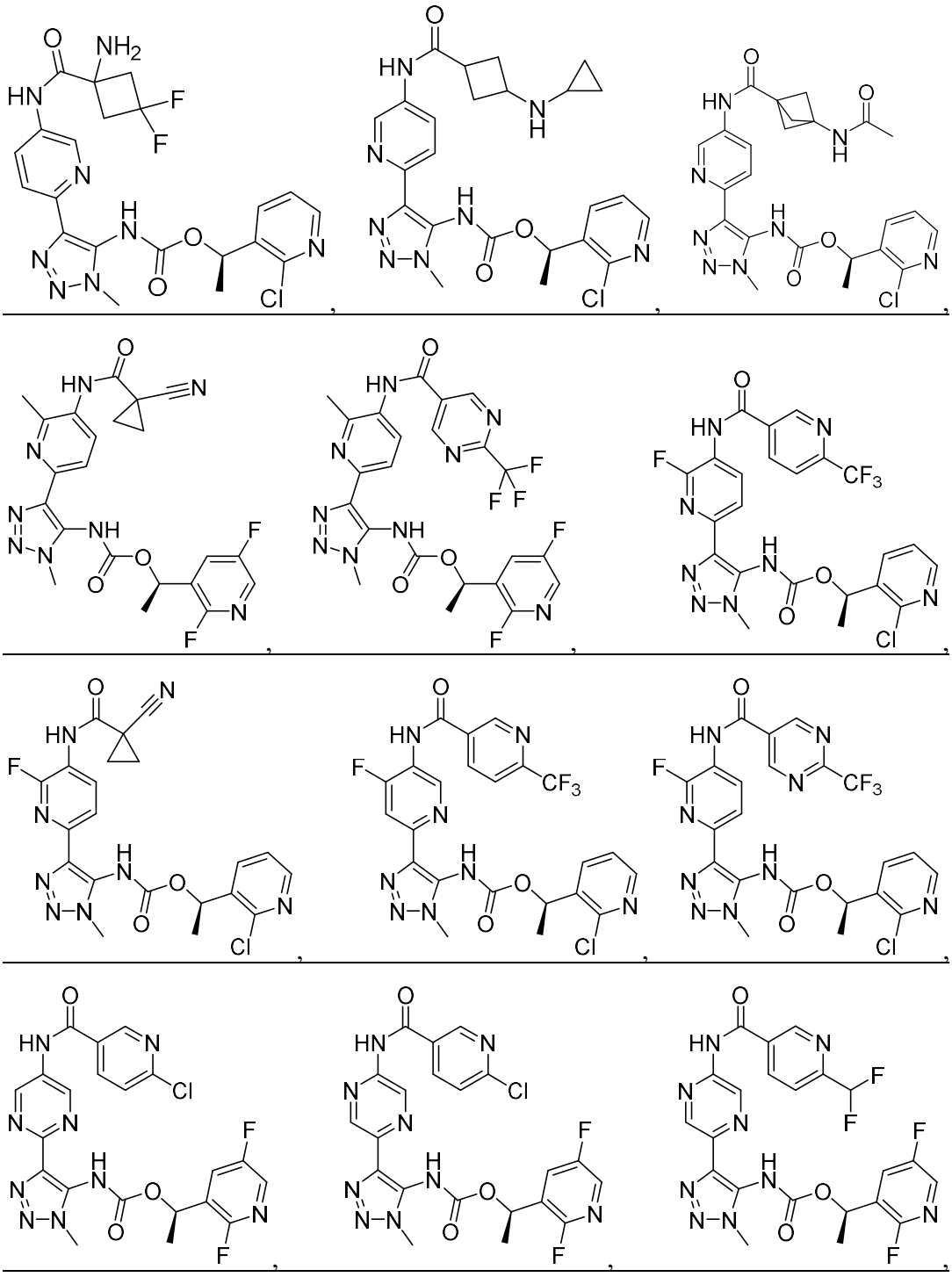

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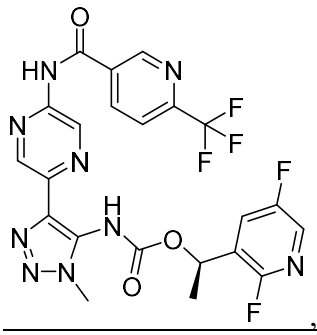
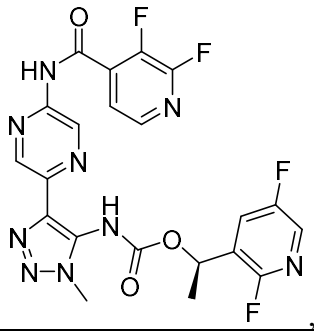
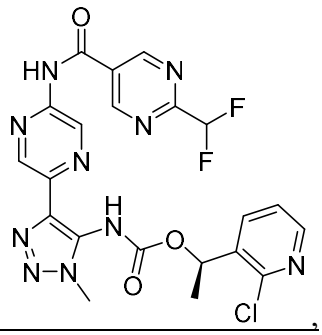
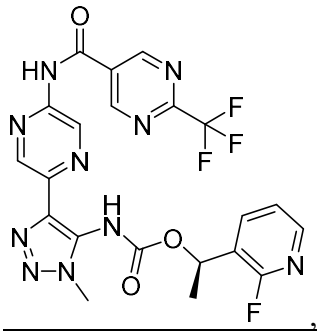
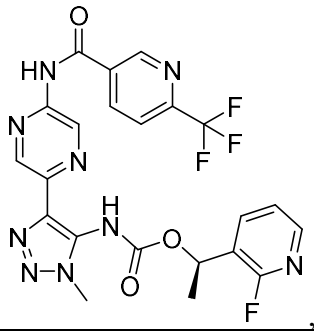
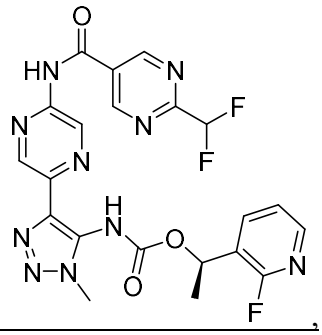
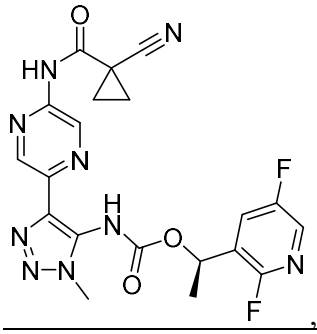
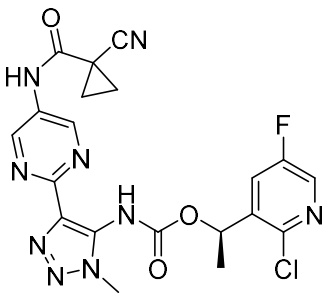
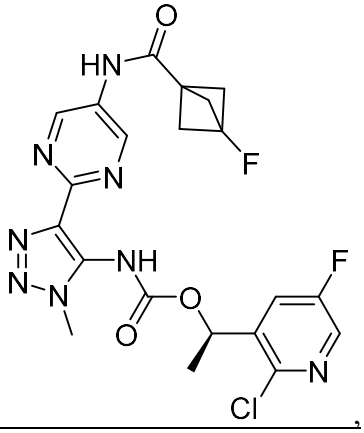
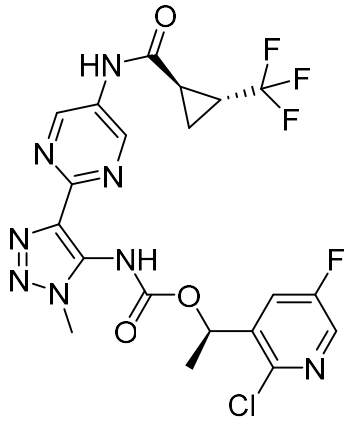
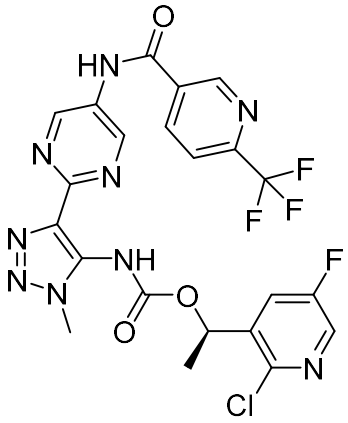
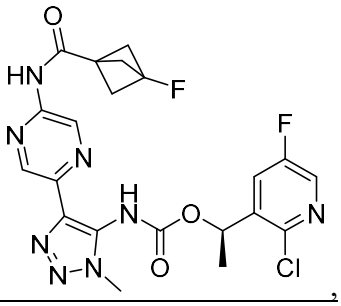


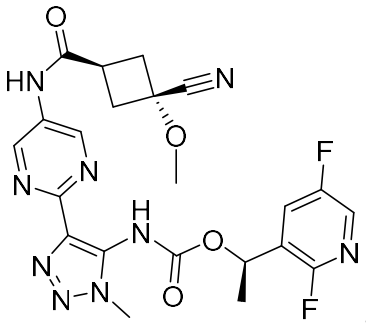
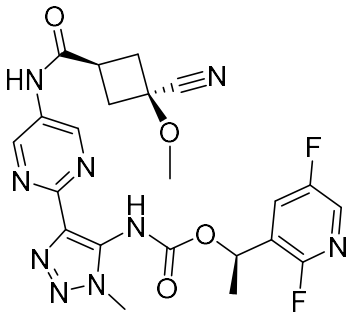
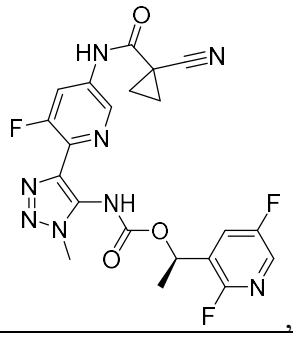


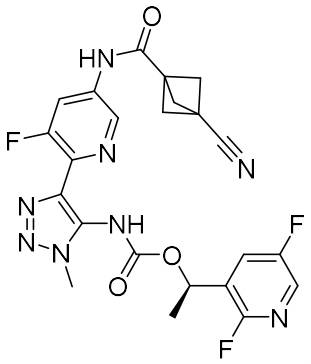
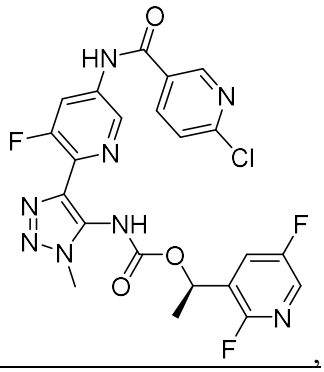






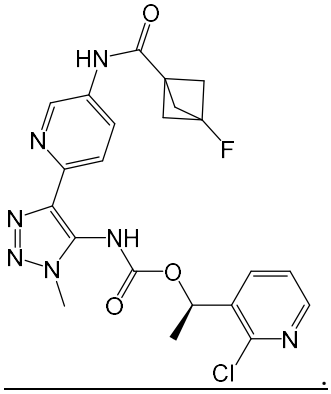

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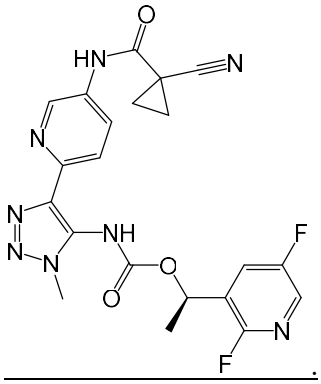
, and ,

or a pharmaceutically acceptable salt thereof.

50. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is

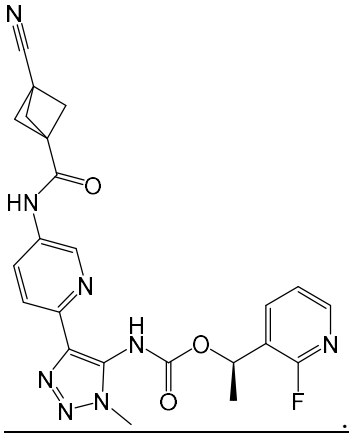
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51. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



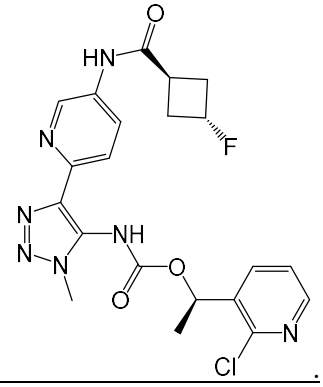
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52. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



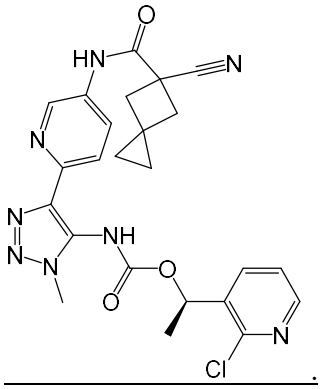
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53. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



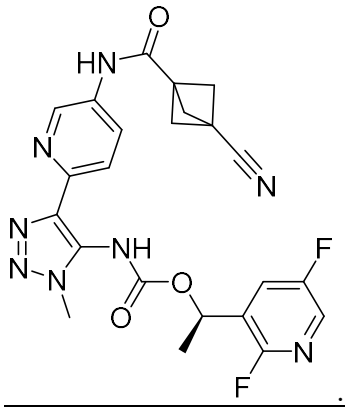
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54. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



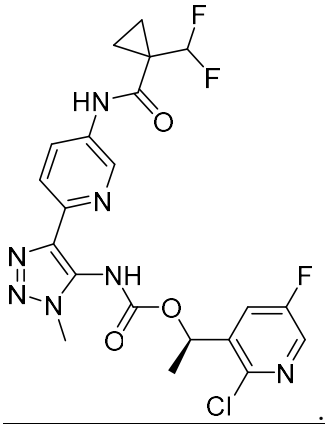
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55. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



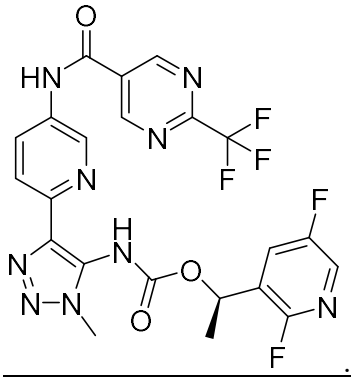
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56. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



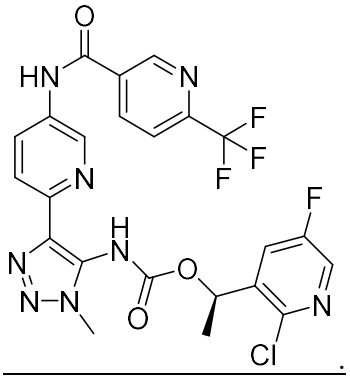
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57. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



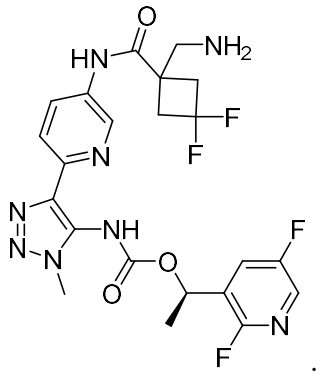
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58. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



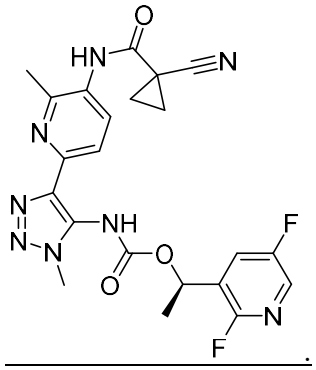
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59. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



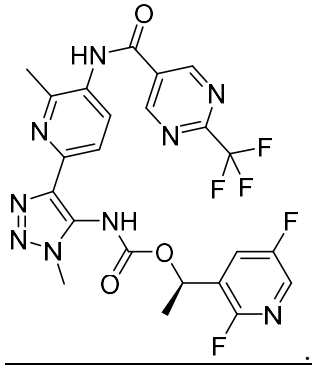
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60. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



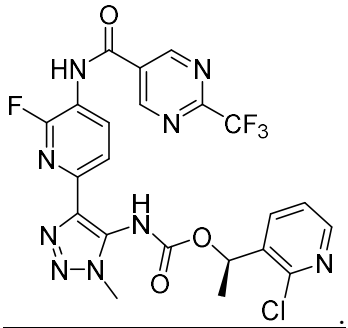
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61. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



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62. A compound or pharmaceutically acceptable salt thereof of claim 1, wherein the compound is



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63. A pharmaceutical composition comprising a therapeutically effective amount of a compound, or pharmaceutically acceptable salt thereof, of any one of claims 1 to 62, and a pharmaceutically acceptable excipient.

64. The pharmaceutical composition of claim 63, further comprising an additional therapeutic agent.

65. Use of a therapeutically effective amount of a compound of any one of claims 1 to 62, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for of treating, stabilizing, or lessening the severity or progression of an LPAR1 mediated disease or condition.

66. The use of claim 65, wherein the LPAR1 mediated disease or condition is an interstitial lung disease (ILD).

67. The use of claim 65, wherein the LPAR1 mediated disease or condition is a chronic kidney disease (CKD).

68. The use of claim 65, wherein the LPAR1 mediated disease or condition comprises fibrosis.

69. The use of claim 68, wherein fibrosis is pulmonary fibrosis, renal fibrosis, hepatic fibrosis, ocular fibrosis, cardiac fibrosis, or systemic sclerosis.

70. The use of claim 69, wherein pulmonary fibrosis is idiopathic pulmonary fibrosis (IPF) or Progressive Fibrotic interstitial lung disease (PF-ILD).

71. The use of claim 65, wherein the LPAR1 mediated disease or condition is a liver disease.

72. The use of claim 71, wherein the liver disease comprises non-alcoholic steatoheptitis (NASH).

73. The use of claim 71 or 72, wherein the liver disease comprises Primary Biliary Cirrhosis (PBC) or Primary Sclerosing Choleangitis (PSC).

74. The use of claim 71 or 72, wherein the liver disease comprises portal hypertension.

75. The use of any one of claims 65-74, wherein the compound or pharmaceutically acceptable salt thereof is to be administered in combination with an additional therapeutic agent.

76. The pharmaceutical composition of claim 63 or the use of claim 75, wherein the additional therapeutic agent is one, two, three, or four additional therapeutic agents.

77. The pharmaceutical composition of claim 63, or the use of claim 75 or 76, wherein the additional therapeutic agent comprises an acetyl-CoA carboxylase (ACC) inhibitor, an apoptotic signal-regulating kinase (ASK-1) inhibitor, a farnesoid X receptor (FXR) agonist, fish oil, a glucagon-like peptide-1 receptor agonist, a peroxisome proliferator-activated receptor alpha (PPARα) agonist, or a TGFβ antagonist.