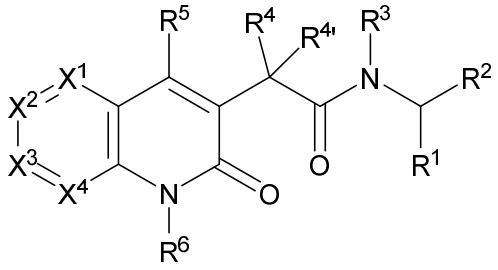
CLAIMS

WHAT IS CLAIMED IS:

1. A compound represented by Formula (I):



(I);

or a salt thereof, wherein:

X^1, X^2, and X^3 are each independently selected from C(R) and N, wherein at least one of X^1, X^2, and X^3 is N and no more than two of X^1, X^2, and X^3 are N;

X^4 is selected from C(R);

each R is independently selected from:

hydrogen, halogen, $-NO_2$, -CN, $-N_3$, $-OR^8$, $-SR^8$, $-N(R^8)_2$, $-C(O)R^8$, $-C(O)N(R^8)_2$, $-N(R^8)C(O)R^8$, $-N(R^8)C(O)N(R^8)_2$, $-OC(O)N(R^8)_2$, $-N(R^8)C(O)OR^8$, $-C(O)OR^8$, $-OC(O)R^8$, $-S(O)R^8$, and $-S(O)_2R^8$;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^8$, $-SR^8$, $-N(R^8)_2$, $-C(O)R^8$, $-C(O)N(R^8)_2$, $-N(R^8)C(O)R^8$, $-C(O)OR^8$, $-OC(O)R^8$, $-N(R^8)C(O)N(R^8)_2$, $-OC(O)N(R^8)_2$, $-N(R^8)C(O)OR^8$, $-S(O)R^8$, $-S(O)_2R^8$, $-NO_2$, =O, =S, $=N(R^8)$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^7; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^8$, $-SR^8$, $-N(R^8)_2$, $-C(O)R^8$, $-C(O)N(R^8)_2$, $-N(R^8)C(O)R^8$, $-N(R^8)C(O)N(R^8)_2$, $-OC(O)N(R^8)_2$, $-N(R^8)C(O)OR^8$, $-C(O)OR^8$, $-OC(O)R^8$, $-S(O)R^8$, $-S(O)_2R^8$, $-NO_2$, =O, =S, $=N(R^8)$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^7;

R^1 is selected from:

hydrogen;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{8a}$, $-SR^{8a}$, -

$N(R^{8a})_2$, $-C(O)R^{8a}$, $-C(O)N(R^{8a})_2$, $-N(R^{8a})C(O)R^{8a}$, $-C(O)OR^{8a}$, $-OC(O)R^{8a}$, $-N(R^{8a})C(O)N(R^{8a})_2$, $-OC(O)N(R^{8a})_2$, $-N(R^{8a})C(O)OR^{8a}$, $-S(O)R^{8a}$, $-S(O)_2R^{8a}$, $-NO_2$, =O, =S, $=N(R^{8a})$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{7a}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{8a}$, $-SR^{8a}$, $-N(R^{8a})_2$, $-C(O)R^{8a}$, $-C(O)N(R^{8a})_2$, $-N(R^{8a})C(O)R^{8a}$, $-N(R^{8a})C(O)N(R^{8a})_2$, $-OC(O)N(R^{8a})_2$, $-N(R^{8a})C(O)OR^{8a}$, $-C(O)OR^{8a}$, $-OC(O)R^{8a}$, $-S(O)R^{8a}$, $-S(O)_2R^{8a}$, $-NO_2$, =O, =S, $=N(R^{8a})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{7a}; or

R^1 together with R^2 form a C_{3-10} carbocycle or 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{8a}$, $-SR^{8a}$, $-N(R^{8a})_2$, $-C(O)R^{8a}$, $-C(O)N(R^{8a})_2$, $-N(R^{8a})C(O)R^{8a}$, $-N(R^{8a})C(O)N(R^{8a})_2$, $-OC(O)N(R^{8a})_2$, $-N(R^{8a})C(O)OR^{8a}$, $-C(O)OR^{8a}$, $-OC(O)R^{8a}$, $-S(O)R^{8a}$, $-S(O)_2R^{8a}$, $-NO_2$, =O, =S, $=N(R^{8a})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{7b};

R^2 is selected from:

hydrogen;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{8b}$, $-SR^{8b}$, $-N(R^{8b})_2$, $-C(O)R^{8b}$, $-C(O)N(R^{8b})_2$, $-N(R^{8b})C(O)R^{8b}$, $-C(O)OR^{8b}$, $-OC(O)R^{8b}$, $-N(R^{8b})C(O)N(R^{8b})_2$, $-OC(O)N(R^{8b})_2$, $-N(R^{8b})C(O)OR^{8b}$, $-S(O)R^{8b}$, $-S(O)_2R^{8b}$, $-NO_2$, =O, =S, $=N(R^{8b})$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{7b}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{8b}$, $-SR^{8b}$, $-N(R^{8b})_2$, $-C(O)R^{8b}$, $-C(O)N(R^{8b})_2$, $-N(R^{8b})C(O)R^{8b}$, $-N(R^{8b})C(O)N(R^{8b})_2$, $-OC(O)N(R^{8b})_2$, $-N(R^{8b})C(O)OR^{8b}$, $-C(O)OR^{8b}$, $-OC(O)R^{8b}$, $-S(O)R^{8b}$, $-S(O)_2R^{8b}$, $-NO_2$, =O, =S, $=N(R^{8b})$, -CN, $-N_3$, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6}

alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{7b}; or

R^1 together with R^2 form a C_{3-10} carbocycle or 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{8a}$, $-SR^{8a}$, $-N(R^{8a})_2$, $-C(O)R^{8a}$, $-C(O)N(R^{8a})_2$, $-N(R^{8a})C(O)R^{8a}$, $-N(R^{8a})C(O)N(R^{8a})_2$, $-OC(O)N(R^{8a})_2$, $-N(R^{8a})C(O)OR^{8a}$, $-C(O)OR^{8a}$, $-OC(O)R^{8a}$, $-S(O)R^{8a}$, $-S(O)_2R^{8a}$, $-NO_2$, =O, =S, $=N(R^{8a})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{7b};

R^3 is selected from:

hydrogen, halogen, $-OR^{8c}$, $-SR^{8c}$, $-N(R^{8c})_2$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from R^{7c};

R^4 is selected from:

hydrogen, halogen, $-OR^{8d}$, $-SR^{8d}$, $-N(R^{8d})_2$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{8d}$, $-SR^{8d}$, $-N(R^{8d})_2$, $-NO_2$, and -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{7d};

or R^4 and $R^{4'}$ together form a C_{3-10} carbocycle or 3- to 10-membered heterocycle, wherein the C_{3-10} carbocycle or 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{7d};

$R^{4'}$ is selected from:

hydrogen, halogen, $-OR^{8d}$, $-SR^{8d}$, $-N(R^{8d})_2$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{8d}$, $-SR^{8d}$, $-N(R^{8d})_2$, $-NO_2$, and -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{7d};

or R^4 and $R^{4'}$ together form a C_{3-10} carbocycle or 3- to 10-membered heterocycle, wherein the C_{3-10} carbocycle or 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{7d};

R^5 is selected from:

hydrogen, halogen, -OR^{8e}, -SR^{8e}, -$N(R^{8e})_2$, -NO_2, -CN, C_{1-6} alkyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{1-6} alkyl, C_{3-10} carbocycle, and 3- to 10- membered heterocycle is optionally substituted with one or more substituents independently selected from R^{7e};

R^6 is selected from:

hydrogen, halogen, -OR^{8f}, -SR^{8f}, -$N(R^{8f})_2$, -NO_2, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from R^{7f};

each R^7, R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, and R^{7f} is independently selected from:

halogen, -OR^{8g}, -SR^{8g}, -$N(R^{8g})_2$, -$C(O)R^{8g}$, -$C(O)N(R^{8g})_2$, -$N(R^{8g})C(O)R^{8g}$, -$N(R^{8g})C(O)N(R^{8g})_2$, -$OC(O)N(R^{8g})_2$, -$N(R^{8g})C(O)OR^{8g}$, -$C(O)OR^{8g}$, -$OC(O)R^{8g}$, -$S(O)R^{8g}$, -$S(O)_2R^{8g}$, -NO_2, =O, =S, =$N(R^{8g})$, and -CN; and

C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{8g}, -SR^{8g}, -$N(R^{8g})_2$, -$C(O)R^{8g}$, -$C(O)N(R^{8g})_2$, -$N(R^{8g})C(O)R^{8g}$, -$N(R^{8g})C(O)N(R^{8g})_2$, -$OC(O)N(R^{8g})_2$, -$N(R^{8g})C(O)OR^{8g}$, -$C(O)OR^{8g}$, -$OC(O)R^{8g}$, -$S(O)R^{8g}$, -$S(O)_2R^{8g}$, -NO_2, =O, =S, =$N(R^{8g})$, and -CN; and

each R^8, R^{8a}, R^{8b}, R^{8c}, R^{8d}, R^{8e}, R^{8f}, and R^{8g} is independently selected from:

hydrogen and halogen; and

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{3-10} carbocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO_2, -NH_2, =O, =S, -O-C_{1-6} alkyl, -S-C_{1-6} alkyl, -$N(C_{1-6}$ alkyl$)_2$, -$NH(C_{1-6}$ alkyl), C_{3-10} carbocycle, and 3- to 10-membered heterocycle; and

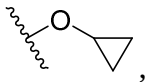
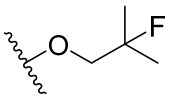
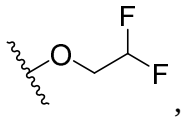
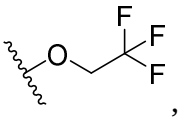
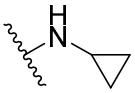
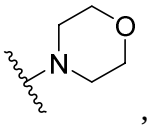
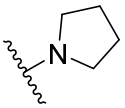
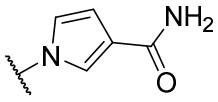
C_{3-10} carbocycle, and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO_2, -NH_2, =O, =S, -O-C_{1-6} alkyl, -S-C_{1-6} alkyl, -SO_2-C_{1-6} alkyl, -$N(C_{1-6}$ alkyl$)_2$, -$NH(C_{1-6}$ alkyl), C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, and C_{1-6} haloalkyl.

2. The compound or salt of claim 1, wherein each R is independently selected from:

hydrogen, halogen, -CN, -N_3, -OR^8, -SR^8, and -$N(R^8)_2$;

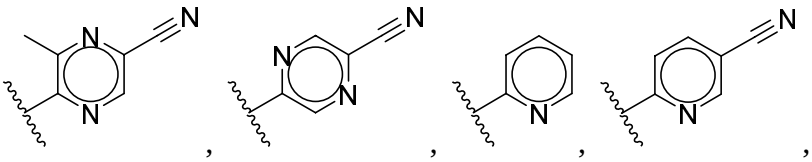
C_{1-6} alkyl and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen; and

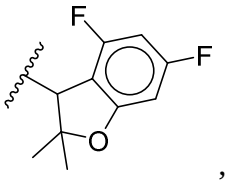
C_{3-10} carbocycle and 3- to 10-membered heterocycle.

3. The compound or salt of claim 1 or 2, wherein each R is independently selected from: hydrogen, -F, -Cl, -Br, -I, -CN, -N_3, -OH, -OMe, -OEt, -O(*n*-Pr), -O(*i*Pr), -O(*i*-Bu),  , -OCF_3,  ,  ,  , -NH_2, -NH(Me), -NH(Et), -$N(Et)_2$, -NH(*i*-Bu), -NH(Ph), -NHBn,  ,  ,  ,  , -CF_3, -methyl, -ethyl, cyclopropyl, -$CH_2N(CH_3)_2$, -CCMe, -CCH, phenyl, *N*-morpholinyl, and *N*-pyrrolidinyl.
4. The compound or salt of any one of claims 1 to 3 wherein each R^8 is independently selected from hydrogen, methyl, ethyl, propyl, isopropyl, cyclopropyl, isobutyl, -CF_3, -CH_2CF_3, -CH_2CHF_2, -$CH_2C(F)(Me)_2$, and -CH_2-phenyl.
5. The compound or salt of any one of claims 1 to 4, wherein R^1 is methyl, -CH_2OH, -CH_2CH_2OH, $C(Me)_2OH$, or -CH_2OMe.
6. The compound or salt of any one of claims 1 to 5, wherein R^1 is methyl.
7. The compound or salt of any one of claims 1 to 6, wherein R^2 is selected from:

$C_{3\text{-}10}$ carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{8b}, -$C(O)R^{8b}$, -$S(O)_2R^{8b}$, -CN, and $C_{1\text{-}6}$ alkyl, wherein $C_{1\text{-}6}$ alkyl is optionally substituted with one or more R^{7b}; or

R^1 together with R^2 form a $C_{3\text{-}10}$ carbocycle, or 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -$C(O)R^{8a}$, -CN, N_3, and $C_{1\text{-}6}$ alkyl, wherein $C_{1\text{-}6}$ alkyl is optionally substituted with one or more R^{7b}.
8. The compound or salt of any one of claims 1 to 7, wherein R^2 is selected from phenyl, pyridinyl, pyrimidinyl, pyrazinyl, and pyridazinyl, each of which is optionally substituted with one or more substituents independently selected from -F, -OH, -OMe, -COMe, -SO_2Me, -CN, and methyl.
9. The compound or salt of any one of claims 1 to 7, wherein :

(i) R^2 is selected from  , , ,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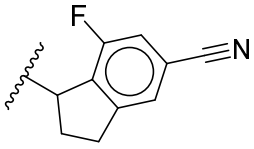
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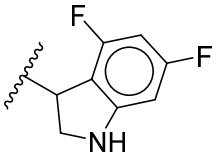
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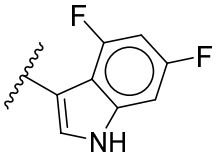
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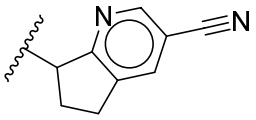
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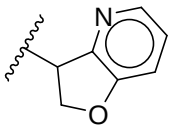
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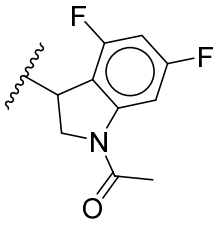
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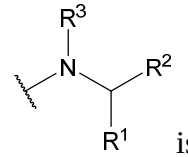
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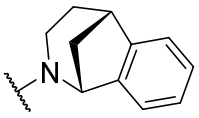
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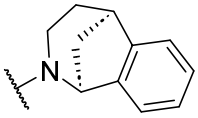
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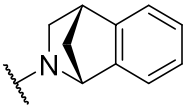
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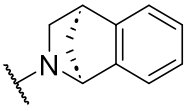
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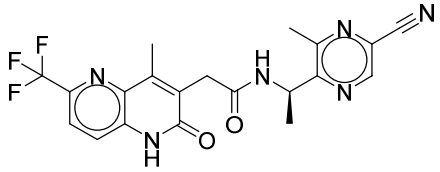
10. The compound or salt of any one of claims 1 to 9, wherein R^3 is hydrogen, and R^6 is hydrogen.
11. The compound or salt of any one of claims 1 to 10, wherein R^4 is selected from hydrogen, and $R^{4'}$ is selected from hydrogen; or R^4 is -F, and $R^{4'}$ is -F; or R^4 and $R^{4'}$ together form an optionally substituted cyclopropyl.
12. The compound or salt of any one of claims 1 to 11, wherein R^4 and $R^{4'}$ together form an unsubstituted cyclopropyl.
13. The compound or salt of claim 1, selected from: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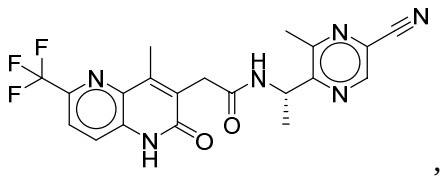
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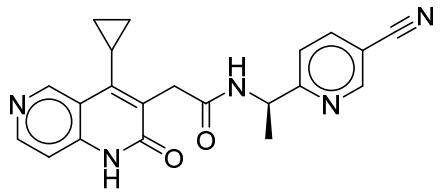
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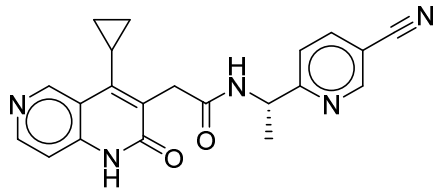
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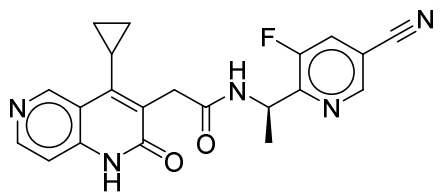
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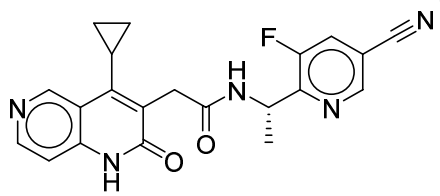
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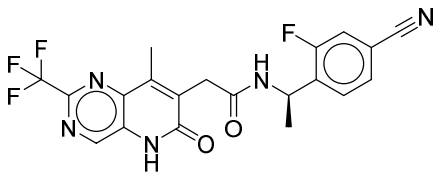
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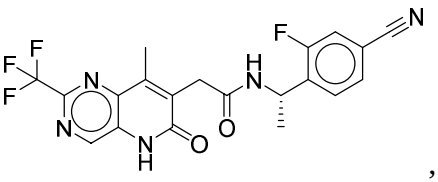
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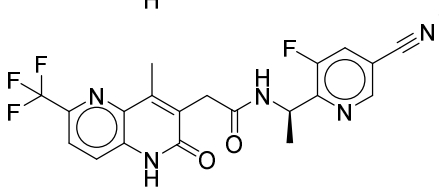
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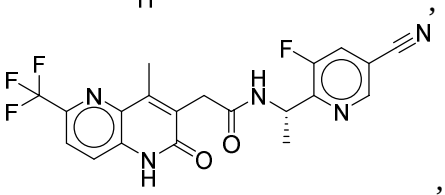
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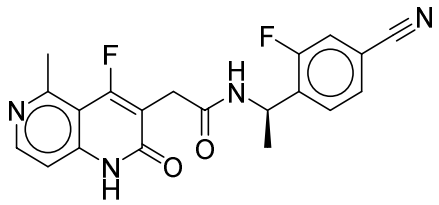
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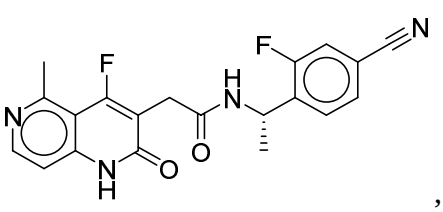
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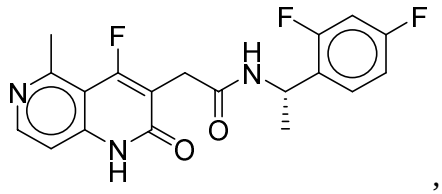
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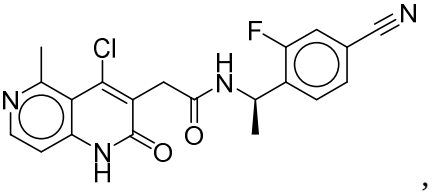
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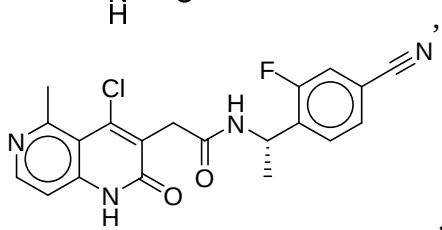
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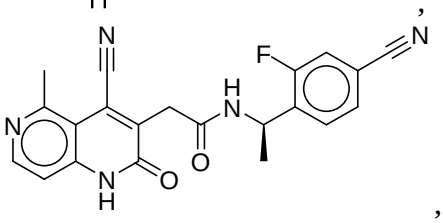
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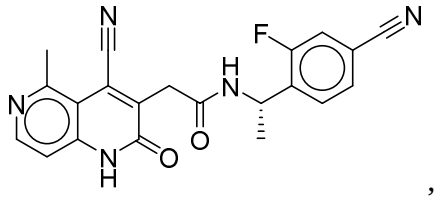
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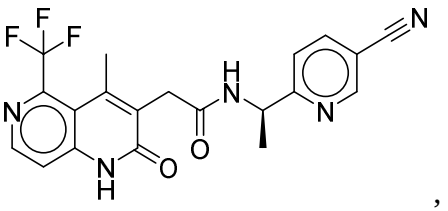
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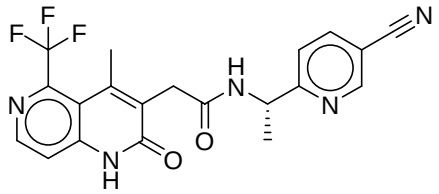
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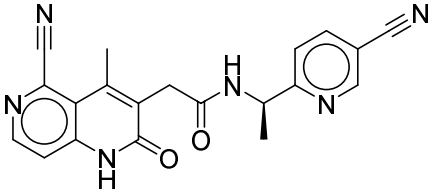
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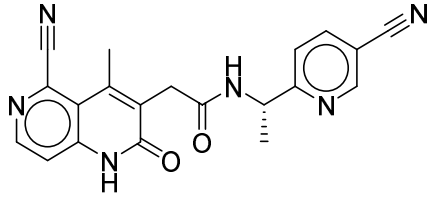
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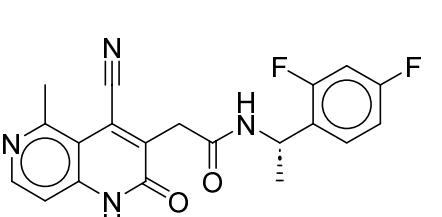
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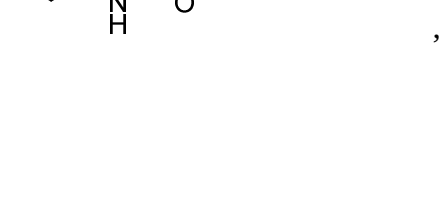
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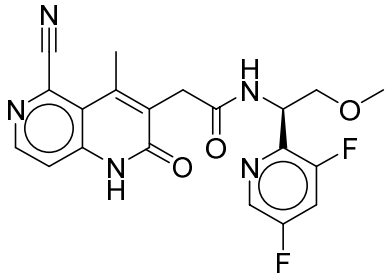
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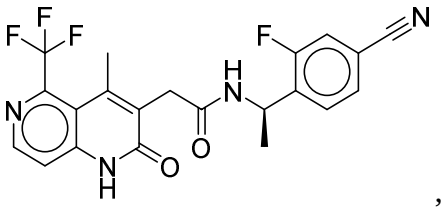
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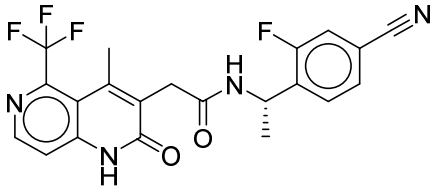
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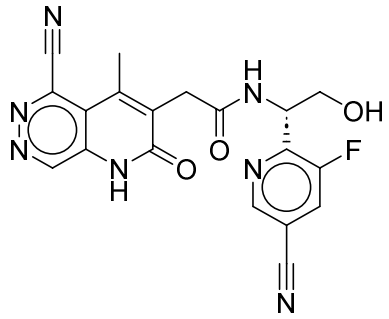
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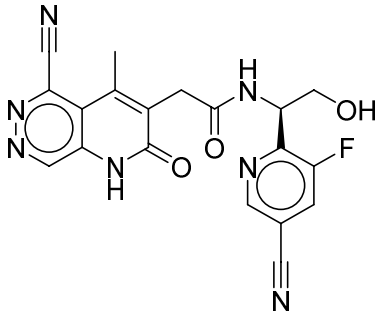
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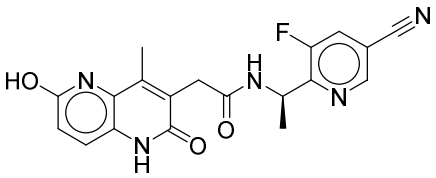
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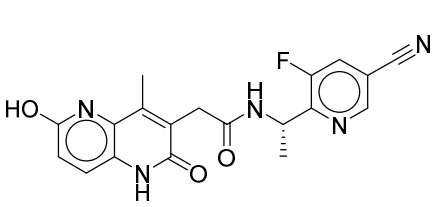
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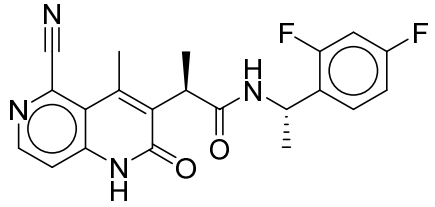
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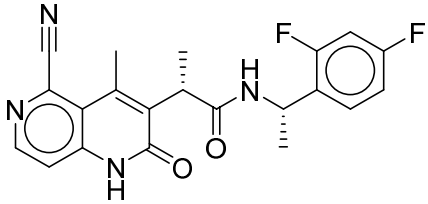
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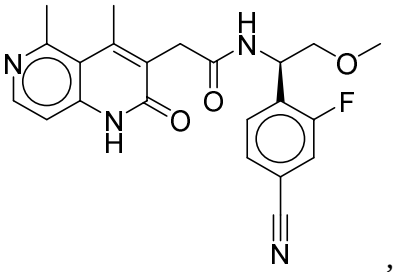
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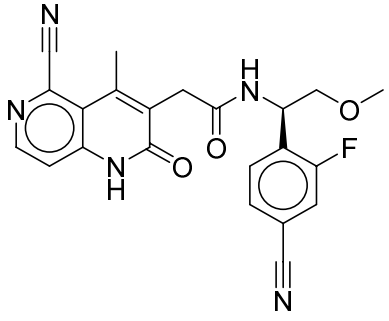
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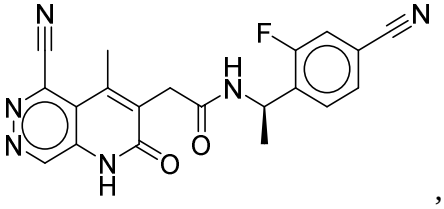
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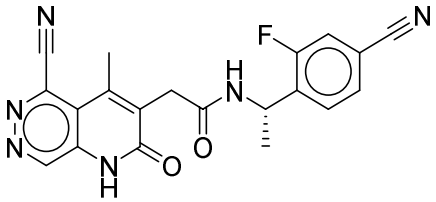
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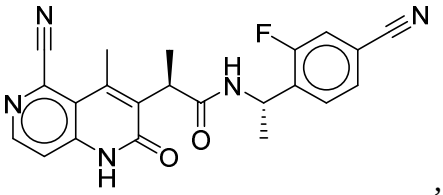
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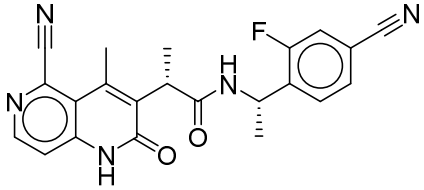
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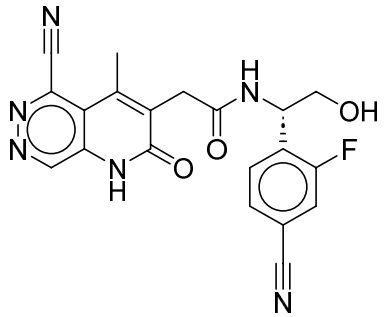
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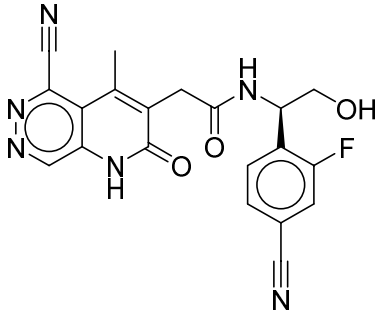
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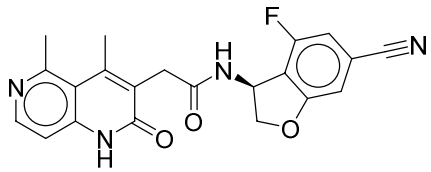
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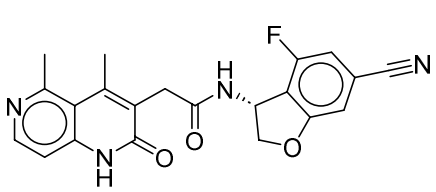
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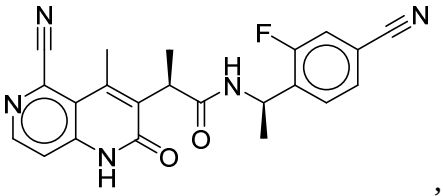
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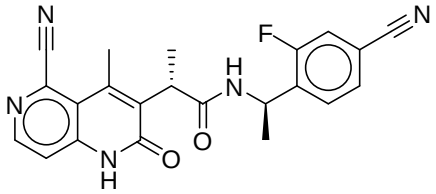
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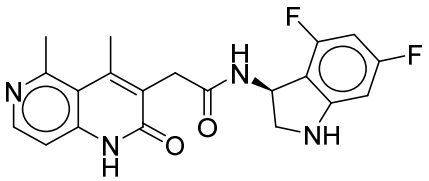
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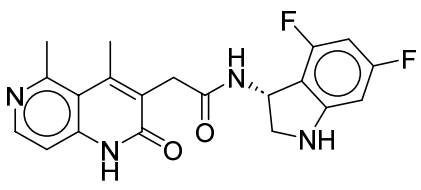
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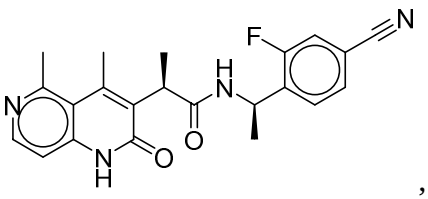
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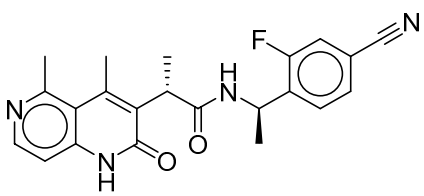
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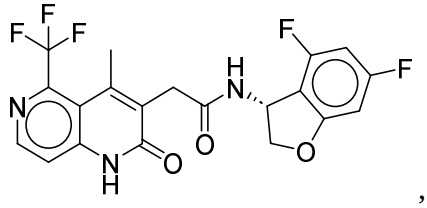
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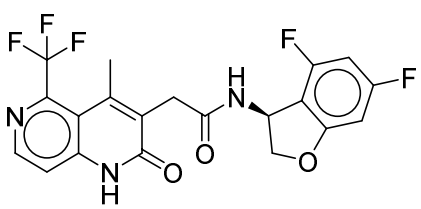
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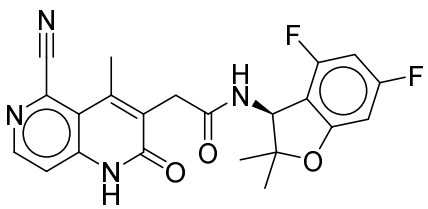
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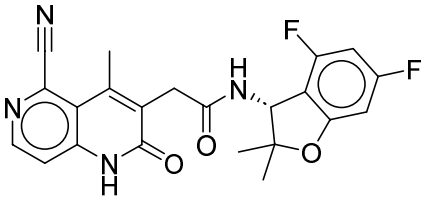
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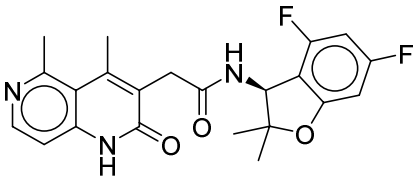
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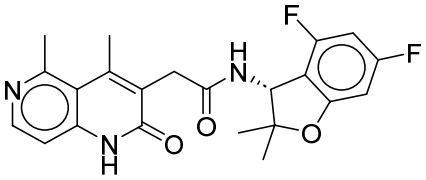
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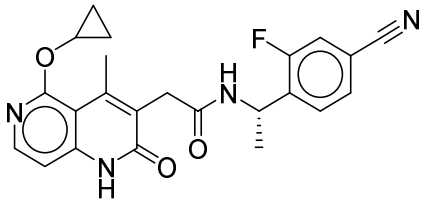
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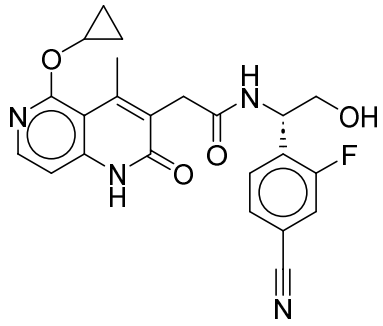
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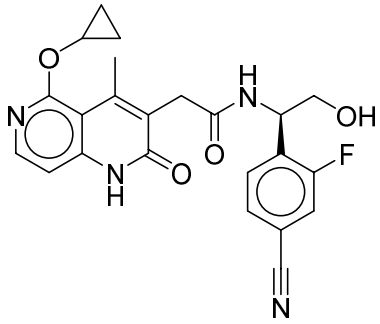
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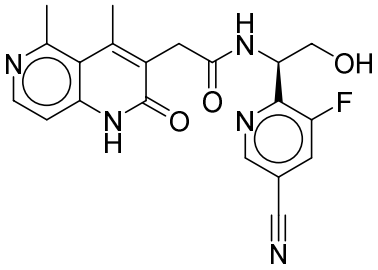
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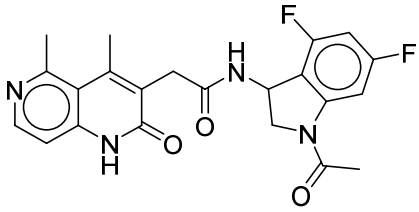
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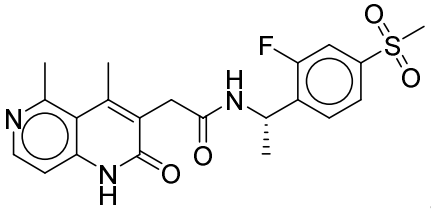
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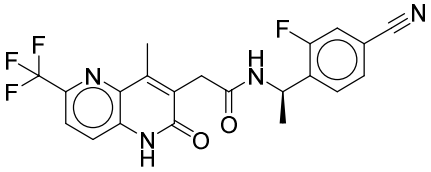
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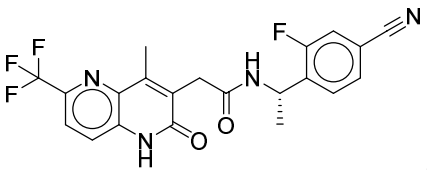
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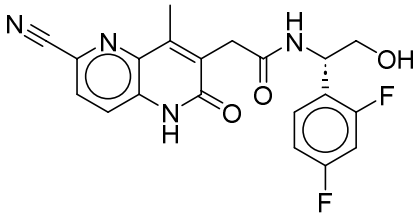
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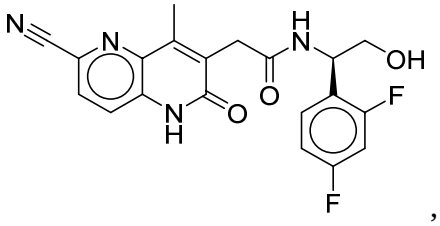
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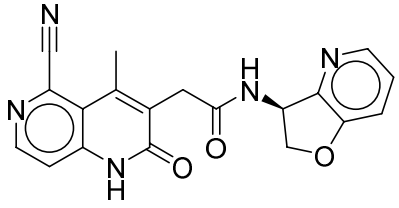
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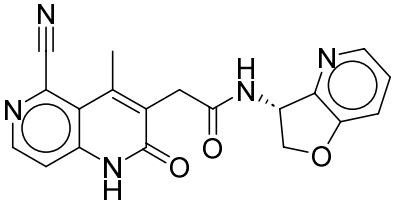
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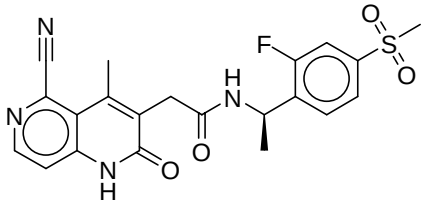
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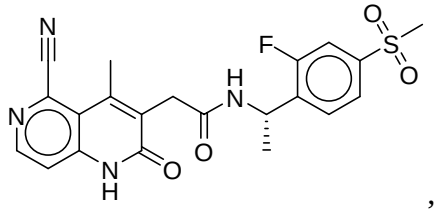
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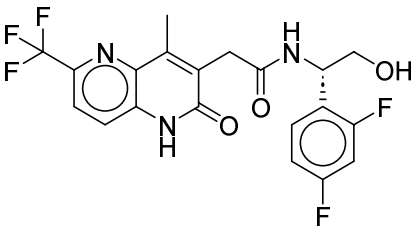
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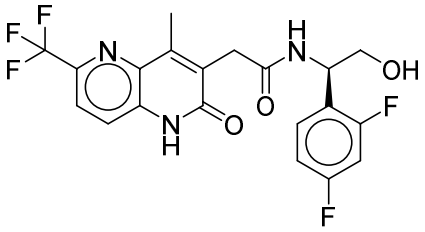
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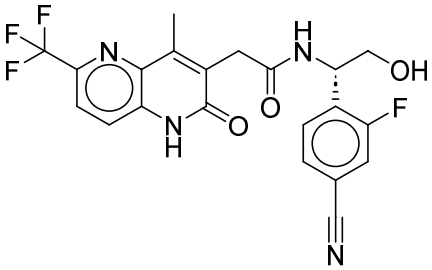
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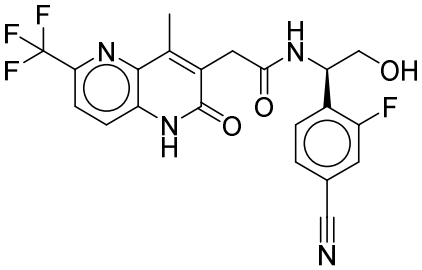
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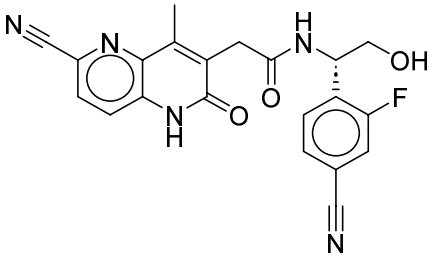
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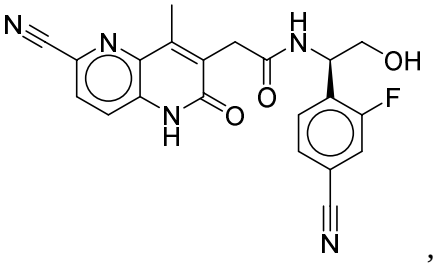
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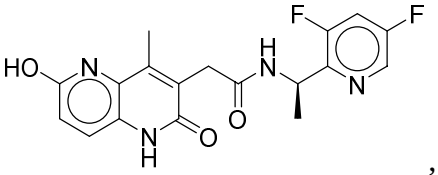
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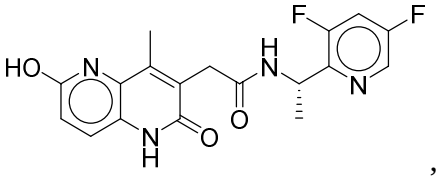
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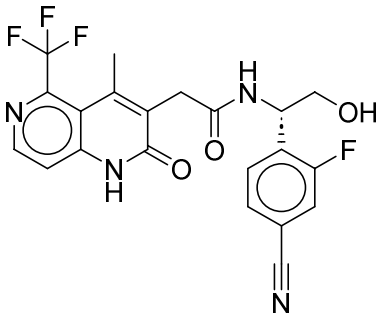
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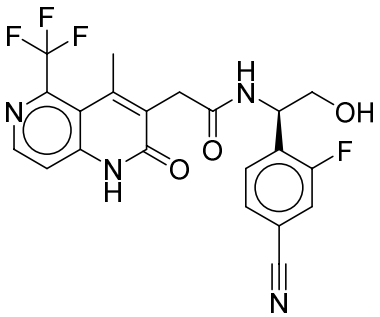
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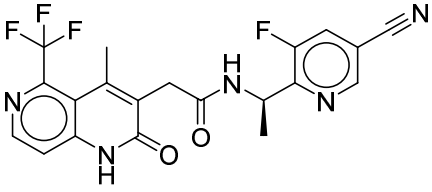
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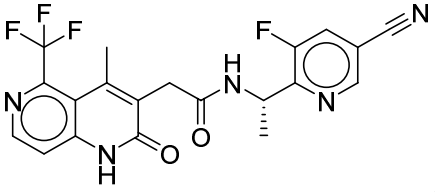
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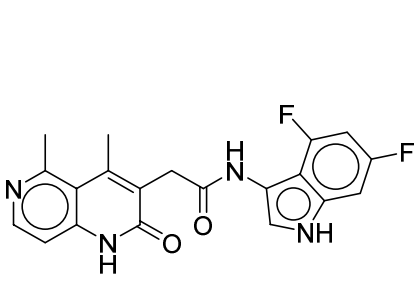
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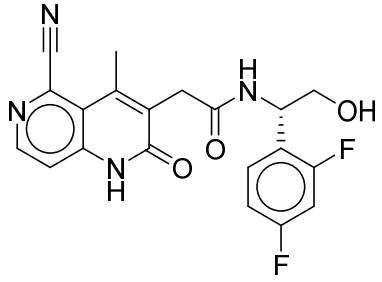
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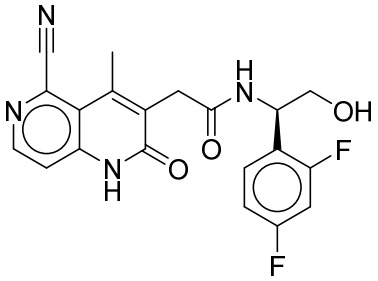
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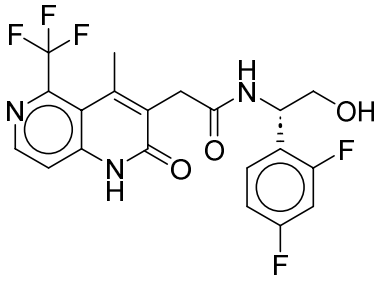
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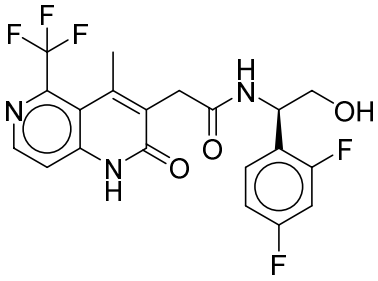
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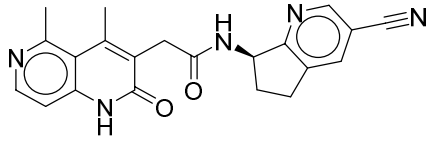
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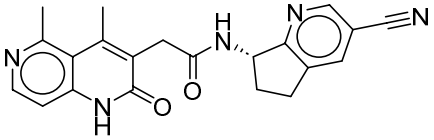
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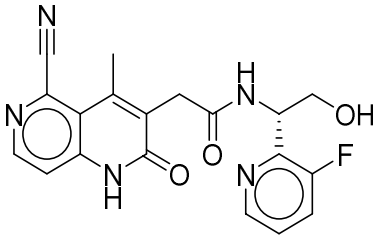
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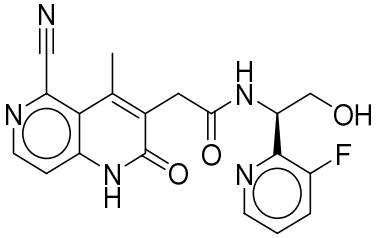
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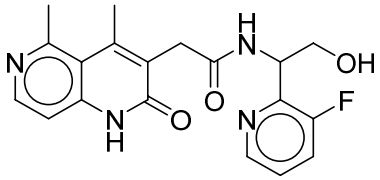
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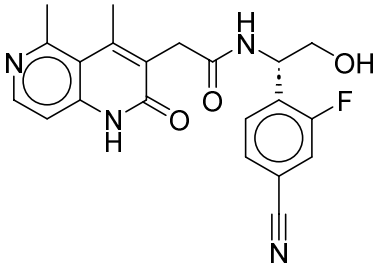
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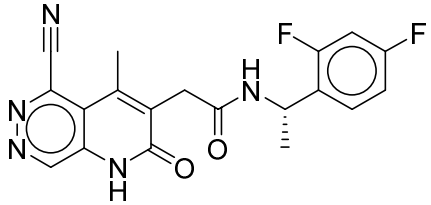
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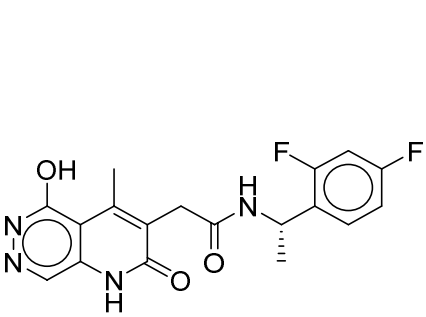
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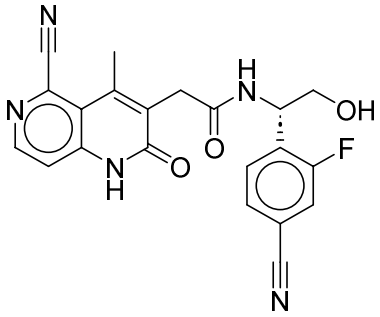
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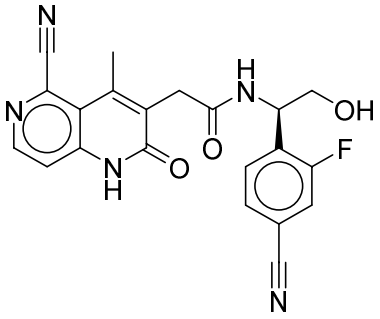
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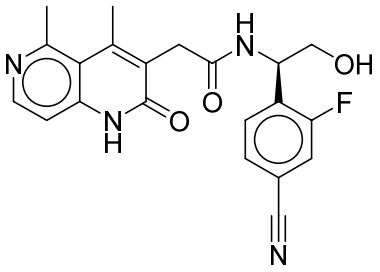
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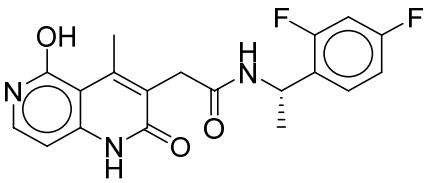
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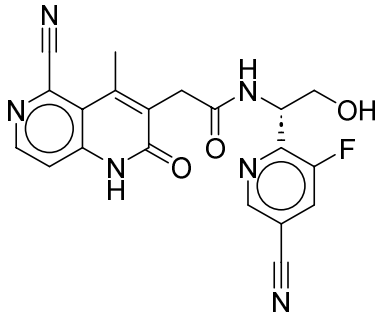
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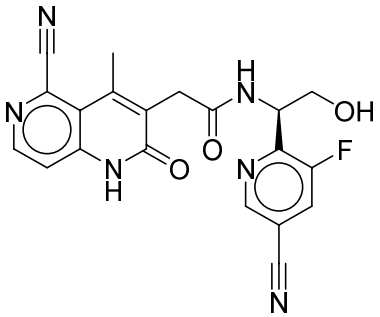
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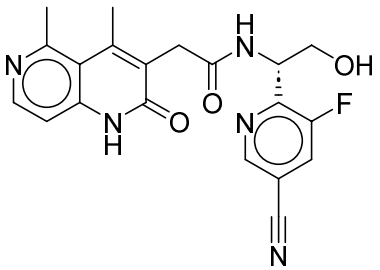
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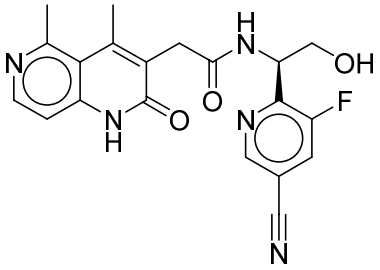
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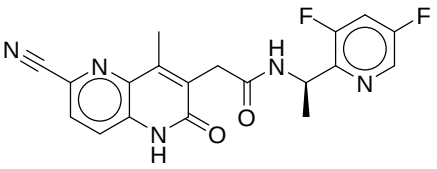
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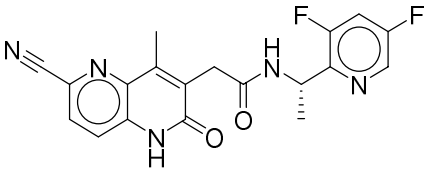
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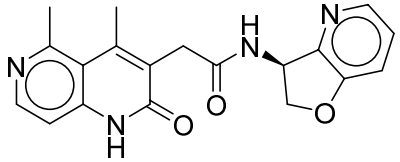
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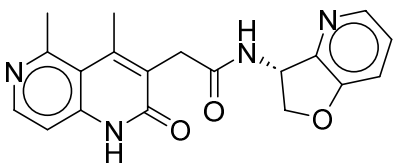
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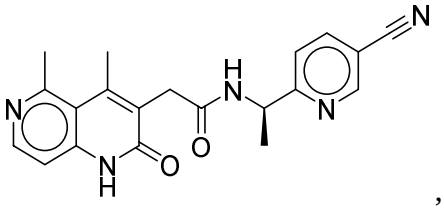
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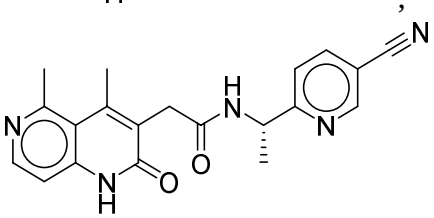
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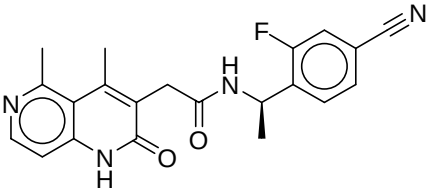
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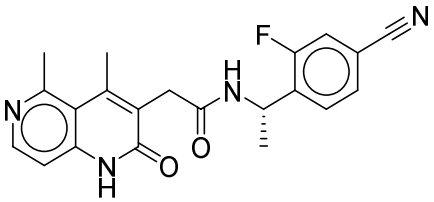
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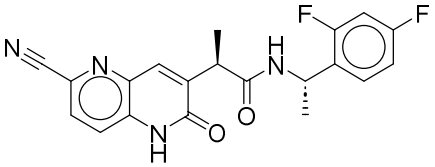
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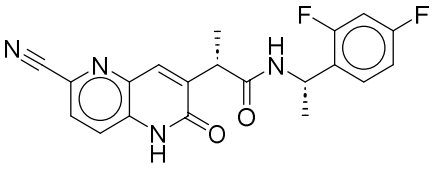
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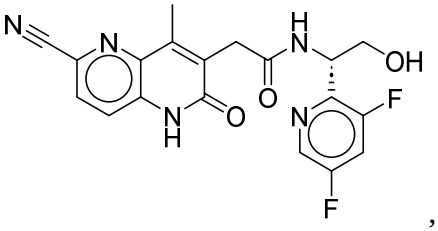
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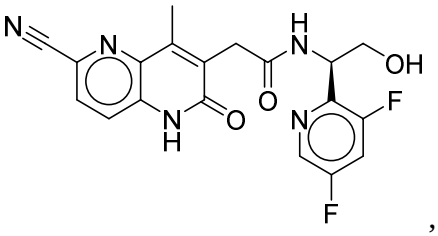
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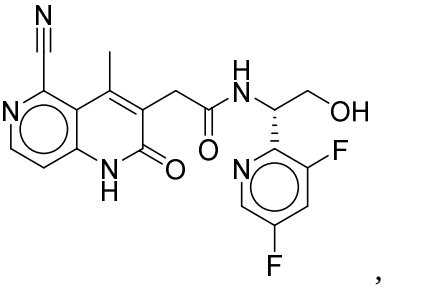
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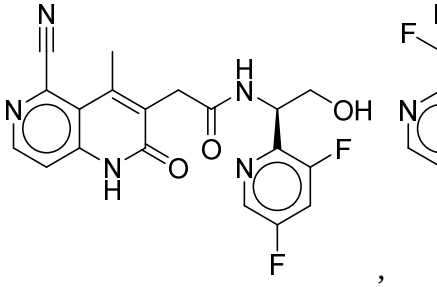
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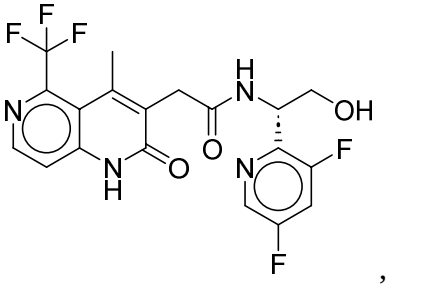
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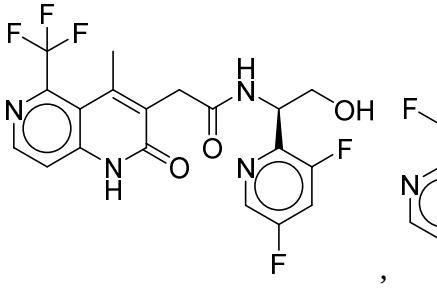
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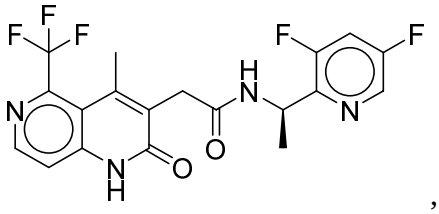
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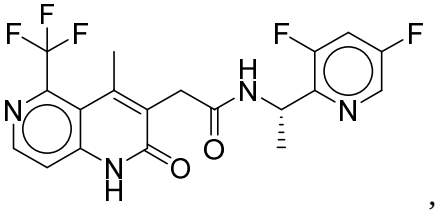
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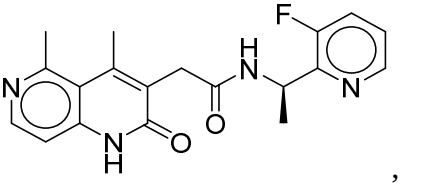
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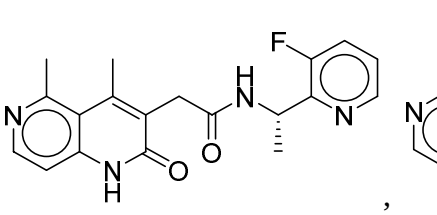
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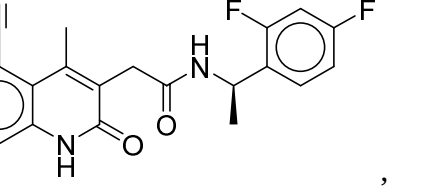
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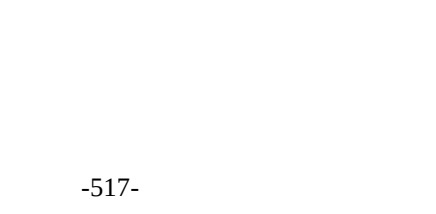
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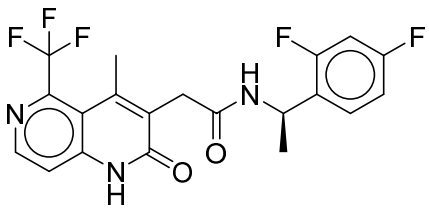
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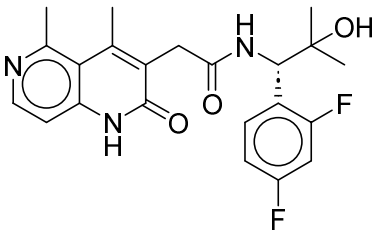
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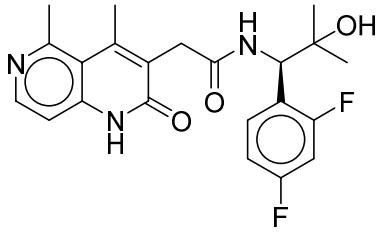
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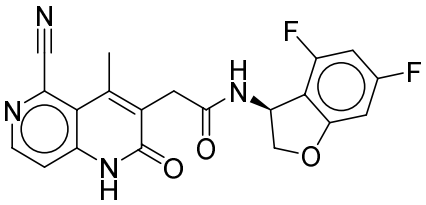
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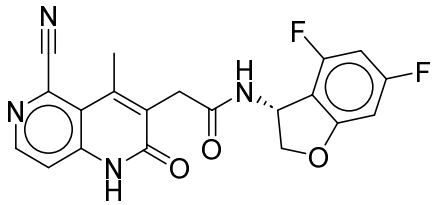
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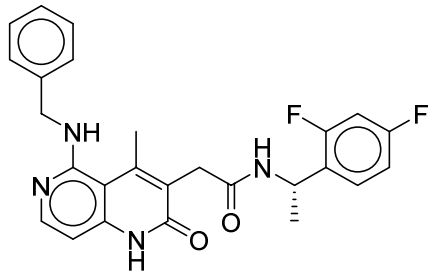
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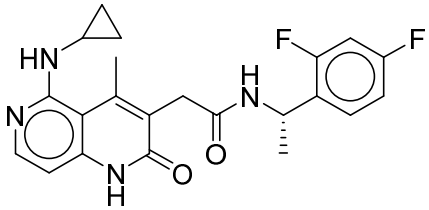
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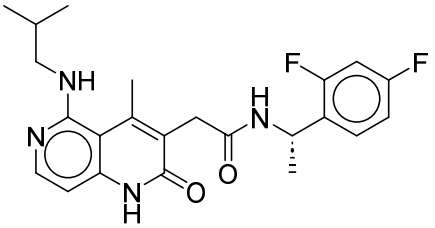
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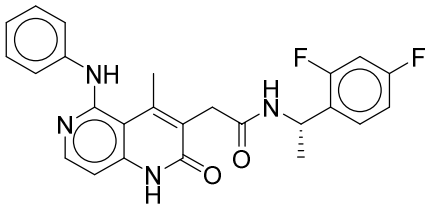
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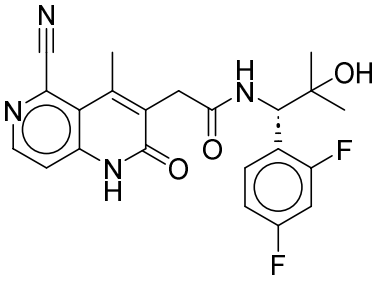
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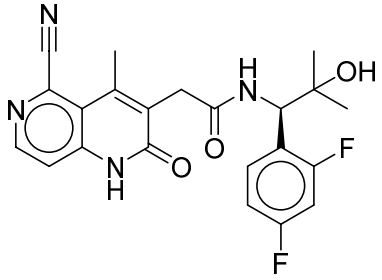
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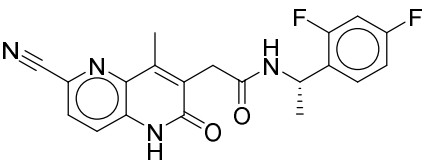
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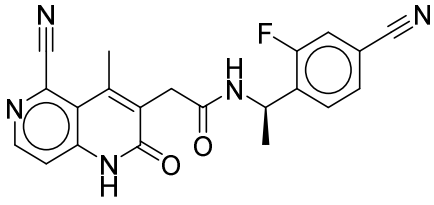
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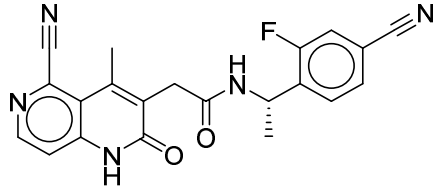

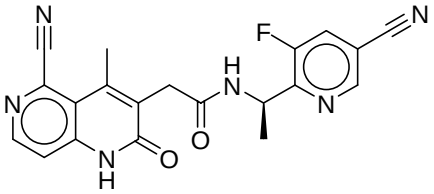
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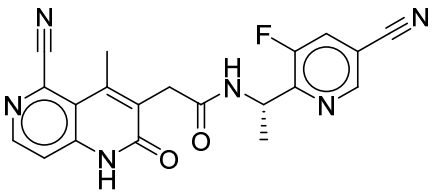
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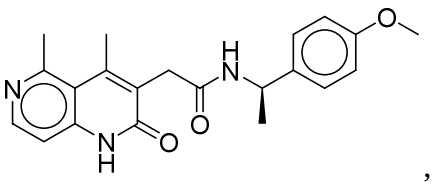
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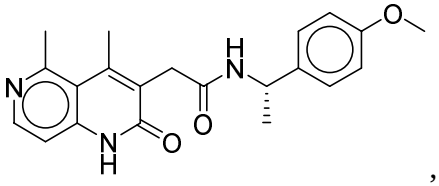
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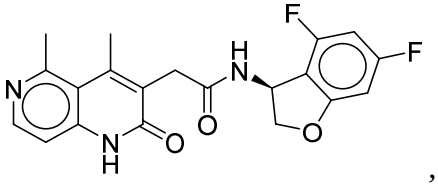
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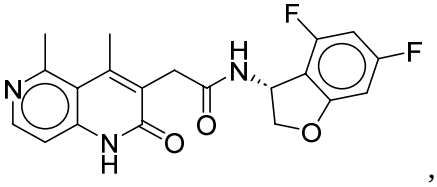
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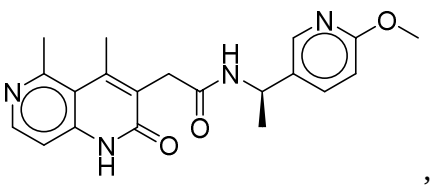
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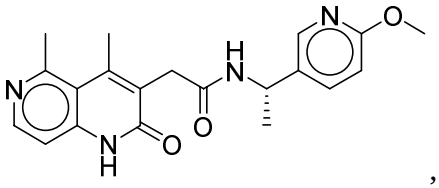
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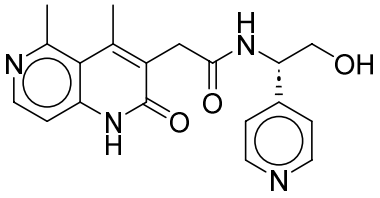
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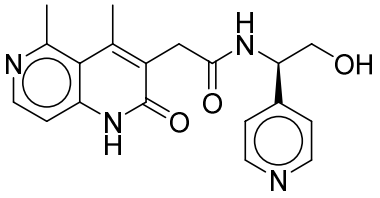
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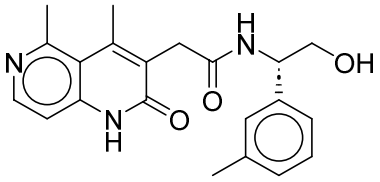
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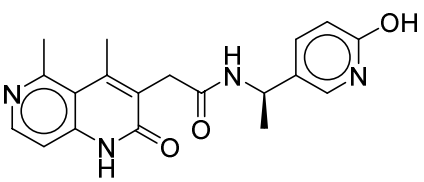
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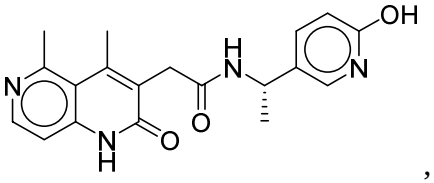
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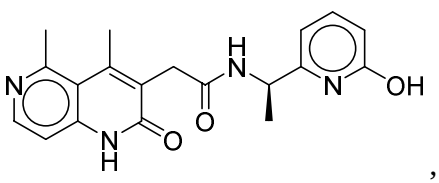
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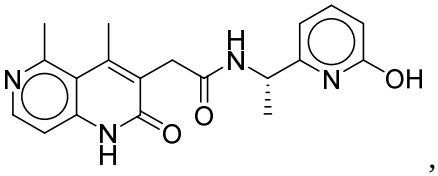
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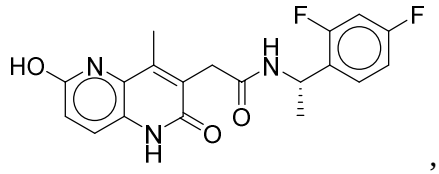
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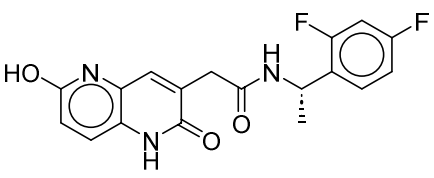
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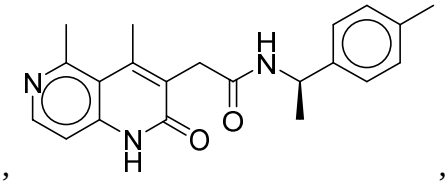
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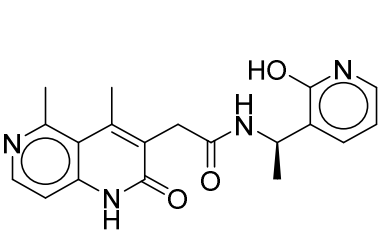
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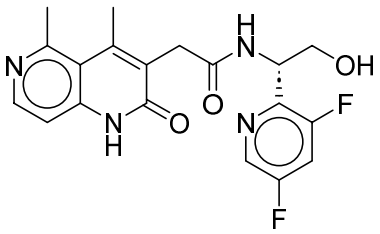
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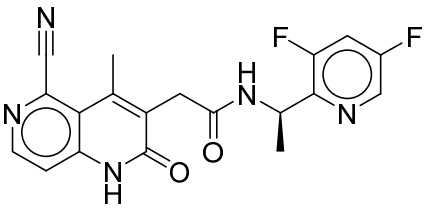
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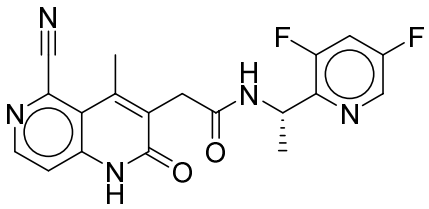
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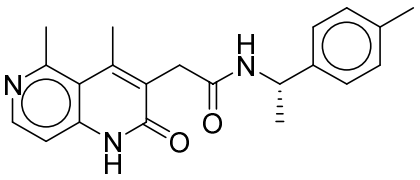
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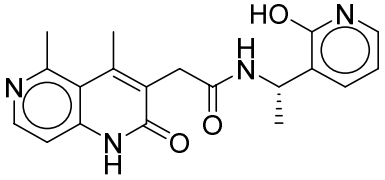
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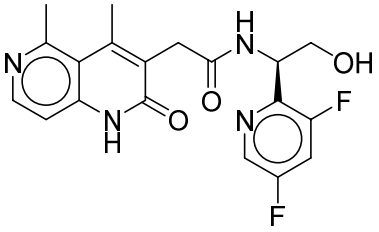
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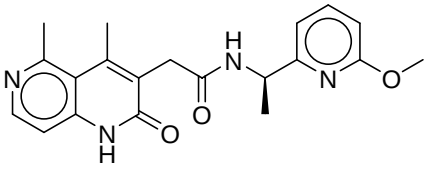
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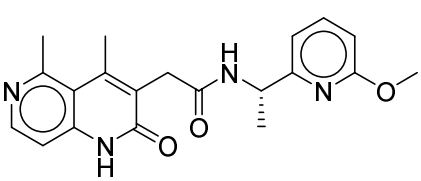
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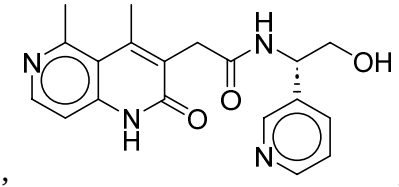
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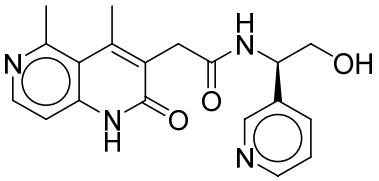
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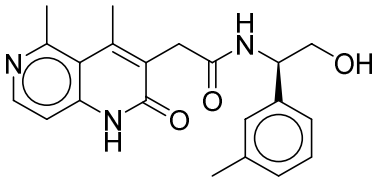
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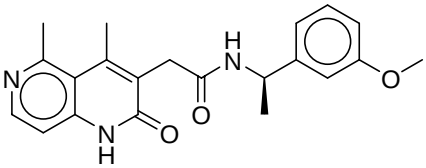
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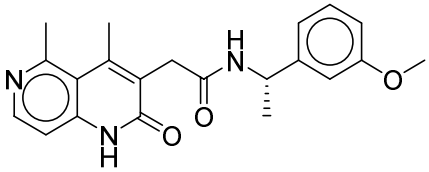
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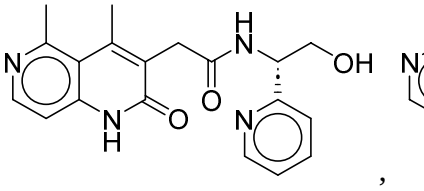
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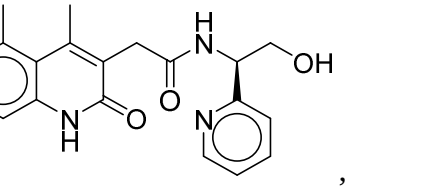
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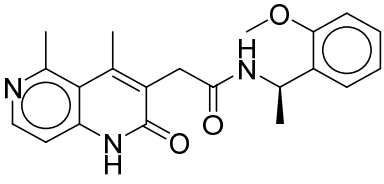
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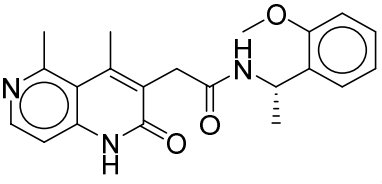
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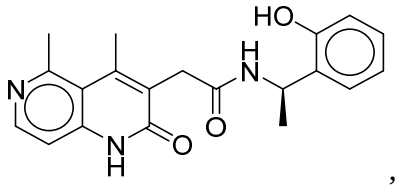
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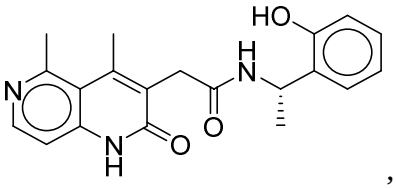
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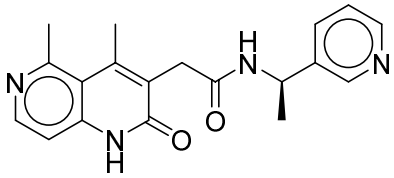
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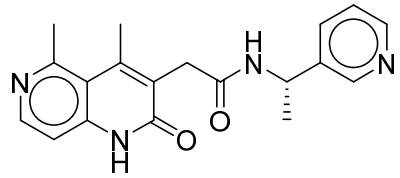
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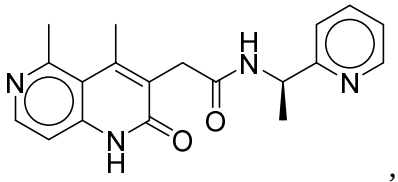
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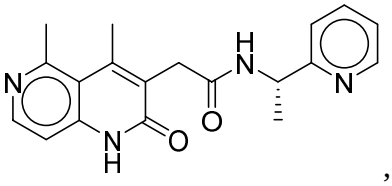
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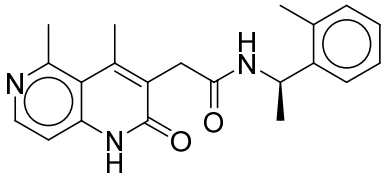
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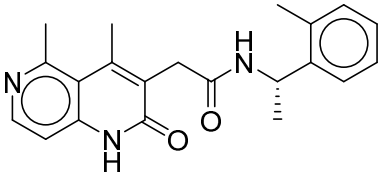
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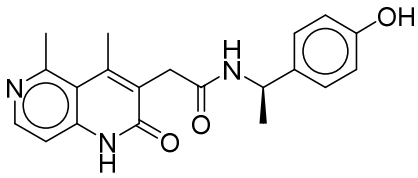
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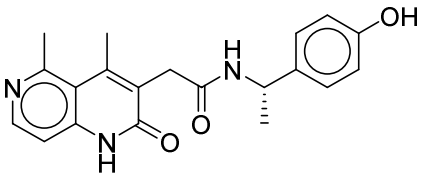
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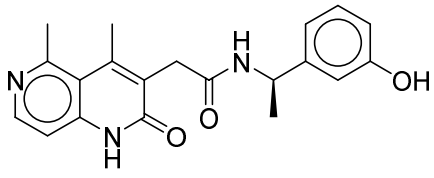
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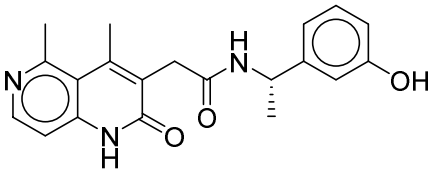
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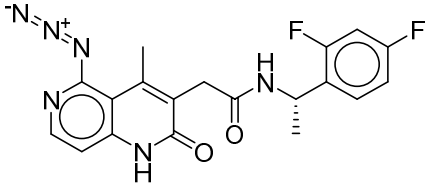
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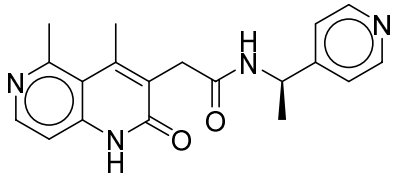
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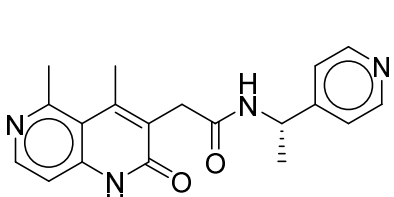
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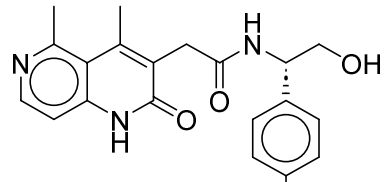
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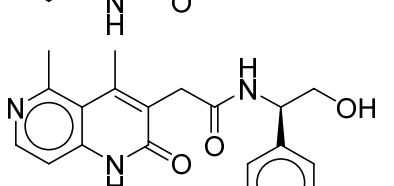
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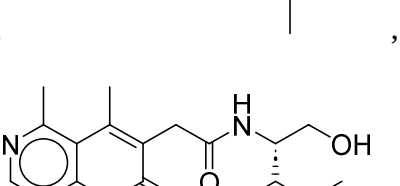
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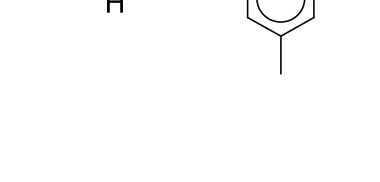
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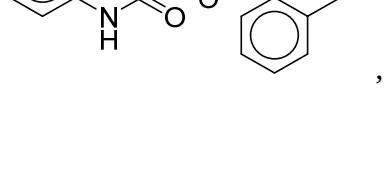
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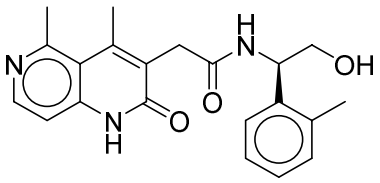
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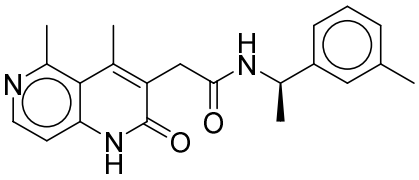
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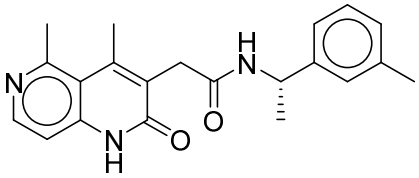
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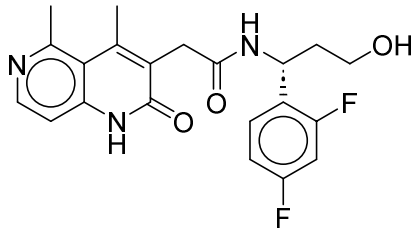
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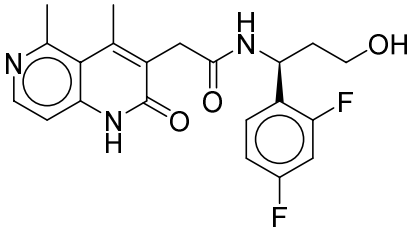
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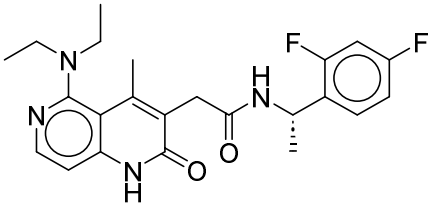
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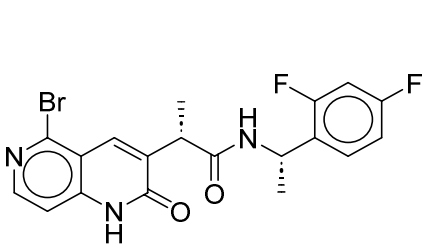
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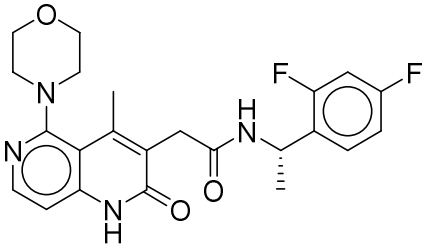
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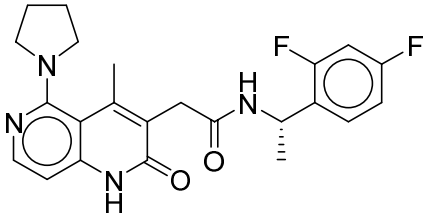
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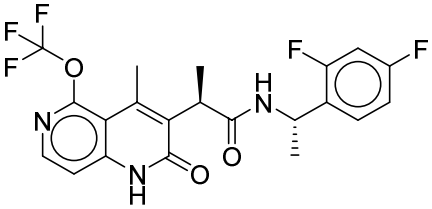
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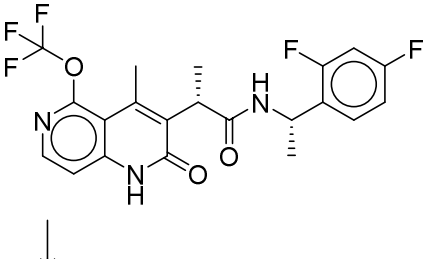
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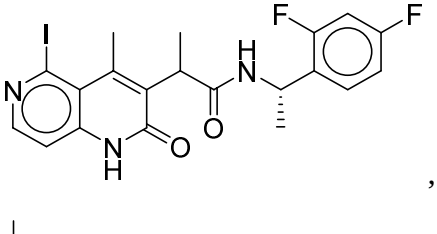
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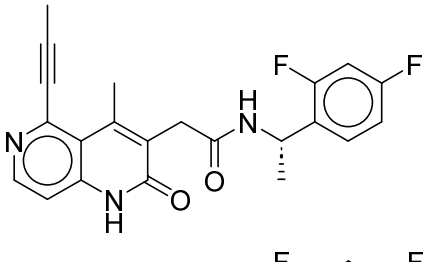
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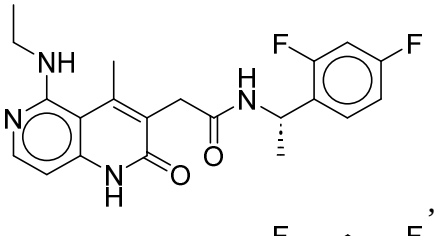
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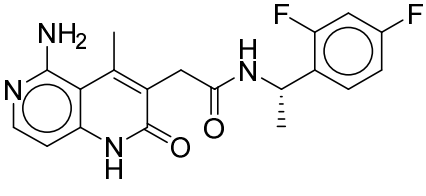
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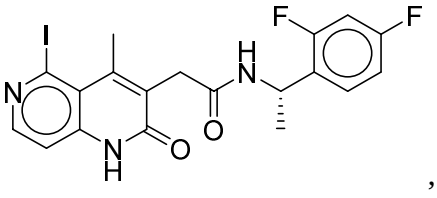
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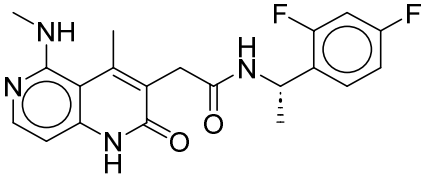
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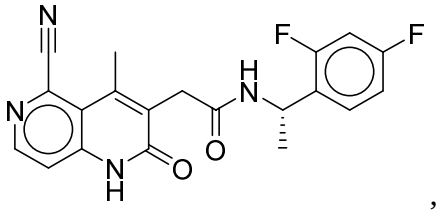
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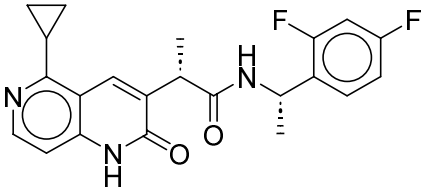
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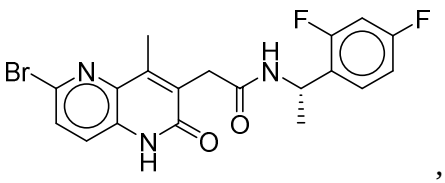
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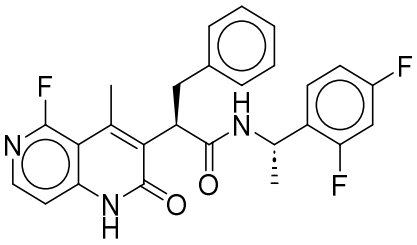
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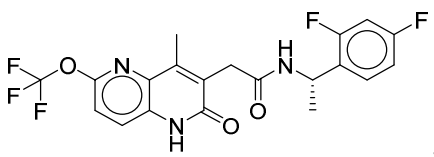
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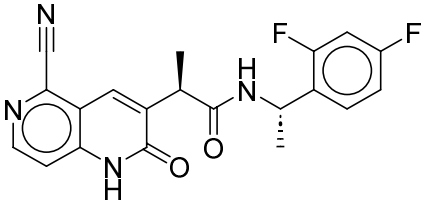
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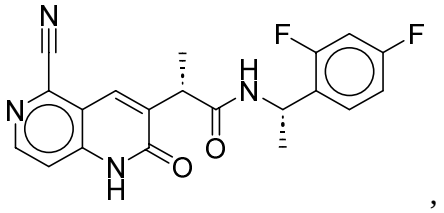
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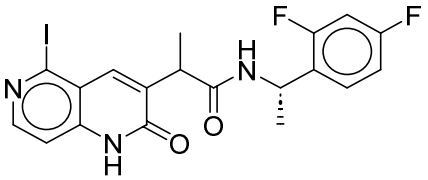
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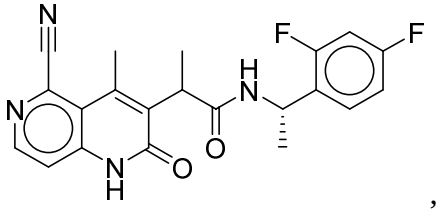
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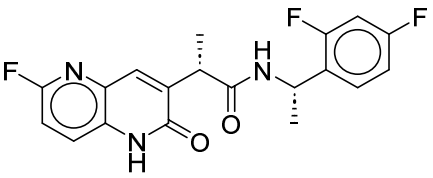
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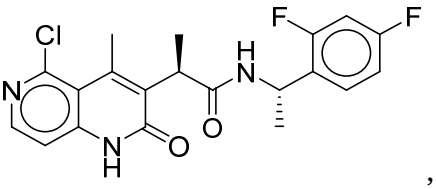
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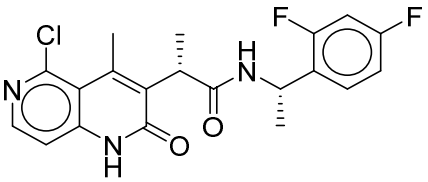
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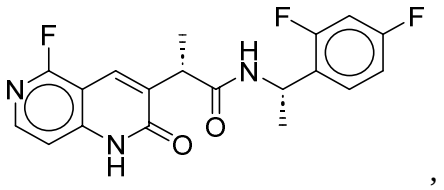
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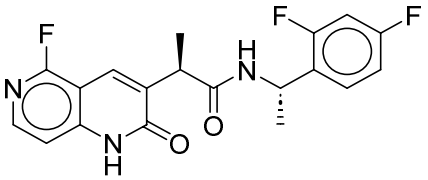
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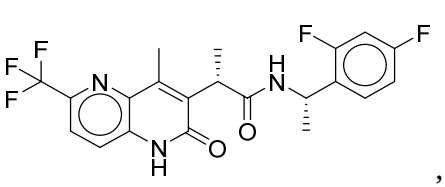
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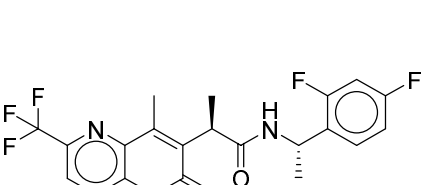
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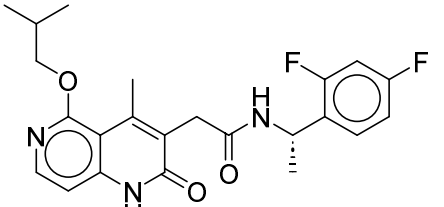
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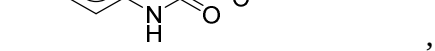
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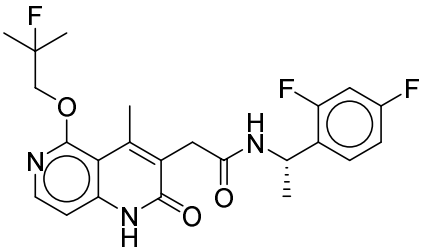
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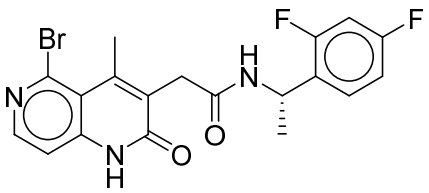
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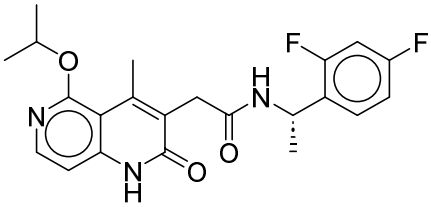
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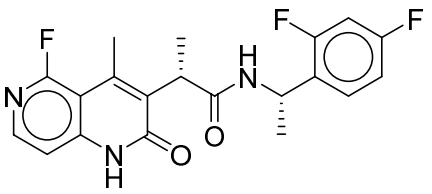
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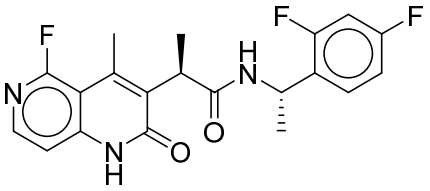
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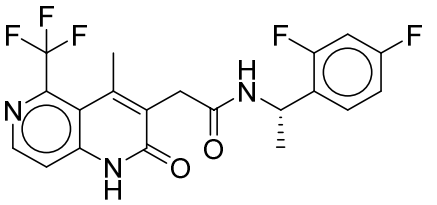
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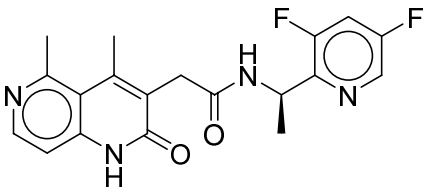
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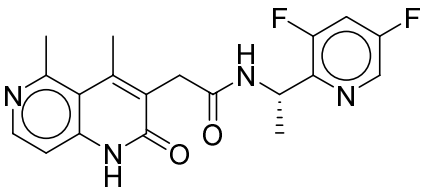
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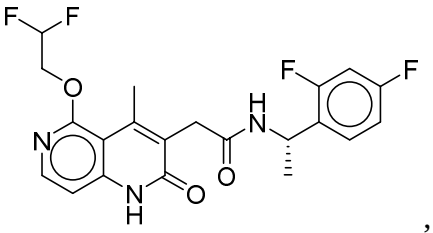
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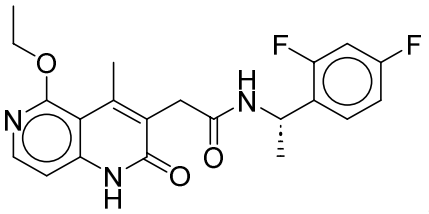
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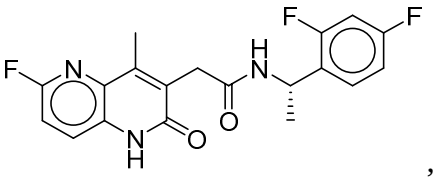
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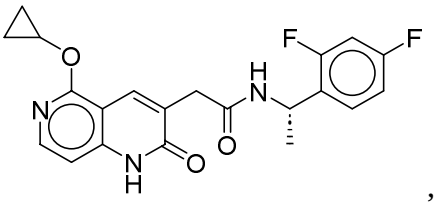
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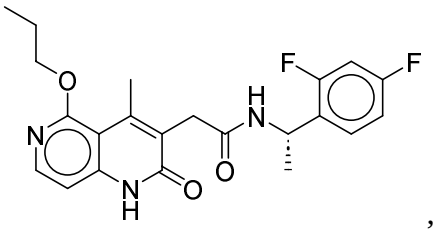
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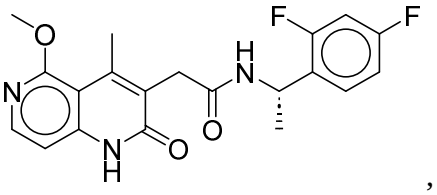
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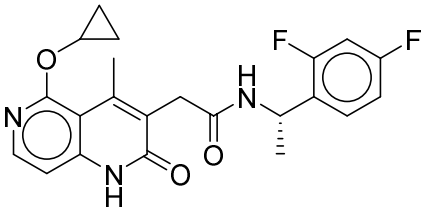
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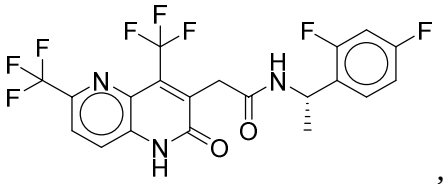
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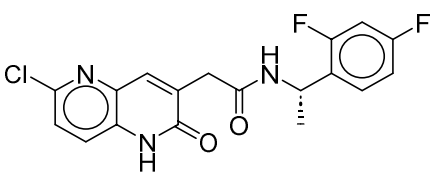
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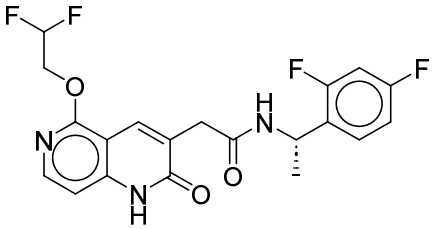
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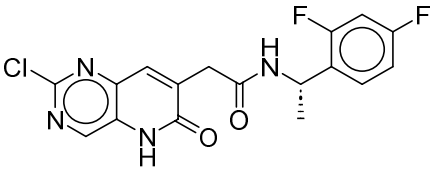
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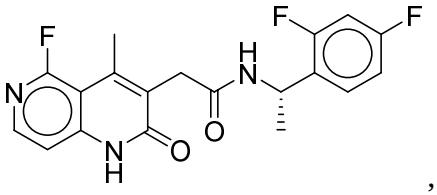
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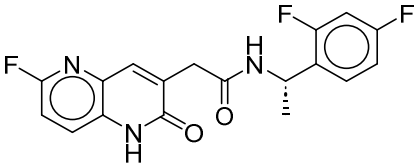
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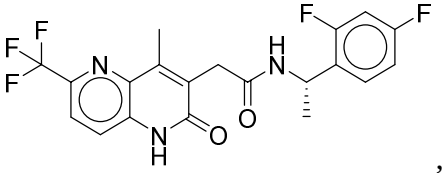
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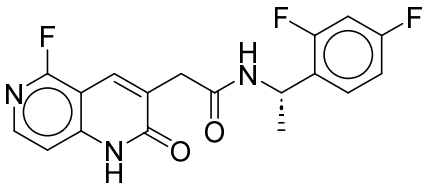
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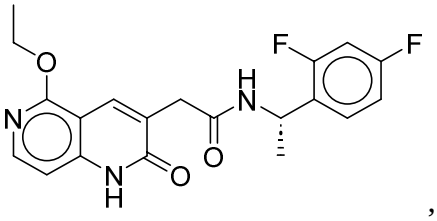
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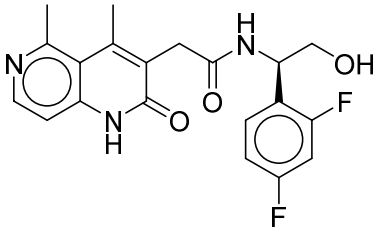
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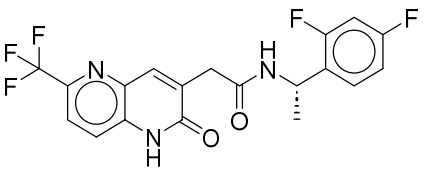
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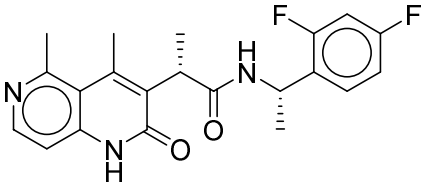
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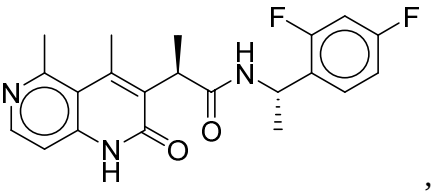
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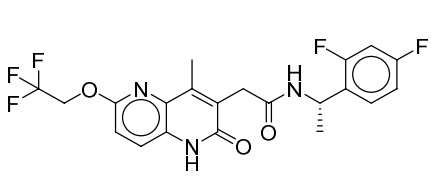
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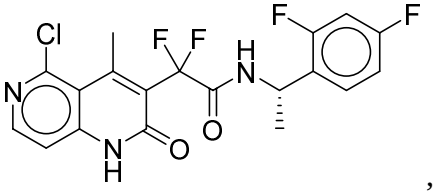
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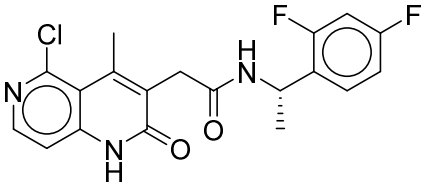
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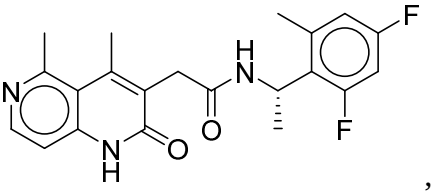
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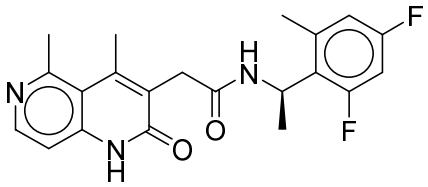
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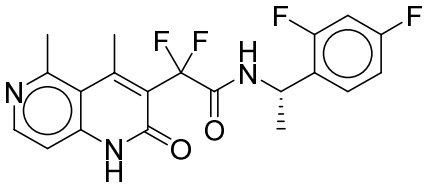
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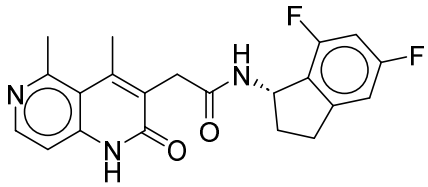
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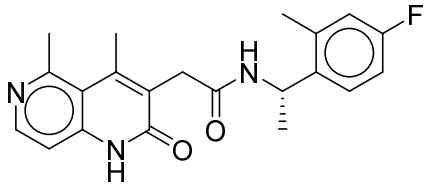
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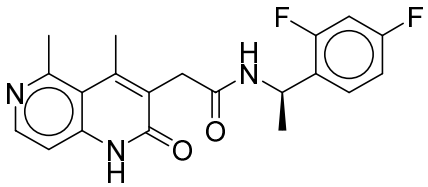
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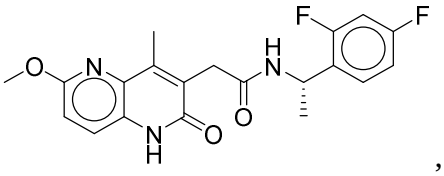
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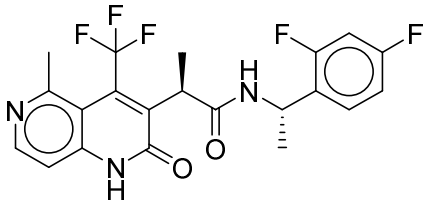
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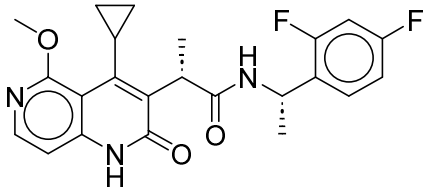
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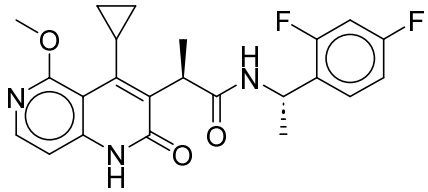
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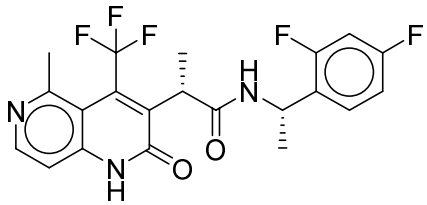
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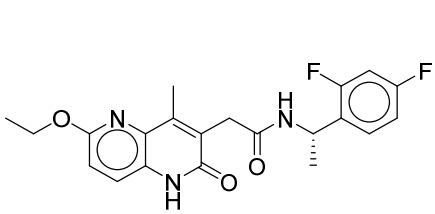
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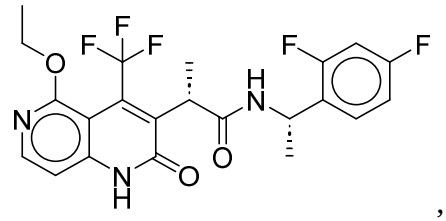
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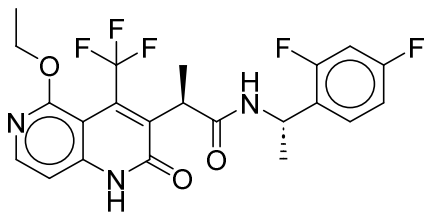
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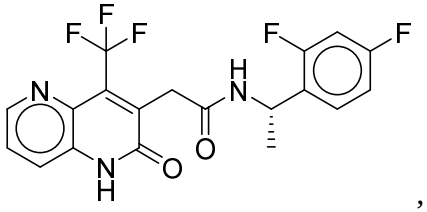
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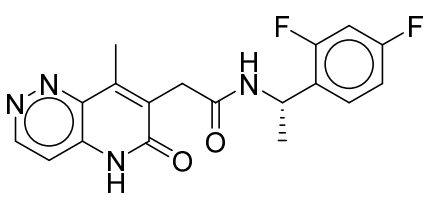
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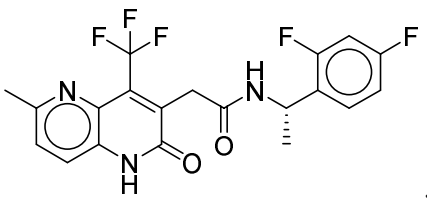
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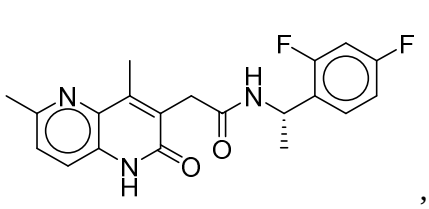
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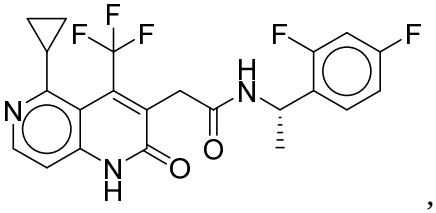
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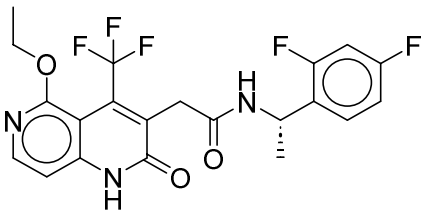
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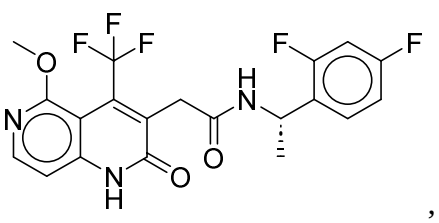
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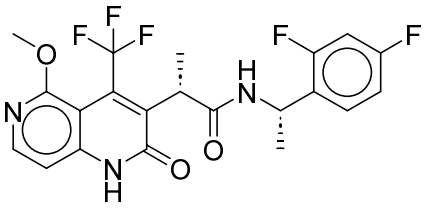
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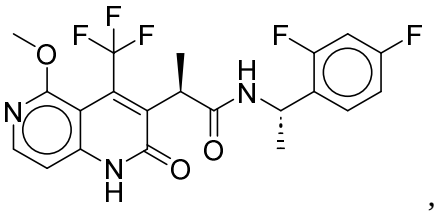
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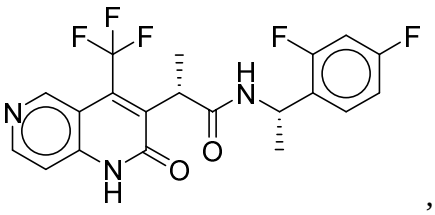
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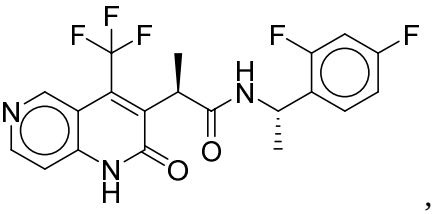
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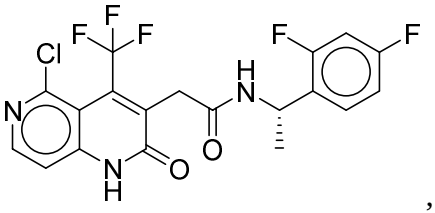
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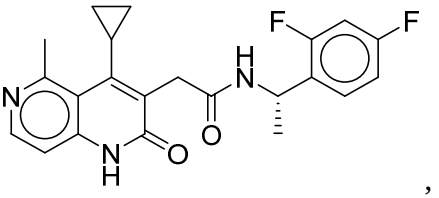
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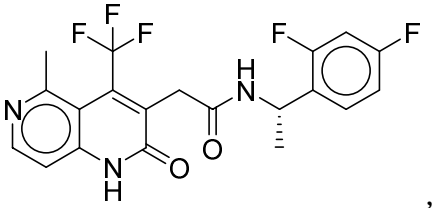
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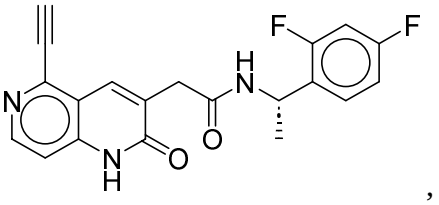
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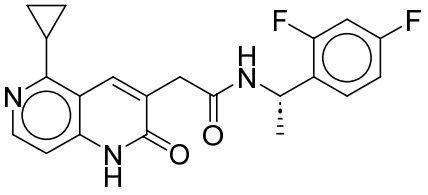
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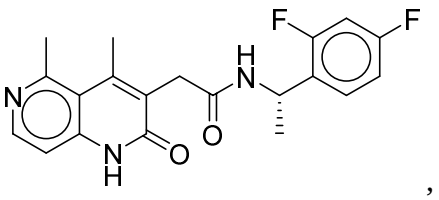
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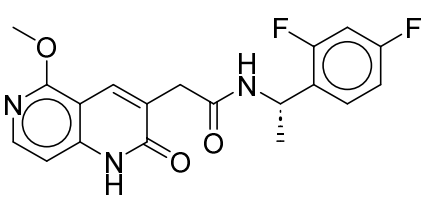
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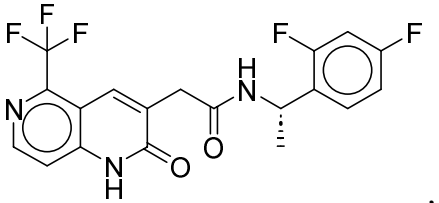
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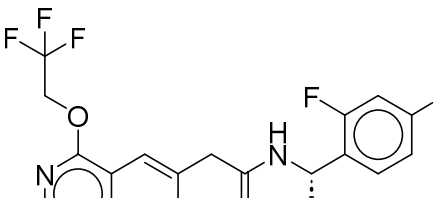
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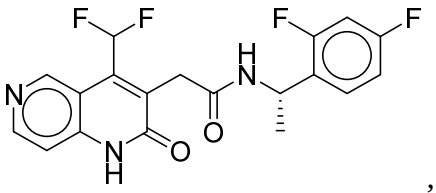
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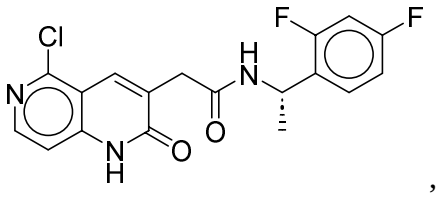
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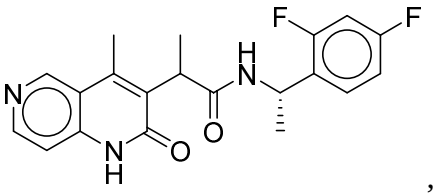
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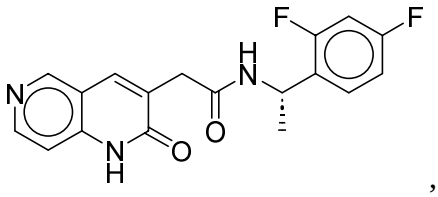
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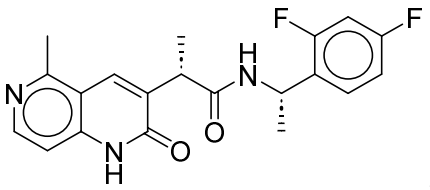
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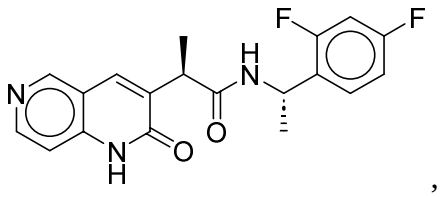
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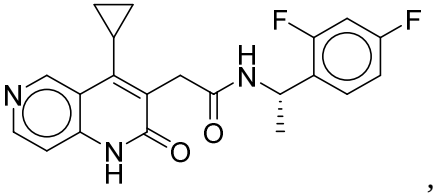
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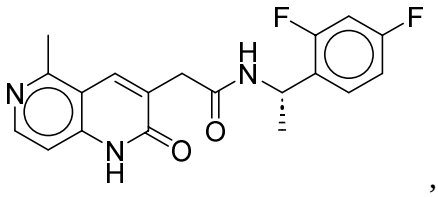
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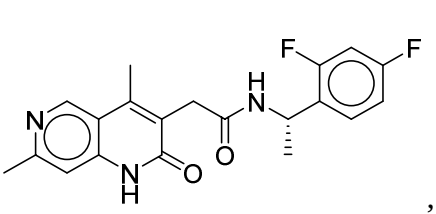
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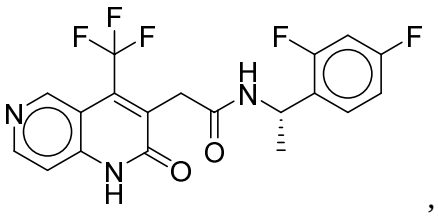
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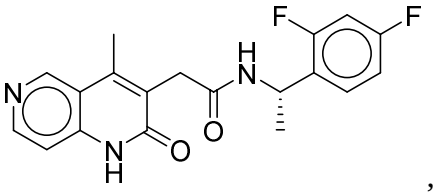
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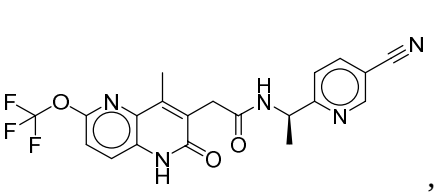
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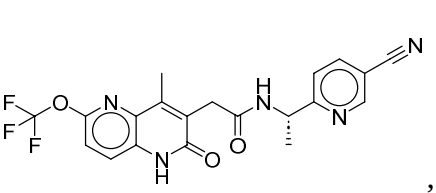
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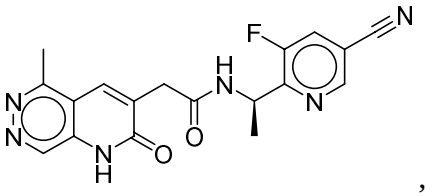
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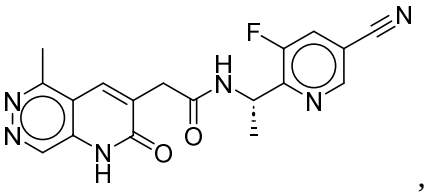
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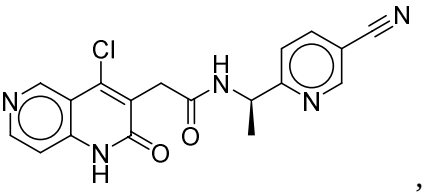
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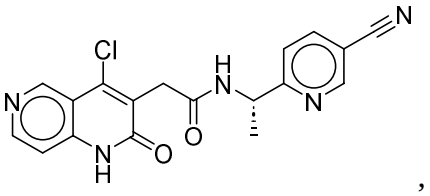
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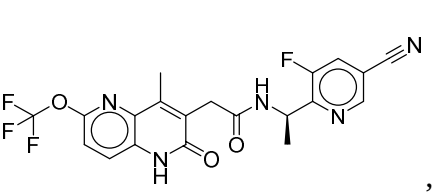
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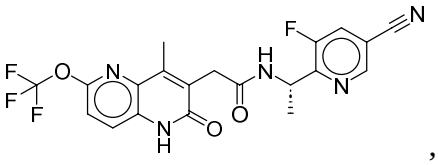
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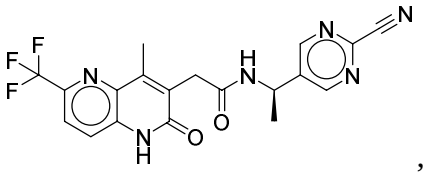
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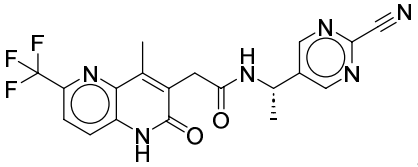
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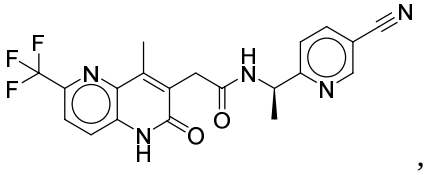
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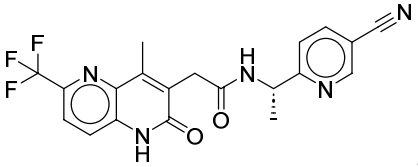
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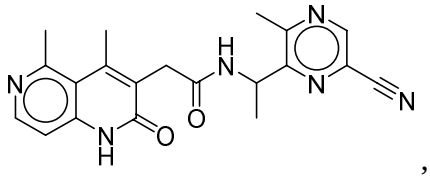
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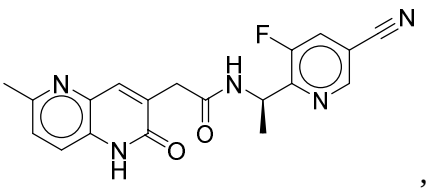
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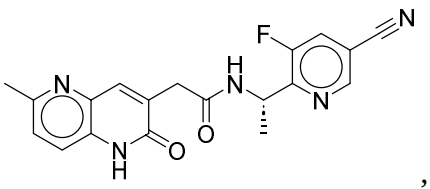
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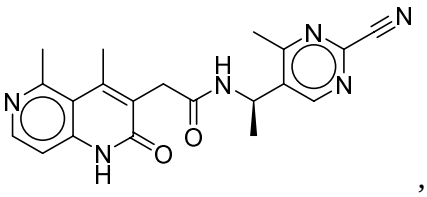
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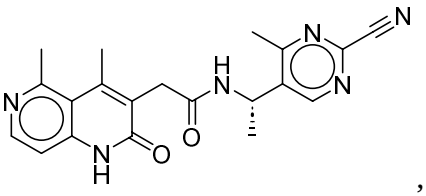
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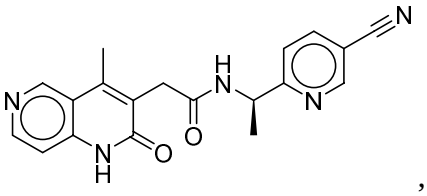
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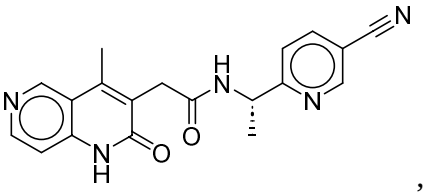
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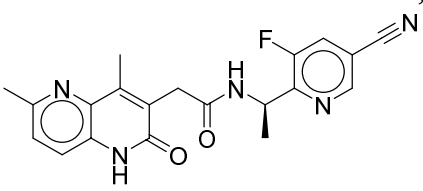
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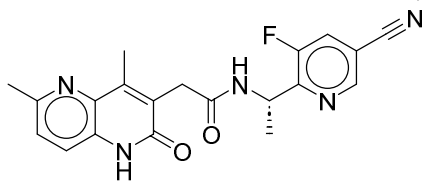
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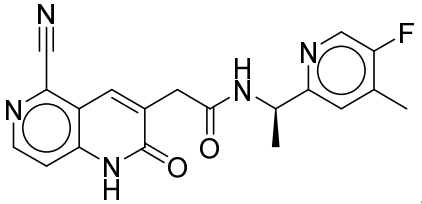
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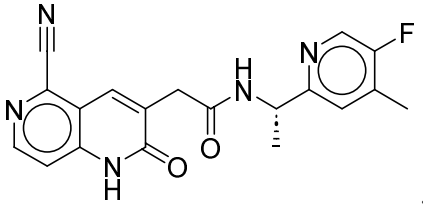
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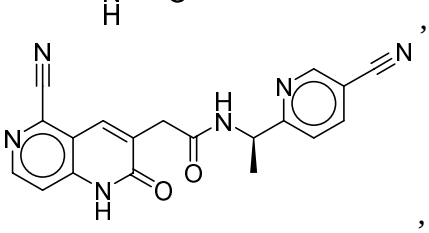
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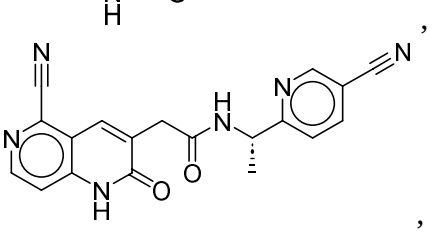
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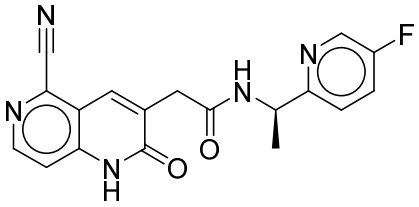
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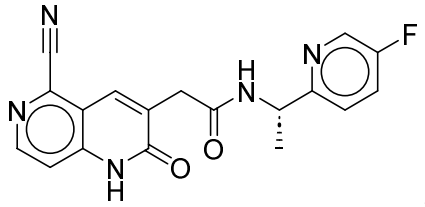
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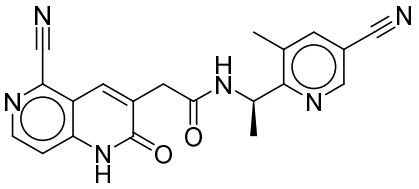
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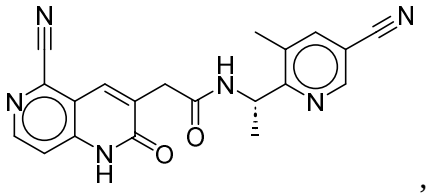
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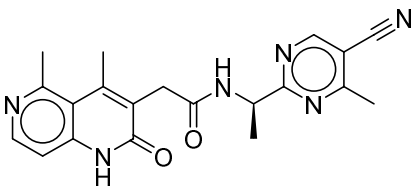
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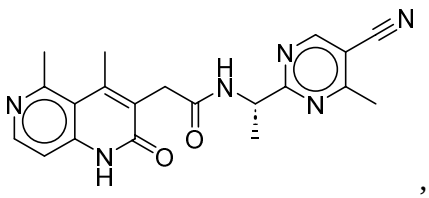
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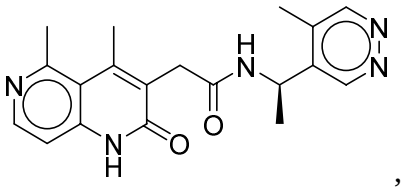
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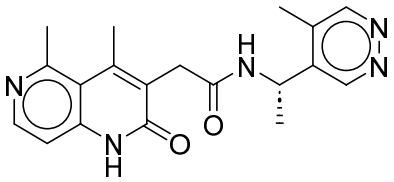
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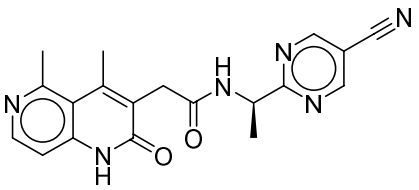
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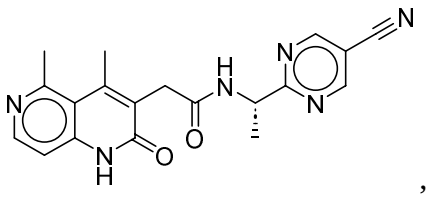
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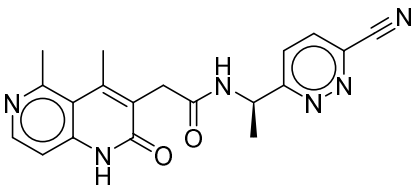
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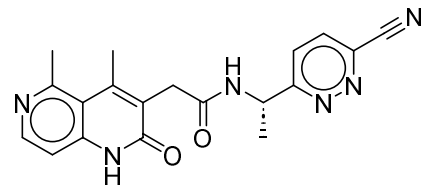
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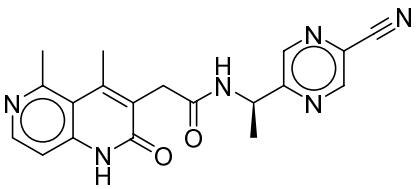
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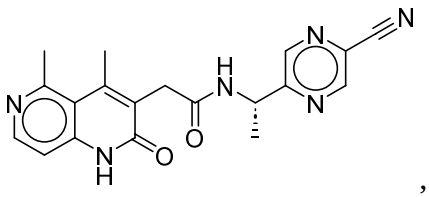
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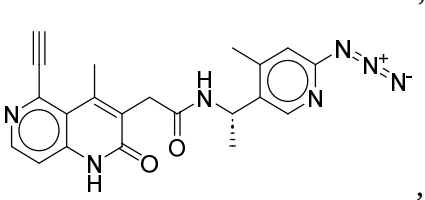
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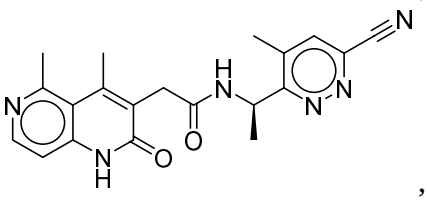
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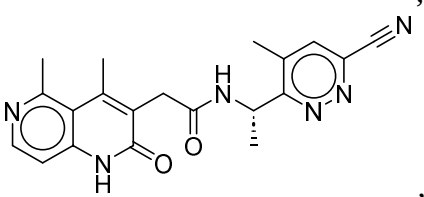
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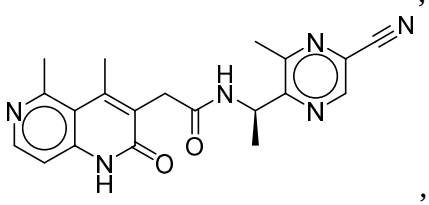
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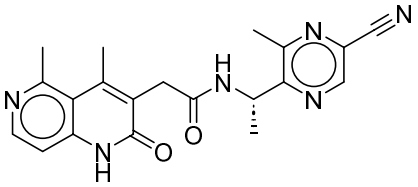
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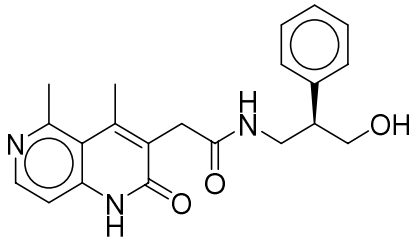
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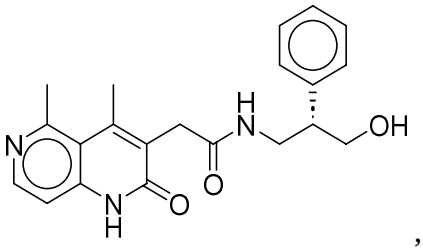
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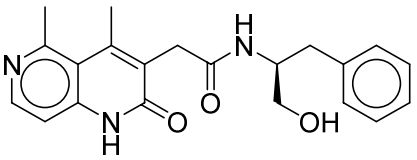
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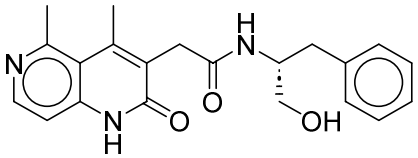
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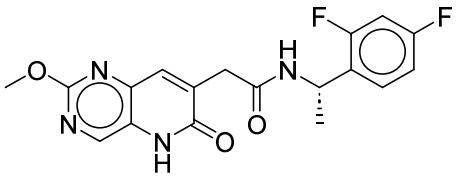
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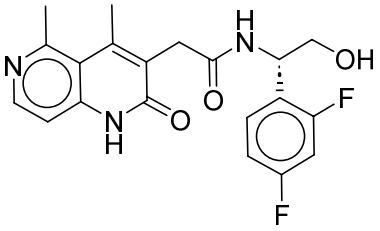
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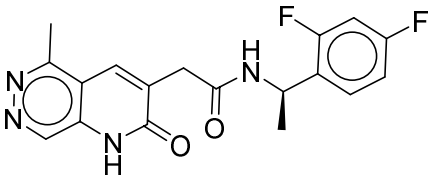
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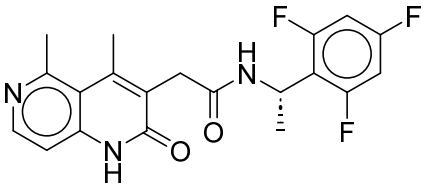
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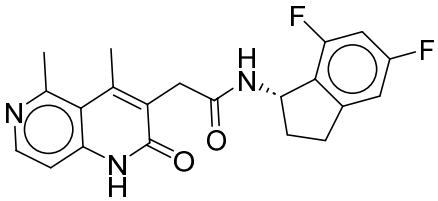
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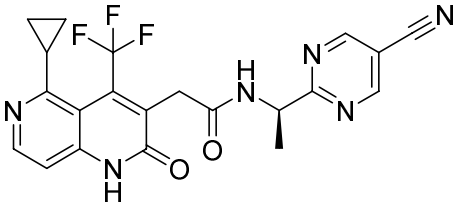
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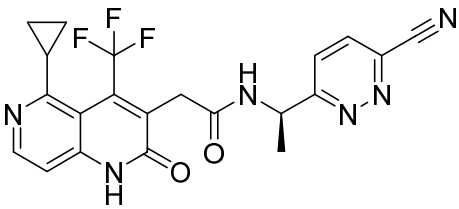
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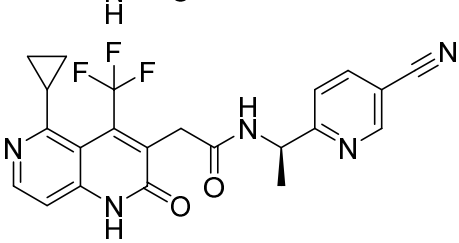
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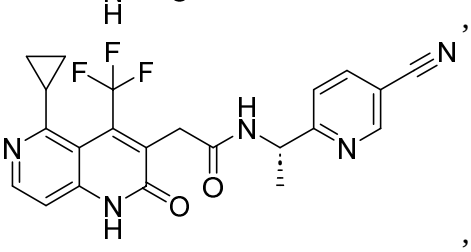
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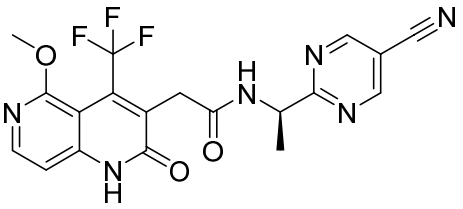
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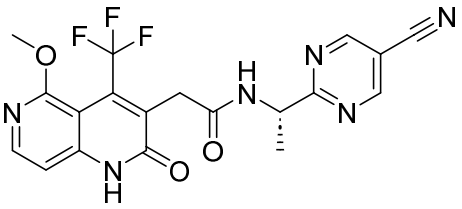
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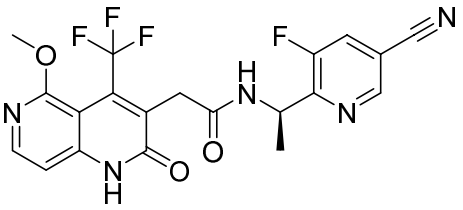
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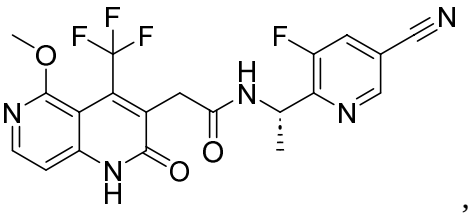
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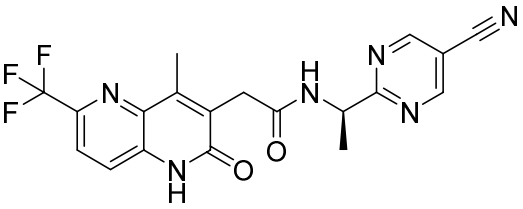
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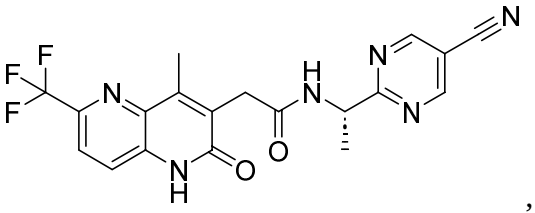
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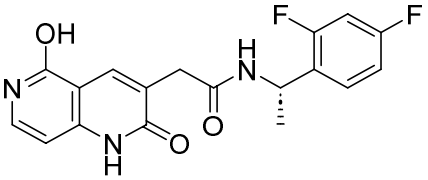
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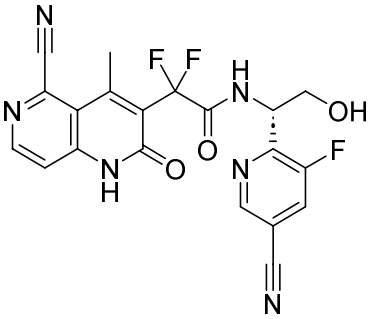
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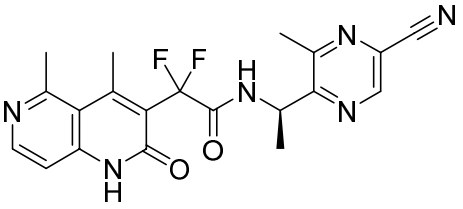
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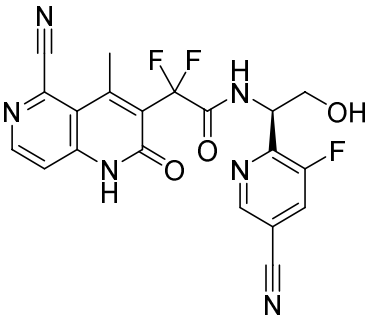
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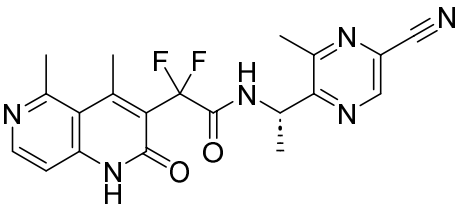
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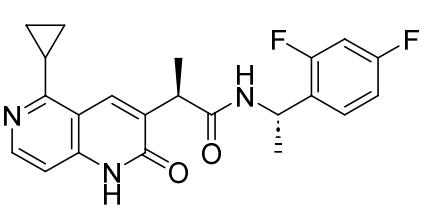
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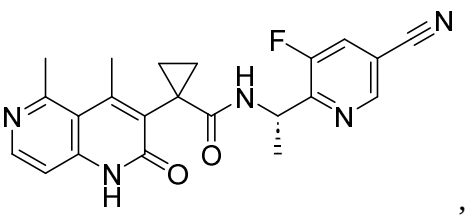
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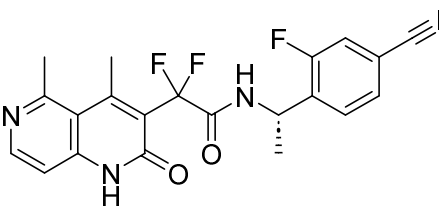
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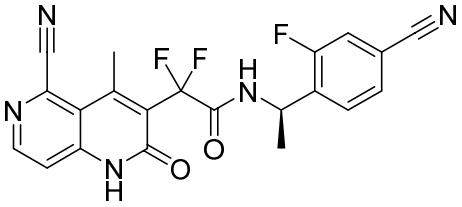
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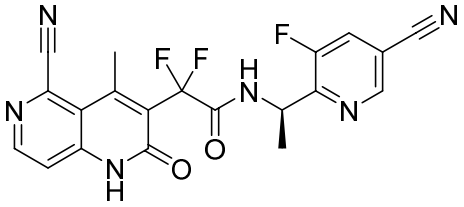
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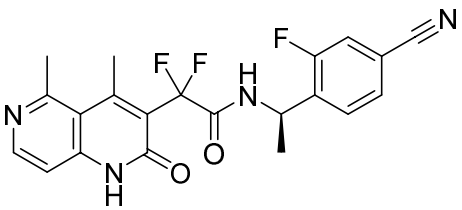
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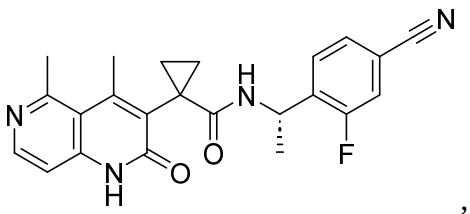
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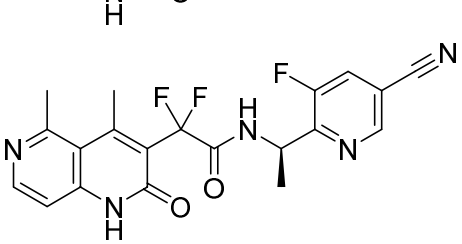
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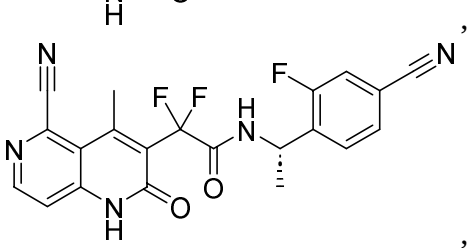
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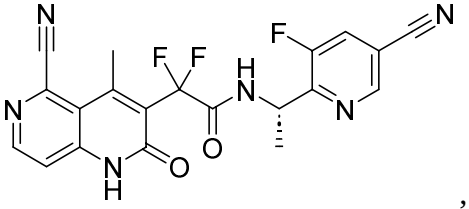
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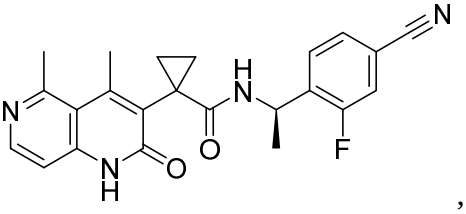
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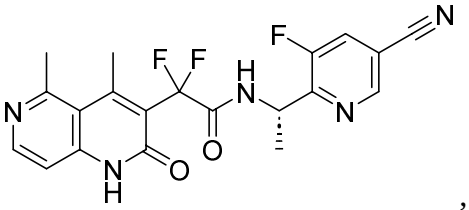
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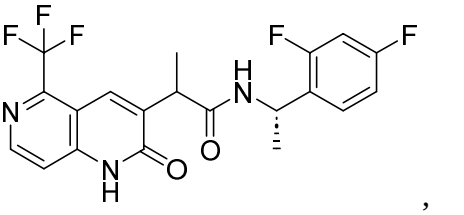
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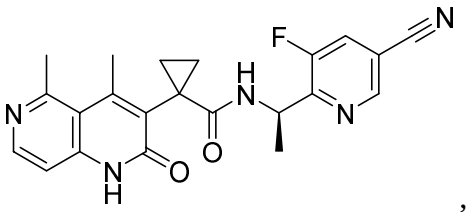
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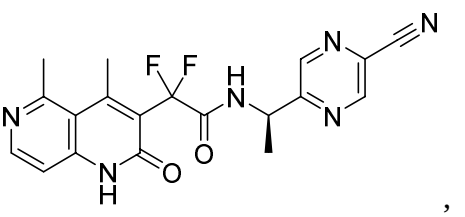
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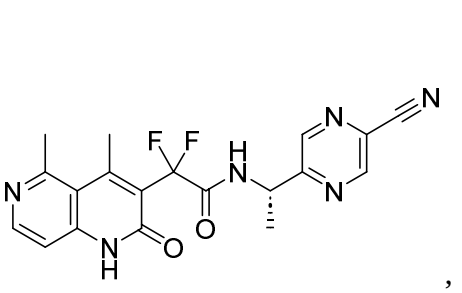
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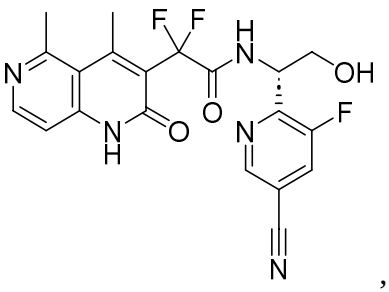
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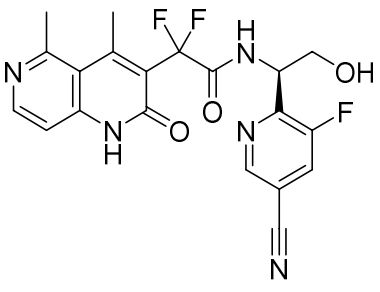
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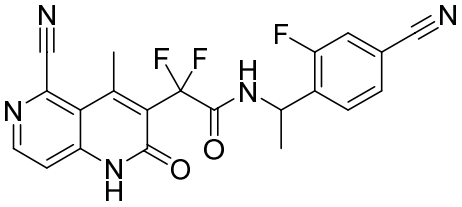
14. The compound or salt of claim 1, selected from: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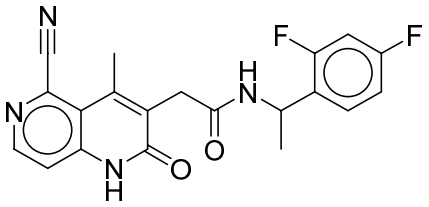
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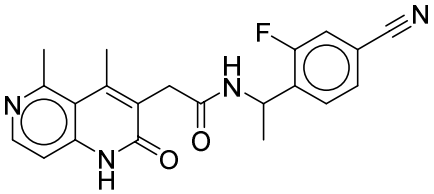
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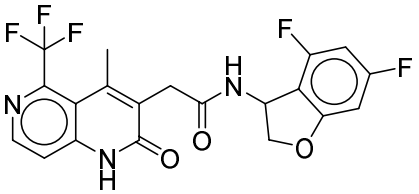
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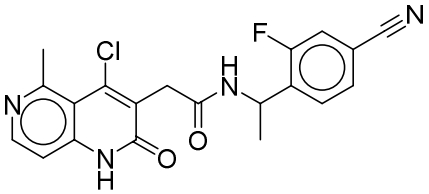
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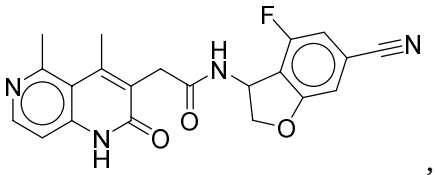
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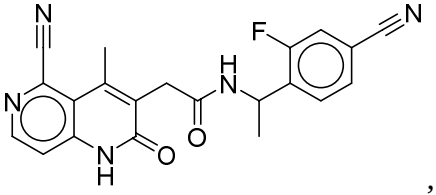
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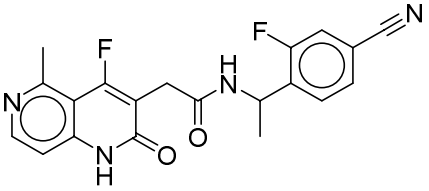
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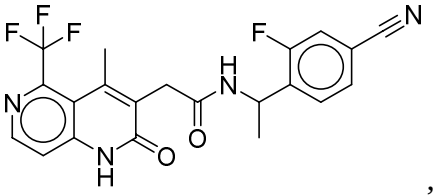
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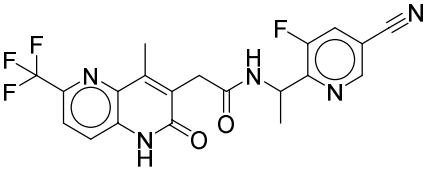
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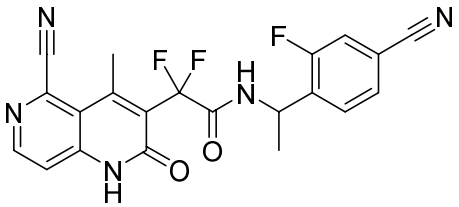
15. The compound or salt of claim 1, selected from: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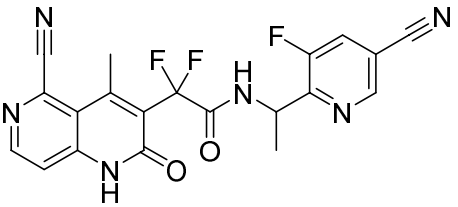
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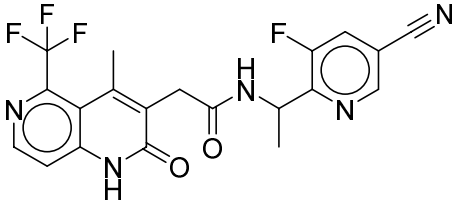
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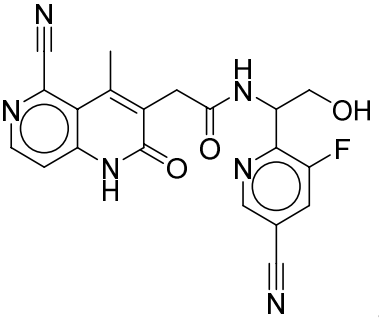
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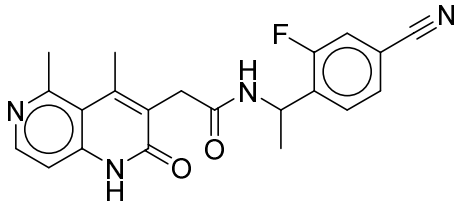
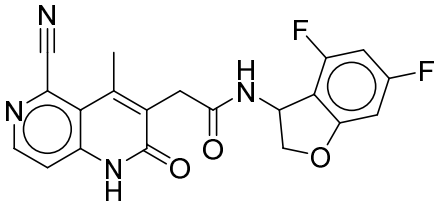
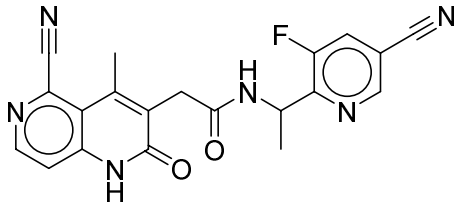
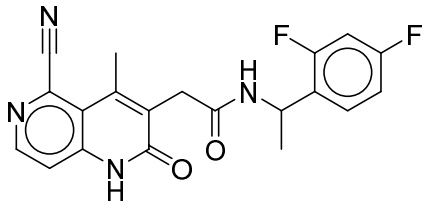
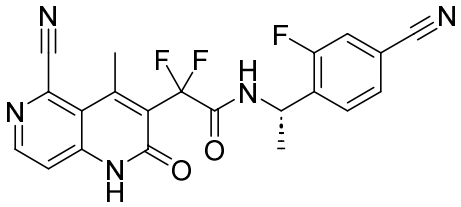
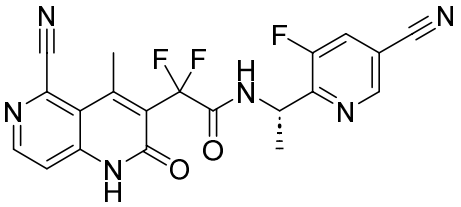
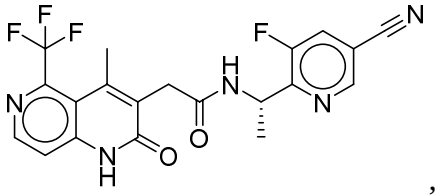
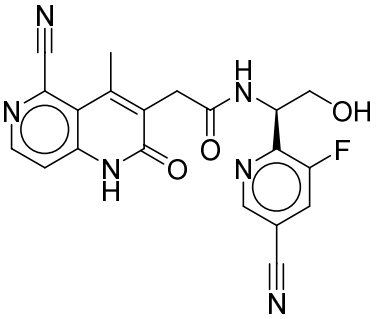
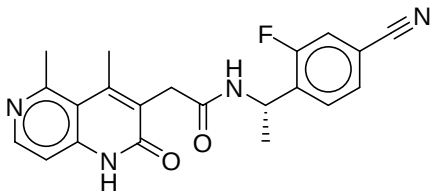
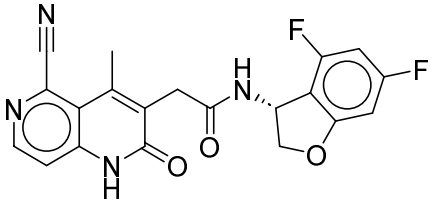
 ,  ,

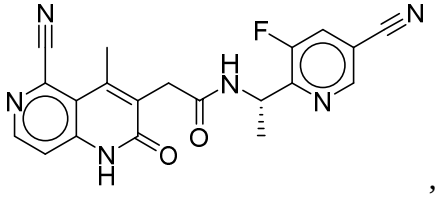
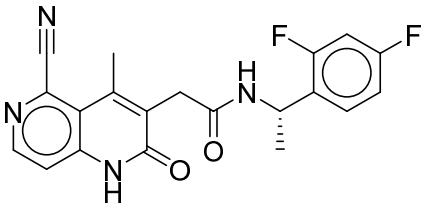
 , and  , or a salt of any one thereof.

16. The compound or salt of claim 1, selected from:

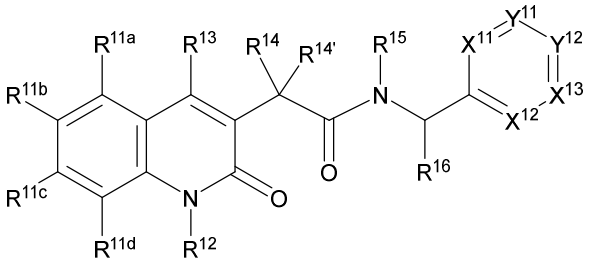
 ,  ,

 ,  ,

 ,  ,

 , and  , or a salt of any one thereof.

17. A compound represented by Formula (II-A):



(II-A);

or a salt thereof, wherein:

X^{11} is selected from C(R^{17a}) and N;

X^{12} is selected from C(R^{17b}) and N;

X^{13} is selected from C(R^{17c}) and N;

Y^{11} is selected from C(R^{17d}) and N;

Y^{12} is selected from C(R^{17e}) and N;

R^{11a}, R^{11b}, R^{11c}, and R^{11d} are each independently selected from:

hydrogen, halogen, -NO_2, -CN, -N_3, -OR^{19a}, -SR^{19a}, -$N(R^{19a})_2$, -$C(O)R^{19a}$, -$C(O)N(R^{19a})_2$, -$N(R^{19a})C(O)R^{19a}$, -$N(R^{19a})C(O)N(R^{19a})_2$, -$OC(O)N(R^{19a})_2$, -$N(R^{19a})C(O)OR^{19a}$, -$C(O)OR^{19a}$, -$OC(O)R^{19a}$, -$S(O)R^{19a}$, and -$S(O)_2R^{19a}$;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{19a}, -SR^{19a}, -$N(R^{19a})_2$, -$C(O)R^{19a}$, -$C(O)N(R^{19a})_2$, -$N(R^{19a})C(O)R^{19a}$, -$C(O)OR^{19a}$, -$OC(O)R^{19a}$, -$N(R^{19a})C(O)N(R^{19a})_2$, -$OC(O)N(R^{19a})_2$, -$N(R^{19a})C(O)OR^{19a}$, -$S(O)R^{19a}$, -$S(O)_2R^{19a}$, -$NO_2$, =O, =S, =$N(R^{19a})$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{18a}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{19a}, -SR^{19a}, -$N(R^{19a})_2$, -$C(O)R^{19a}$, -$C(O)N(R^{19a})_2$, -$N(R^{19a})C(O)R^{19a}$, -$N(R^{19a})C(O)N(R^{19a})_2$, -$OC(O)N(R^{19a})_2$, -$N(R^{19a})C(O)OR^{19a}$, -$C(O)OR^{19a}$, -$OC(O)R^{19a}$, -$S(O)R^{19a}$, -$S(O)_2R^{19a}$, -$NO_2$, =O, =S, =$N(R^{19a})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{18a};

wherein when R^{11a}, R^{11b}, and R^{11c} are each hydrogen, then R^{11d} is not hydrogen;

wherein when R^{11b} is -OCH_3, then R^{11c} is not -OCH_3;

R^{12} is selected from:

hydrogen, halogen, -NO_2, -CN, -OR^{19b}, -SR^{19b}, -$N(R^{19b})_2$, -$C(O)R^{19b}$, -$C(O)N(R^{19b})_2$, -$N(R^{19b})C(O)R^{19b}$, -$N(R^{19b})C(O)N(R^{19b})_2$, -$OC(O)N(R^{19b})_2$, -$N(R^{19b})C(O)OR^{19b}$, -$C(O)OR^{19b}$, -$OC(O)R^{19b}$, -$S(O)R^{19b}$, and -$S(O)_2R^{19b}$;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{19b}$, $-SR^{19b}$, $-N(R^{19b})_2$, $-C(O)R^{19b}$, $-C(O)N(R^{19b})_2$, $-N(R^{19b})C(O)R^{19b}$, $-C(O)OR^{19b}$, $-OC(O)R^{19b}$, $-N(R^{19b})C(O)N(R^{19b})_2$, $-OC(O)N(R^{19b})_2$, $-N(R^{19b})C(O)OR^{19b}$, $-S(O)R^{19b}$, $-S(O)_2R^{19b}$, $-NO_2$, =O, =S, $=N(R^{19b})$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{18b}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{19b}$, $-SR^{19b}$, $-N(R^{19b})_2$, $-C(O)R^{19b}$, $-C(O)N(R^{19b})_2$, $-N(R^{19b})C(O)R^{19b}$, $-N(R^{19b})C(O)N(R^{19b})_2$, $-OC(O)N(R^{19b})_2$, $-N(R^{19b})C(O)OR^{19b}$, $-C(O)OR^{19b}$, $-OC(O)R^{19b}$, $-S(O)R^{19b}$, $-S(O)_2R^{19b}$, $-NO_2$, =O, =S, $=N(R^{19b})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{18b};

R^{13} is selected from:

hydrogen, halogen, $-OR^{19c}$, $-SR^{19c}$, $-N(R^{19c})_2$, $-NO_2$, and -CN;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{19c}$, $-SR^{19c}$, $-N(R^{19c})_2$, $-NO_2$, and -CN; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{19c}$, $-SR^{19c}$, $-N(R^{19c})_2$, $-C(O)R^{19c}$, $-C(O)N(R^{19c})_2$, $-N(R^{19c})C(O)R^{19c}$, $-N(R^{19c})C(O)N(R^{19c})_2$, $-OC(O)N(R^{19c})_2$, $-N(R^{19c})C(O)OR^{19c}$, $-C(O)OR^{19c}$, $-OC(O)R^{19c}$, $-S(O)R^{19c}$, $-S(O)_2R^{19c}$, $-NO_2$, and -CN;

R^{14} is selected from:

hydrogen, halogen, $-OR^{19d}$, $-SR^{19d}$, $-N(R^{19d})_2$, $-NO_2$, and -CN;

C_{1-6} alkyl which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{19d}$, $-SR^{19d}$, $-N(R^{19d})_2$, $-NO_2$, and -CN; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{19d}$, $-SR^{19d}$, $-N(R^{19d})_2$, $-C(O)R^{19d}$, $-C(O)N(R^{19d})_2$, $-N(R^{19d})C(O)R^{19d}$, $-N(R^{19d})C(O)N(R^{19d})_2$, $-OC(O)N(R^{19d})_2$, $-N(R^{19d})C(O)OR^{19d}$, $-C(O)OR^{19d}$, $-OC(O)R^{19d}$, $-S(O)R^{19d}$, $-S(O)_2R^{19d}$, $-NO_2$, =O, =S, $=N(R^{19d})$, and -CN; or

R^{14} together with $R^{14'}$ form a C_{3-10} carbocycle or 3- to 10-membered heterocycle, wherein the C_{3-10} carbocycle or 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{18c};

$R^{14'}$ is selected from:

hydrogen, halogen, $-OR^{19d}$, $-SR^{19d}$, $-N(R^{19d})_2$, $-NO_2$, and -CN;

C_{1-6} alkyl which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{19d}$, $-SR^{19d}$, $-N(R^{19d})_2$, $-NO_2$, and -CN; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{19d}$, $-SR^{19d}$, $-N(R^{19d})_2$, $-C(O)R^{19d}$, $-C(O)N(R^{19d})_2$, $-N(R^{19d})C(O)R^{19d}$, $-N(R^{19d})C(O)N(R^{19d})_2$, $-OC(O)N(R^{19d})_2$, $-N(R^{19d})C(O)OR^{19d}$, $-C(O)OR^{19d}$, $-OC(O)R^{19d}$, $-S(O)R^{19d}$, $-S(O)_2R^{19d}$, $-NO_2$, =O, =S, $=N(R^{19d})$, and -CN; or

R^{14} together with $R^{14'}$ form a C_{3-10} carbocycle or 3- to 10-membered heterocycle, wherein the C_{3-10} carbocycle or 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{18c};

R^{15} is selected from:

hydrogen, halogen, $-OR^{19e}$, $-SR^{19e}$, $-N(R^{19e})_2$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from R^{18d}; or

R^{15} together with R^{17a} form a 3- to 10-membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more R^{18f}; or

R^{15} together with R^{17b} form a 3- to 10-membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more substituents independently selected from R^{18f}; or

R^{15}, R^{16}, and R^{17b} together form a bridged heterocycle, wherein the bridged heterocycle is optionally substituted with one or more substituents independently selected from R^{18f};

R^{16} is selected from:

hydrogen, halogen, $-OR^{19f}$, $-SR^{19f}$, $-N(R^{19f})_2$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from R^{18e}; or

R^{16} together with R^{17a} form a 3- to 10-membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more substituents independently selected from R^{18f}; or

R^{16} together with R^{17b} form a 3- to 10-membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more substituents independently selected from R^{18f};

R^{17a}, R^{17b}, R^{17c}, R^{17d}, and R^{17e} are each independently selected from:

hydrogen, halogen, $-OR^{19g}$, $-SR^{19g}$, $-N(R^{19g})_2$, $-NO_2$, -CN, and $-N_3$;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from R^{18f}; or

R^{15} together with R^{17a} form a 3- to 10-membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more substituents independently selected from R^{18f}; or

R^{15} together with R^{17b} form a 3- to 10-membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more substituents independently selected from R^{18f}; or

R^{16} together with R^{17a} form a 3- to 10-membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more substituents independently selected from R^{18f}; or

R^{16} together with R^{17b} form a 3- to 10-membered heterocycle, wherein the 3- to 10- membered heterocycle is optionally substituted with one or more substituents independently selected from R^{18f}; or

R^{15}, R^{16}, and R^{17b} together form a bridged heterocycle, wherein the bridged heterocycle is optionally substituted with one or more substituents independently selected from R^{18f};

each R^{18a}, R^{18b}, R^{18c}, R^{18d}, R^{18e}, and R^{18f} is independently selected from:

halogen, $-OR^{19h}$, $-SR^{19h}$, $-N(R^{19h})_2$, $-C(O)R^{19h}$, $-C(O)N(R^{19h})_2$, $-N(R^{19h})C(O)R^{19h}$, $-N(R^{19h})C(O)N(R^{19h})_2$, $-OC(O)N(R^{19h})_2$, $-N(R^{19h})C(O)OR^{19h}$, $-C(O)OR^{19h}$, $-OC(O)R^{19h}$, $-S(O)R^{19h}$, $-S(O)_2R^{19h}$, $-NO_2$, =O, =S, $=N(R^{19h})$, and -CN; and

C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{19h}$, $-SR^{19h}$, $-N(R^{19h})_2$, $-C(O)R^{19h}$, $-C(O)N(R^{19h})_2$, $-N(R^{19h})C(O)R^{19h}$, $-N(R^{19h})C(O)N(R^{19h})_2$, $-OC(O)N(R^{19h})_2$, $-N(R^{19h})C(O)OR^{19h}$, $-C(O)OR^{19h}$, $-OC(O)R^{19h}$, $-S(O)R^{19h}$, $-S(O)_2R^{19h}$, $-NO_2$, =O, =S, $=N(R^{19h})$, and -CN; and

each R^{19a}, R^{19b}, R^{19c}, R^{19d}, R^{19e}, R^{19f}, R^{19g}, and R^{19h} is independently selected from:

hydrogen;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO_2, -NH_2, =O, =S, -O-C_{1-6} alkyl, -S-C_{1-6} alkyl, -N(C_{1-6} alkyl)$_2$, -NH(C_{1-6} alkyl), C_{3-10} carbocycle, 3- to 10-membered heterocycle; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, -NO_2, -NH_2, =O, =S, -O-C_{1-6} alkyl, -S-C_{1-6} alkyl, -N(C_{1-6} alkyl)$_2$, -NH(C_{1-6} alkyl), C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, and C_{1-6} haloalkyl.

18. The compound or salt of claim 17, wherein X^{11} is C(R^{17a}).
19. The compound or salt of claim 17, wherein X^{11} is N.
20. The compound or salt of any one of claims 17 to 19, wherein X^{12} is C(R^{17b}).
21. The compound or salt of any one of claims 17 to 19, wherein X^{12} is N.
22. The compound or salt of any one of claims 17 to 21, wherein Y^{12} is C(R^{17e}).
23. The compound or salt of any one of claims 17 to 22, wherein Y^{12} is C(CN).
24. The compound or salt of any one of claims 17 to 23, wherein X^{13} is C(R^{17c}), and Y^{11} is C(R^{17d}).
25. The compound or salt of claim 17, 19, 20, 22, or 24, wherein X^{11} is N, X^{12} is C(R^{17b}), X^{13} is C(R^{17c}), Y^{11} is C(R^{17d}), and Y^{12} is C(R^{17e}).
26. The compound or salt of any one of claims 17 to 25, wherein Y^{11} is C(H), and X^{13} is C(H).
27. The compound or salt of any one of any one of claims 17 to 26, wherein:

R^{11a} is hydrogen, halogen, -NO_2, -CN, -OR^{19a}, -SR^{19a}, -N(R^{19a})$_2$, or C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, -OR^{19a}, -SR^{19a}, -N(R^{19a})$_2$, =O, and -CN;

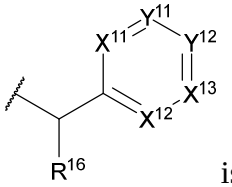
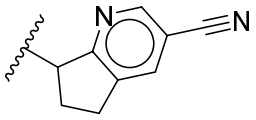
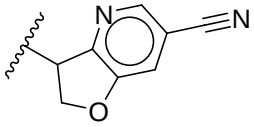
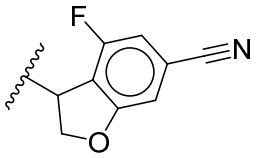
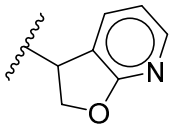
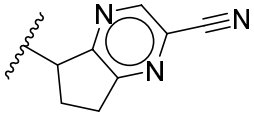
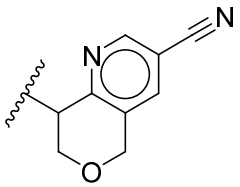
R^{11b} is halogen, -NO_2, -CN, -N_3, -OR^{19a}, -SR^{19a}, -N(R^{19a})$_2$, or C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, -OR^{19a}, -SR^{19a}, -N(R^{19a})$_2$, =O, and -CN;

R^{11c} is hydrogen; and

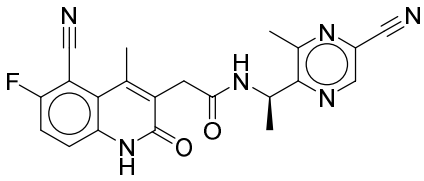
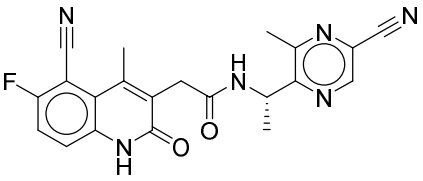
R^{11d} is hydrogen.

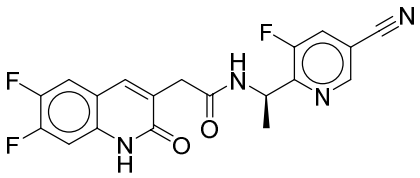
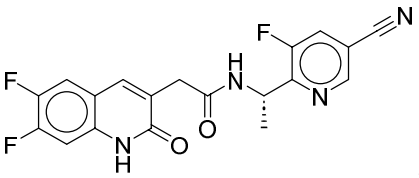
28. The compound or salt of any one of claims 17 to 27, wherein R^{11a}, R^{11b}, R^{11c}, and R^{11d} are each independently selected from hydrogen, -F, -CN, and methyl;
wherein when R^{11a}, R^{11b}, and R^{11c} are each hydrogen; then R^{11d} is selected from -F, -CN, and methyl.

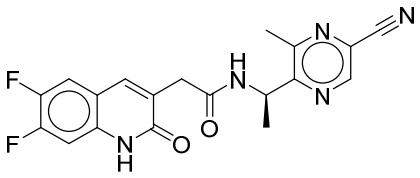
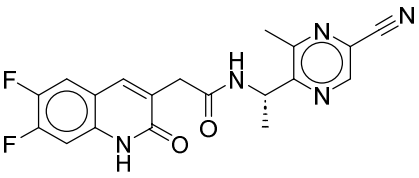
29. The compound or salt of any one of claims 17 to 28, wherein R^{11b} is -F; and R^{11a}, R^{11c}, and R^{11d} are each independently selected from hydrogen, -F, -CN, and methyl.
30. The compound or salt of any one of claims 17 to 29, wherein R^{11a} is -F, R^{11b} is -F, R^{11c} is -H, and R^{11d} is -H.
31. The compound or salt of any one of claims 17 to 30, wherein R^{12} is hydrogen.
32. The compound or salt of any one of claims 17 to 31, wherein R^{13} is selected from:
hydrogen;
C_{1-6} alkyl which is optionally substituted with one or more substituents independently selected from halogen, -OH, -OMe, and -CN; and
C_{3-10} carbocycle which is optionally substituted with one or more substituents independently selected from halogen, -OH, -OMe, and -CN.
33. The compound or salt of any one of claims 17 to 32, wherein R^{13} is selected from hydrogen and $-CH_3$.
34. The compound or salt of any one of claims 17 to 33, wherein R^{14} is selected from hydrogen, C_{1-6} alkyl, and halogen; and $R^{14'}$ is selected from hydrogen, C_{1-6} alkyl, and halogen.
35. The compound or salt of any one of claims 17 to 34, wherein R^{14} is selected from hydrogen, and $R^{14'}$ is selected from hydrogen.
36. The compound or salt of any one of claims 17 to 34, wherein R^{14} is selected from fluoro and $R^{14'}$ is selected from fluoro.
37. The compound or salt of any one of claims 17 to 34, wherein R^{14} and $R^{14'}$ together form an optionally substituted C_3 carbocycle.
38. The compound or salt of claim 37, wherein R^{14} and $R^{14'}$ together form a C_3 carbocycle.
39. The compound or salt of any one of claims 17 to 38, wherein R^{15} is hydrogen.
40. The compound or salt of any one of claims 17 to 39, wherein R^{16} is hydrogen, methyl, or CH_2OH.
41. The compound or salt of any one of claims 17 to 40, wherein R^{16} is methyl.
42. The compound or salt of any one of claims 17 to 41, wherein each R^{17a}, R^{17b}, R^{17c}, R^{17d}, and R^{17e} is independently selected from hydrogen, methyl, -CCH, -F, and -CN.

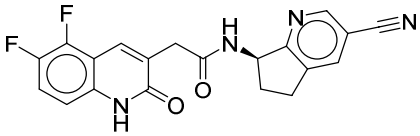
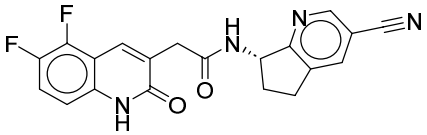
43. The compound or salt of any one of claims 17 to 41, wherein  is selected from  ,  ,  ,  ,  , and  .

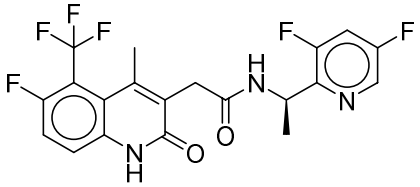
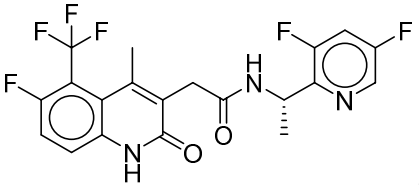
44. The compound or salt of claim 17, selected from:

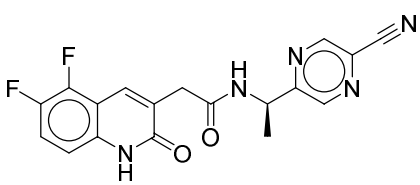
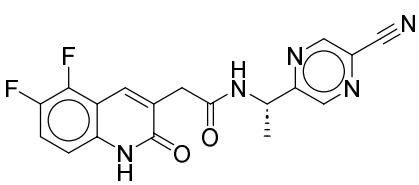
 ,  ,

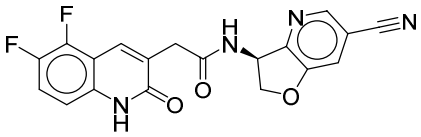
 ,  ,

 ,  ,

 ,  ,

 ,  ,

 ,  ,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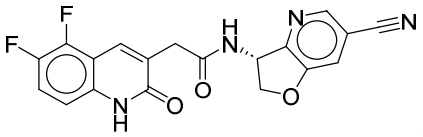
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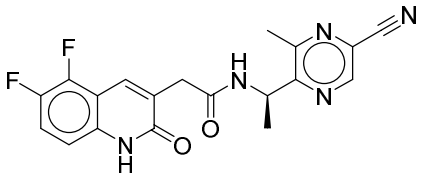
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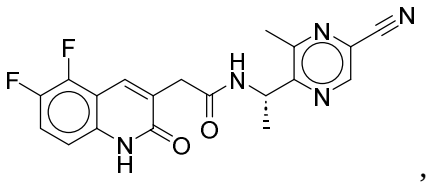
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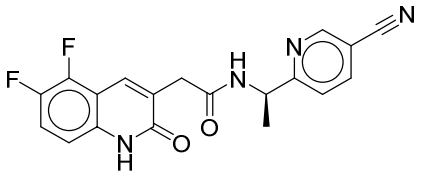
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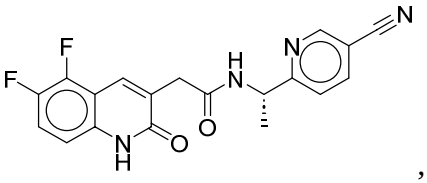
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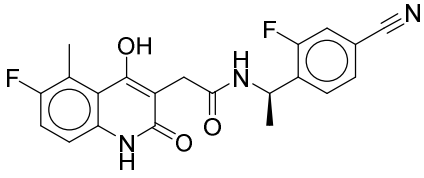
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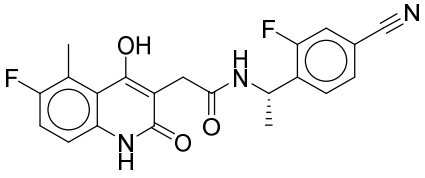
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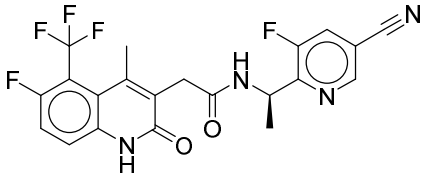
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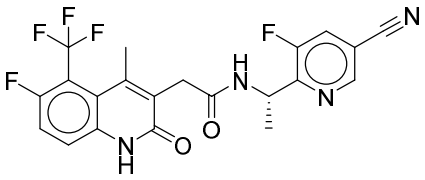
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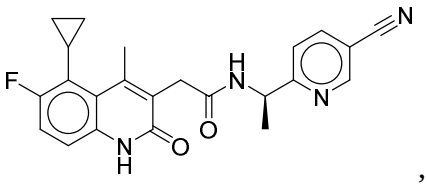
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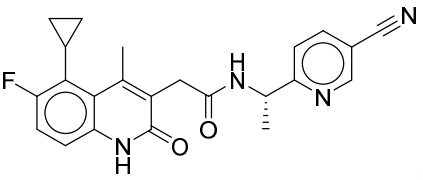
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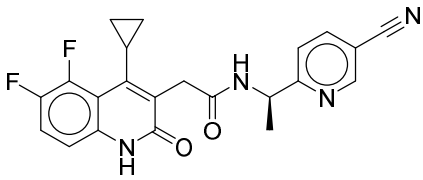
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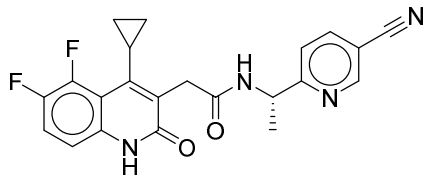
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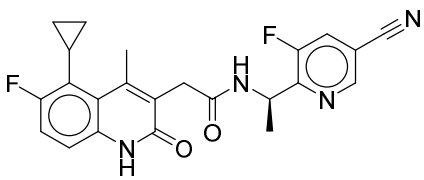
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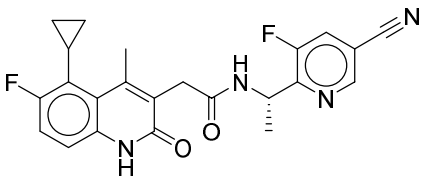
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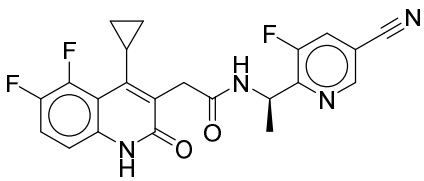
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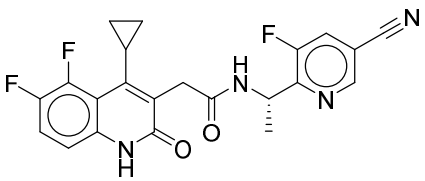
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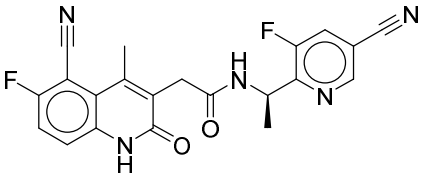
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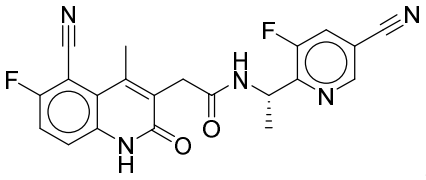
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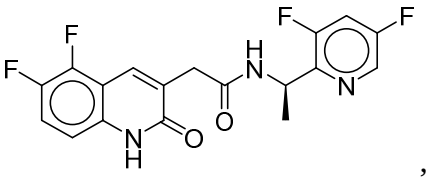
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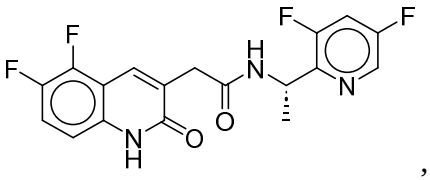
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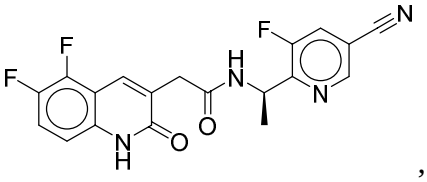
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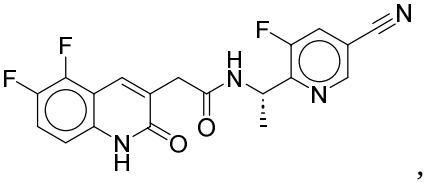
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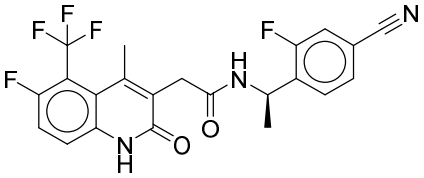
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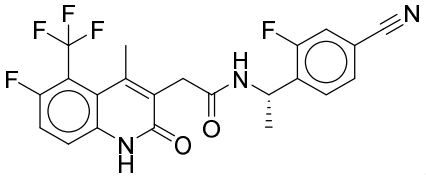
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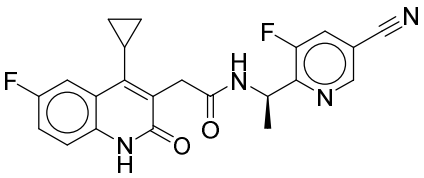
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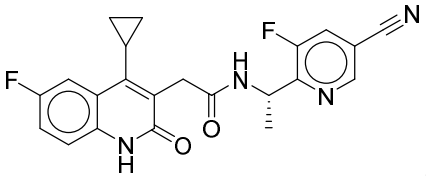
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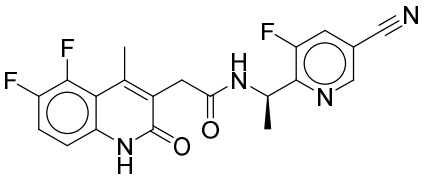
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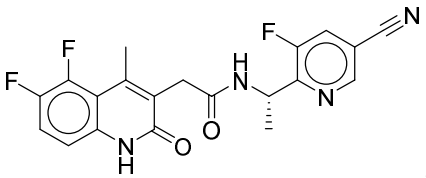
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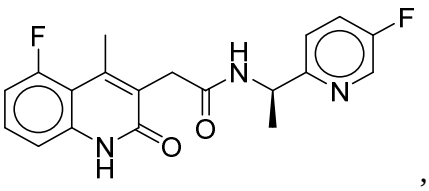
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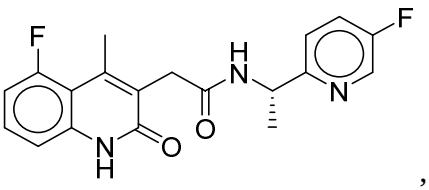
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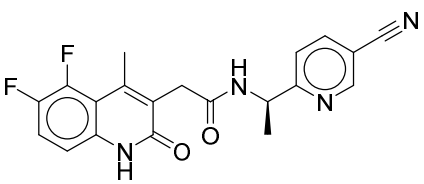
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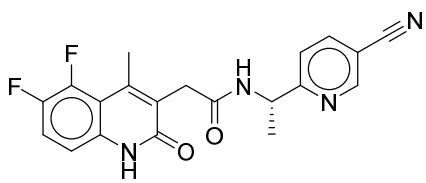
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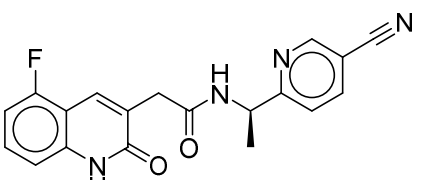
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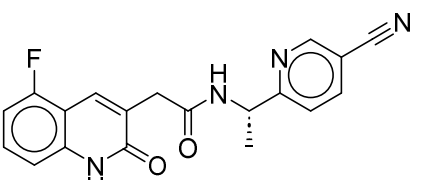
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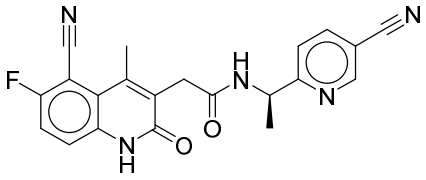
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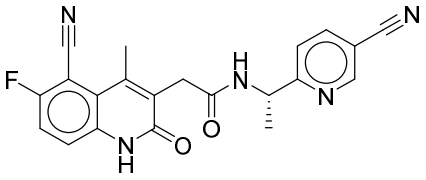
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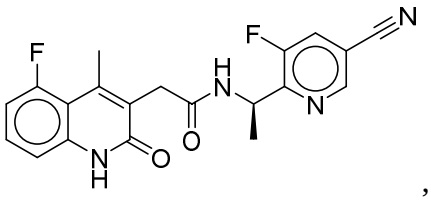
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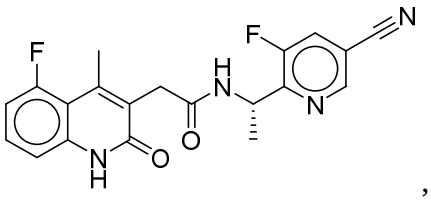
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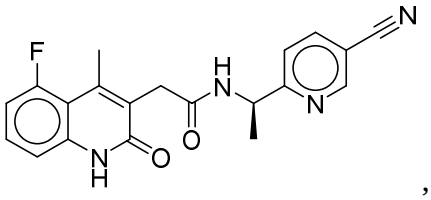
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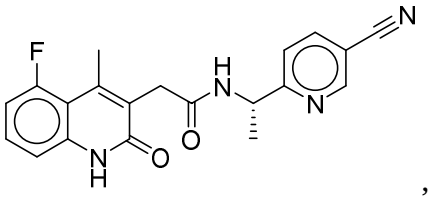
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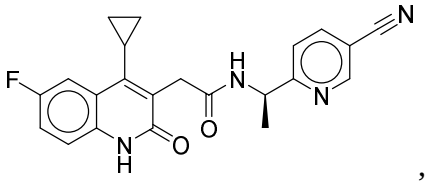
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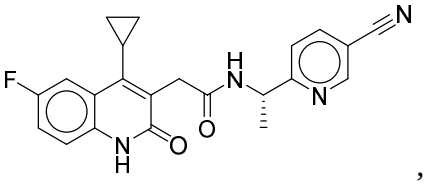
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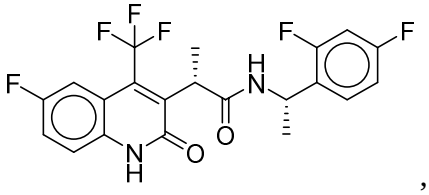
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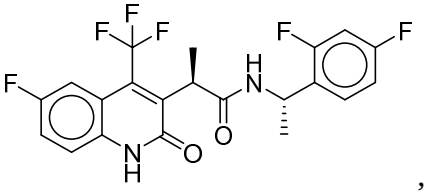
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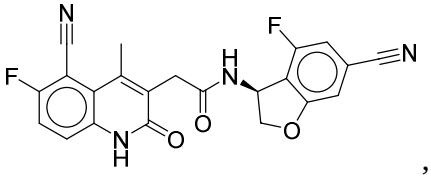
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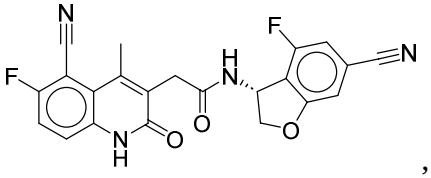
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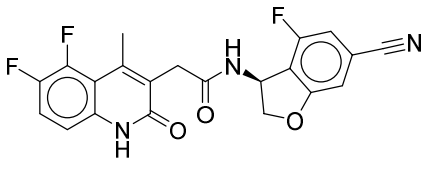
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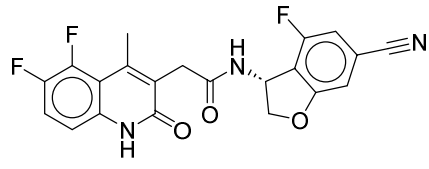
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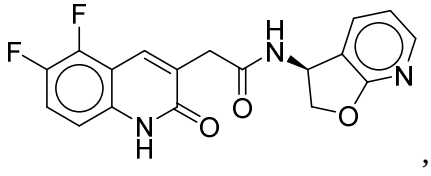
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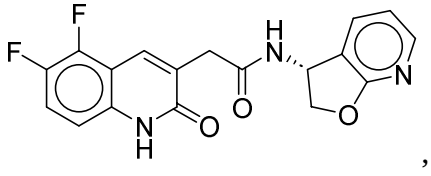
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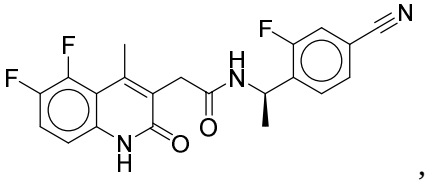
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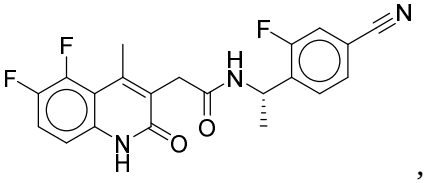
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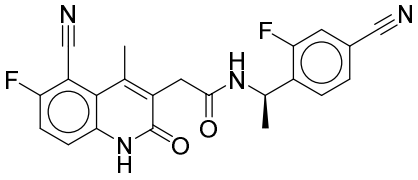
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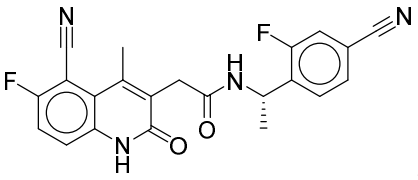
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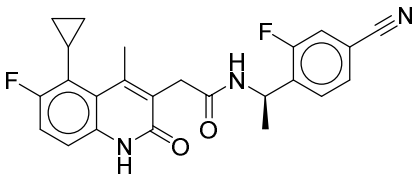
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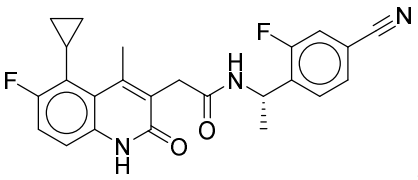
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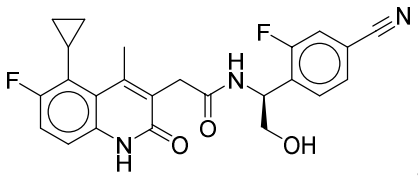
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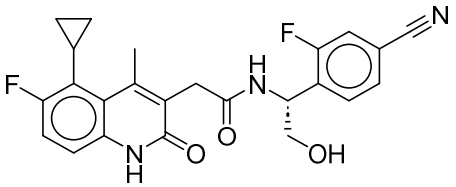
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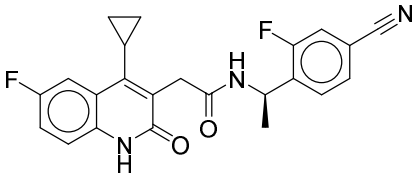
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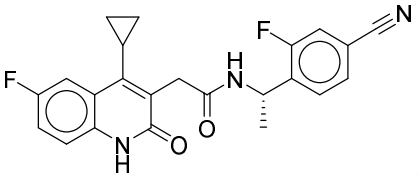
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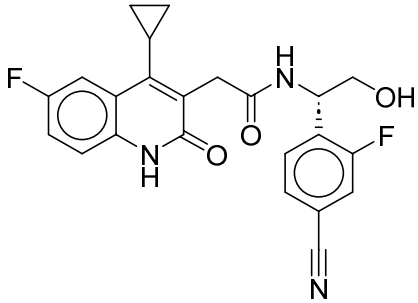
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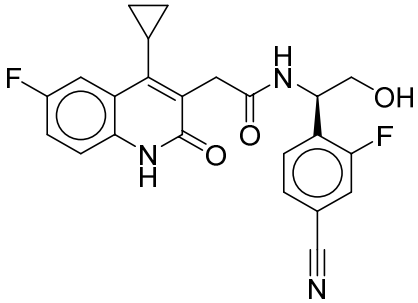
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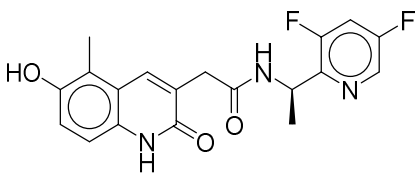
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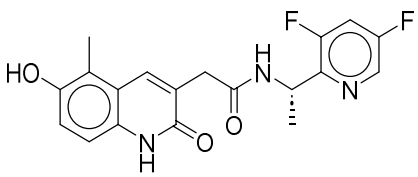
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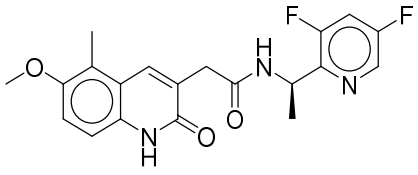
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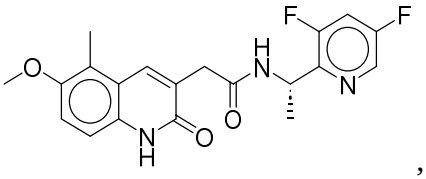
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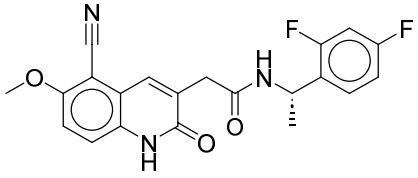
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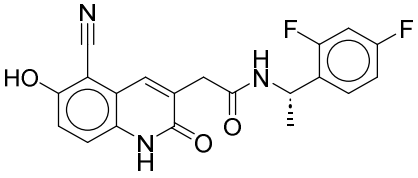
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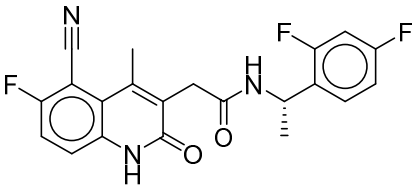
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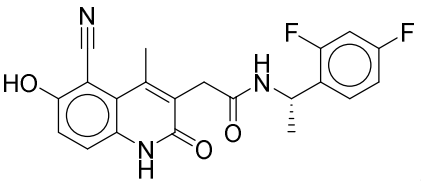
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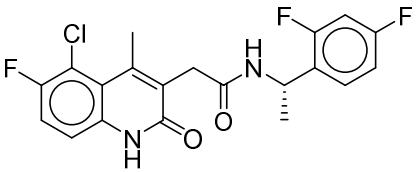
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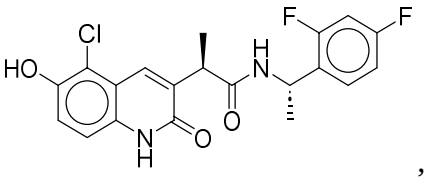
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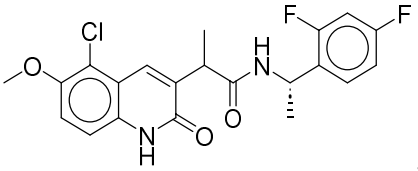
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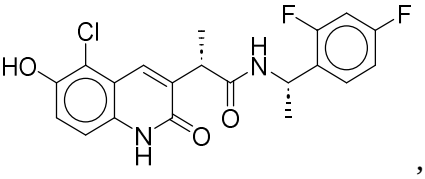
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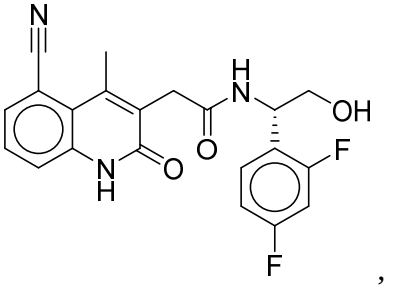
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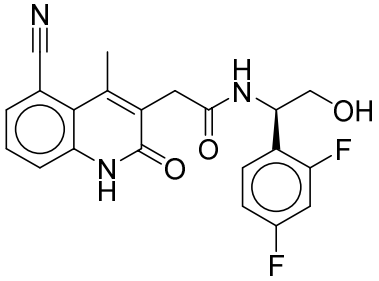
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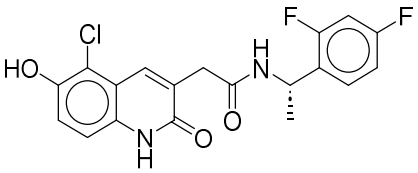
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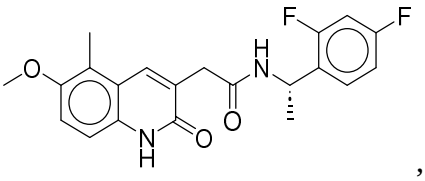
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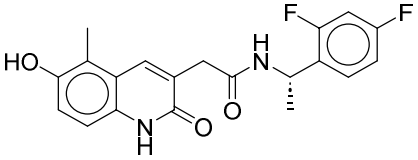
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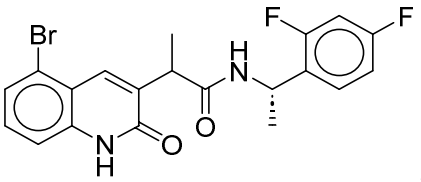
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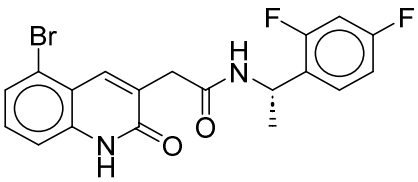
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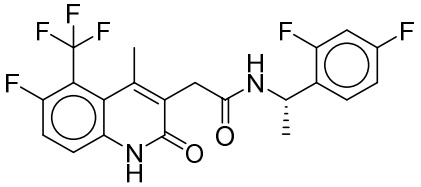
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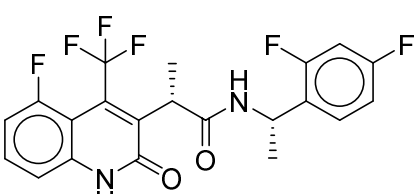
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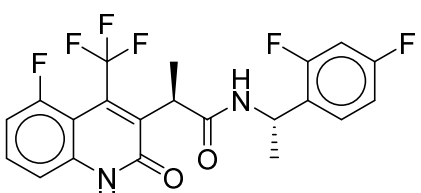
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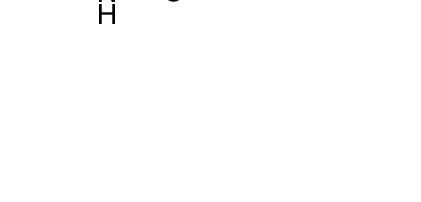
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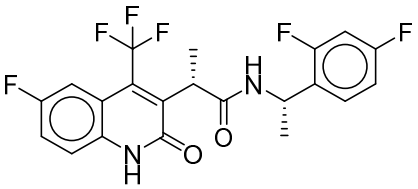
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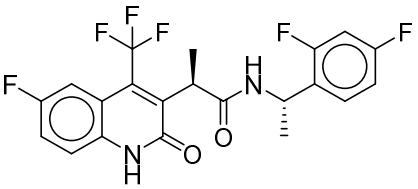
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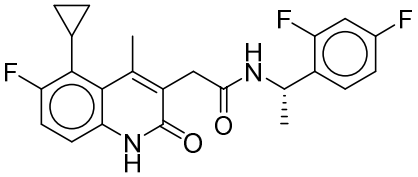
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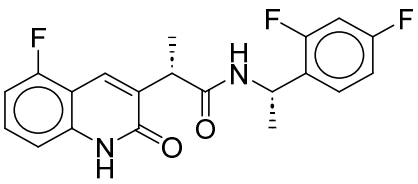
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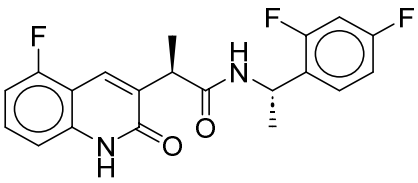
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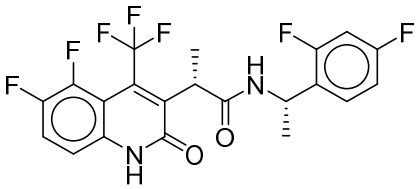
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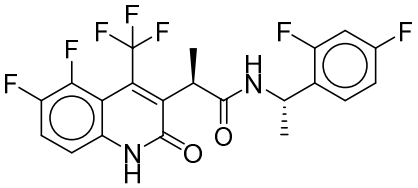
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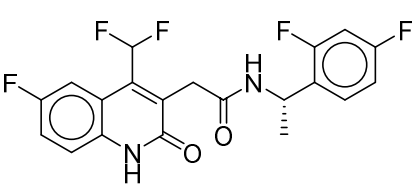
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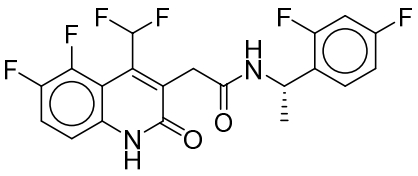
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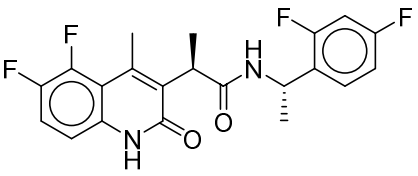
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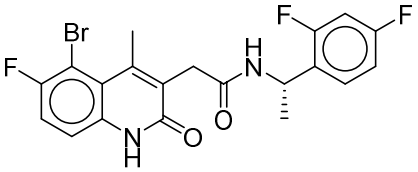
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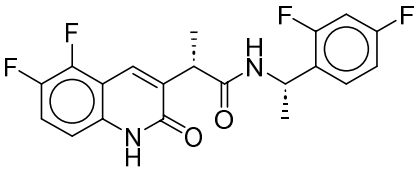
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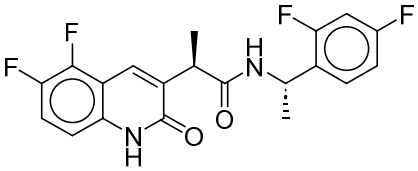
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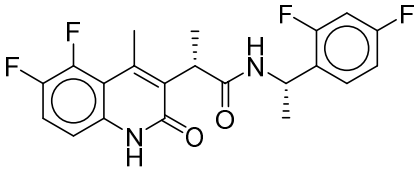
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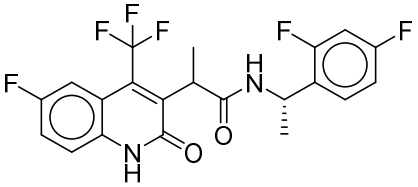
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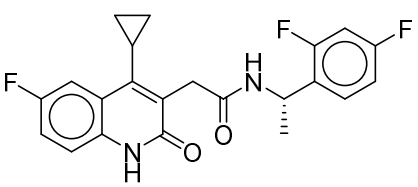
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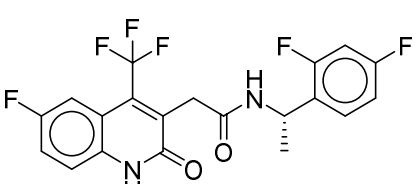
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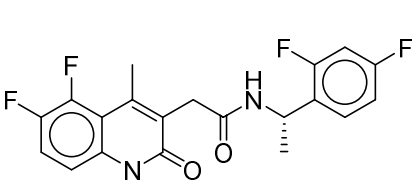
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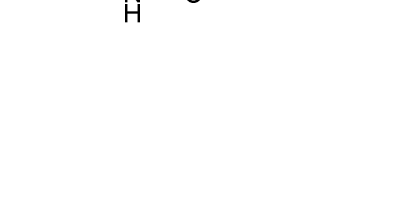
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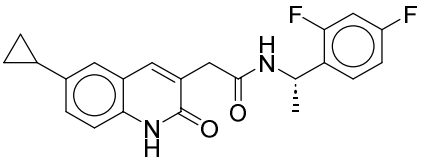
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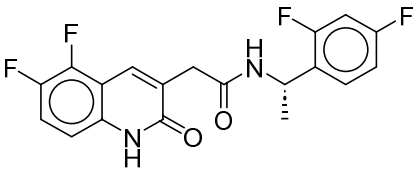
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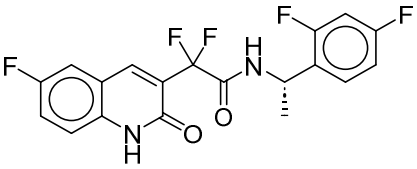
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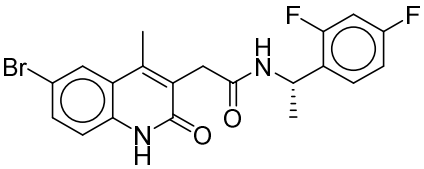
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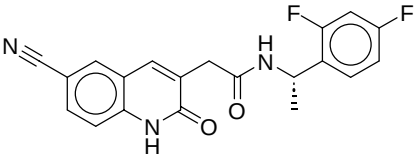
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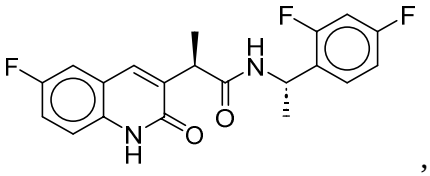
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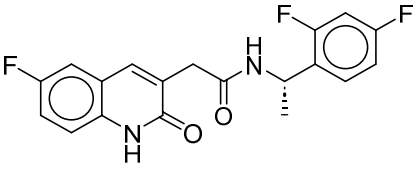
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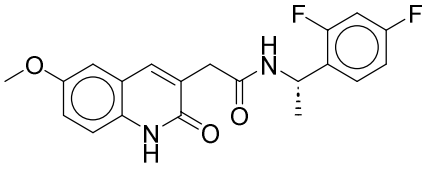
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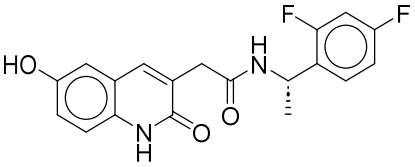
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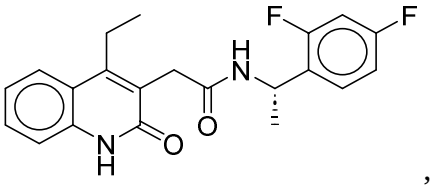
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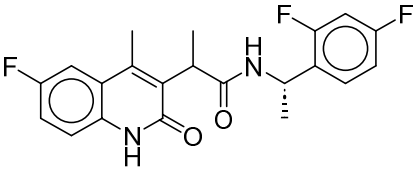
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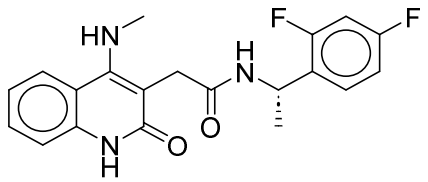
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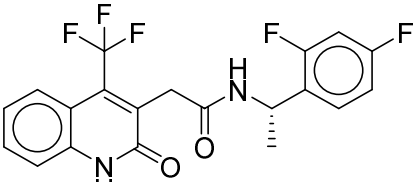
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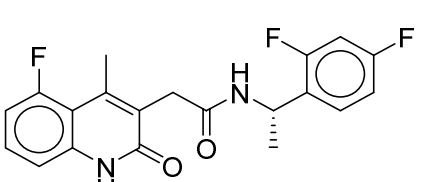
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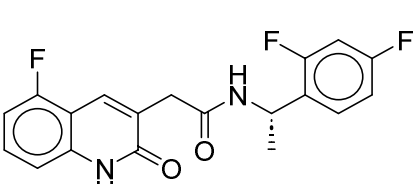
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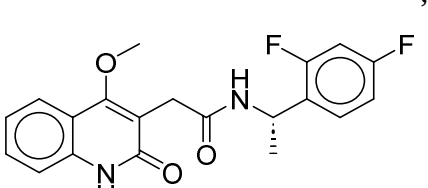
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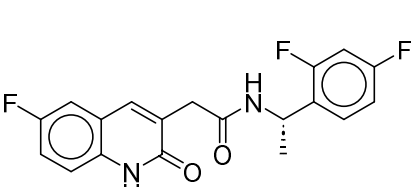
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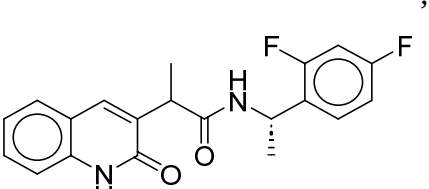
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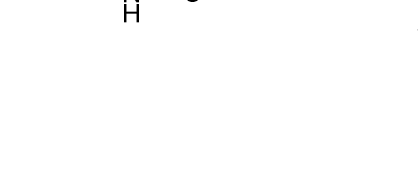
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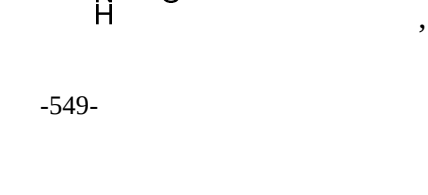
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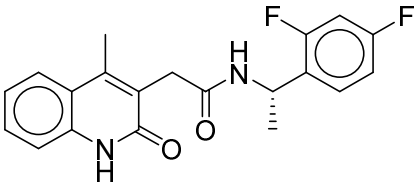
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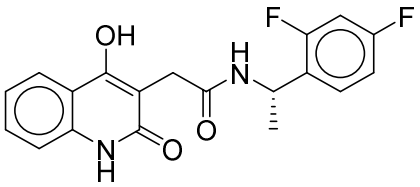
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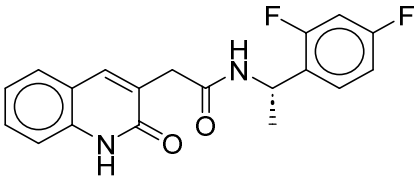
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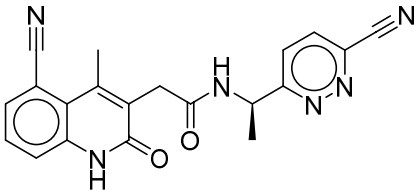
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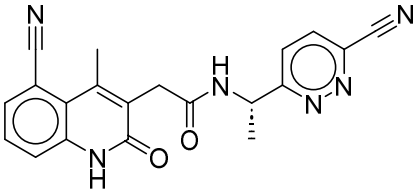
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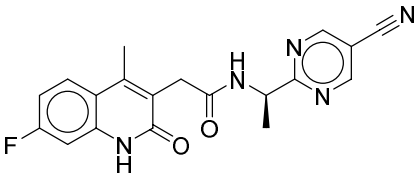
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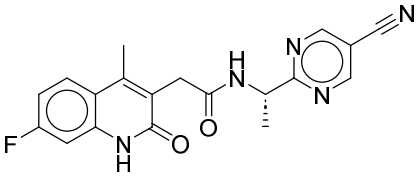
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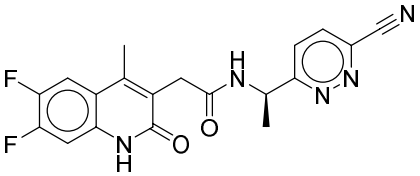
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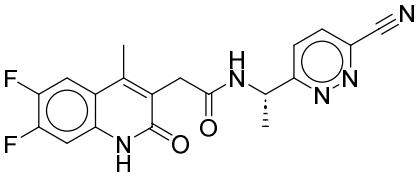
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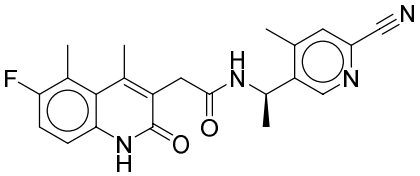
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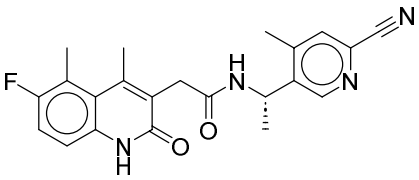
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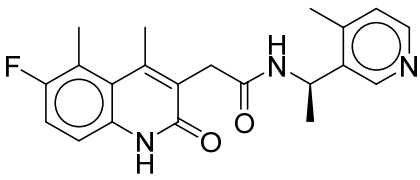
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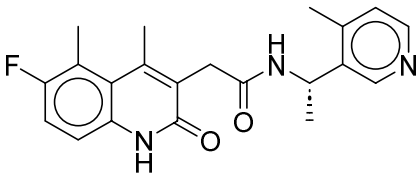
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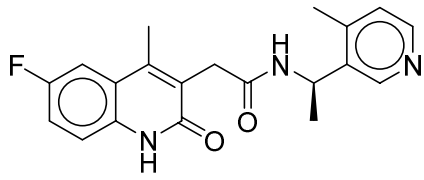
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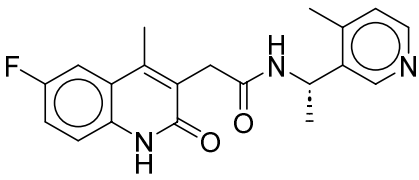
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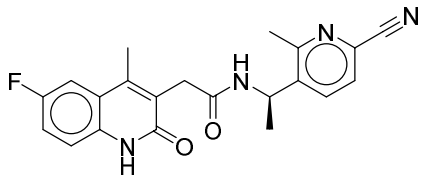
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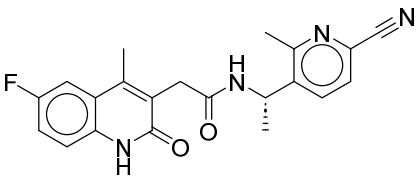
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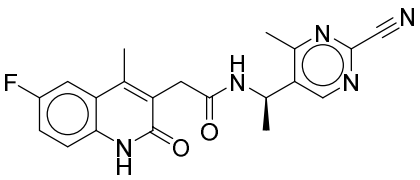
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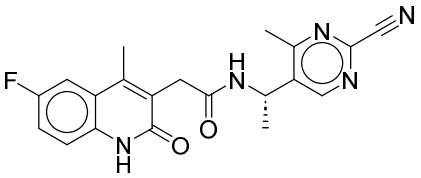
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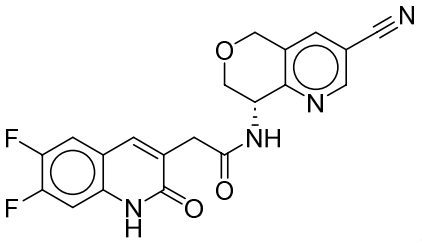
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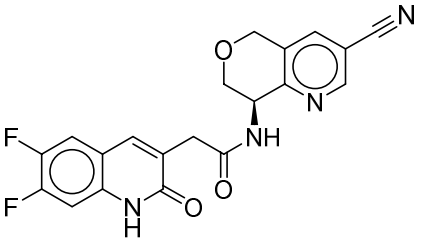
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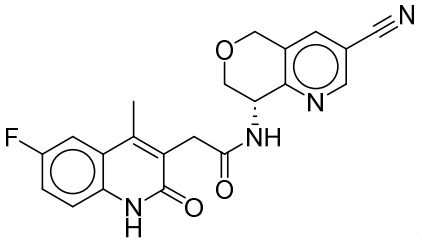
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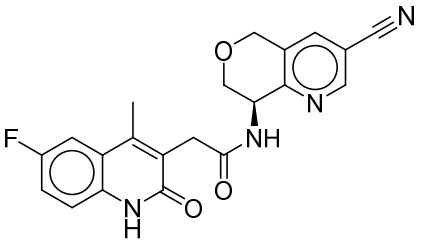
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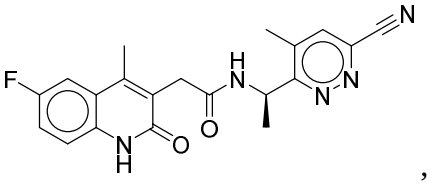
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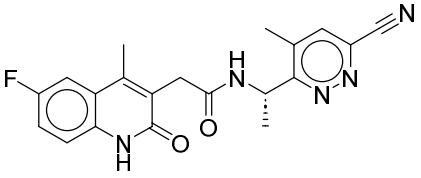
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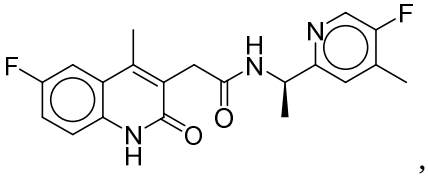
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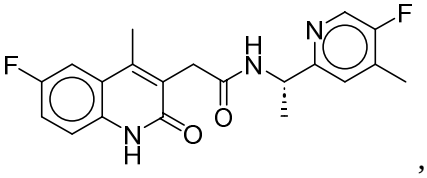
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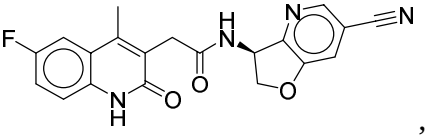
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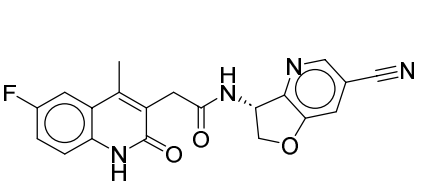
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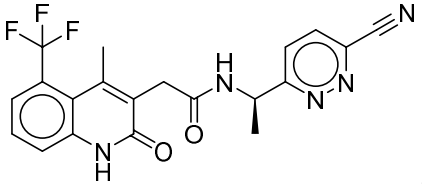
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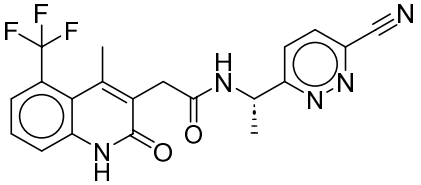
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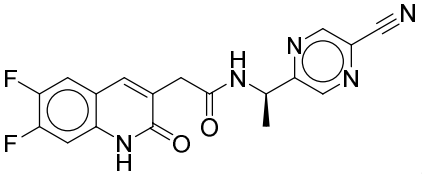
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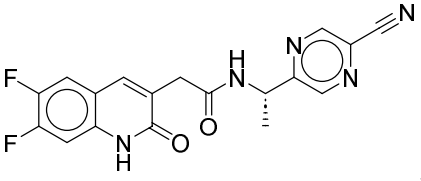
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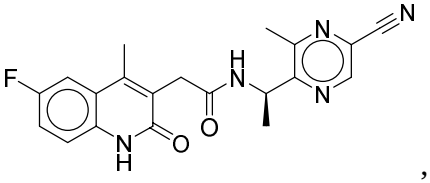
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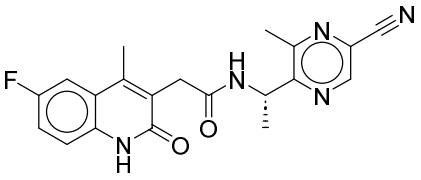
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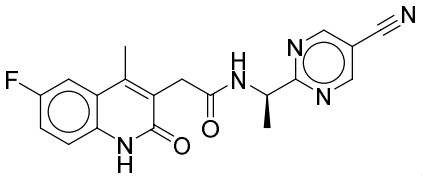
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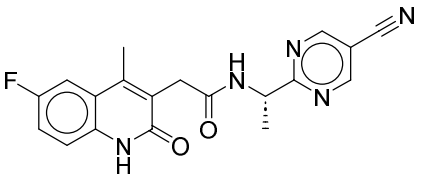
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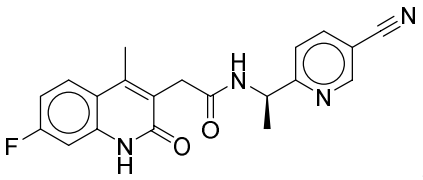
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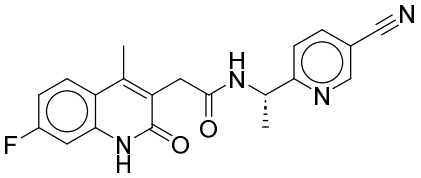
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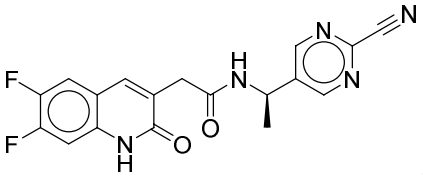
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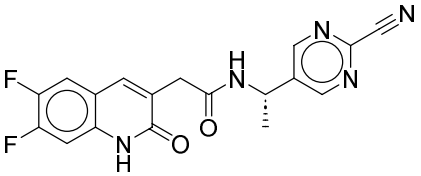
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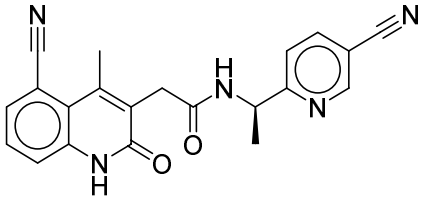
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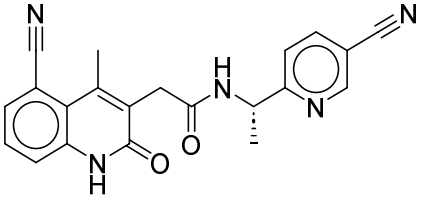
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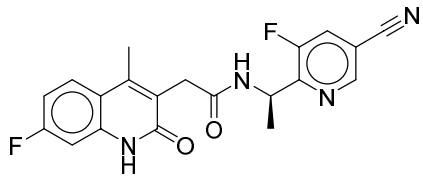
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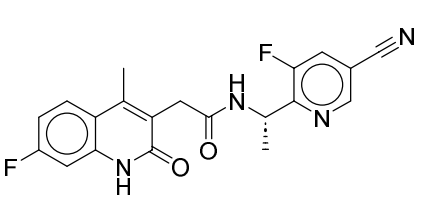
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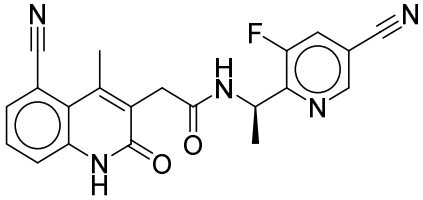
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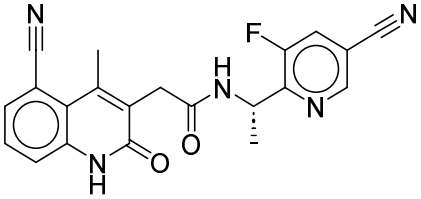
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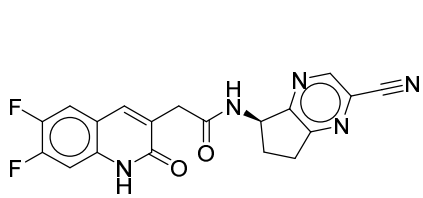
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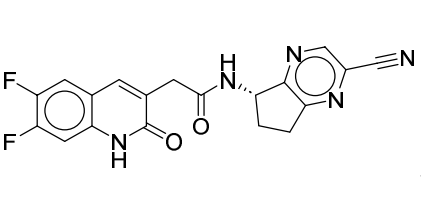
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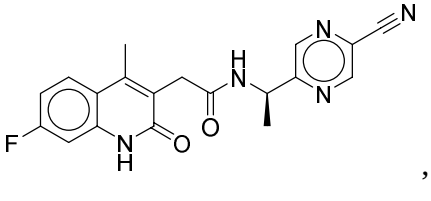
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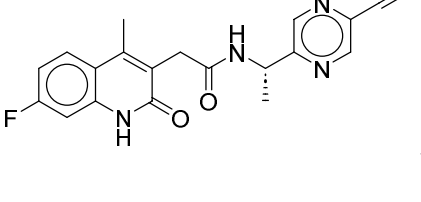
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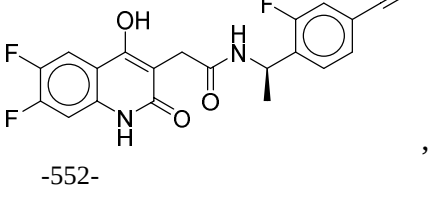
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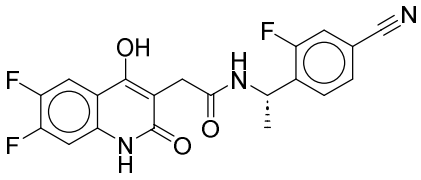
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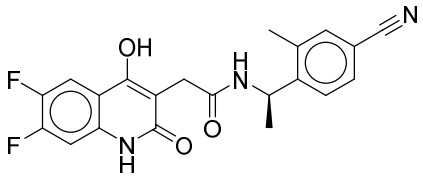
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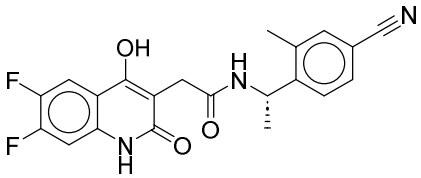
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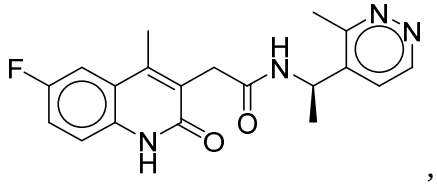
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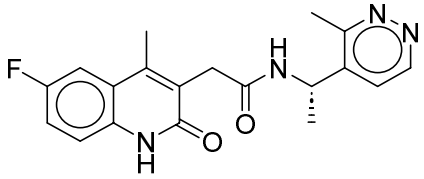
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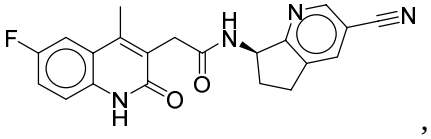
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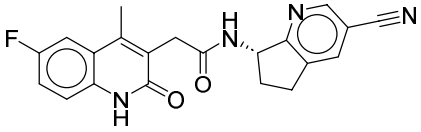
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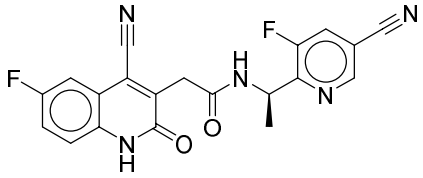
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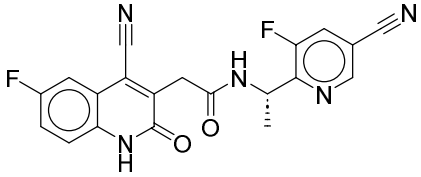
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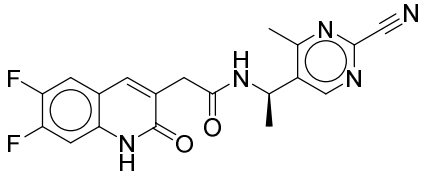
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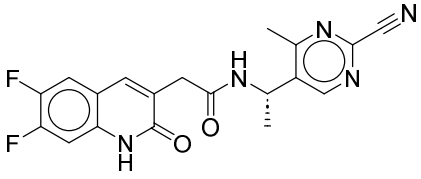
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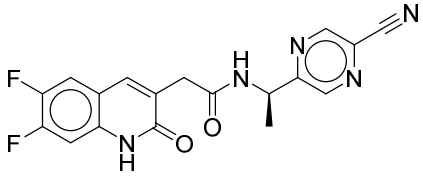
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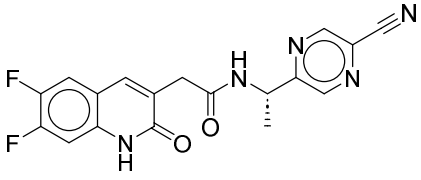
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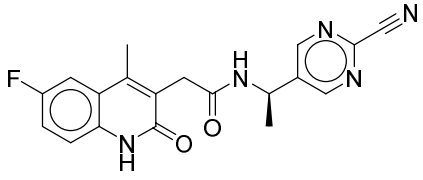
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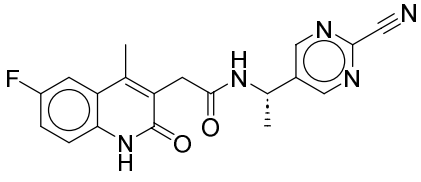
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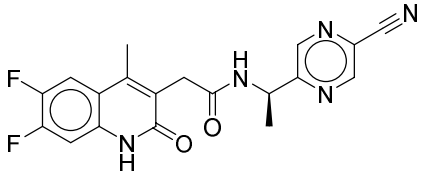
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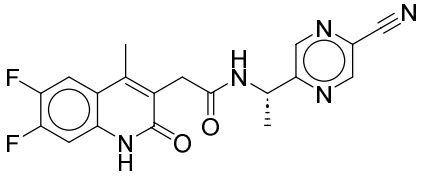
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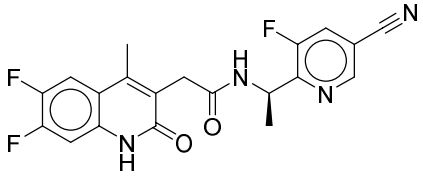
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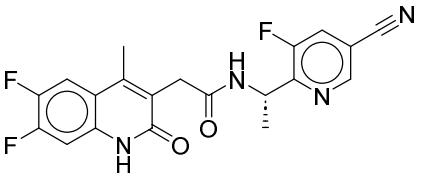
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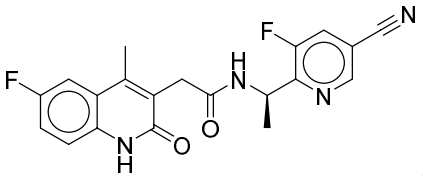
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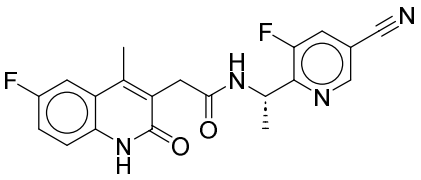
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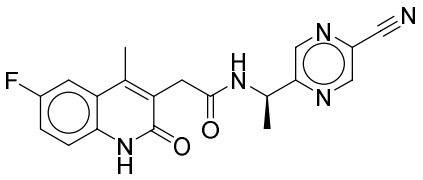
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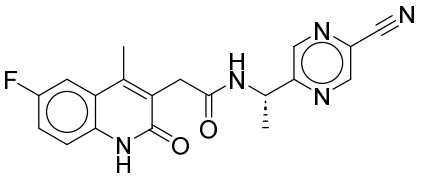
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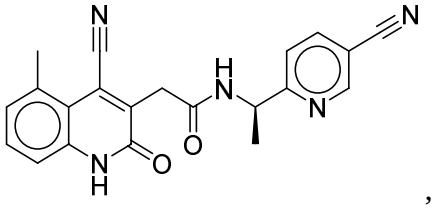
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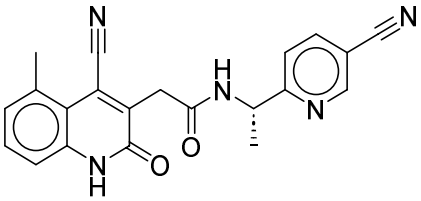
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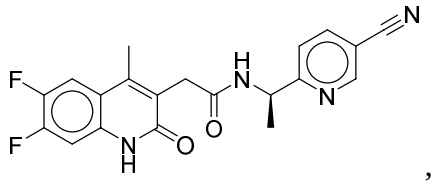
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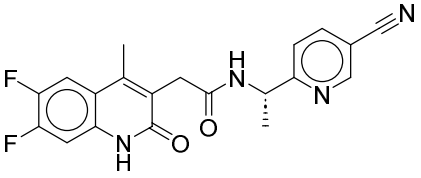
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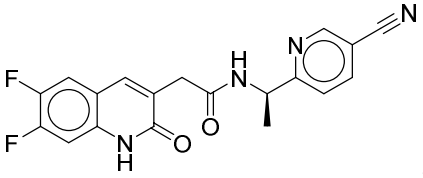
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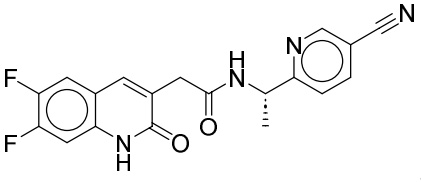
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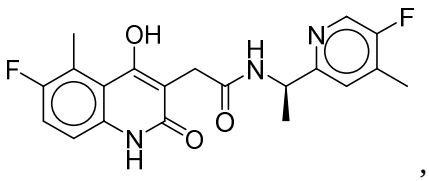
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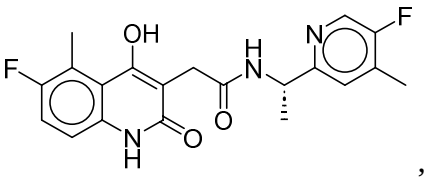
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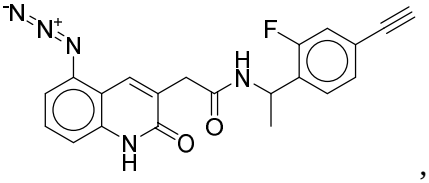
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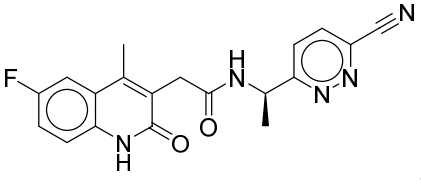
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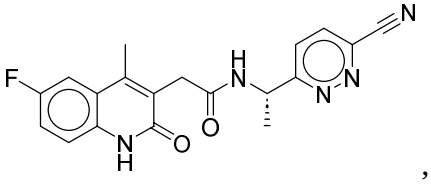
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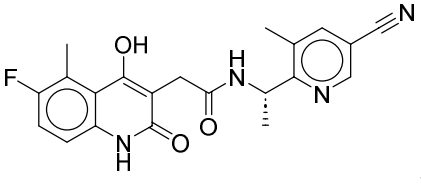
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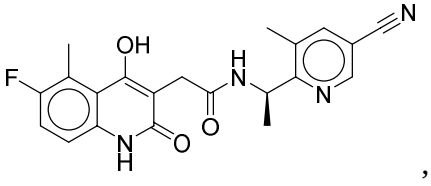
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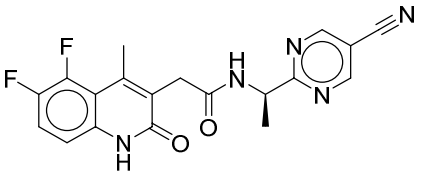
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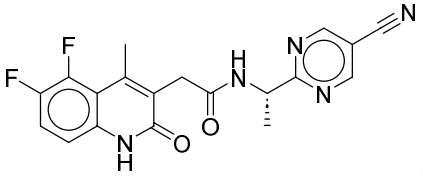
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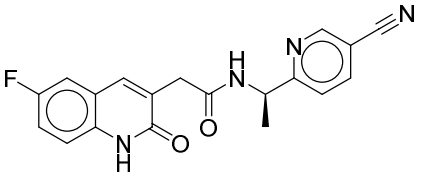
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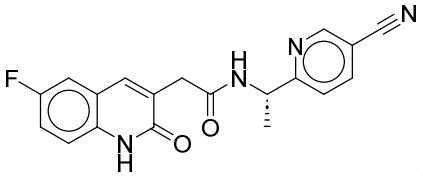
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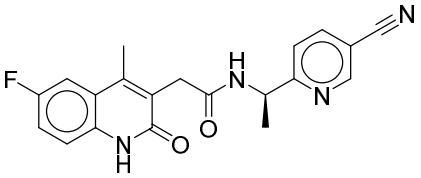
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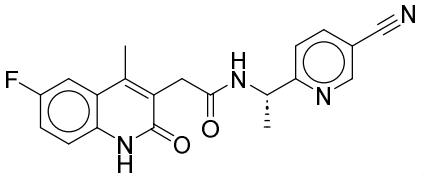
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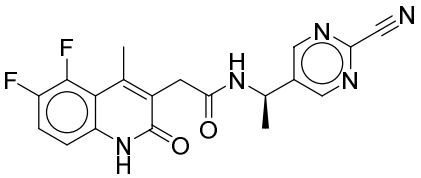
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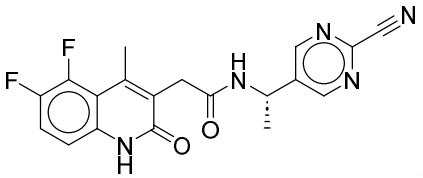
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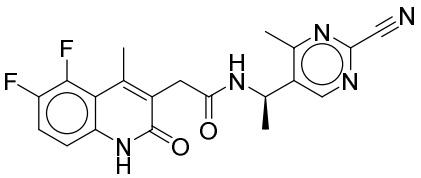
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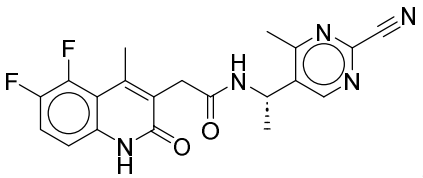
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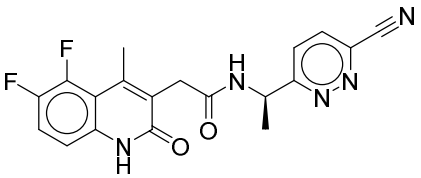
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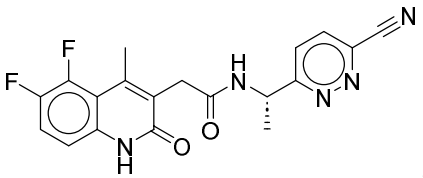
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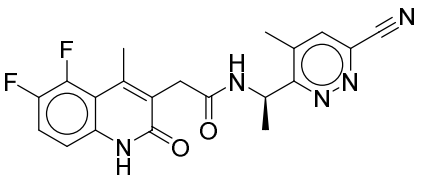
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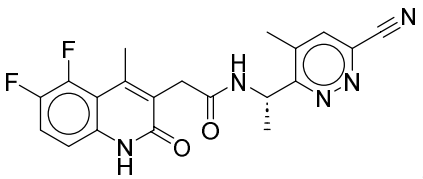
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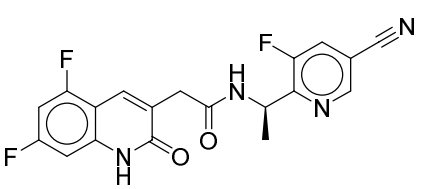
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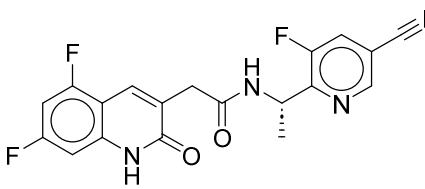
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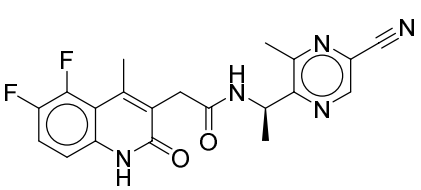
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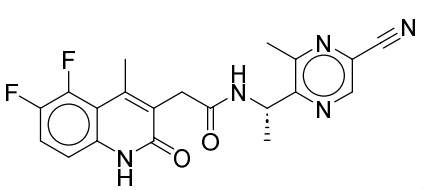
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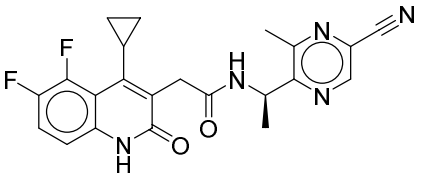
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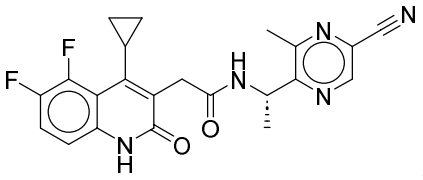
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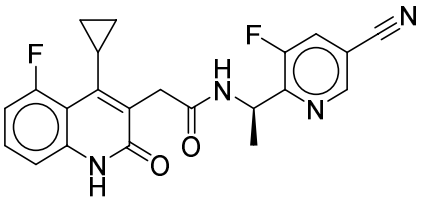
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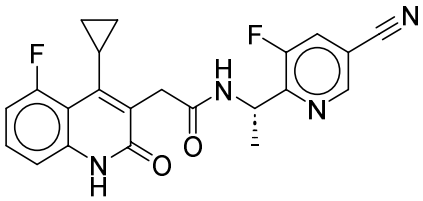
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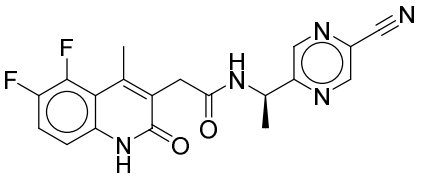
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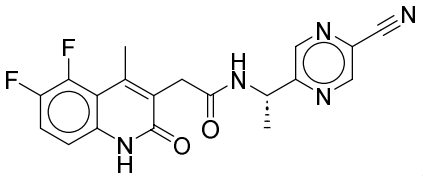
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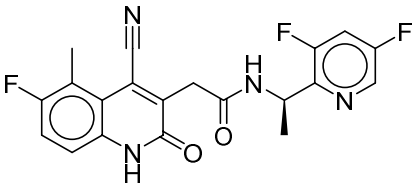
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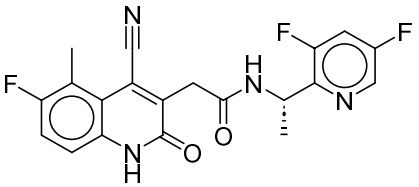
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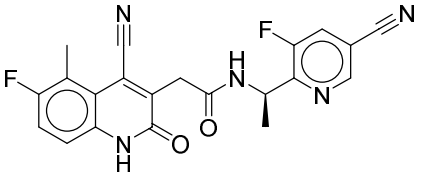
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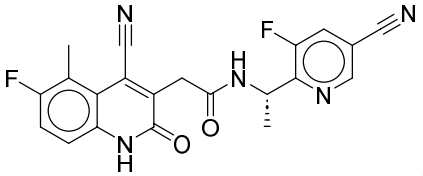
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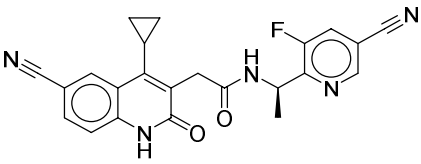
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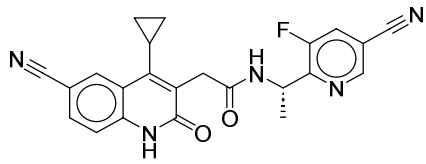
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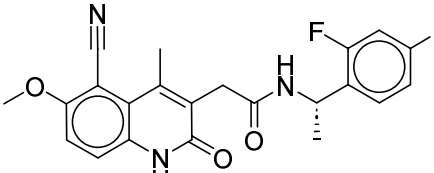
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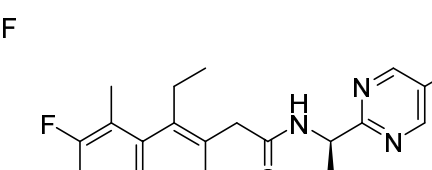
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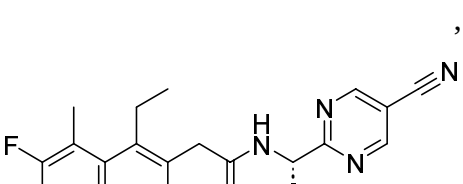
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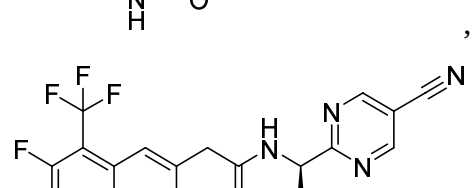
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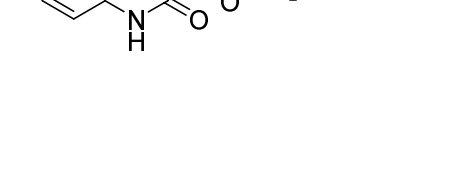
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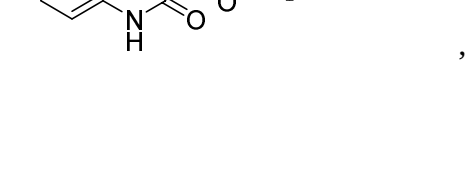
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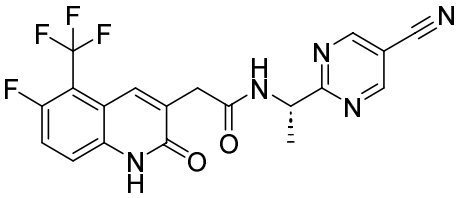
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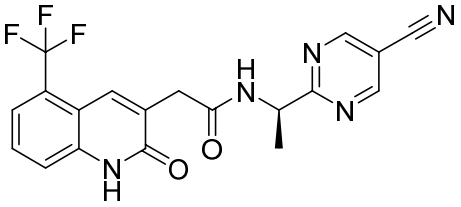
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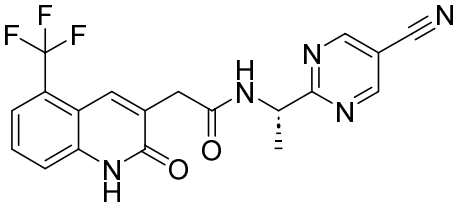
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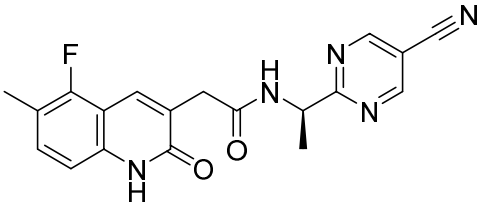
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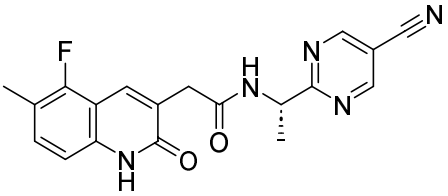
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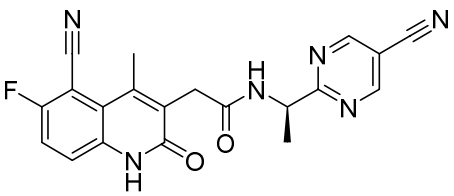
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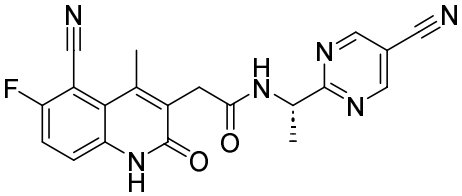
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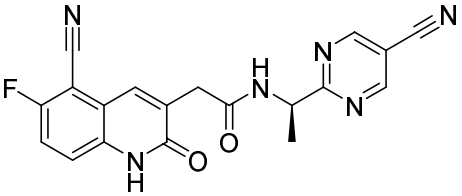
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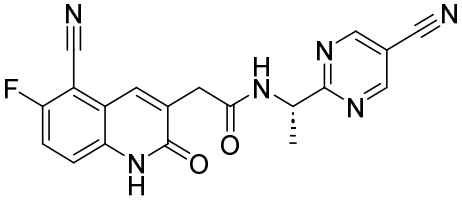
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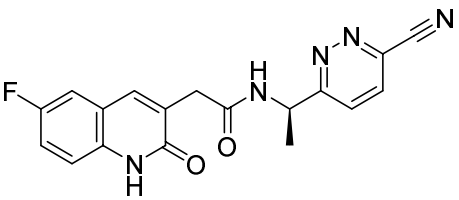
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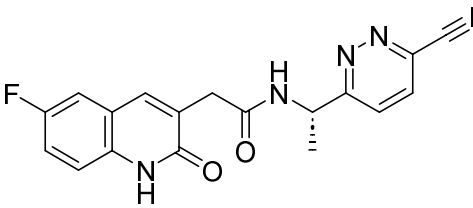
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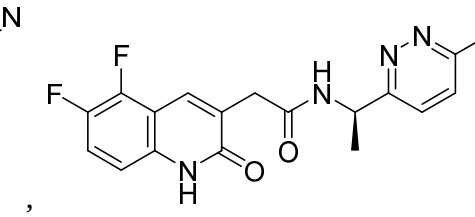
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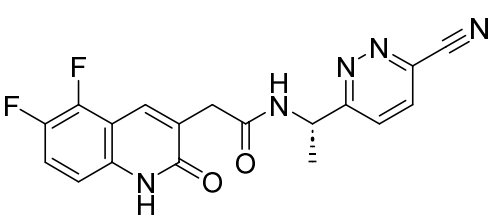
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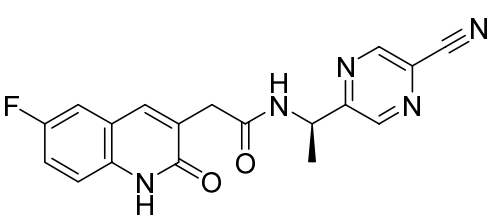
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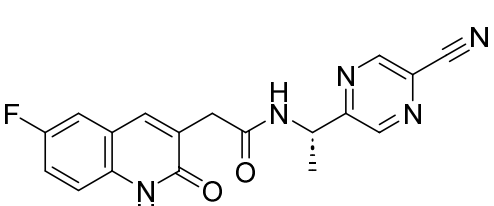
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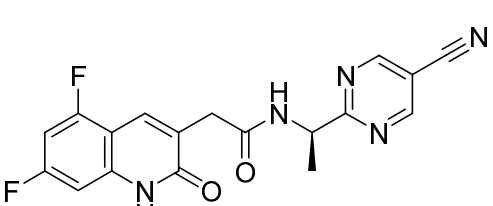
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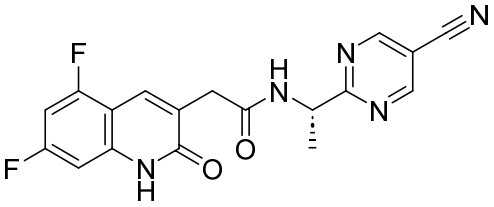
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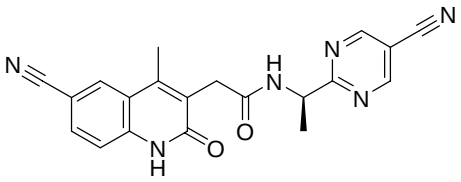
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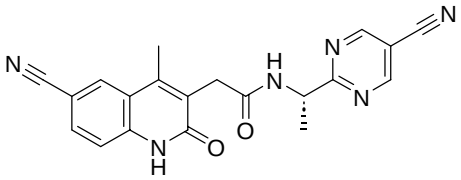
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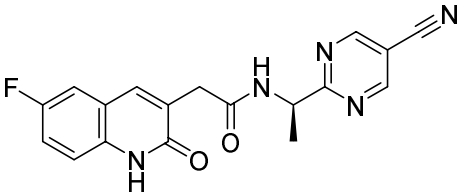
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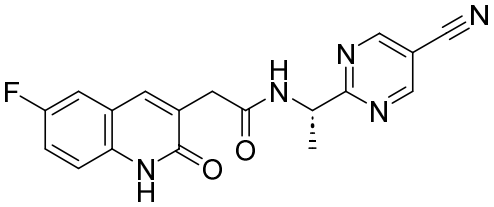
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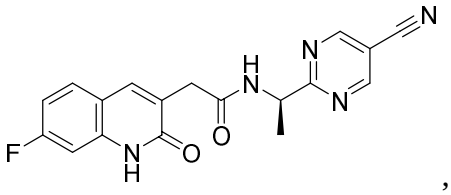
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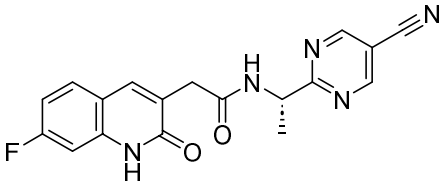
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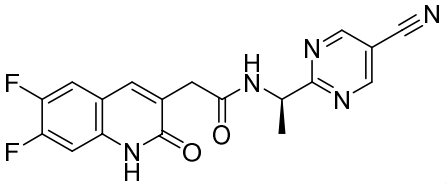
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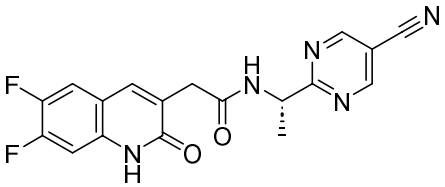
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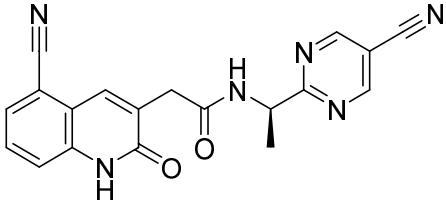
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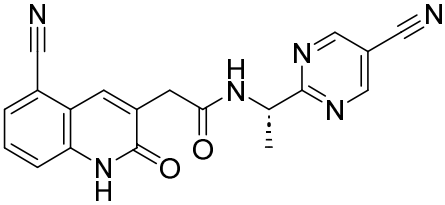
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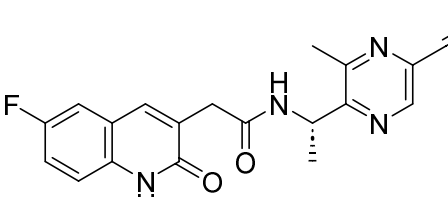
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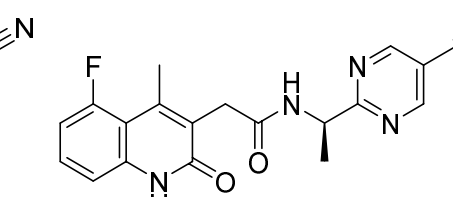
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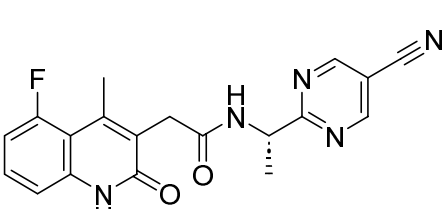
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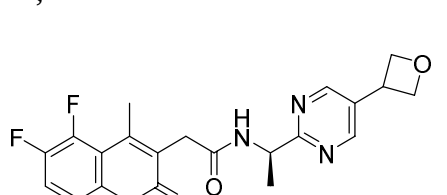
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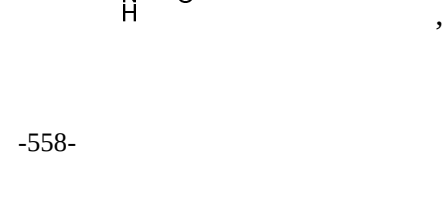
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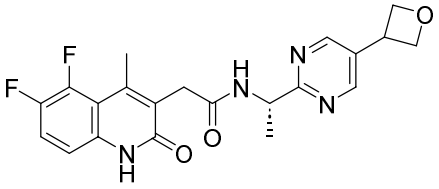
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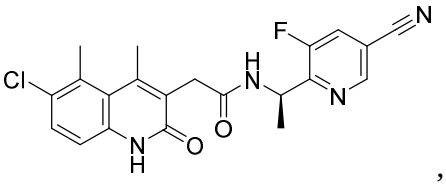
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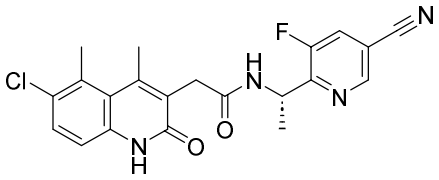
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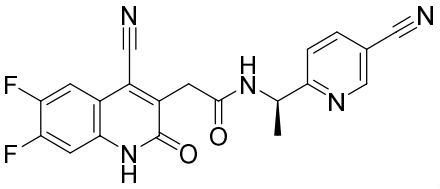
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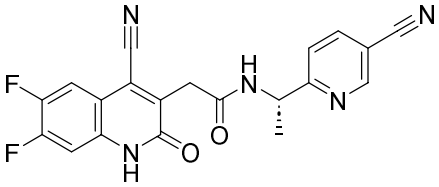
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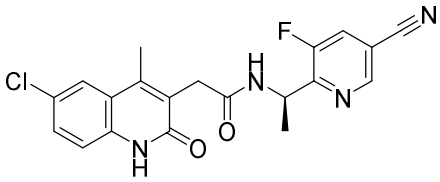
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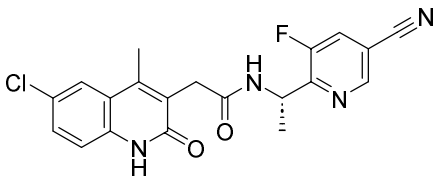
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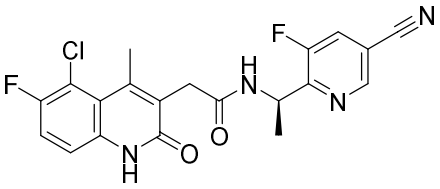
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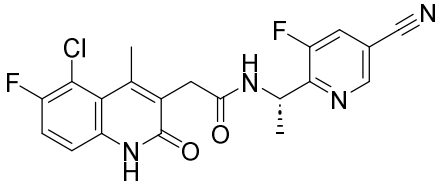
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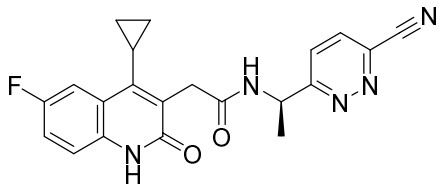
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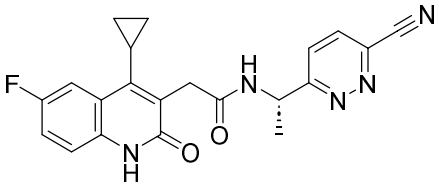
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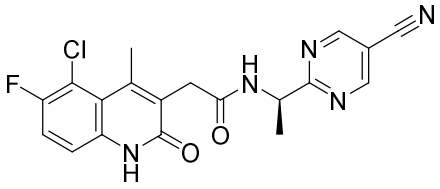
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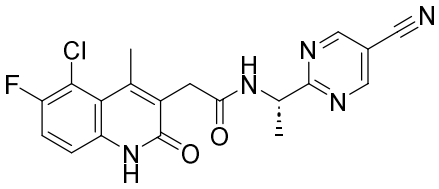
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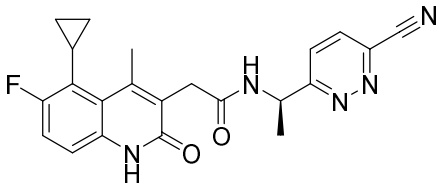
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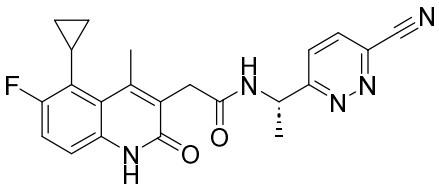
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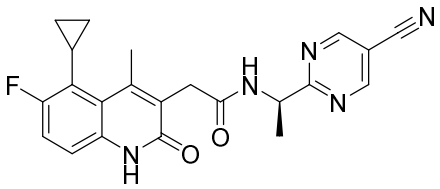
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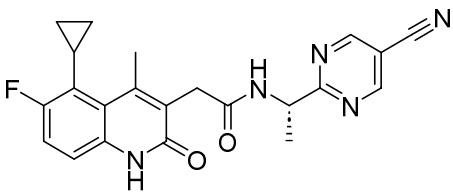
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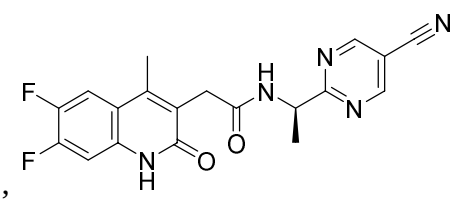
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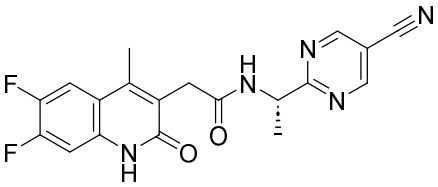
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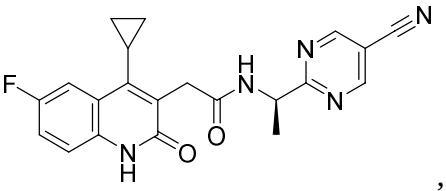
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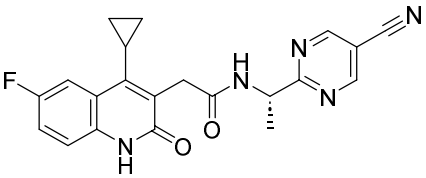
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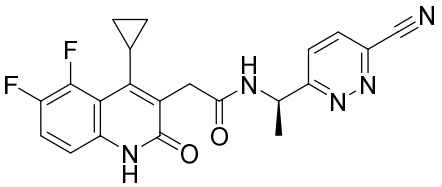
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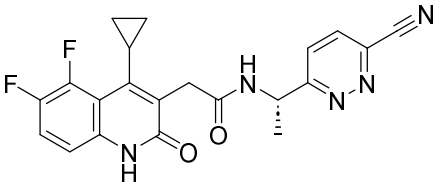
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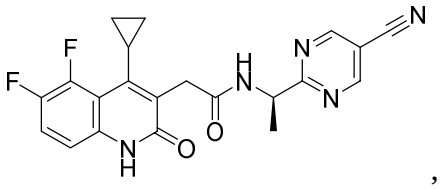
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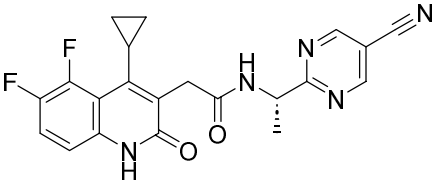
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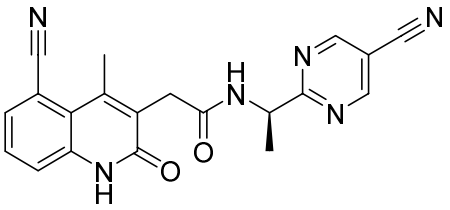
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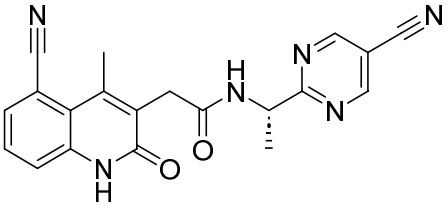
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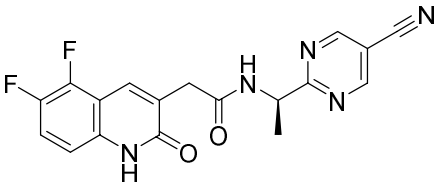
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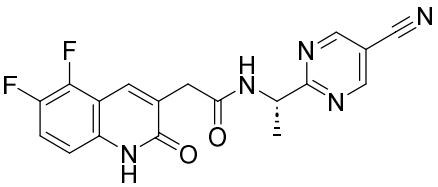
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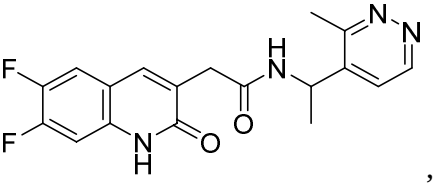
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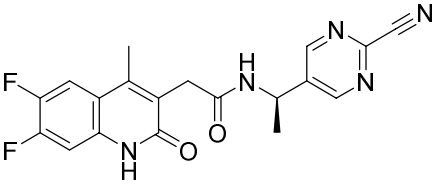
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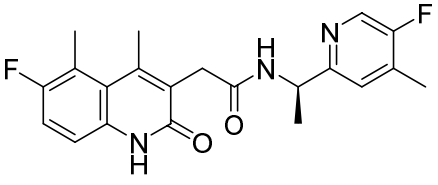
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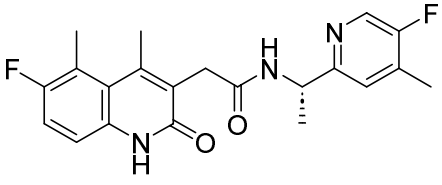
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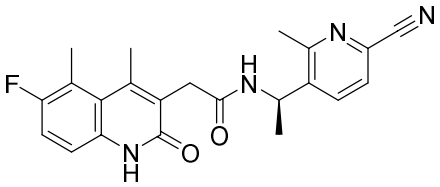
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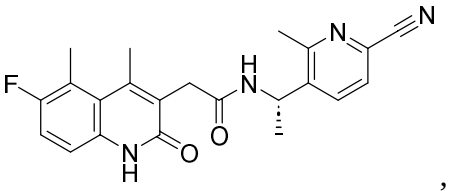
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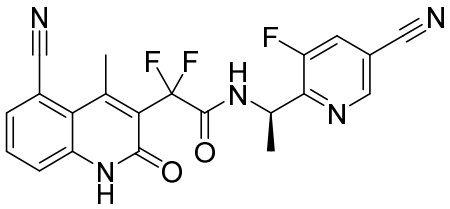
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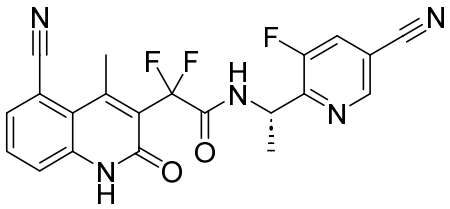
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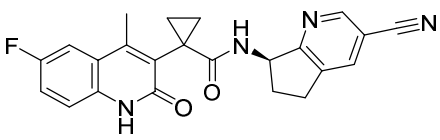
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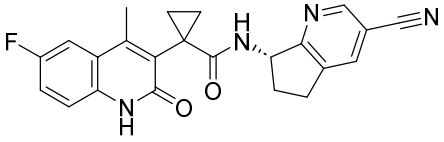
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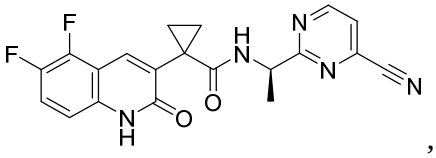
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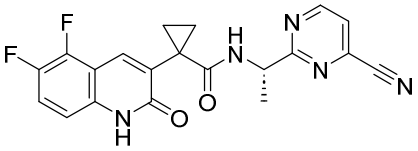
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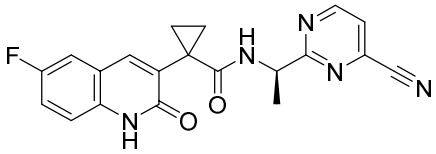
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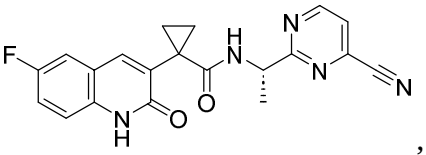
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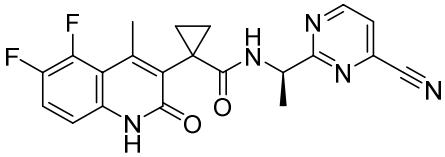
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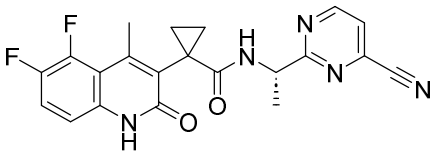
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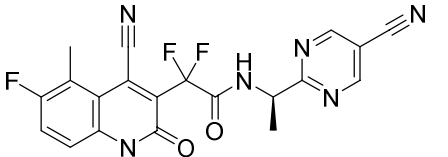
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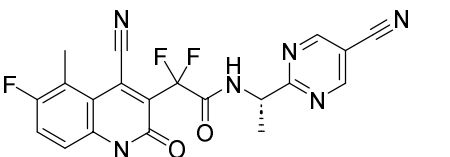
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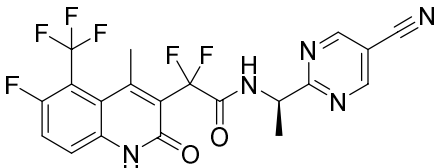
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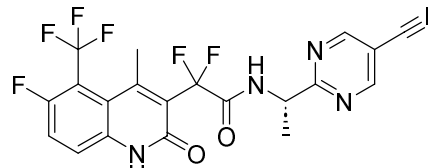
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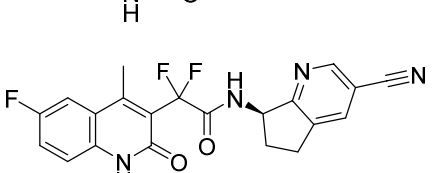
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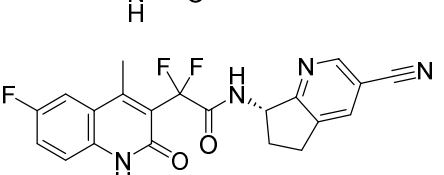
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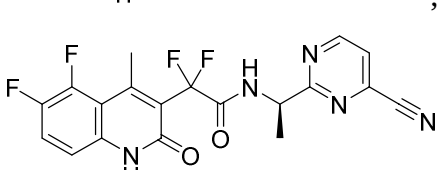
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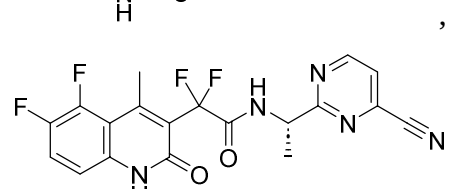
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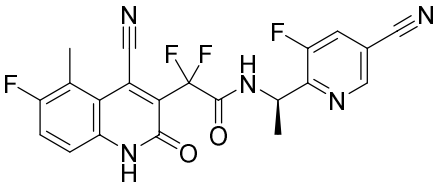
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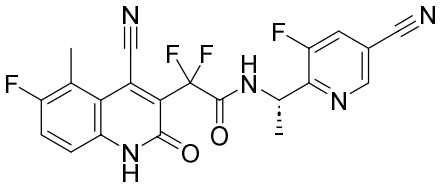
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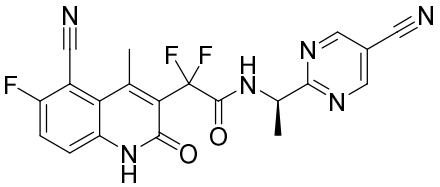
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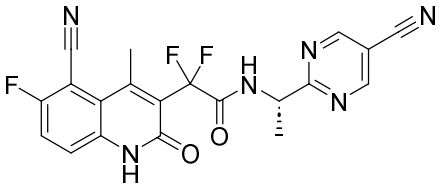
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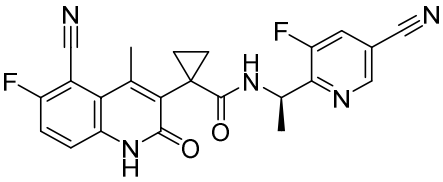
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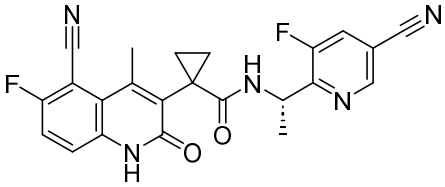
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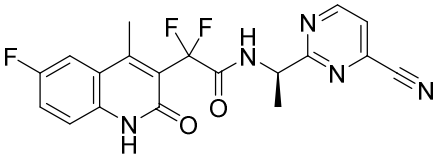
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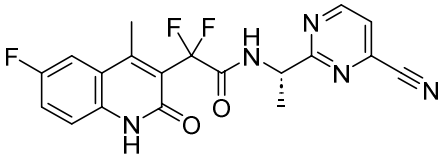
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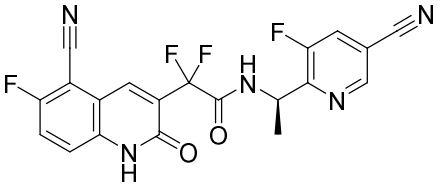
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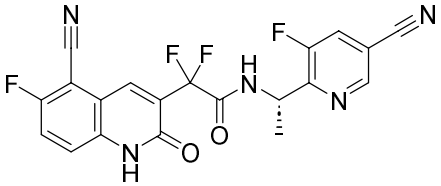
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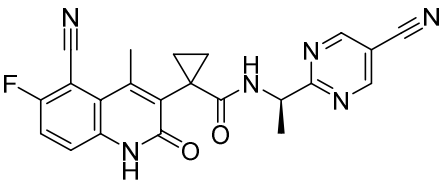
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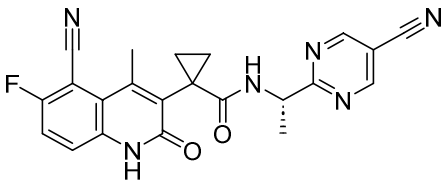
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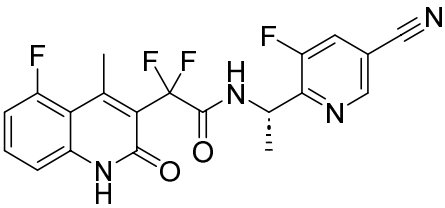
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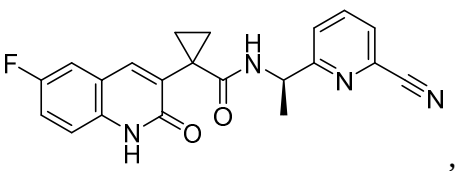
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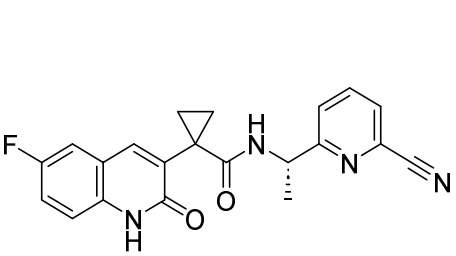
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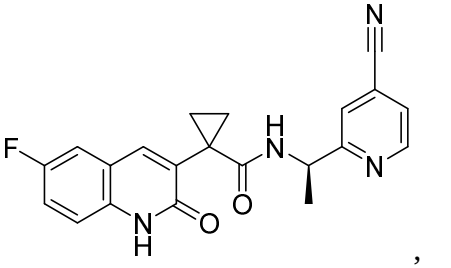
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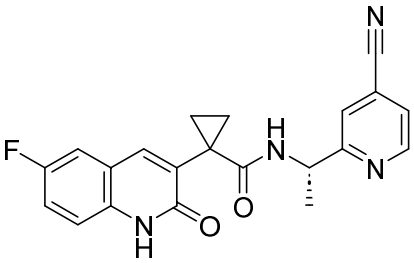
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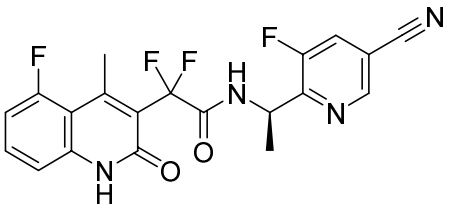
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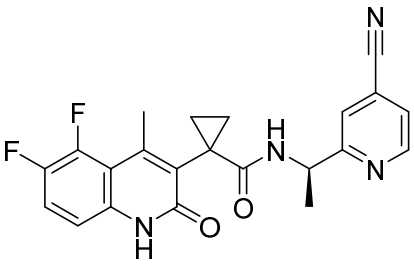
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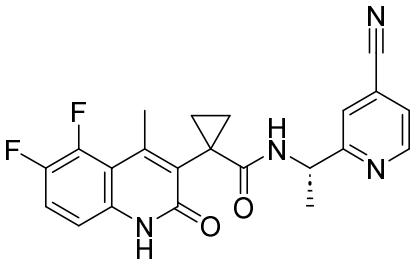
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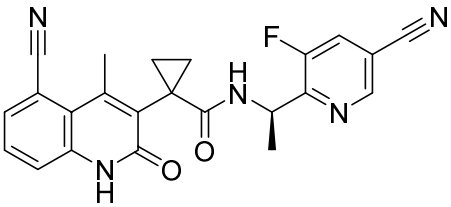
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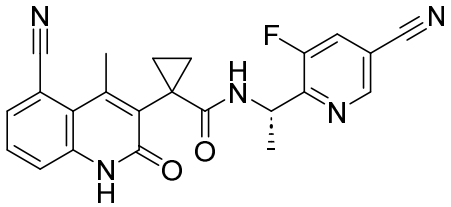
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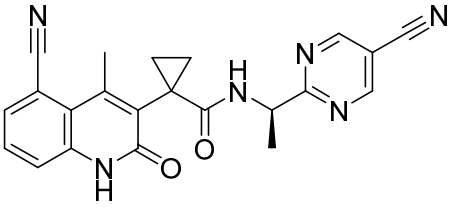
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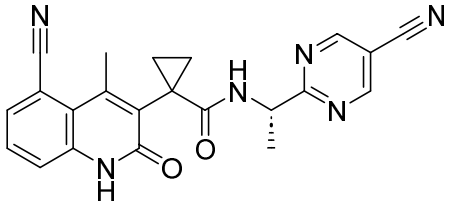
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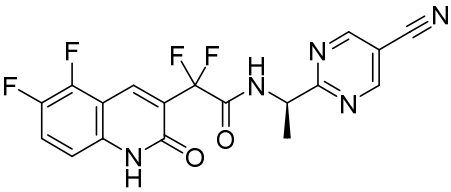
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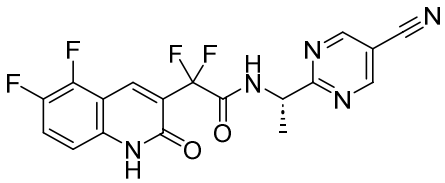
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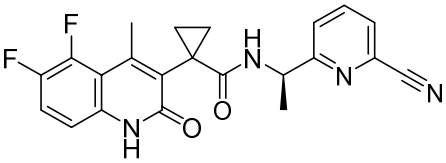
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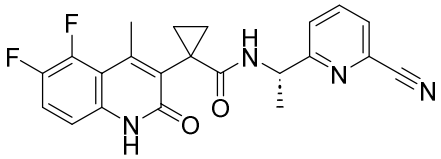
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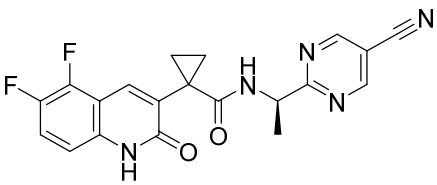
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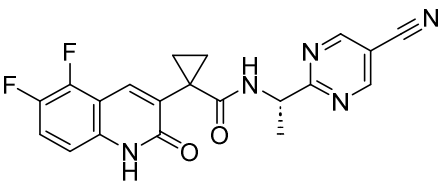
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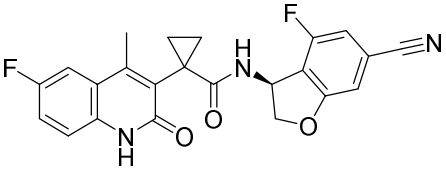
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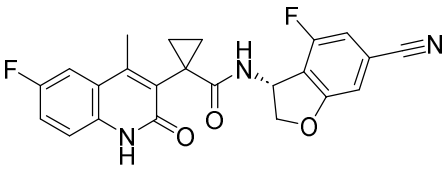
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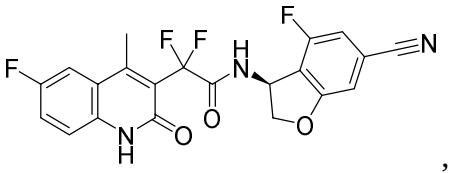
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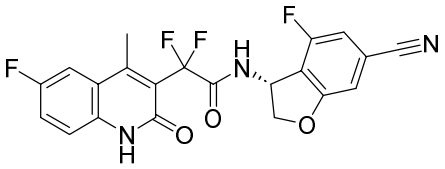
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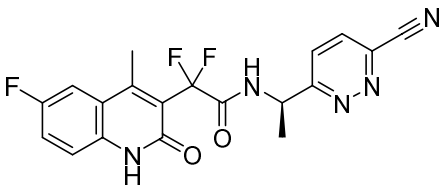
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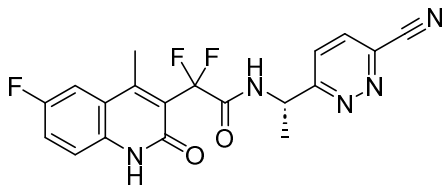
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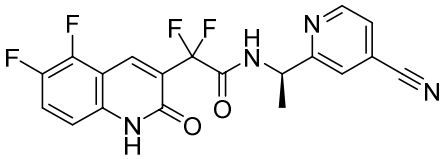
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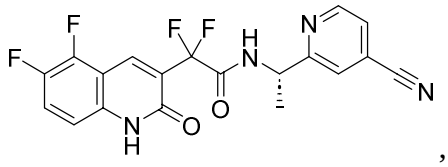
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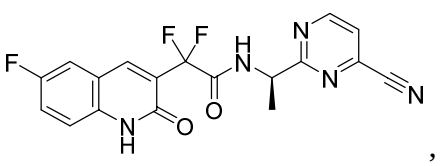
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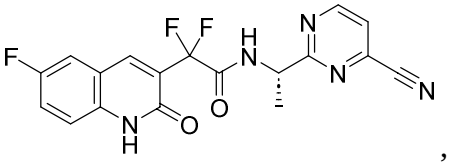
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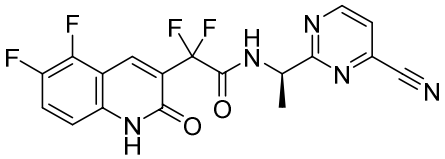
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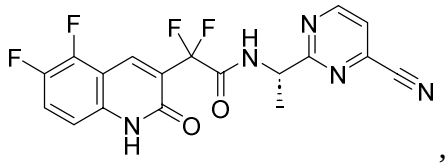
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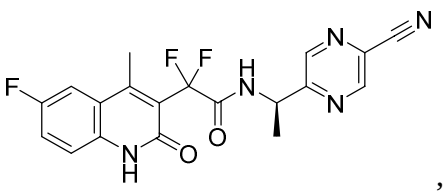
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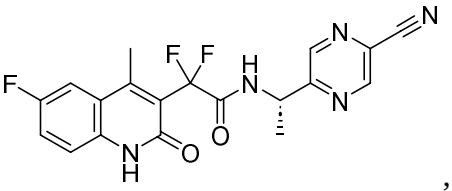
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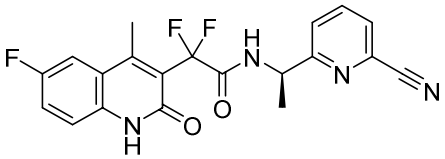
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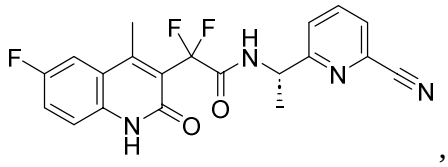
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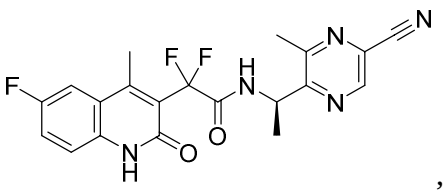
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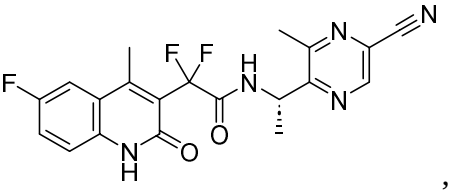
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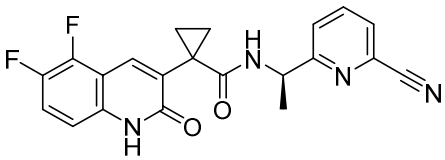
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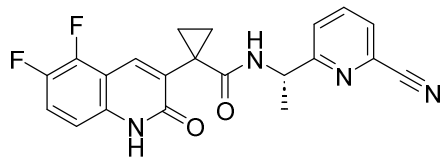
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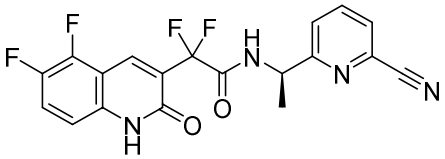
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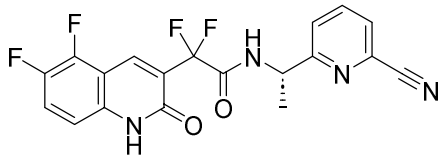
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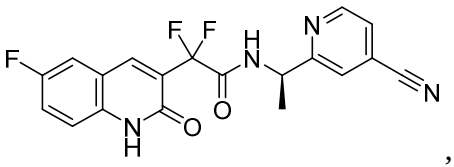
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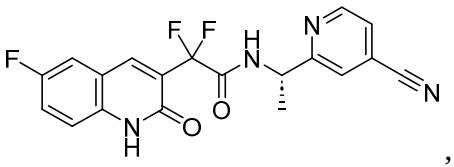
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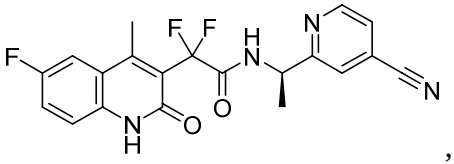
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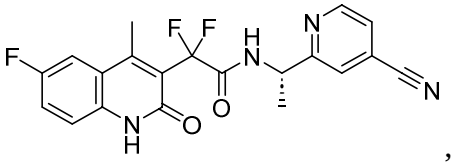
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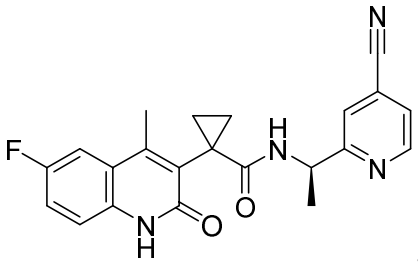
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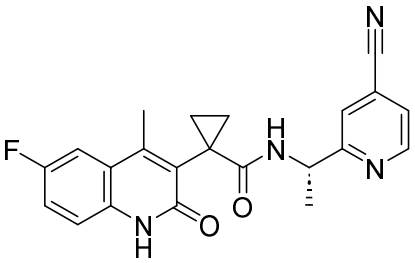
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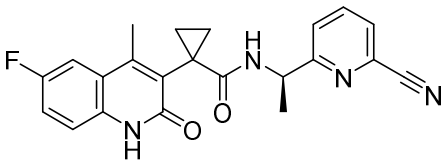
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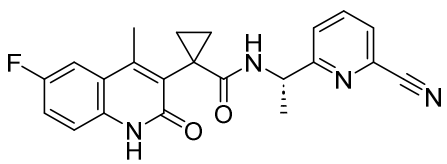
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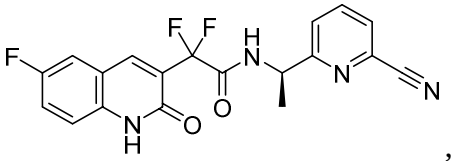
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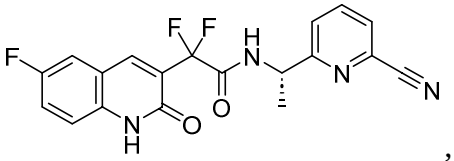
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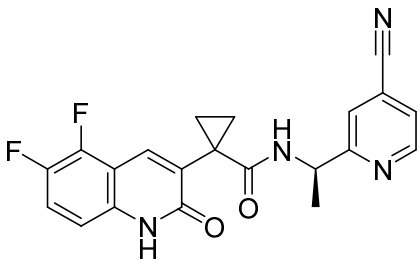
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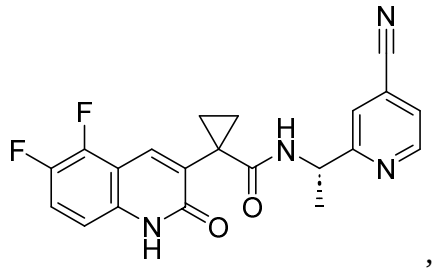
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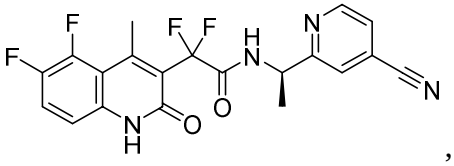
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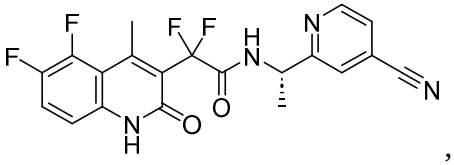
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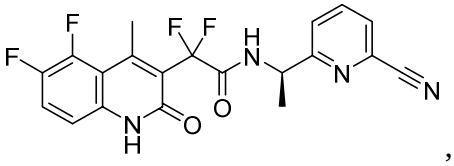
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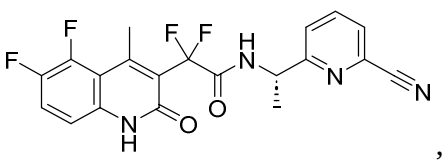
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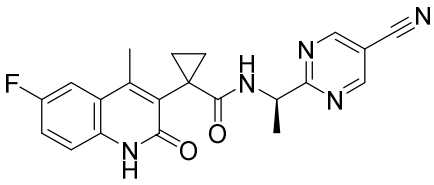
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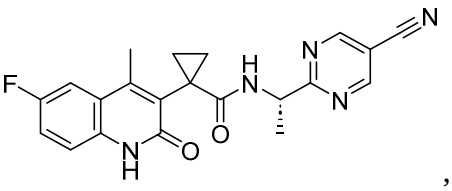
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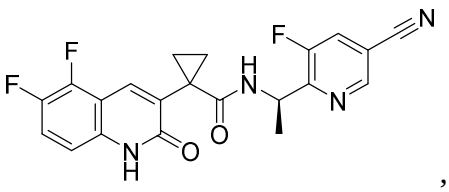
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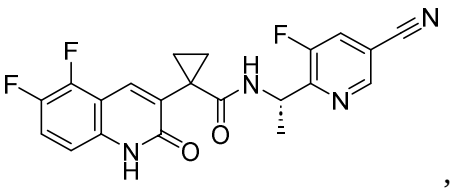
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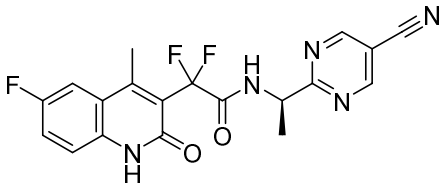
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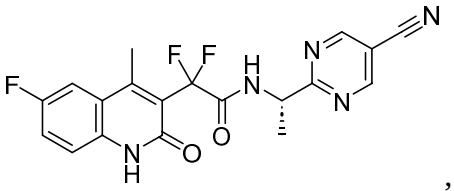
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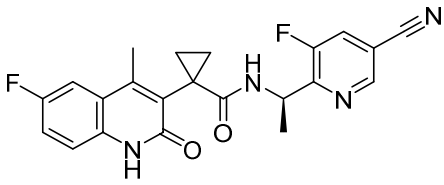
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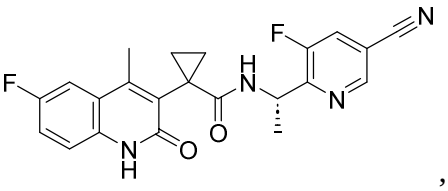
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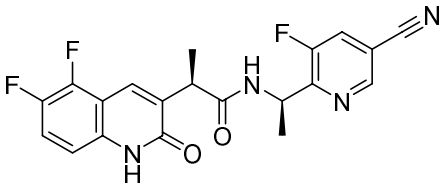
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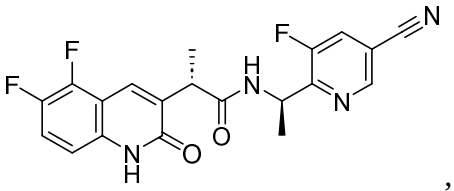
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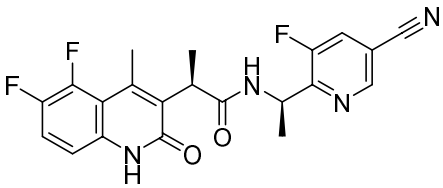
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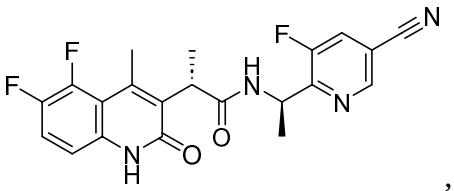
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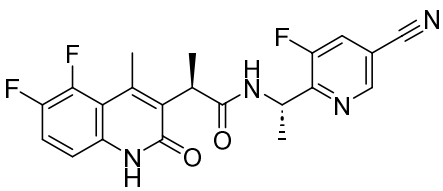
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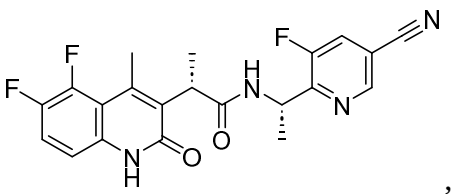
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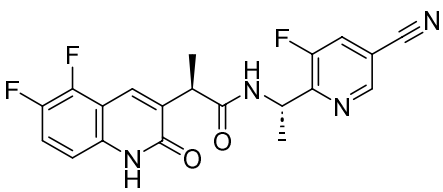
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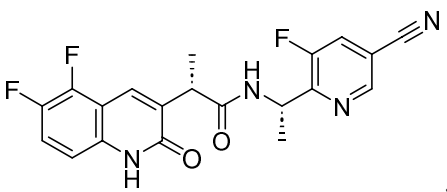
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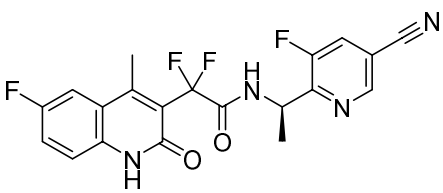
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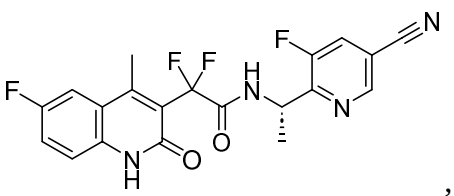
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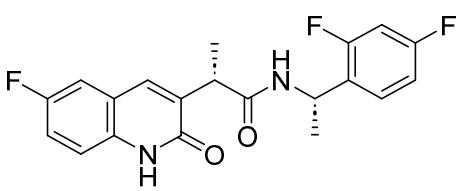
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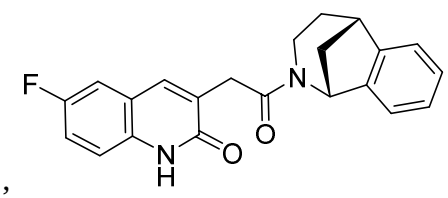
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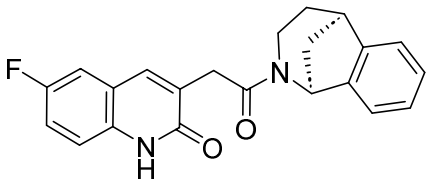
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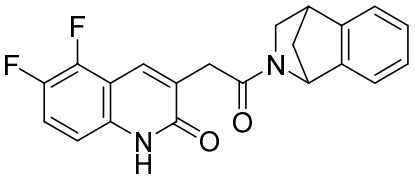
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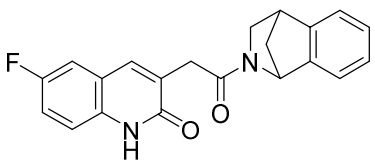
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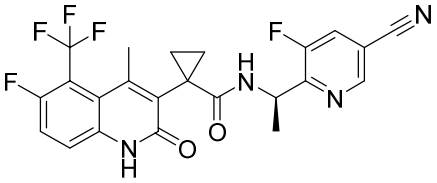
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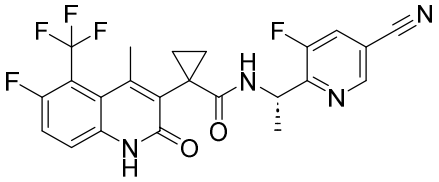
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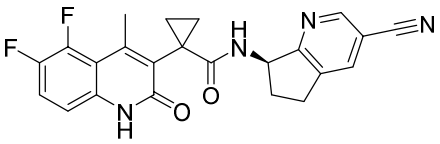
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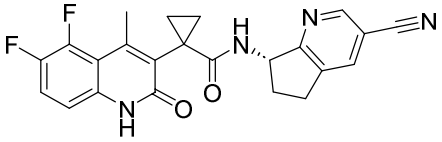
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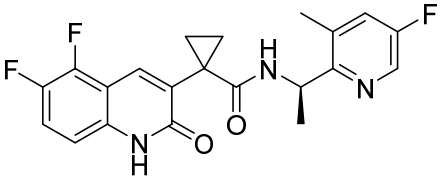
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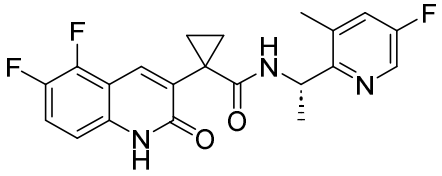
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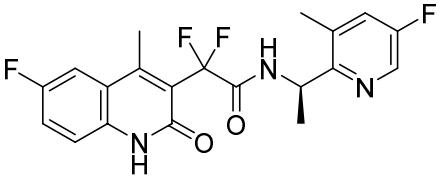
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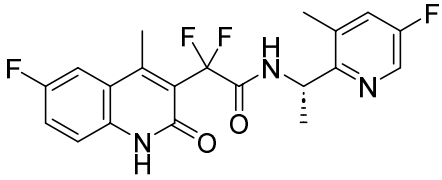
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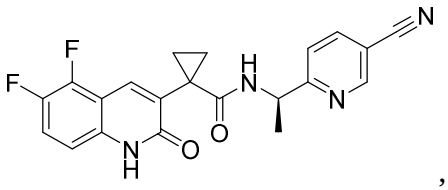
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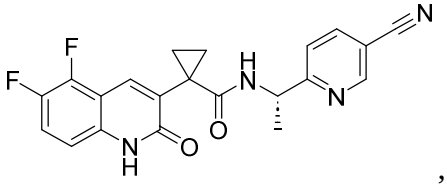
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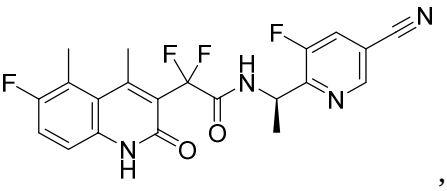
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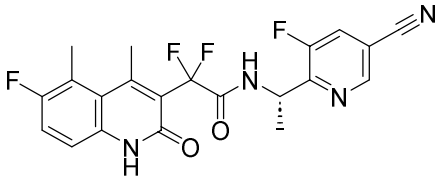
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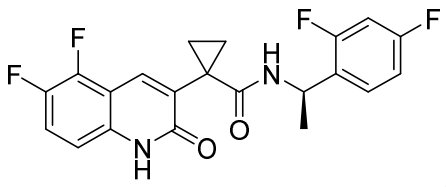
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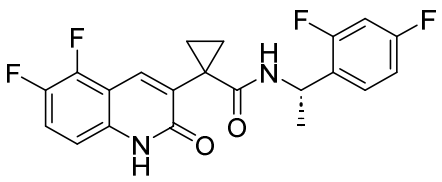
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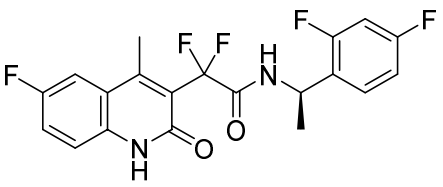
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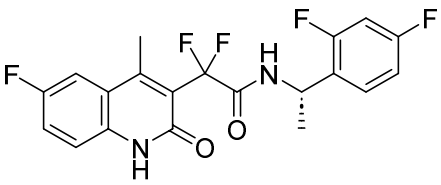
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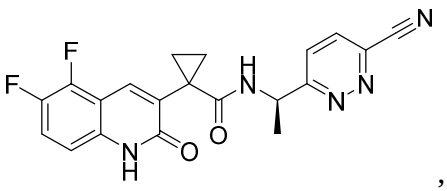
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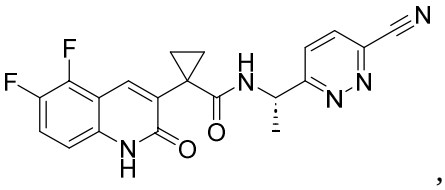
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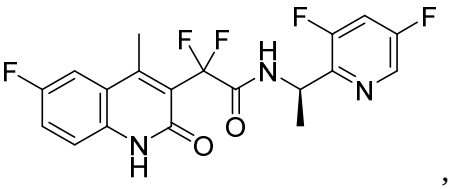
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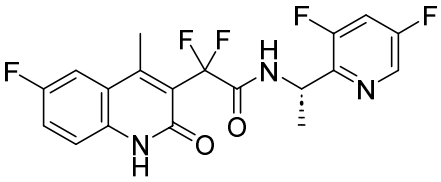
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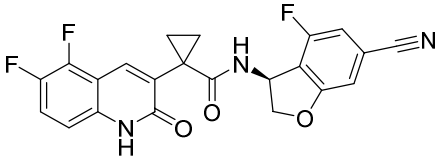
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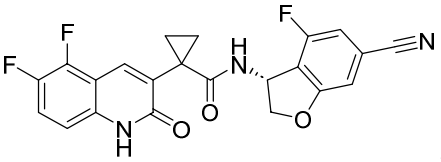
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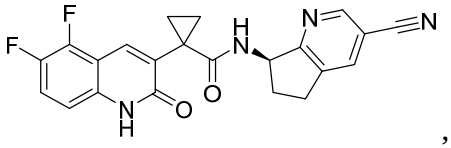
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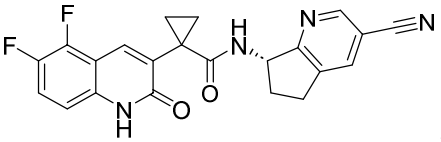
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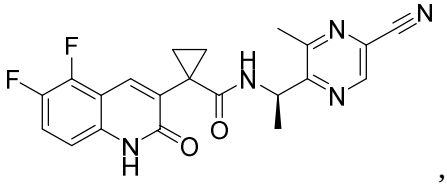
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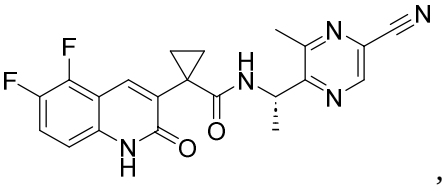
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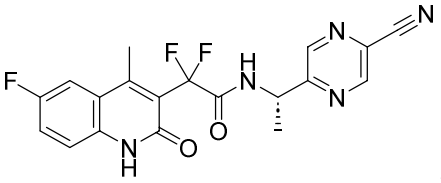
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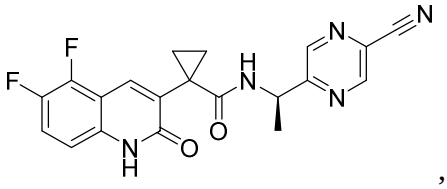
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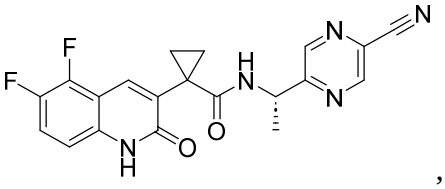
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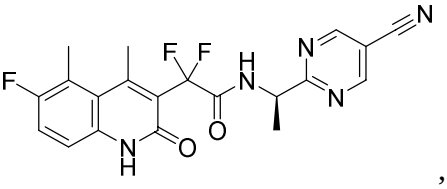
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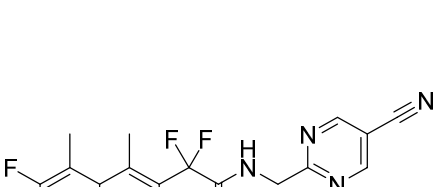
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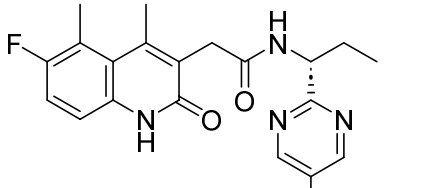
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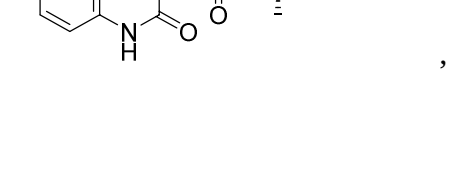
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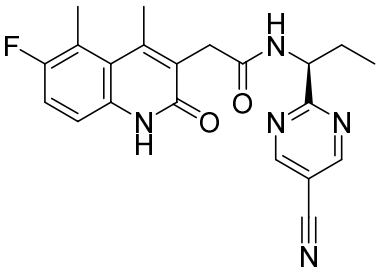
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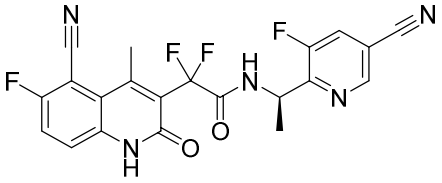
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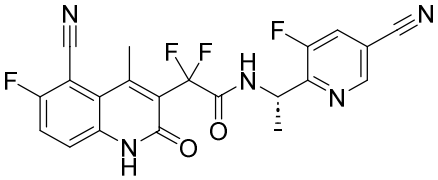
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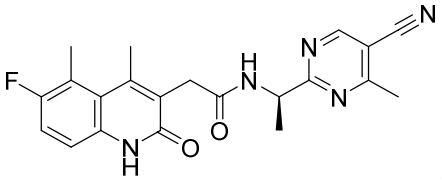
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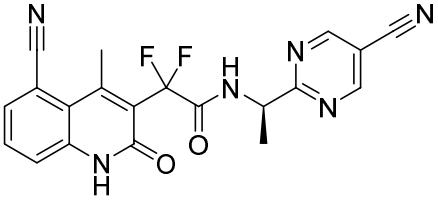
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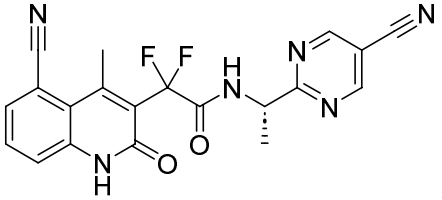
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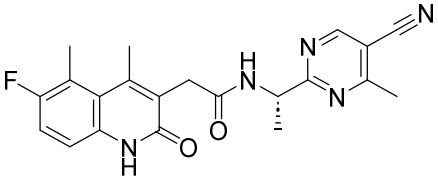
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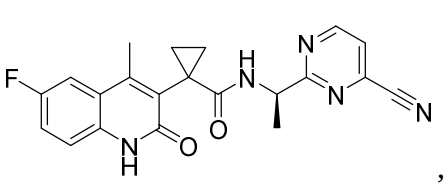
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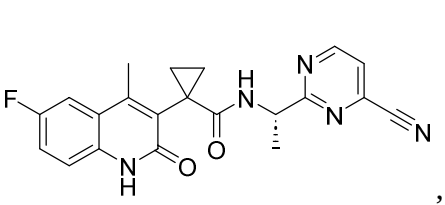
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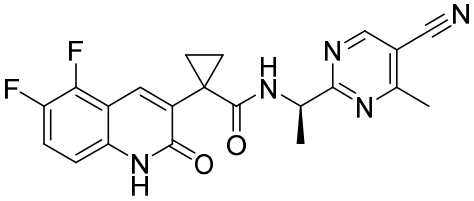
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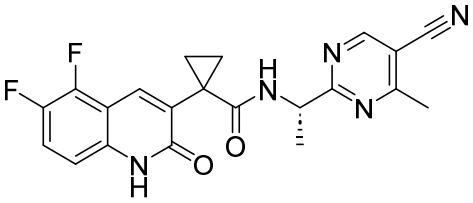
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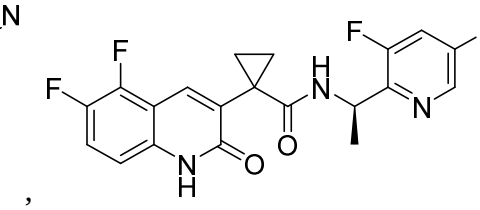
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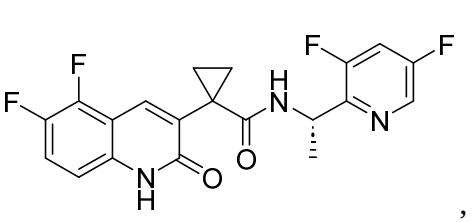
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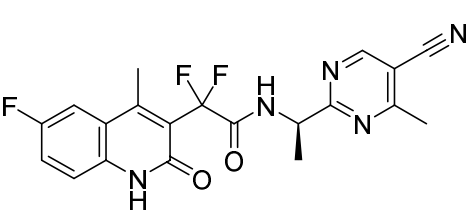
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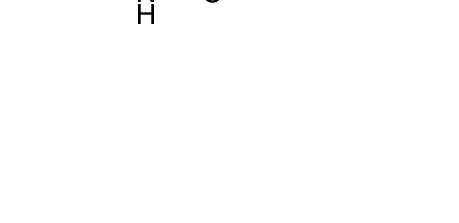
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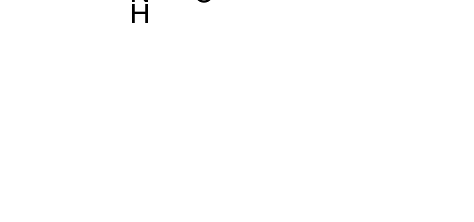
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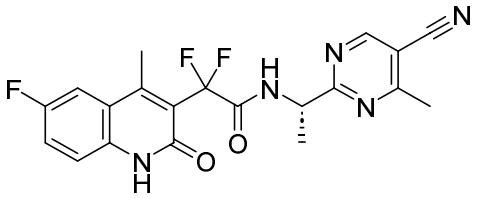
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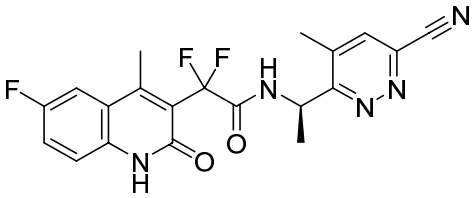
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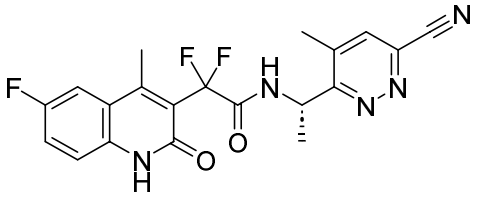
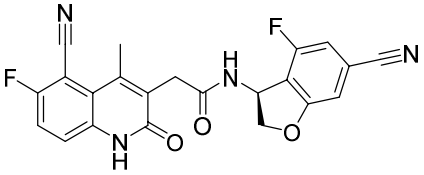

, or a salt of any one thereof.

45. The compound or salt of claim 17, selected from:

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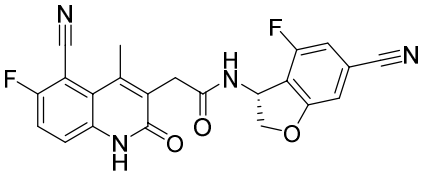
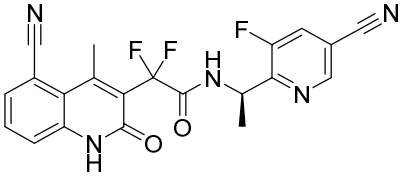
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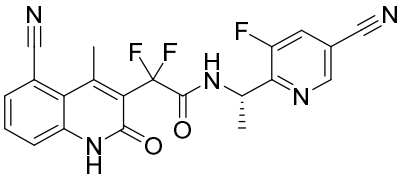
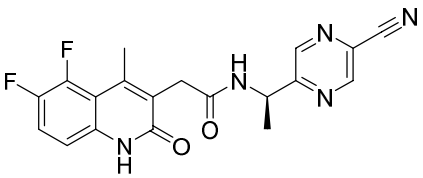
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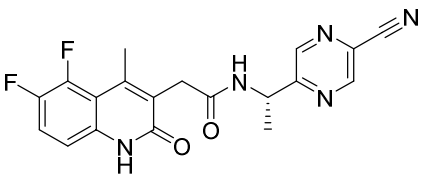
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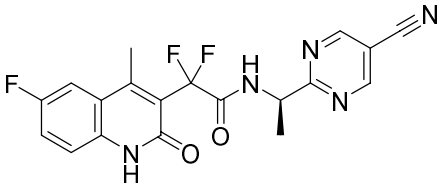
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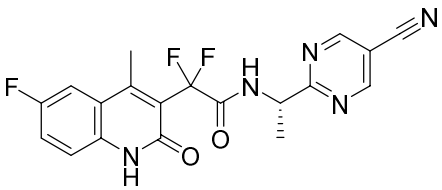
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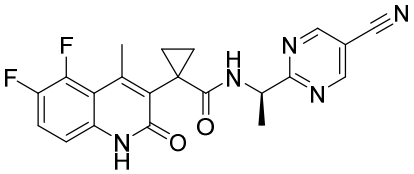
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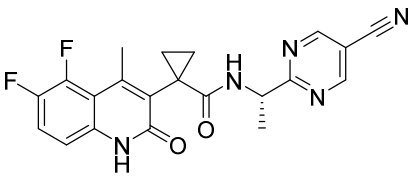
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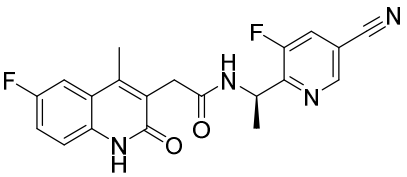
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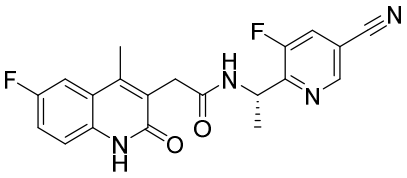
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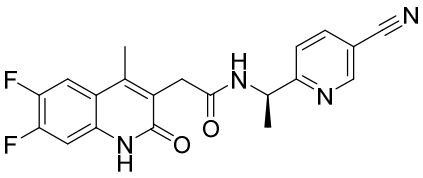
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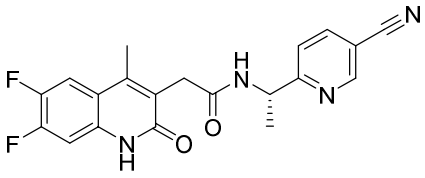
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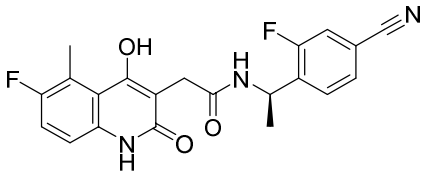
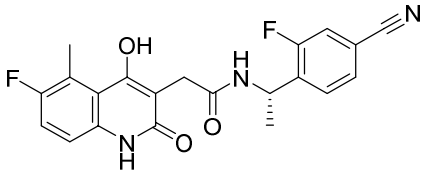
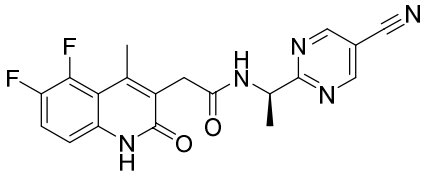
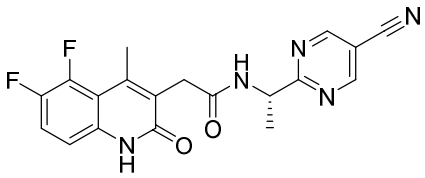

, and


, or a salt of any one thereof.

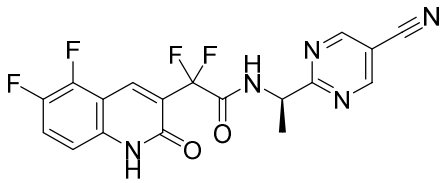
46. The compound or salt of claim 17, wherein the compound is


or a salt thereof.

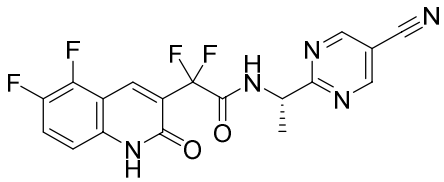
47. The compound or salt of claim 17, wherein the compound is


or a salt thereof.

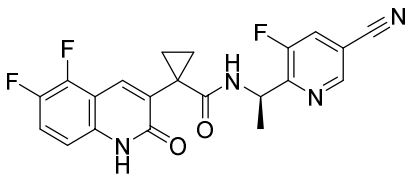
48. The compound or salt of claim 17, wherein the compound is


or a salt thereof.

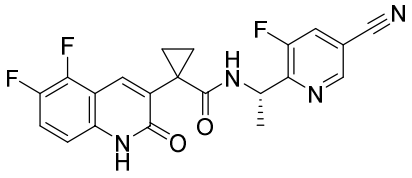
49. The compound or salt of claim 17, wherein the compound is


or a salt thereof.

50. The compound or salt of claim 17, wherein the compound is

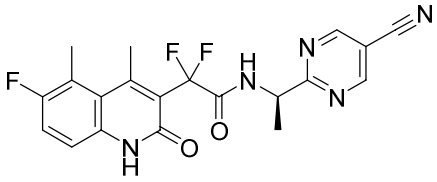

or a salt thereof.

51. The compound or salt of claim 17, wherein the compound is



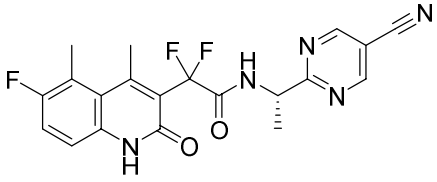
or a salt thereof.

52. The compound or salt of claim 17, wherein the compound is



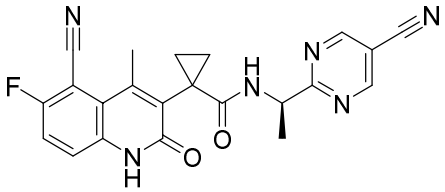
or a salt thereof.

53. The compound or salt of claim 17, wherein the compound is



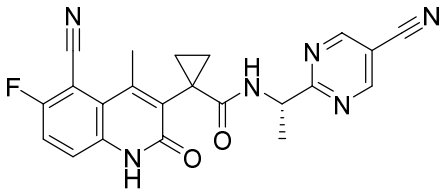
or a salt thereof.

54. The compound or salt of claim 17, wherein the compound is



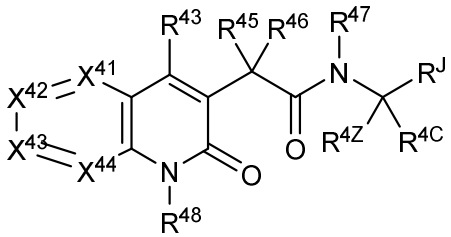
or a salt thereof.

55. The compound or salt of claim 17, wherein the compound is



or a salt thereof.

56. A compound represented by Formula (IV):



(IV);

or a salt thereof, wherein:

R^J is a 3- to 10-membered heterocycle, wherein the 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410b}$, $-SR^{410b}$, $-N(R^{410b})_2$, $-C(O)R^{410b}$, $-C(O)N(R^{410b})_2$, $-N(R^{410b})C(O)R^{410b}$, $-N(R^{410b})C(O)N(R^{410b})_2$, $-OC(O)N(R^{410b})_2$, $-N(R^{410b})C(O)OR^{410b}$, $-C(O)OR^{410b}$, -

$OC(O)R^{410b}$, $-S(O)R^{410b}$, $-S(O)_2R^{410b}$, $-NO_2$, =O, =S, $=N(R^{410b})$, $-N_3$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{49a};

X^{41} is selected from $C(R^{41a})$ and N;

X^{42} is selected from $C(R^{41b})$ and N;

X^{43} is selected from $C(R^{41c})$ and N;

X^{44} is selected from $C(R^{41d})$ and N;

wherein no more than two of X^{41}, X^{42}, X^{43}, and X^{44} are N;

R^{41a}, R^{41b}, R^{41c}, and R^{41d} are each independently selected from:

hydrogen;

halogen, $-NO_2$, $-N_3$, -CN, $-OR^{410a}$, $-SR^{410a}$, $-N(R^{410a})_2$, $-C(O)R^{410a}$, $-C(O)N(R^{410a})_2$, $-N(R^{410a})C(O)R^{410a}$, $-N(R^{410a})C(O)N(R^{410a})_2$, $-OC(O)N(R^{410a})_2$, $-N(R^{410a})C(O)OR^{410a}$, $-C(O)OR^{410a}$, $-OC(O)R^{410a}$, $-S(O)R^{410a}$, and $-S(O)_2R^{410a}$;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410a}$, $-SR^{410a}$, $-N(R^{410a})_2$, $-C(O)R^{410a}$, $-C(O)N(R^{410a})_2$, $-N(R^{410a})C(O)R^{410a}$, $-C(O)OR^{410a}$, $-OC(O)R^{410a}$, $-N(R^{410a})C(O)N(R^{410a})_2$, $-OC(O)N(R^{410a})_2$, $-N(R^{410a})C(O)OR^{410a}$, $-S(O)R^{410a}$, $-S(O)_2R^{410a}$, $-NO_2$, =O, =S, $=N(R^{410a})$, $-N_3$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{49a}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410a}$, $-SR^{410a}$, $-N(R^{410a})_2$, $-C(O)R^{410a}$, $-C(O)N(R^{410a})_2$, $-N(R^{410a})C(O)R^{410a}$, $-N(R^{410a})C(O)N(R^{410a})_2$, $-OC(O)N(R^{410a})_2$, $-N(R^{410a})C(O)OR^{410a}$, $-C(O)OR^{410a}$, $-OC(O)R^{410a}$, $-S(O)R^{410a}$, $-S(O)_2R^{410a}$, $-NO_2$, =O, =S, $=N(R^{410a})$, $-N_3$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{49a};

wherein when X^{41} is C(H), X^{42} is C(H), and X^{43} is C(H); then R^{41d} is not hydrogen;

R^{43} is selected from:

hydrogen, halogen, $-OR^{410x}$, $-SR^{410x}$, $-N(R^{410x})_2$, $-NO_2$, -CN, C_{1-6} alkyl, C_{3-10} carbocycle and 3- to 10-membered heterocycle, wherein each C_{1-6} alkyl, C_{3-10} carbocycle,

and 3- to 10- membered heterocycle is optionally substituted with one or more substituents independently selected from R^{47e};

R^{4Z} is selected from:

$-C(O)R^{410z}$, $-C(O)N(R^{410z})_2$, $-C(O)OR^{410z}$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410z}$, $-SR^{410z}$, $-N(R^{410z})_2$, $-C(O)R^{410z}$, $-C(O)N(R^{410z})_2$, $-N(R^{410z})C(O)R^{410z}$, $-C(O)OR^{410z}$, $-OC(O)R^{410z}$, $-N(R^{410z})C(O)N(R^{410z})_2$, $-OC(O)N(R^{410z})_2$, $-N(R^{410z})C(O)OR^{410z}$, $-S(O)R^{410z}$, $-S(O)_2R^{410z}$, $-NO_2$, =O, =S, $=N(R^{410z})$, $-N_3$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{49z}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410z}$, $-SR^{410z}$, $-N(R^{410z})_2$, $-C(O)R^{410z}$, $-C(O)N(R^{410z})_2$, $-N(R^{410z})C(O)R^{410z}$, $-N(R^{410z})C(O)N(R^{410z})_2$, $-OC(O)N(R^{410z})_2$, $-N(R^{410z})C(O)OR^{410z}$, $-C(O)OR^{410z}$, $-OC(O)R^{410z}$, $-S(O)R^{410z}$, $-S(O)_2R^{410z}$, $-NO_2$, =O, =S, $=N(R^{410z})$, $-N_3$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{49z};

R^{4C} is selected from:

hydrogen;

$-C(O)R^{410c}$, $-C(O)N(R^{410c})_2$, $-C(O)OR^{410c}$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410c}$, $-SR^{410c}$, $-N(R^{410c})_2$, $-C(O)R^{410c}$, $-C(O)N(R^{410c})_2$, $-N(R^{410c})C(O)R^{410c}$, $-C(O)OR^{410c}$, $-OC(O)R^{410c}$, $-N(R^{410c})C(O)N(R^{410c})_2$, $-OC(O)N(R^{410c})_2$, $-N(R^{410c})C(O)OR^{410c}$, $-S(O)R^{410c}$, $-S(O)_2R^{410c}$, $-NO_2$, =O, =S, $=N(R^{410c})$, $-N_3$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{49c}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410c}$, $-SR^{410c}$, $-N(R^{410c})_2$, $-C(O)R^{410c}$, $-C(O)N(R^{410c})_2$, $-N(R^{410c})C(O)R^{410c}$, -

$N(R^{410c})C(O)N(R^{410c})_2$, $-OC(O)N(R^{410c})_2$, $-N(R^{410c})C(O)OR^{410c}$, $-C(O)OR^{410c}$, $-OC(O)R^{410c}$, $-S(O)R^{410c}$, $-S(O)_2R^{410c}$, $-NO_2$, =O, =S, $=N(R^{410c})$, $-N_3$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{49c};

R^{45} is selected from:

hydrogen;

halogen, $-OR^{410d}$, $-SR^{410d}$, $-N(R^{410d})_2$, $-C(O)R^{410d}$, $-C(O)N(R^{410d})_2$, $-N(R^{410d})C(O)R^{410d}$, $-C(O)OR^{410d}$, $-OC(O)R^{410d}$, $-N(R^{410d})C(O)N(R^{410d})_2$, $-OC(O)N(R^{410d})_2$, $-N(R^{410d})C(O)OR^{410d}$, $-S(O)R^{410d}$, $-S(O)_2R^{410d}$, $-NO_2$, $-N_3$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410d}$, $-SR^{410d}$, $-N(R^{410d})_2$, $-C(O)R^{410d}$, $-C(O)N(R^{410d})_2$, $-N(R^{410d})C(O)R^{410d}$, $-C(O)OR^{410d}$, $-OC(O)R^{410d}$, $-N(R^{410d})C(O)N(R^{410d})_2$, $-OC(O)N(R^{410d})_2$, $-N(R^{410d})C(O)OR^{410d}$, $-S(O)R^{410d}$, $-S(O)_2R^{410d}$, $-NO_2$, =O, =S, $=N(R^{410d})$, $-N_3$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{49d}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410d}$, $-SR^{410d}$, $-N(R^{410d})_2$, $-C(O)R^{410d}$, $-C(O)N(R^{410d})_2$, $-N(R^{410d})C(O)R^{410d}$, $-N(R^{410d})C(O)N(R^{410d})_2$, $-OC(O)N(R^{410d})_2$, $-N(R^{410d})C(O)OR^{410d}$, $-C(O)OR^{410d}$, $-OC(O)R^{410d}$, $-S(O)R^{410d}$, $-S(O)_2R^{410d}$, $-NO_2$, =O, =S, $=N(R^{410d})$, $-N_3$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more R^{49d}; or

R^{45} together with R^{46} form a 3- to 10- membered heterocycle or C_{3-10} carbocycle, wherein the 3- to 10- membered heterocycle or C_{3-10} carbocycle is optionally substituted with one or more R^{49d};

R^{46} is selected from:

hydrogen;

halogen, $-OR^{410e}$, $-SR^{410e}$, $-N(R^{410e})_2$, $-C(O)R^{410e}$, $-C(O)N(R^{410e})_2$, $-N(R^{410e})C(O)R^{410e}$, $-C(O)OR^{410e}$, $-OC(O)R^{410e}$, $-N(R^{410e})C(O)N(R^{410e})_2$, $-OC(O)N(R^{410e})_2$, $-N(R^{410e})C(O)OR^{410e}$, $-S(O)R^{410e}$, $-S(O)_2R^{410e}$, $-NO_2$, $-N_3$, and -CN;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410e}$, $-SR^{410e}$, $-N(R^{410e})_2$, $-C(O)R^{410e}$, $-C(O)N(R^{410e})_2$, $-N(R^{410e})C(O)R^{410e}$, $-C(O)OR^{410e}$, $-OC(O)R^{410e}$, $-N(R^{410e})C(O)N(R^{410e})_2$, $-OC(O)N(R^{410e})_2$, $-N(R^{410e})C(O)OR^{410e}$, $-S(O)R^{410e}$, $-S(O)_2R^{410e}$, $-NO_2$, =O, =S, $=N(R^{410e})$, $-N_3$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{49e}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410e}$, $-SR^{410e}$, $-N(R^{410e})_2$, $-C(O)R^{410e}$, $-C(O)N(R^{410e})_2$, $-N(R^{410e})C(O)R^{410e}$, $-N(R^{410e})C(O)N(R^{410e})_2$, $-OC(O)N(R^{410e})_2$, $-N(R^{410e})C(O)OR^{410e}$, $-C(O)OR^{410e}$, $-OC(O)R^{410e}$, $-S(O)R^{410e}$, $-S(O)_2R^{410e}$, $-NO_2$, =O, =S, $=N(R^{410e})$, $-N_3$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{49e};

R^{47} is selected from:

hydrogen;

$-C(O)R^{410f}$, $-C(O)N(R^{410f})_2$, $-C(O)OR^{410f}$, $-S(O)R^{410f}$, and $-S(O)_2R^{410f}$;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{410f}$, $-SR^{410f}$, $-N(R^{410f})_2$, $-C(O)R^{410f}$, $-C(O)N(R^{410f})_2$, $-N(R^{410f})C(O)R^{410f}$, $-C(O)OR^{410f}$, $-OC(O)R^{410f}$, $-N(R^{410f})C(O)N(R^{410f})_2$, $-OC(O)N(R^{410f})_2$, $-N(R^{410f})C(O)OR^{410f}$, $-S(O)R^{410f}$, $-S(O)_2R^{410f}$, $-NO_2$, =O, =S, $=N(R^{410f})$, $-N_3$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{49f}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410f}$, $-SR^{410f}$, $-N(R^{410f})_2$, $-C(O)R^{410f}$, $-C(O)N(R^{410f})_2$, $-N(R^{410f})C(O)R^{410f}$, $-N(R^{410f})C(O)N(R^{410f})_2$, $-OC(O)N(R^{410f})_2$, $-N(R^{410f})C(O)OR^{410f}$, $-C(O)OR^{410f}$, $-OC(O)R^{410f}$, $-S(O)R^{410f}$, $-S(O)_2R^{410f}$, $-NO_2$, =O, =S, $=N(R^{410f})$, $-N_3$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{49f};

each R^{47e} is independently selected from:

halogen, $-OR^{410y}$, $-SR^{410y}$, $-N(R^{410y})_2$, $-C(O)R^{410y}$, $-C(O)N(R^{410y})_2$, $-N(R^{410y})C(O)R^{410y}$, $-N(R^{410y})C(O)N(R^{410y})_2$, $-OC(O)N(R^{410y})_2$, $-N(R^{410y})C(O)OR^{410y}$, $-C(O)OR^{410y}$, $-OC(O)R^{410y}$, $-S(O)R^{410y}$, $-S(O)_2R^{410y}$, $-NO_2$, =O, =S, $=N(R^{410y})$, and -CN; and

C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410y}$, $-SR^{410y}$, $-N(R^{410y})_2$, $-C(O)R^{410y}$, $-C(O)N(R^{410y})_2$, $-N(R^{410y})C(O)R^{410y}$, $-N(R^{410y})C(O)N(R^{410y})_2$, $-OC(O)N(R^{410y})_2$, $-N(R^{410y})C(O)OR^{410y}$, $-C(O)OR^{410y}$, $-OC(O)R^{410y}$, $-S(O)R^{410y}$, $-S(O)_2R^{410y}$, $-NO_2$, =O, =S, $=N(R^{410y})$, and -CN;

R^{48} is selected from:

hydrogen;

$-C(O)R^{410g}$, $-C(O)N(R^{410g})_2$, $-C(O)OR^{410g}$, $-S(O)R^{410g}$, and $-S(O)_2R^{410g}$;

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{410g}$, $-SR^{410g}$, $-N(R^{410g})_2$, $-C(O)R^{410g}$, $-C(O)N(R^{410g})_2$, $-N(R^{410g})C(O)R^{410g}$, $-C(O)OR^{410g}$, $-OC(O)R^{410g}$, $-N(R^{410g})C(O)N(R^{410g})_2$, $-OC(O)N(R^{410g})_2$, $-N(R^{410g})C(O)OR^{410g}$, $-S(O)R^{410g}$, $-S(O)_2R^{410g}$, $-NO_2$, =O, =S, $=N(R^{410g})$, $-N_3$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{49g}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410g}$, $-SR^{410g}$, $-N(R^{410g})_2$, $-C(O)R^{410g}$, $-C(O)N(R^{410g})_2$, $-N(R^{410g})C(O)R^{410g}$, $-N(R^{410g})C(O)N(R^{410g})_2$, $-OC(O)N(R^{410g})_2$, $-N(R^{410g})C(O)OR^{410g}$, $-C(O)OR^{410g}$, $-OC(O)R^{410g}$, $-S(O)R^{410g}$, $-S(O)_2R^{410g}$, $-NO_2$, =O, =S, $=N(R^{410g})$, $-N_3$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{49g};

each R^{49a} is independently selected from:

halogen, $-OR^{410a}$, $-SR^{410a}$, $-N(R^{410a})_2$, $-C(O)R^{410a}$, $-C(O)N(R^{410a})_2$, $-N(R^{410a})C(O)R^{410a}$, $-N(R^{410a})C(O)N(R^{410a})_2$, $-OC(O)N(R^{410a})_2$, $-N(R^{410a})C(O)OR^{410a}$, $-C(O)OR^{410a}$, $-OC(O)R^{410a}$, $-S(O)R^{410a}$, $-S(O)_2R^{410a}$, $-NO_2$, =O, =S, $=N(R^{410a})$, $-N_3$, and -CN; and

C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410a}$, $-SR^{410a}$, $-N(R^{410a})_2$, $-C(O)R^{410a}$, $-C(O)N(R^{410a})_2$, $-N(R^{410a})C(O)R^{410a}$, $-N(R^{410a})C(O)N(R^{410a})_2$,

-OC(O)N(R^{410a})$_2$, -N(R^{410a})C(O)OR^{410a}, -C(O)OR^{410a}, -OC(O)R^{410a}, -S(O)R^{410a}, -S(O)$_2$$R^{410a}$, -$NO_2$, =O, =S, =N($R^{410a}$), -$N_3$, and -CN;

each R^{49z} is independently selected from:

halogen, -OR^{410z}, -SR^{410z}, -N(R^{410z})$_2$, -C(O)R^{410z}, -C(O)N(R^{410z})$_2$, -N(R^{410z})C(O)R^{410z}, -N(R^{410z})C(O)N(R^{410z})$_2$, -OC(O)N(R^{410z})$_2$, -N(R^{410z})C(O)OR^{410z}, -C(O)OR^{410z}, -OC(O)R^{410z}, -S(O)R^{410z}, -S(O)$_2$$R^{410z}$, -$NO_2$, =O, =S, =N($R^{410z}$), -$N_3$, and -CN; and

C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{410z}, -SR^{410z}, -N(R^{410z})$_2$, -C(O)R^{410z}, -C(O)N(R^{410z})$_2$, -N(R^{410z})C(O)R^{410z}, -N(R^{410z})C(O)N(R^{410z})$_2$, -OC(O)N(R^{410z})$_2$, -N(R^{410z})C(O)OR^{410z}, -C(O)OR^{410z}, -OC(O)R^{410z}, -S(O)R^{410z}, -S(O)$_2$$R^{410z}$, -$NO_2$, =O, =S, =N($R^{410z}$), -$N_3$, and -CN;

each R^{49c} is independently selected from:

halogen, -OR^{410c}, -SR^{410c}, -N(R^{410c})$_2$, -C(O)R^{410c}, -C(O)N(R^{410c})$_2$, -N(R^{410c})C(O)R^{410c}, -N(R^{410c})C(O)N(R^{410c})$_2$, -OC(O)N(R^{410c})$_2$, -N(R^{410c})C(O)OR^{410c}, -C(O)OR^{410c}, -OC(O)R^{410c}, -S(O)R^{410c}, -S(O)$_2$$R^{410c}$, -$NO_2$, =O, =S, =N($R^{410c}$), -$N_3$, and -CN; and

C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{410c}, -SR^{410c}, -N(R^{410c})$_2$, -C(O)R^{410c}, -C(O)N(R^{410c})$_2$, -N(R^{410c})C(O)R^{410c}, -N(R^{410c})C(O)N(R^{410c})$_2$, -OC(O)N(R^{410c})$_2$, -N(R^{410c})C(O)OR^{410c}, -C(O)OR^{410c}, -OC(O)R^{410c}, -S(O)R^{410c}, -S(O)$_2$$R^{410c}$, -$NO_2$, =O, =S, =N($R^{410c}$), -$N_3$, and -CN;

each R^{49d} is independently selected from:

halogen, -OR^{410d}, -SR^{410d}, -N(R^{410d})$_2$, -C(O)R^{410d}, -C(O)N(R^{410d})$_2$, -N(R^{410d})C(O)R^{410d}, -N(R^{410d})C(O)N(R^{410d})$_2$, -OC(O)N(R^{410d})$_2$, -N(R^{410d})C(O)OR^{410d}, -C(O)OR^{410d}, -OC(O)R^{410d}, -S(O)R^{410d}, -S(O)$_2$$R^{410d}$, -$NO_2$, =O, =S, =N($R^{410d}$), -$N_3$, and -CN; and

C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -OR^{410d}, -SR^{410d}, -N(R^{410d})$_2$, -C(O)R^{410d}, -C(O)N(R^{410d})$_2$, -N(R^{410d})C(O)R^{410d}, -N(R^{410d})C(O)N(R^{410d})$_2$, -OC(O)N(R^{410d})$_2$, -N(R^{410d})C(O)OR^{410d}, -C(O)OR^{410d}, -OC(O)R^{410d}, -S(O)R^{410d}, -S(O)$_2$$R^{410d}$, -$NO_2$, =O, =S, =N($R^{410d}$), -$N_3$, and -CN;

each R^{49e} is independently selected from:

halogen, -OR^{410e}, -SR^{410e}, -N(R^{410e})$_2$, -C(O)R^{410e}, -C(O)N(R^{410e})$_2$, -N(R^{410e})C(O)R^{410e}, -N(R^{410e})C(O)N(R^{410e})$_2$, -OC(O)N(R^{410e})$_2$, -N(R^{410e})C(O)OR^{410e}, -C(O)OR^{410e}, -OC(O)R^{410e}, -S(O)R^{410e}, -S(O)$_2$$R^{410e}$, -$NO_2$, =O, =S, =N($R^{410e}$), -$N_3$, and -CN; and

C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410e}$, $-SR^{410e}$, $-N(R^{410e})_2$, $-C(O)R^{410e}$, $-C(O)N(R^{410e})_2$, $-N(R^{410e})C(O)R^{410e}$, $-N(R^{410e})C(O)N(R^{410e})_2$, $-OC(O)N(R^{410e})_2$, $-N(R^{410e})C(O)OR^{410e}$, $-C(O)OR^{410e}$, $-OC(O)R^{410e}$, $-S(O)R^{410e}$, $-S(O)_2R^{410e}$, $-NO_2$, =O, =S, $=N(R^{410e})$, $-N_3$, and -CN;

each R^{49f} is independently selected from:

halogen, $-OR^{410f}$, $-SR^{410f}$, $-N(R^{410f})_2$, $-C(O)R^{410f}$, $-C(O)N(R^{410f})_2$, $-N(R^{410f})C(O)R^{410f}$, $-N(R^{410f})C(O)N(R^{410f})_2$, $-OC(O)N(R^{410f})_2$, $-N(R^{410f})C(O)OR^{410f}$, $-C(O)OR^{410f}$, $-OC(O)R^{410f}$, $-S(O)R^{410f}$, $-S(O)_2R^{410f}$, $-NO_2$, =O, =S, $=N(R^{410f})$, $-N_3$, and -CN; and

C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410f}$, $-SR^{410f}$, $-N(R^{410f})_2$, $-C(O)R^{410f}$, $-C(O)N(R^{410f})_2$, $-N(R^{410f})C(O)R^{410f}$, $-N(R^{410f})C(O)N(R^{410f})_2$, $-OC(O)N(R^{410f})_2$, $-N(R^{410f})C(O)OR^{410f}$, $-C(O)OR^{410f}$, $-OC(O)R^{410f}$, $-S(O)R^{410f}$, $-S(O)_2R^{410f}$, $-NO_2$, =O, =S, $=N(R^{410f})$, $-N_3$, and -CN;

each R^{49g} is independently selected from:

halogen, $-OR^{410g}$, $-SR^{410g}$, $-N(R^{410g})_2$, $-C(O)R^{410g}$, $-C(O)N(R^{410g})_2$, $-N(R^{410g})C(O)R^{410g}$, $-N(R^{410g})C(O)N(R^{410g})_2$, $-OC(O)N(R^{410g})_2$, $-N(R^{410g})C(O)OR^{410g}$, $-C(O)OR^{410g}$, $-OC(O)R^{410g}$, $-S(O)R^{410g}$, $-S(O)_2R^{410g}$, $-NO_2$, =O, =S, $=N(R^{410g})$, $-N_3$, and -CN; and

C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410g}$, $-SR^{410g}$, $-N(R^{410g})_2$, $-C(O)R^{410g}$, $-C(O)N(R^{410g})_2$, $-N(R^{410g})C(O)R^{410g}$, $-N(R^{410g})C(O)N(R^{410g})_2$, $-OC(O)N(R^{410g})_2$, $-N(R^{410g})C(O)OR^{410g}$, $-C(O)OR^{410g}$, $-OC(O)R^{410g}$, $-S(O)R^{410g}$, $-S(O)_2R^{410g}$, $-NO_2$, =O, =S, $=N(R^{410g})$, $-N_3$, and -CN; and

each R^{410a}, R^{410b}, R^{410c}, R^{410d}, R^{410e}, R^{410f}, R^{410g}, R^{410x}, R^{410y} and R^{410z} is independently selected from:

hydrogen;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, $-NO_2$, $-NH_2$, =O, =S, -O-C_{1-6} alkyl, -S-C_{1-6} alkyl, $-N(C_{1-6}$ alkyl$)_2$, $-NH(C_{1-6}$ alkyl), C_{3-10} carbocycle, 3- to 10-membered heterocycle; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, $-NO_2$, $-NH_2$, =O, =S, -O-C_{1-6} alkyl, -S-C_{1-6} alkyl, $-N(C_{1-6}$ alkyl$)_2$, -

$NH(C_{1-6}$ alkyl), C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, and C_{1-6} haloalkyl.

57. The compound or salt of claim 56, wherein

X^{41} is $C(R^{41a})$;

X^{42} is $C(R^{41b})$;

X^{43} is $C(R^{41c})$; and

X^{44} is $C(R^{41d})$.

58. The compound or salt of claim 56 or 57, wherein:

(i) X^{41} is C(F), X^{42} is C(F), X^{43} is C(H), and X^{44} is C(H); or

(ii) X^{41} is C(H), X^{42} is C(F), X^{43} is C(H), and X^{44} is C(H).

59. The compound or salt of any one of claim 56 to 58, wherein

(i) R^{41a}, R^{41b}, R^{41c}, and R^{41d} are each independently selected from: hydrogen, -F, -Cl, -OH, and -CN; and

(ii) each R^{410b}, R^{410y}, and R^{410z} is independently selected from: hydrogen, methyl, ethyl, propyl, isopropyl, cyclopropyl, isobutyl, $-CF_3$, $-CH_2CF_3$, $-CH_2CHF_2$, $-CH_2C(F)(Me)_2$, and $-CH_2$-phenyl; and

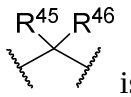
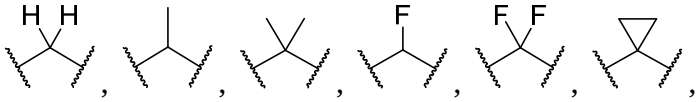
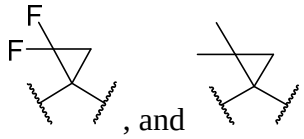
(iii) R^{4Z} is methyl, $-CH_2OH$, $-CH_2CH_2OH$, $-C(Me)_2OH$, or $-CH_2OMe$; and

(iv) R^{4C} is hydrogen; and

(v) R^{47} is hydrogen; and

(vi) R^{43} is selected from: hydrogen and CH_3; and

(vii) R^{48} is selected from: hydrogen and methyl; and

(viii)  is selected from:  ,  , and .

60. The compound or salt of any one of claims 56 to 59, wherein R^{4Z} is methyl, and R^{48} is selected from: hydrogen.

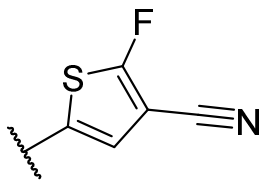
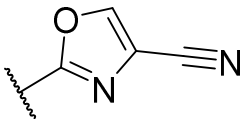
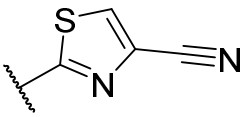
61. The compound or salt of any one of claims 56 to 60, wherein R^J is a 5- to 10-membered heteroaryl optionally substituted with one or more substituents independently selected from halogen, $-OR^{410b}$, $-SR^{410b}$, $-N(R^{410b})_2$, $-C(O)R^{410b}$, $-C(O)N(R^{410b})_2$, $-N(R^{410b})C(O)R^{410b}$, $-N(R^{410b})C(O)N(R^{410b})_2$, $-OC(O)N(R^{410b})_2$, $-N(R^{410b})C(O)OR^{410b}$, $-C(O)OR^{410b}$, $-OC(O)R^{410b}$, $-S(O)R^{410b}$, $-S(O)_2R^{410b}$, $-NO_2$, =O, =S,

$=N(R^{410b})$, $-N_3$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more R^{49a}.

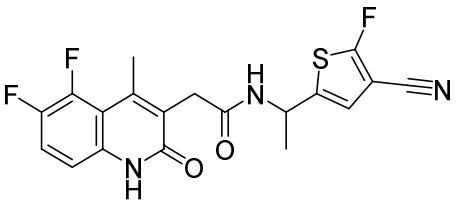
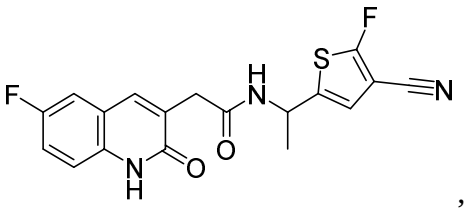
62. The compound or salt of any one of claims 56 to 61, wherein R^J is a 5-membered heteroaryl optionally substituted with one or more substituents independently selected from halogen, $-OR^{410b}$, $-SR^{410b}$, $-N(R^{410b})_2$, $-C(O)R^{410b}$, $-C(O)N(R^{410b})_2$, $-N(R^{410b})C(O)R^{410b}$, $-N(R^{410b})C(O)N(R^{410b})_2$, $-OC(O)N(R^{410b})_2$, $-N(R^{410b})C(O)OR^{410b}$, $-C(O)OR^{410b}$, $-OC(O)R^{410b}$, $-S(O)R^{410b}$, $-S(O)_2R^{410b}$, $-NO_2$, =O, =S, $=N(R^{410b})$, $-N_3$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more R^{49a}.

63. The compound or salt of any one of claims 59 to 73, wherein R^J is a thiophene, thiazole, thiadiazole, furan, isoxazole, oxazole, oxadiazole, pyrrole, pyrazole, imidazole, or triazole, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{410b}$, $-N(R^{410b})_2$, $-C(O)R^{410b}$, $-C(O)N(R^{410b})_2$, $-N(R^{410b})C(O)R^{410b}$, $-OC(O)N(R^{410b})_2$, $-C(O)OR^{410b}$, $-OC(O)R^{410b}$, =O, =S, $=N(R^{410b})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{49a}.

64. The compound or salt of any one of claims 56 to 63, wherein R^J is selected from:


, 
, and 
.

65. The compound or salt of claim 56, selected from:


, 
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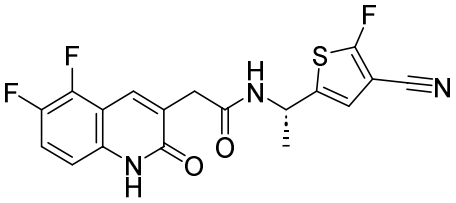
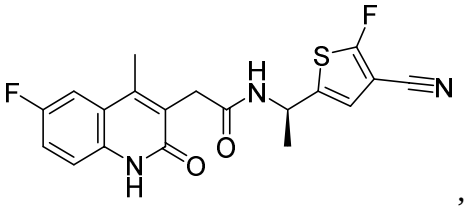

, 
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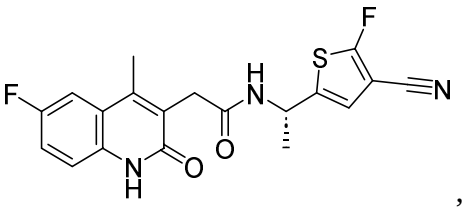
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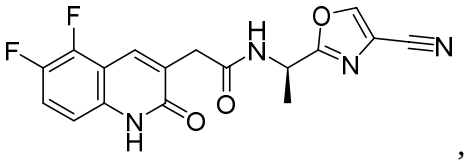
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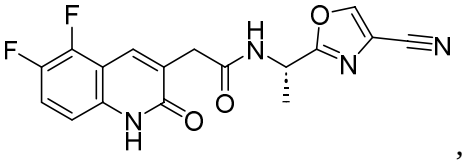
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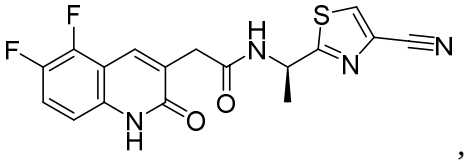
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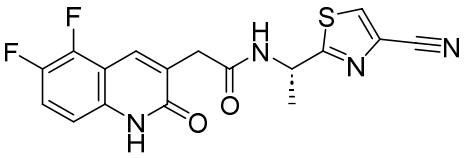
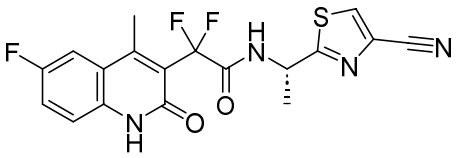
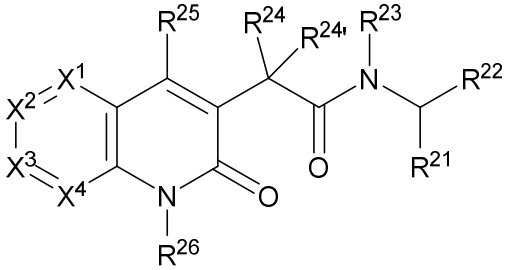

, and

, or a salt of any one thereof.

66. The compound of any one of claims 1 to 65 for use as a medicament.

67. Use of the compound of any one of claims 1 to 65 in the manufacture of a medicament for treating cardiovascular disease or a related condition.

68. A pharmaceutical composition comprising the compound or salt of any one of claims 1 to 65 and a pharmaceutically acceptable excipient.

69. Use of a compound of Formula (III) in the manufacture of a medicament for treating a cardiovascular disease or related condition in an individual in need thereof:



Formula (III)

or a salt thereof, wherein:

X^1, X^2, X^3, and X^4 are each independently selected from C(R) and N, wherein no more than two of X^1, X^2, X^3, and X^4 are N;

each R is independently selected from:

hydrogen, halogen, $-NO_2$, -CN, $-N_3$, $-OR^{28}$, $-SR^{28}$, $-N(R^{28})_2$, $-C(O)R^{28}$, $-C(O)N(R^{28})_2$, $-N(R^{28})C(O)R^{28}$, $-N(R^{28})C(O)N(R^{28})_2$, $-OC(O)N(R^{28})_2$, $-N(R^{28})C(O)OR^{28}$, $-C(O)OR^{28}$, $-OC(O)R^{28}$, $-S(O)R^{28}$, and $-S(O)_2R^{28}$;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{28}$, $-SR^{28}$, $-N(R^{28})_2$, $-C(O)R^{28}$, $-C(O)N(R^{28})_2$, $-N(R^{28})C(O)R^{28}$, $-C(O)OR^{28}$, $-OC(O)R^{28}$, -

$N(R^{28})C(O)N(R^{28})_2$, $-OC(O)N(R^{28})_2$, $-N(R^{28})C(O)OR^{28}$, $-S(O)R^{28}$, $-S(O)_2R^{28}$, $-NO_2$, =O, =S, $=N(R^{28})$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{27}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{28}$, $-SR^{28}$, $-N(R^{28})_2$, $-C(O)R^{28}$, $-C(O)N(R^{28})_2$, $-N(R^{28})C(O)R^{28}$, $-N(R^{28})C(O)N(R^{28})_2$, $-OC(O)N(R^{28})_2$, $-N(R^{28})C(O)OR^{28}$, $-C(O)OR^{28}$, $-OC(O)R^{28}$, $-S(O)R^{28}$, $-S(O)_2R^{28}$, $-NO_2$, =O, =S, $=N(R^{28})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{27};

R^{21} is selected from:

hydrogen,

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{28a}$, $-SR^{28a}$, $-N(R^{28a})_2$, $-C(O)R^{28a}$, $-C(O)N(R^{28a})_2$, $-N(R^{28a})C(O)R^{28a}$, $-C(O)OR^{28a}$, $-OC(O)R^{28a}$, $-N(R^{28a})C(O)N(R^{28a})_2$, $-OC(O)N(R^{28a})_2$, $-N(R^{28a})C(O)OR^{28a}$, $-S(O)R^{28a}$, $-S(O)_2R^{28a}$, $-NO_2$, =O, =S, $=N(R^{28a})$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{27a}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{28a}$, $-SR^{28a}$, $-N(R^{28a})_2$, $-C(O)R^{28a}$, $-C(O)N(R^{28a})_2$, $-N(R^{28a})C(O)R^{28a}$, $-N(R^{28a})C(O)N(R^{28a})_2$, $-OC(O)N(R^{28a})_2$, $-N(R^{28a})C(O)OR^{28a}$, $-C(O)OR^{28a}$, $-OC(O)R^{28a}$, $-S(O)R^{28a}$, $-S(O)_2R^{28a}$, $-NO_2$, =O, =S, $=N(R^{28a})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{27a};

R^{22} is selected from:

hydrogen;

C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{28b}$, $-SR^{28b}$, $-C(O)R^{28b}$, $-C(O)N(R^{28b})_2$, $-N(R^{28b})C(O)R^{28b}$, $-C(O)OR^{28b}$, $-OC(O)R^{28b}$, $-N(R^{28b})C(O)N(R^{28b})_2$, $-OC(O)N(R^{28b})_2$, $-N(R^{28b})C(O)OR^{28b}$, $-S(O)R^{28b}$, $-S(O)_2R^{28b}$, $-NO_2$, =O, =S, $=N(R^{28b})$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein

each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{27b}; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{28b}$, $-SR^{28b}$, $-N(R^{28b})_2$, $-C(O)R^{28b}$, $-C(O)N(R^{28b})_2$, $-N(R^{28b})C(O)R^{28b}$, $-N(R^{28b})C(O)N(R^{28b})_2$, $-OC(O)N(R^{28b})_2$, $-N(R^{28b})C(O)OR^{28b}$, $-C(O)OR^{28b}$, $-OC(O)R^{28b}$, $-S(O)R^{28b}$, $-S(O)_2R^{28b}$, $-NO_2$, =O, =S, $=N(R^{28b})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{27b}; or

R^{21} together with R^{22} form a C_{3-10} carbocycle or 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{28a}$, $-SR^{28a}$, $-N(R^{28a})_2$, $-C(O)R^{28a}$, $-C(O)N(R^{28a})_2$, $-N(R^{28a})C(O)R^{28a}$, $-N(R^{28a})C(O)N(R^{28a})_2$, $-OC(O)N(R^{28a})_2$, $-N(R^{28a})C(O)OR^{28a}$, $-C(O)OR^{28a}$, $-OC(O)R^{28a}$, $-S(O)R^{28a}$, $-S(O)_2R^{28a}$, $-NO_2$, =O, =S, $=N(R^{28a})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{27b};

R^{23} is selected from:

hydrogen, halogen, $-OR^{28c}$, $-SR^{28c}$, $-N(R^{28c})_2$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from R^{27c}; or

R^{21} together with R^{23} form a 3- to 10-membered heterocycle, which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{28a}$, $-SR^{28a}$, $-N(R^{28a})_2$, $-C(O)R^{28a}$, $-C(O)N(R^{28a})_2$, $-N(R^{28a})C(O)R^{28a}$, $-N(R^{28a})C(O)N(R^{28a})_2$, $-OC(O)N(R^{28a})_2$, $-N(R^{28a})C(O)OR^{28a}$, $-C(O)OR^{28a}$, $-OC(O)R^{28a}$, $-S(O)R^{28a}$, $-S(O)_2R^{28a}$, $-NO_2$, =O, =S, $=N(R^{28a})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{27c}; or

R^{22} together with R^{23} form a C_{3-10} carbocycle or 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{28a}$, $-SR^{28a}$, $-N(R^{28a})_2$, $-C(O)R^{28a}$, $-C(O)N(R^{28a})_2$, $-N(R^{28a})C(O)R^{28a}$, $-N(R^{28a})C(O)N(R^{28a})_2$, $-OC(O)N(R^{28a})_2$, $-N(R^{28a})C(O)OR^{28a}$, $-C(O)OR^{28a}$, $-OC(O)R^{28a}$, $-S(O)R^{28a}$, $-S(O)_2R^{28a}$, $-NO_2$, =O–, =S, $=N(R^{28a})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6}

alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{27c}; or

R^{21}, R^{22}, and R^{23} together form a bicyclic heterocycle which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{28a}$, $-SR^{28a}$, $-N(R^{28a})_2$, $-C(O)R^{28a}$, $-C(O)N(R^{28a})_2$, $-N(R^{28a})C(O)R^{28a}$, $-N(R^{28a})C(O)N(R^{28a})_2$, $-OC(O)N(R^{28a})_2$, $-N(R^{28a})C(O)OR^{28a}$, $-C(O)OR^{28a}$, $-OC(O)R^{28a}$, $-S(O)R^{28a}$, $-S(O)_2R^{28a}$, $-NO_2$, =O, =S, $=N(R^{28a})$, -CN, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl, wherein each C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl is optionally substituted with one or more substituents independently selected from R^{27c};

R^{24} is selected from:

hydrogen, halogen, $-OR^{28d}$, $-SR^{28d}$, $-N(R^{28d})_2$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{28d}$, $-SR^{28d}$, $-N(R^{28d})_2$, $-NO_2$, -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{27d};

$R^{24'}$ is selected from:

hydrogen, halogen, $-OR^{28d}$, $-SR^{28d}$, $-N(R^{28d})_2$, $-NO_2$, and -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from halogen, $-OR^{28d}$, $-SR^{28d}$, $-N(R^{28d})_2$, $-NO_2$, and -CN, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{3-10} carbocycle and 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{27d};

or R^{24} and $R^{24'}$ together form a C_{3-10} carbocycle or 3- to 10-membered heterocycle, wherein the C_{3-10} carbocycle or 3- to 10-membered heterocycle is optionally substituted with one or more substituents independently selected from R^{27d};

R^{25} is selected from:

hydrogen, halogen, $-OR^{28e}$, $-SR^{28e}$, $-N(R^{28e})_2$, $-NO_2$, -CN, C_{1-6} alkyl, C_{3-10} carbocycle, and 3- to 10-membered heterocycle, wherein each C_{1-6} alkyl, C_{3-10} carbocycle, and 3- to 10- membered heterocycle is optionally substituted with one or more R^{27e};

R^{26} is selected from:

hydrogen, halogen, $-OR^{28f}$, $-SR^{28f}$, $-N(R^{28f})_2$, $-NO_2$, -CN; and

C_{1-6} alkyl optionally substituted with one or more substituents independently selected from R^{27f};

each R^{27}, R^{27a}, R^{27b}, R^{27c}, R^{27d}, R^{27e}, and R^{27f} is independently selected from:

halogen, $-OR^{28g}$, $-SR^{28g}$, $-N(R^{28g})_2$, $-C(O)R^{28g}$, $-C(O)N(R^{28g})_2$, $-N(R^{28g})C(O)R^{28g}$, $-N(R^{28g})C(O)N(R^{28g})_2$, $-OC(O)N(R^{28g})_2$, $-N(R^{28g})C(O)OR^{28g}$, $-C(O)OR^{28g}$, $-OC(O)R^{28g}$, $-S(O)R^{28g}$, $-S(O)_2R^{28g}$, $-NO_2$, =O, =S, $=N(R^{28g})$, and -CN; and

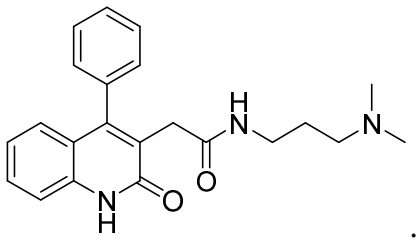
C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, each of which is optionally substituted with one or more substituents independently selected from halogen, $-OR^{28g}$, $-SR^{28g}$, $-N(R^{28g})_2$, $-C(O)R^{28g}$, $-C(O)N(R^{28g})_2$, $-N(R^{28g})C(O)R^{28g}$, $-N(R^{28g})C(O)N(R^{28g})_2$, $-OC(O)N(R^{28g})_2$, $-N(R^{28g})C(O)OR^{28g}$, $-C(O)OR^{28g}$, $-OC(O)R^{28g}$, $-S(O)R^{28g}$, $-S(O)_2R^{28g}$, $-NO_2$, =O, =S, $=N(R^{28g})$, and -CN; and

each R^{28}, R^{28a}, R^{28b}, R^{28c}, R^{28d}, R^{28e}, R^{28f}, and R^{28g} is independently selected from:

hydrogen and halogen;

C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{3-10} carbocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, $-NO_2$, $-NH_2$, =O, =S, -O-C_{1-6} alkyl, -S-C_{1-6} alkyl, $-N(C_{1-6}$ alkyl$)_2$, $-NH(C_{1-6}$ alkyl), C_{3-10} carbocycle, 3- to 10-membered heterocycle; and

C_{3-10} carbocycle and 3- to 10-membered heterocycle, each of which is optionally substituted with one or more substituents independently selected from halogen, -CN, -OH, -SH, $-NO_2$, $-NH_2$, =O, =S, -O-C_{1-6} alkyl, -S-C_{1-6} alkyl, $-SO_2$-C_{1-6} alkyl, $-N(C_{1-6}$ alkyl$)_2$, $-NH(C_{1-6}$ alkyl), C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} carbocycle, 3- to 10-membered heterocycle, and C_{1-6} haloalkyl;

provided the compound of Formula (III) is not  .

70. The use of claim 69, wherein R^{21} is methyl; and R^{22} is phenyl or 6-membered heteroaryl; and R^{26} is hydrogen; and R^{23} is hydrogen; and R^{24} is hydrogen; and $R^{24'}$ is hydrogen; and R^{25} is hydrogen or methyl.

71. The use of claim 67, 69 or 70, wherein the cardiovascular disease or related condition comprises one or more condition(s) selected from: heart failure with preserved ejection fraction (HFpEF), heart failure with mid-ranged ejection fraction (HFmrEF), heart failure

with reduced ejection fraction (HFrEF), cardiomyopathy, cardiac transplant allograft vasculopathy, valve disease, left ventricular (LV) hypertrophy, right ventricular (RV) hypertrophy, acute myocardial infarction, acute revascularization, abnormal heart rhythms, aorta disease, Marfan syndrome, coronary artery disease, heart attack, heart failure, rhematic heart disease, peripheral vascular disease, stroke, deep vein thrombosis, and pulmonary embolism.

72. The use of of claim 67, 69, 70, or 71, wherein the cardiovascular disease or related condition is obstructive hypertrophic cardiomyopathy.
73. The use of claim 67, 69, 70, or 71, wherein the cardiovascular disease or related condition is non-obstructive hypertrophic cardiomyopathy.
74. The use of claim 67, 69, 70, or 71, wherein the cardiovascular disease or related condition is heart failure with preserved ejection fraction (HFpEF).
75. The use of claim 74, wherein said heart failure with preserved ejection fraction (HFpEF) comprises disorders of relaxation.
76. The use of claim 74, wherein said heart failure with preserved ejection fraction (HFpEF) comprises disorders of chamber stiffness.
77. The use of claim 74, wherein said heart failure with preserved ejection fraction (HFpEF) comprises diabetic HFpEF.
78. The use of claim 67, 69, 70, or 71, wherein the cardiovascular disease or related condition is heart failure with reduced ejection fraction (HFrEF).
79. The use of claim 67, 69, 70, or 71, wherein the cardiovascular disease or related condition is heart failure with mid-ranged ejection fraction (HFmrEF).
80. The use of claim 67, 69, 70, or 71, wherein the cardiovascular disease or related condition is valve disease.
81. The use of claim 67, 69, 70, or 71, wherein the cardiovascular disease or related condition is cardiomyopathy, wherein the cardiomyopathy is ischemic cardiomyopathy, toxic cardiomyopathy, restrictive cardiomyopathy, or dilated cardiomyopathy; wherein the restrictive cardiomyopathy comprises Loefllers Endocarditis, Endomyocardial fibrosis (EMF), hemochromatosis, Fabry cardiomyopathy, glycogen storage disease, a pressure-overloaded right ventricle (RV), Tetralogy of Fallot, pulmonic stenosis, amyloidosis, sarcoidosis, heart conditions related to chest radiation therapy, heart conditions related to mutations in the gene encoding Troponin I (beta myosin HC), heart conditions related to mutations in a gene encoding Troponin T (alpha cardiac actin), or heart conditions related to mutations in a desmin gene.

82. The use of claim 67, 69, 70, or 71, wherein the cardiovascular disease or related condition comprises diastolic dysfunction, left ventricle stiffness, heart failure, or a hypertrophy.
83. The use of claim 67, 69, 70, or 71, wherein the cardiovascular disease or related condition comprises diastolic dysfunction or a related condition.
84. The use of claim 67, 69, 70, or 71, wherein the patient exhibits arrhythmia, stroke, ischemia, angina, or myocarditis.
85. The use of claim 67, 69, 70, or 71, wherein the cardiovascular disease comprises heart failure.
86. The use of any one of claims 66-67 or 69-85, wherein the medicament further comprises an additional active agent