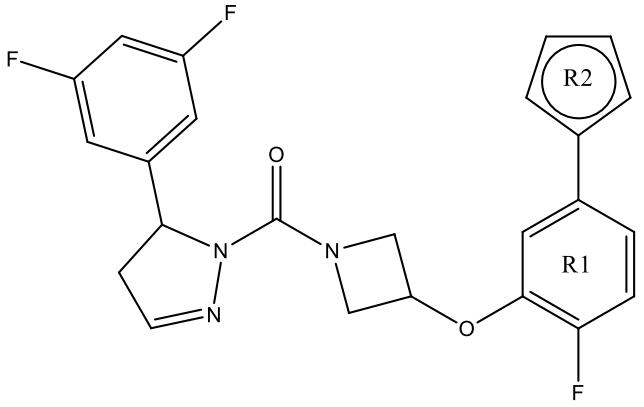
CLAIMS

1. A compound of formula I:



I

or a salt, hydrate or stereoisomer thereof, wherein:

R1 is an F substituted 6-membered aryl, or an F substituted 6-membered heteroaryl comprising 1 or 2 N heteroatoms; and

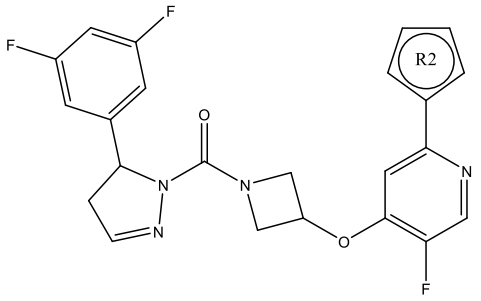
R2 is a 5-membered heteroaryl comprising 1, 2 or 3 N heteroatoms, or 1 or 2 N heteroatoms and an O or S heteroatom, substituted with 0-3 substituents selected from

halogen, -R', -OR', =O, -NR'R", -SR', -OC(O)R', -C(O)R', -CO2R', -CONR'R", -OC(O)NR'R", -NR"C(O)R', -NR'-C(O)NR"R'", -NR'-SO2NR'", -NR"CO2R', -S(O)R', -SO2R', -SO2NR'R", -NR"SO2R, -CN, -NO2, -CH(Ph)2, perfluoro(C1-C4)alkoxy and perfluoro(C1-C4)alkyl,

wherein R', R" and R'" each independently refer to hydrogen, unsubstituted C1-C8 alkyl, unsubstituted C1-C8 heteroalkyl, C1-C8 alkyl substituted with one to three halogens, C1-C8 heteroalkyl substituted with one to three halogens, unsubstituted C6-C14 aryl, C6-C14 aryl substituted with one to three halogens, or unsubstituted aryl-(C1-C4)alkyl groups,

wherein when R' and R" are attached to the same nitrogen atom, they optionally combine with the nitrogen atom to form a 5-, 6- or 7-membered ring.

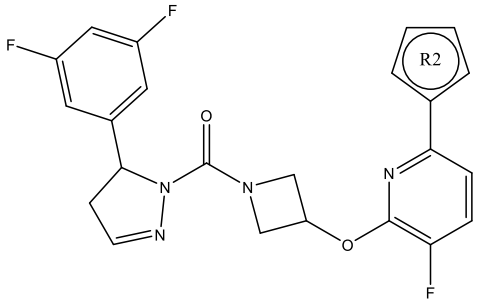
2. The compound, salt, hydrate, or stereoisomer of claim 1, wherein the compound has one of the following structural formula II(1):



II(1)

wherein R2 is as defined in claim 1.

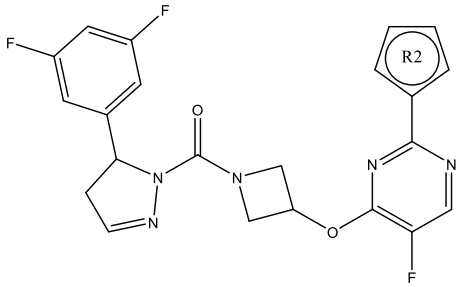
3. The compound, salt, hydrate, or stereoisomer of claim 1, wherein the compound has one of the following structural formula II(2):



II(2)

wherein R2 is as defined in claim 1.

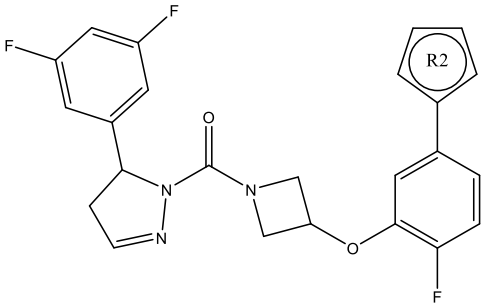
4. The compound, salt, hydrate, or stereoisomer of claim 1, wherein the compound has one of the following structural formula II(3):



II(3)

wherein R2 is as defined in claim 1.

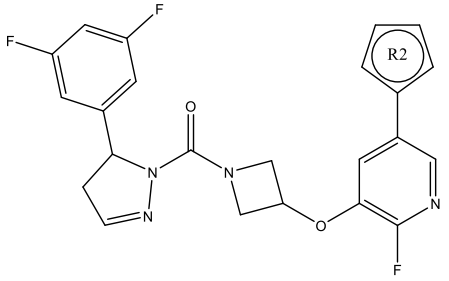
5. The compound, salt, hydrate, or stereoisomer of claim 1, wherein the compound has one of the following structural formula II(4):



II(4)

wherein R2 is as defined in claim 1.

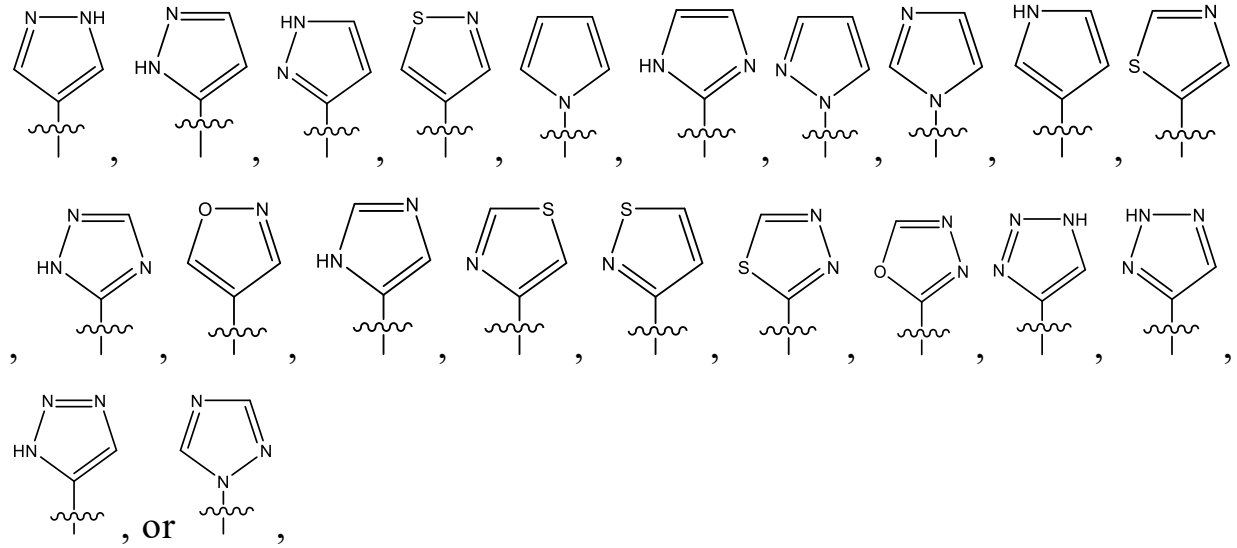
6. The compound, salt, hydrate, or stereoisomer of claim 1, wherein the compound has one of the following structural formula II(5):



II(5)

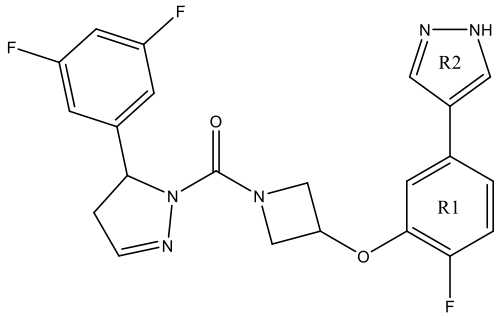
wherein R2 is as defined in claim 1.

7. The compound, salt, hydrate, or stereoisomer of any one of claims 1-6, wherein R2 is



substituted with the 0-3 substituents of R2 as set forth in claim 1.

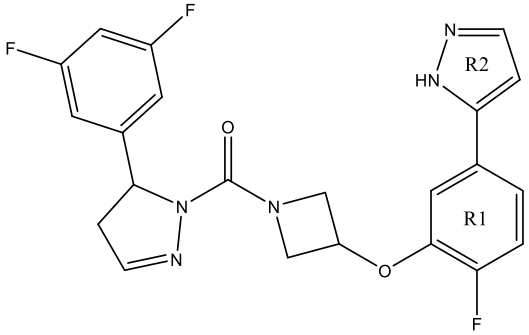
8. The compound, salt, hydrate, or stereoisomer of claim 1, wherein the compound has one of the following structural formula III(1):



III(1)

wherein R1 is an F substituted 6-membered aryl, or an F substituted 6-membered heteroaryl comprising 1 or 2 N heteroatoms; and wherein R2 is a 5-membered heteroaryl as set forth in structural formula III(1), substituted with the 0-3 substituents of R2 as set forth in claim 1.

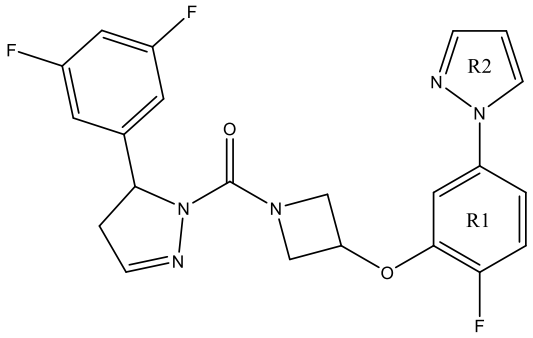
9. The compound, salt, hydrate, or stereoisomer of claim 1, wherein the compound has one of the following structural formula III(2):



III(2)

wherein R1 is an F substituted 6-membered aryl, or an F substituted 6-membered heteroaryl comprising 1 or 2 N heteroatoms; and wherein R2 is a 5-membered heteroaryl as set forth in structural formula III(2), substituted with the 0-3 substituents of R2 as set forth in claim 1.

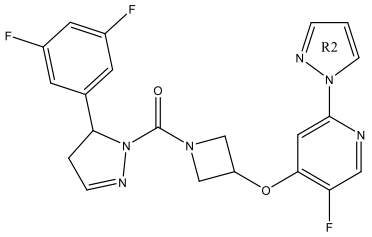
10. The compound, salt, hydrate, or stereoisomer of claims 1, wherein the compound has one of the following structural formula III(3):



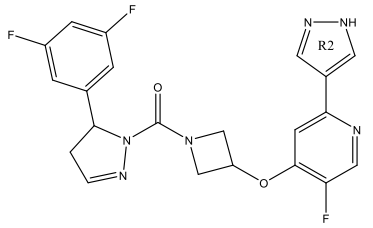
III(3)

wherein R1 is an F substituted 6-membered aryl, or an F substituted 6-membered heteroaryl comprising 1 or 2 N heteroatoms; and wherein R2 is a 5-membered heteroaryl as set forth in structural formula III(3), substituted with the 0-3 substituents of R2 as set forth in claim 1.

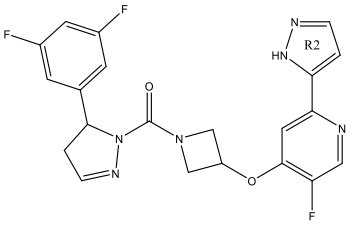
11. The compound, salt, hydrate, or stereoisomer of claim 1, wherein the compound has one of the following structural formulae IV(1)-IV(5):



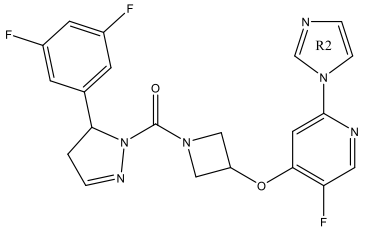
IV(1)



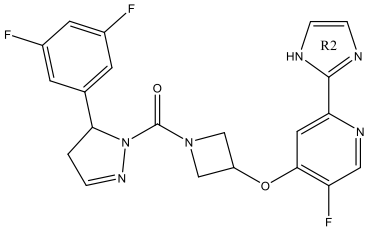
IV(2)



IV(3)



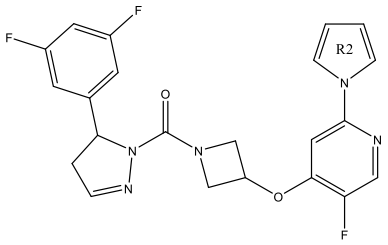
IV(4)



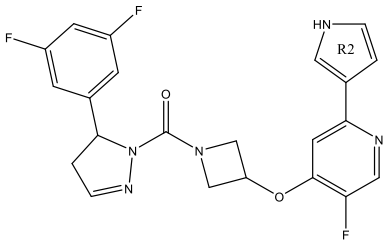
IV(5)

wherein R2 is a 5-membered heteroaryl as set forth in structural formulae IV(1)-IV(5), substituted with the 0-3 substituents of R2 as set forth in claim 1.

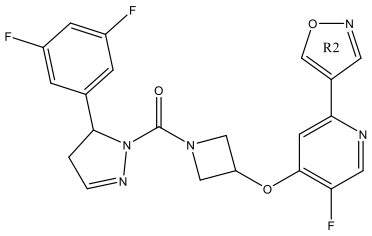
12. The compound, salt, hydrate, or stereoisomer of claim 1, wherein the compound has one of the following structural formulae IV(6)-IV(10):



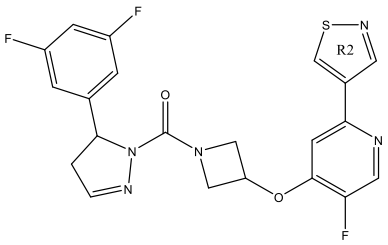
IV(6)



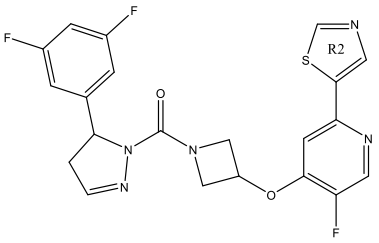
IV(7)



IV(8)



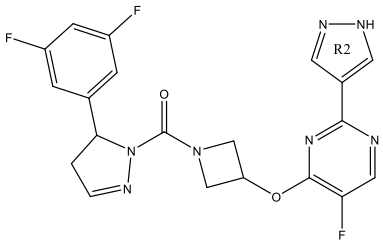
IV(9)



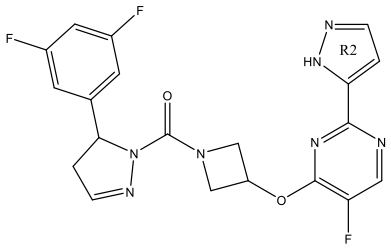
IV(10)

wherein R2 is a 5-membered heteroaryl as set forth in structural formulae IV(6)-IV(10), substituted with the 0-3 substituents of R2 as set forth in claim 1.

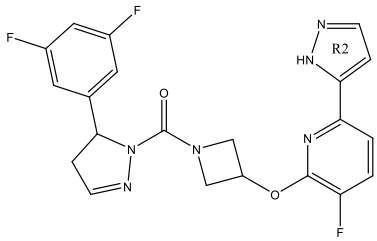
13. The compound, salt, hydrate, or stereoisomer of claim 1, wherein the compound has one of the following structural formulae IV(11)-IV(15):



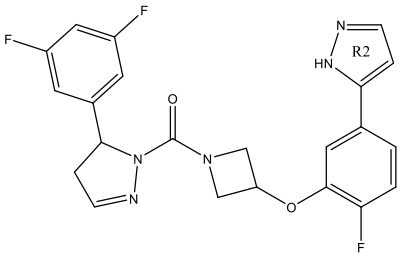
IV(11)



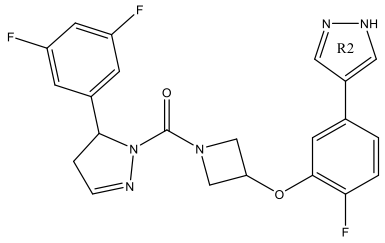
IV(12)



IV(13)



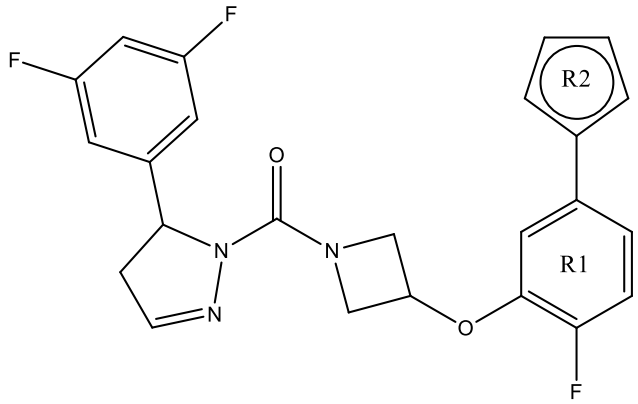
IV(14)



IV(15)

wherein R2 is a 5-membered heteroaryl as set forth in structural formulae IV(11)-IV(15), substituted with the 0-3 substituents of R2 as set forth in claim 1.

14. A compound of formula I, or a salt, hydrate or stereoisomer thereof:



I

wherein:

R1 is an F substituted 6-membered aryl, or an F substituted 6-membered heteroaryl comprising 1 or 2 N heteroatoms; and

R2 is a 5-membered heteroaryl comprising 1, 2 or 3 N heteroatoms, or 1 or 2 N heteroatoms and an O or S heteroatom,

wherein R2 is substituted with 0-3 R^a, wherein R^a, for each occurrence, is independently selected from:

halogen, cyano, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, 3- to 6-membered heterocyclyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, -C(=O)(C_1-C_6 alkyl), -C(=O)(C_3-C_6 cycloalkyl), -C(=O)(3- to 6-membered heterocyclyl), =O, $-NO_2$, -$C(=O)OR^s$, -$C(=O)NR^pR^q$, -NR^pR^q, -$NR^pC(=O)R^s$, -$NR^pC(=O)OR^s$, -$NR^pC(=O)NR^qR^r$, -$NR^pS(=O)_wR^s$, -OR^s, -$OC(=O)R^s$, -$OC(=O)OR^s$, -$OC(=O)NR^pR^q$, -$S(=O)_wR^s$, and -$S(=O)_wNR^pR^q$; wherein

the C_1-C_6 alkyl, C_3-C_6 cycloalkyl, 3- to 6-membered heterocyclyl, C_2-C_6 alkenyl, and C_1-C_6 alkoxy of R^a, the C_1-C_6 alkyl of -C(=O)(C_1-C_6 alkyl), the C_3-C_6 cycloalkyl of -C(=O)(C_3-C_6 cycloalkyl), and the 3- to 6-membered heterocyclyl of -C(=O)(3- to 6-membered heterocyclyl) are each optionally substituted with 1 to 3 groups selected from halogen, cyano, =O, -$C(=O)R^s$, -$C(=O)OR^s$, -$C(=O)NR^pR^q$, -NR^pR^q, -$NR^pC(=O)R^s$, -$NR^pC(=O)OR^s$, -$NR^pC(=O)NR^qR^r$, -$NR^pS(=O)_wR^s$, -OR^s, -$OC(=O)R^s$, -$OC(=O)OR^s$, -$OC(=O)NR^pR^q$, -$S(=O)_wR^s$, -$S(=O)_wNR^pR^q$, C_3-C_6 cycloalkyl, and 3- to 6-

membered heterocyclyl; wherein

R^p, R^q, R^r, and R^s, for each occurrence, are each independently selected from hydrogen, OH, NH_2, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, and 3- to 6-membered heterocyclyl; wherein

the C_1-C_4 alkyl, C_3-C_6 cycloalkyl, and 3- to 6-membered heterocyclyl of any one of R^p, R^q, R^r, and R^s are optionally substituted with 1 to 3 groups selected from halogen, cyano, -OH, C_1-C_6 alkyl, -O(C_1-C_6 alkyl), -C(=O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -C(=O)NH(C_1-C_6 alkyl), -C(=O)(3- to 6-membered heterocyclyl), -C(=O)(C_3-C_6 cycloalkyl), C_3-C_6 cycloalkyl, phenyl, and 3- to 6-membered heterocyclyl; and wherein

w is an integer selected from 0, 1, and 2.

15. The compound, salt, hydrate or stereoisomer of claim 14, wherein R2 is substituted with 1-3 R^a, wherein R^a, for each occurrence, is independently selected from: halogen; cyano; 4- to 6-membered heterocyclyl optionally substituted with oxo; -C(=O)(C_1-C_6 alkyl); -C(=O)(C_3-C_6 cycloalkyl); -C(=O)(4- to 6-membered heterocyclyl); 3- to 4-membered cycloalkyl;

-C(=O)OR^s, wherein R^s is H or C_1-C_3 alkyl;

C_1-C_3 alkyl, optionally substituted with OH, NH_2, cyano, halogen, C_1-C_3 alkoxyl, 3- to 4-membered cycloalkyl, 4- to 6-membered heterocyclyl, -C(=O)OH, -C(=O)(4- to 6-membered heterocyclyl), -C(=O)NH$(CH_2)_2$OH, or -C(=O)NH_2;

-C(=O)NR^pR^q, wherein R^p and R^q each are independently selected from H; OH; CN; 4- to 6-membered heterocyclyl; C_1-C_3 alkyl optionally substituted with OH; and 3- to 4-membered cycloalkyl optionally substituted with OH;

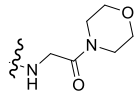
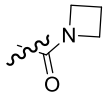
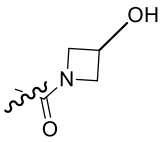
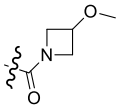
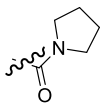
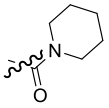
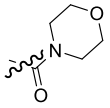
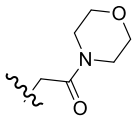
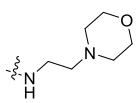
-NR^pR^q, wherein R^p and R^q each are independently selected from H, OH, -C(=O)CH_3, and C_1-C_3 alkyl optionally substituted with OH, 3- to 4-membered cycloalkyl, or 6-membered heterocyclyl;

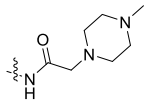
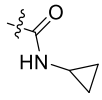
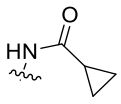
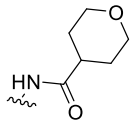
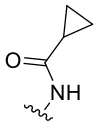
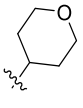
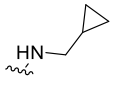
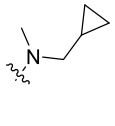
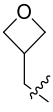
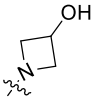
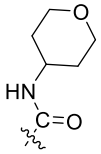
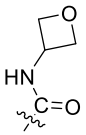
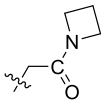
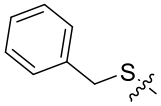
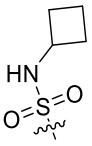
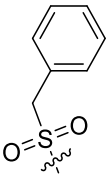
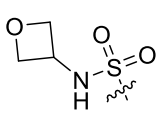
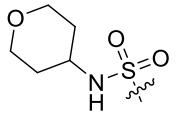
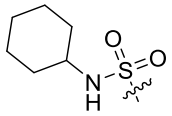
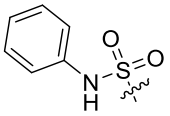
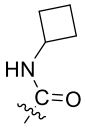
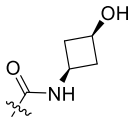
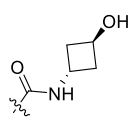
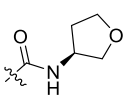
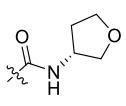
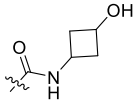
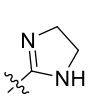
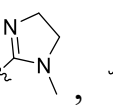
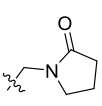
-$NR^pC(=O)NR^qR^r$, wherein R^p, R^q and R^r each are independently selected from H and C_1-C_3 alkyl;

-$NR^pC(=O)R^s$, wherein R^p is selected from H and C_1-C_3 alkyl, and R^s is selected from C_1-C_3 alkyl and 3- to 4-membered cycloalkyl;

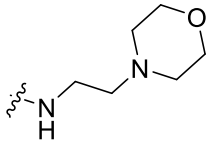
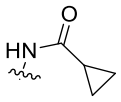
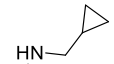
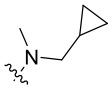
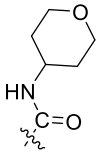
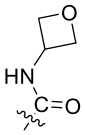
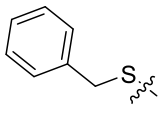
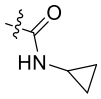
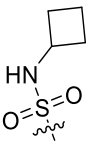
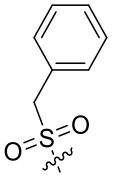
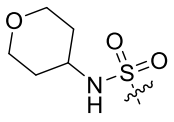
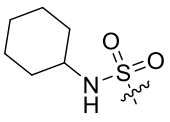
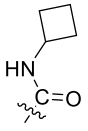
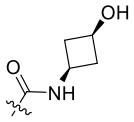
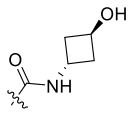
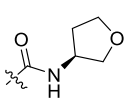
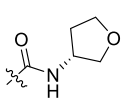
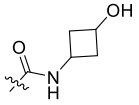
-$S(=O)_wR^s$, wherein R^s is selected from C_1-C_3 alkyl optionally substituted with phenyl or NH_2, and wherein w is 0 or 2; and

-$S(=O)_wNR^pR^q$, wherein R^p and R^q each are independently selected from H, 3- to 6- membered cycloalkyl, 4- to 6-membered heterocyclyl, and C_1-C_3 alkyl optionally substituted with OH, C_1-C_3 alkoxyl, or phenyl, and wherein w is 2.

16. The compound, salt, hydrate, or stereoisomer of claim 14, wherein R2 is substituted with 1-3 R^a, wherein R^a, for each occurrence, is independently selected from methyl, ethyl, -NH_2, -CN, -OCH_3, -$O(CH_2)_2N(CH_3)_2$, -$NHCH_3$, -$O(CH_2)_2OCH_3$, -$N(CH_3)_2$, -$NH(CH_2)OCH_3$, -$NHC(=O)CH_3$, -$NHC(=O)CH_2CH_3$, -$NHC(=O)CH(CH_3)_2$, -$NHC(=O)CH_2CH(CH_3)_2$, -$NHCH_2C(=O)NHCH_3$, -$NHCH_2C(=O)NHCH_3$, , -$NHCH_2C(=O)N(CH_3)_2$, -$C(=O)OCH_3$, -C(=O)OH, -$C(=O)CH_3$, -$C(=O)NH_2$, -$C(=O)NHCH_3$, -$C(=O)NH(CH_2)_2N(CH_3)_2$, -$C(=O)NHCH_2N(CH_3)_2$, -$C(=O)NHCH_2CH_3$, , , , , , , -CH_2OH, -$CH_2N(CH_3)_2$, -CH_2OCH_3, -F, -Cl, -$(CH_2)_2OCH_3$, -$CH_2C(=O)NH_2$, -$CH_2C(=O)N(CH_3)_2$, , -$CH_2C(=O)NHCH_3$, -NO_2, -$(CH_2)_2OH$, -$CH_2C(=O)OCH_3$, -$NH(CH_2)_2N(CH_3)_2$, , -$NHC(=O)CH_2OCH_3$, -

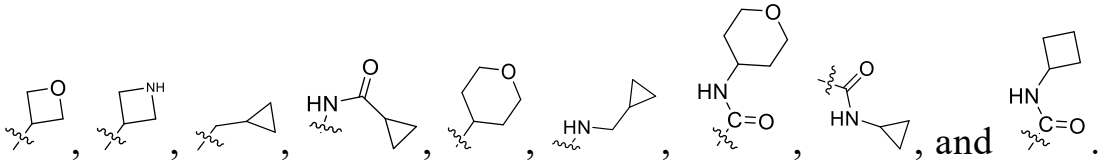
NHC(=O)CH$_2$N(CH$_3$)$_2$, , -NHCH$_3$, -C(=O)OCH$_2$CH$_3$, , , , -C(=O)NHCH(CH$_3$)$_2$, , -N(C(=O)CH$_3$)$_2$, , , , -NHC(=O)NHCH(CH$_3$)$_2$, -NHC(=O)NHCH$_3$, -NHCH$_2$C(=O)NH$_2$, -CH$_2$CH$_2$OH, , -NH(CH$_2$)$_2$CH$_3$, -NHCH(CH$_3$)$_2$, , , -NH(CH$_3$)$_2$, -S(=O)$_2$CH$_2$CH$_3$, -CF$_3$, , -C(=O)N(CH$_3$)$_2$, -SCH$_3$, -S(=O)CH$_3$, -CHOHCH$_3$, , -S(=O)$_2$CH$_3$, -CH$_2$F, -CH$_2$NH$_2$, -NH(CH$_2$)$_2$OH, , -C(=O)NH(CH$_2$)$_2$OH, , , -S(=O)$_2$NH$_2$, , -CH$_2$C(=O)NH(CH$_2$)$_2$OH, , -S(=O)$_2$NHCH$_3$, , , , , , , -S(=O)$_2$NH(CH$_2$)$_2$OH, -S(=O)$_2$NHOCH$_3$, , -C(=O)NHOH,-C(=O)NHCN, , , , , , , , , -CH$_2$CN, , -CH$_2$C(=O)OH, -C(CH$_3$)$_2$C(=O)OH, and -C(CH$_3$)$_2$C(=O)NH$_2$.

17. The compound, salt, hydrate, or stereoisomer of claim 14, wherein

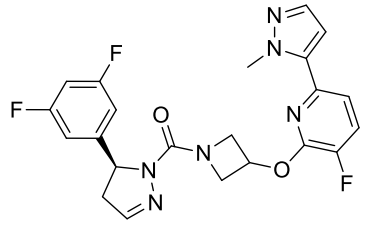
R2 is substituted with 1-3 R^a, wherein R^a, for each occurrence, is independently selected from methyl, ethyl, $-NH_2$, $-NHCH_3$, -CN, $-CH_2CH_2OH$, , $-NHC(=O)CH_3$, $-C(=O)OCH_3$, , , , $-N(C=OCH_3)_2$, $-NHCH_2C(=O)NH_2$, , $-C(=O)OCH_2CH_3$, $-NHCH_3$, $-CH_2OCH_3$, $-CH_2CH_2OH$, , -NHCH2CH2OCH3, $-NHCH(CH_3)_2$, , , $-N(CH_3)_2$, $-C(=O)N(CH_3)_2$, $-C(=O)NH_2$, -Cl, $-SCH_3$, $-S(=O)_2CH_3$, CH_2OH, , $-C(=O)NHCH_3$, CH_2F, $-NHCH_2OH$, $-C(=O)NHCH_2CH_2OH$, , , $-S(=O)_2NH_2$, $-CH_2C(=O)NH_2$, ; $-C(=O)NHCH_2CH_3$, $-C(=O)OH$, , , , , , , $-C(=O)NHCH_3$, $-S(=O)_2NHOCH_3$, , $-C(=O)NHOH$, , , , , , $-C(=O)NHCH_2CH_2OH$, and $-CH_2CN$.

18. The compound, salt, hydrate, or stereoisomer of claim 14, wherein R2 is substituted with 1-3 R^a, wherein R^a, for each occurrence, is independently selected from methyl, ethyl, $-NH_2$, $-C(=O)NH_2$, $-NHCH_3$, -

CN, -CH_2CN, -$NHCH_2OH$, -CH_2NH_2, -SCH_3, $CONHCH_3$, -SO_2CH_3, -CH_2OH, -Cl, -$N(CH_3)_2$, -$NHCH(CH_3)_2$, -$NHCH_2CH_2OCH_3$, -CH_2CH_2OH, -$C(=O)OCH_2CH_3$, -$C(=O)OCH_3$, -$C(=O)OH$, -$S(=O)_2NH_2$, -$CH_2C(=O)NH_2$, -$C(=O)NHCH_2CH_2OH$,



19. A compound, or a salt, hydrate, or stereoisomer thereof, wherein the compound has a structure selected from:



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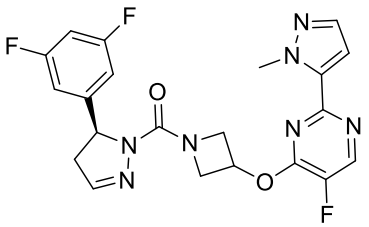

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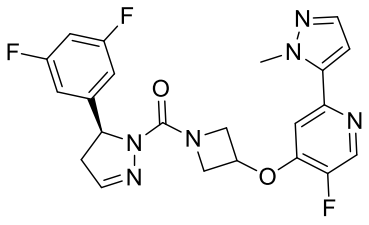

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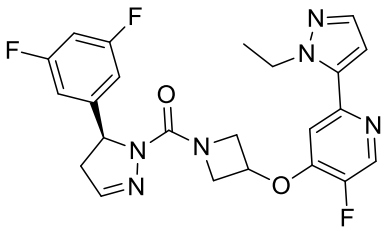

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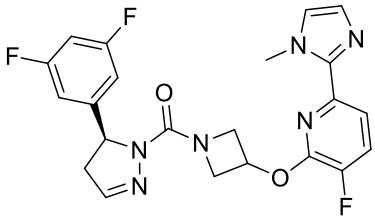

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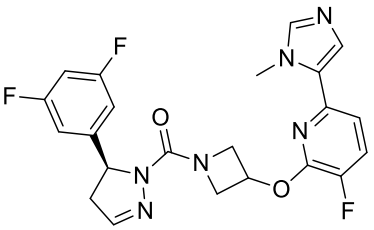

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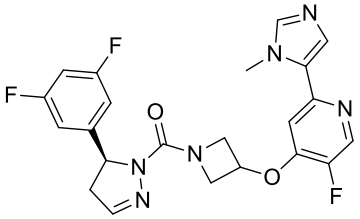

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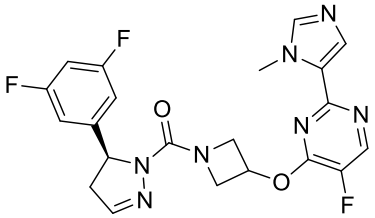

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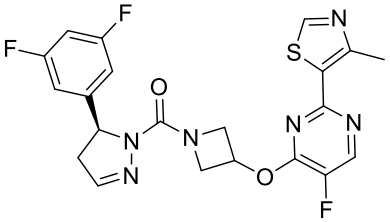

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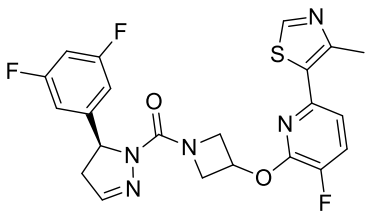

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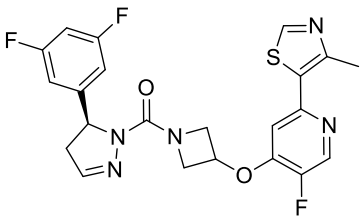

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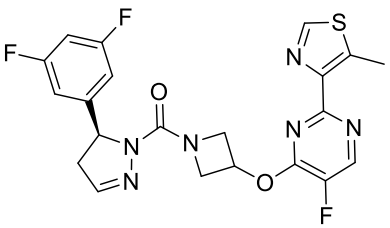

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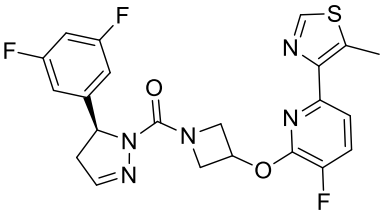

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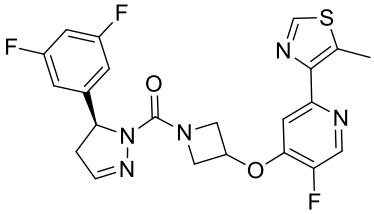

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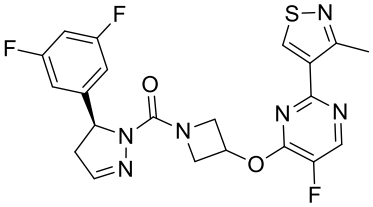

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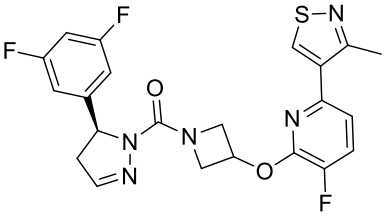

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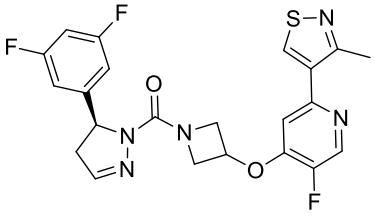

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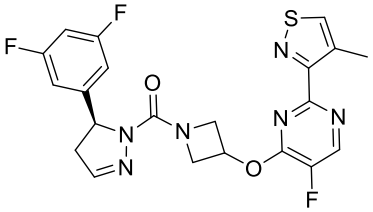

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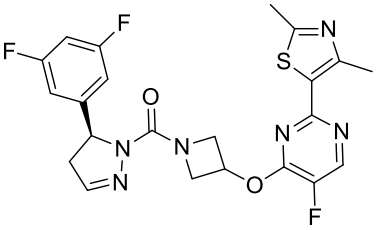

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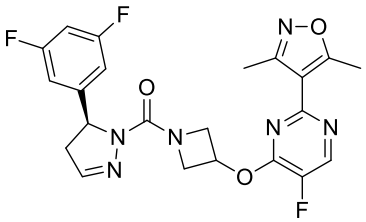

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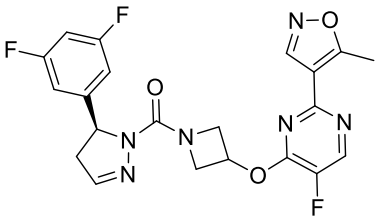

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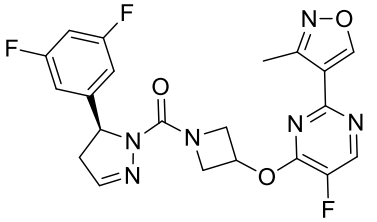

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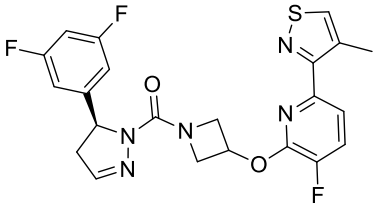

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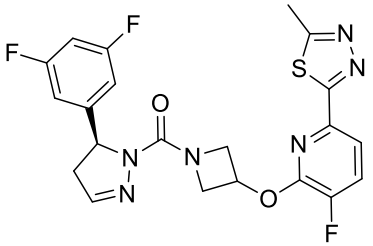

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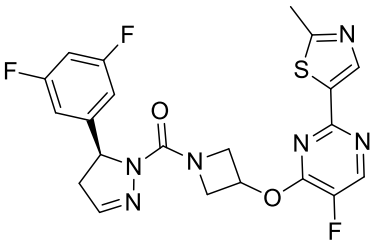

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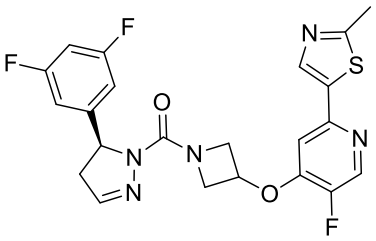

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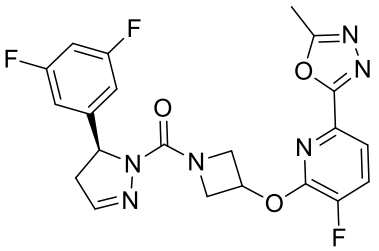

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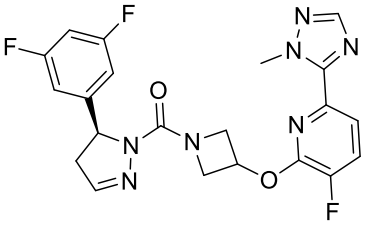

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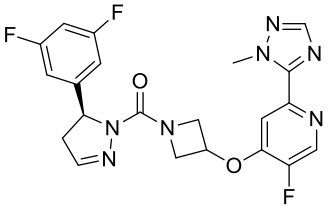

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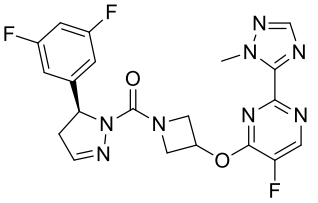

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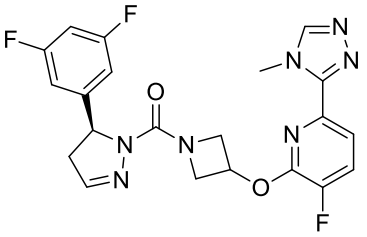

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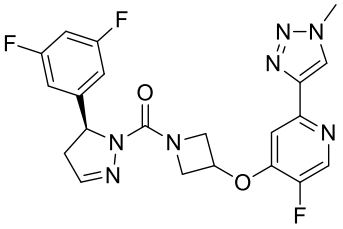

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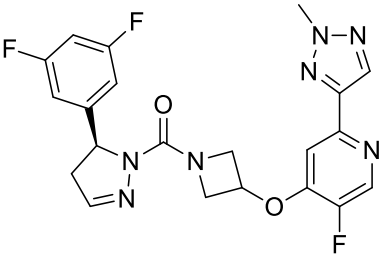

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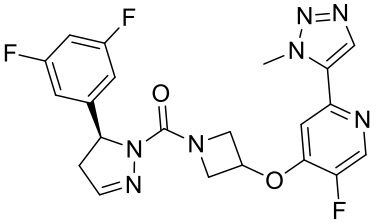

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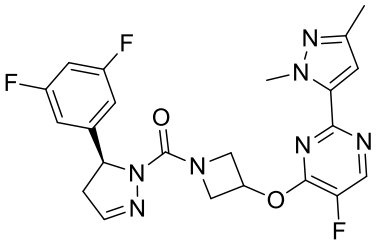

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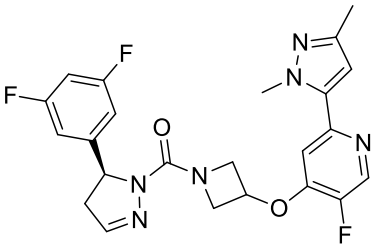

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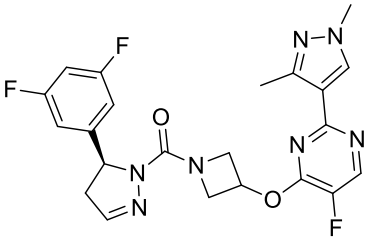

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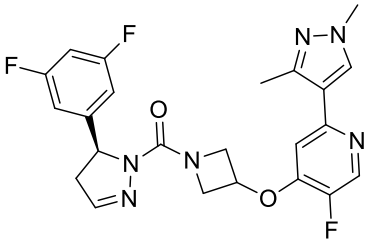

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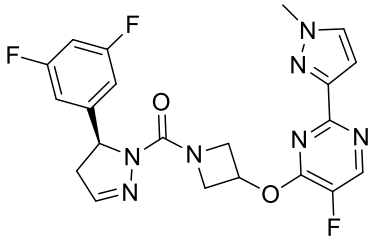

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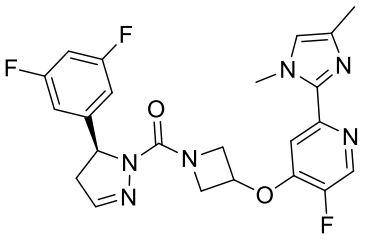

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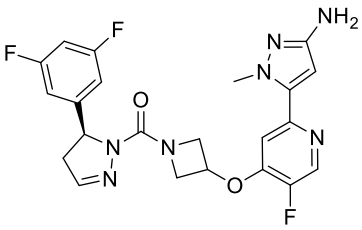

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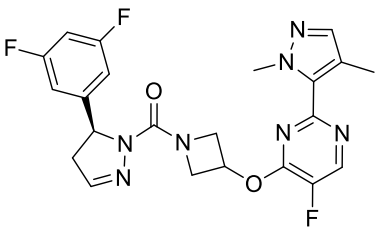

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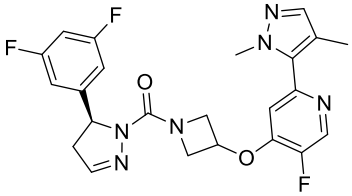

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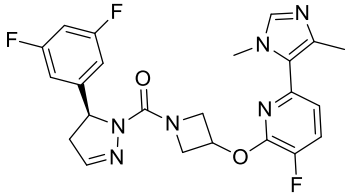

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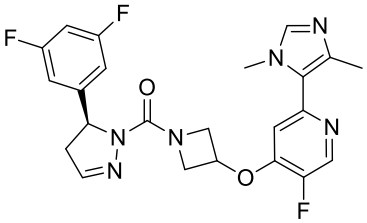

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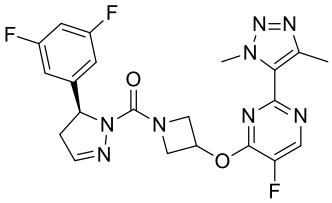

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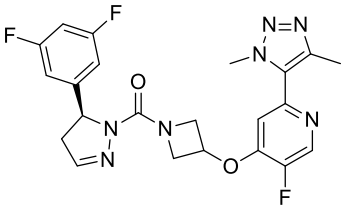

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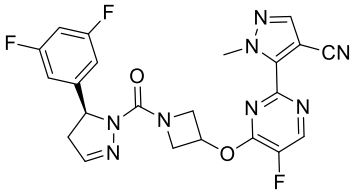

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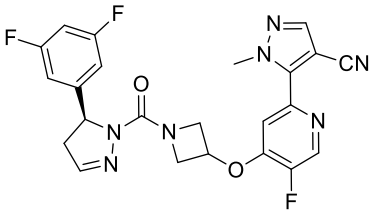

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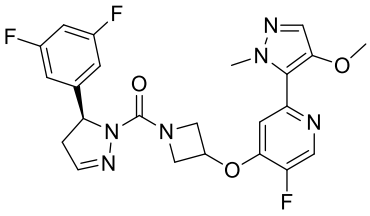

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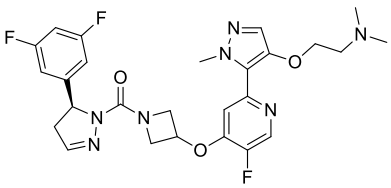

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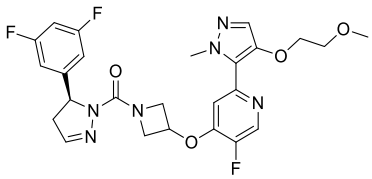

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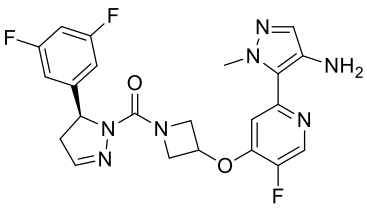

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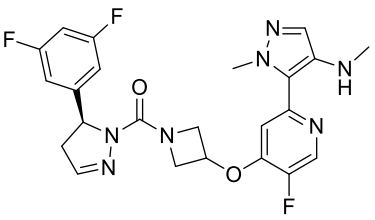

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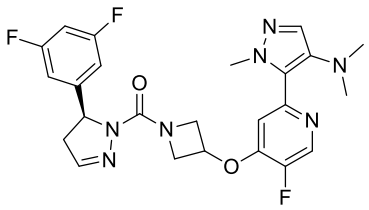

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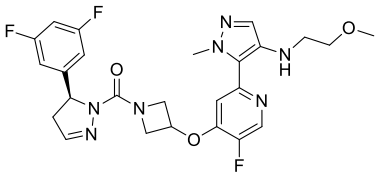

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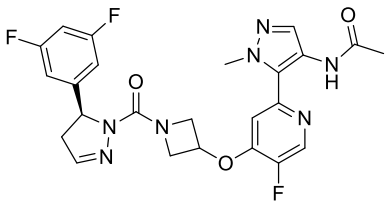

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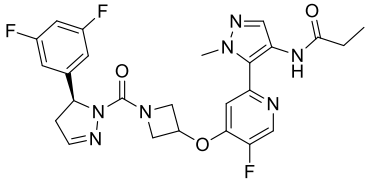

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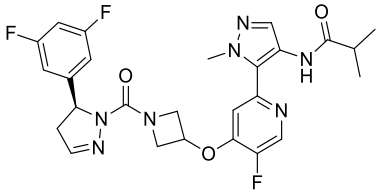

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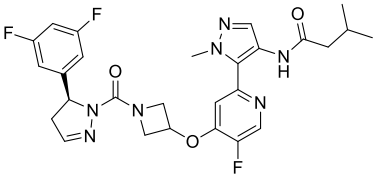

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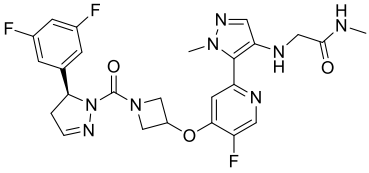

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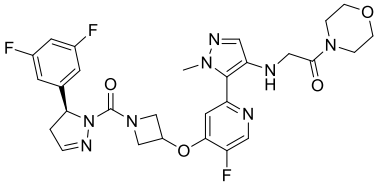

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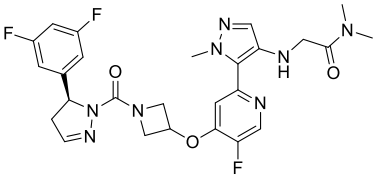

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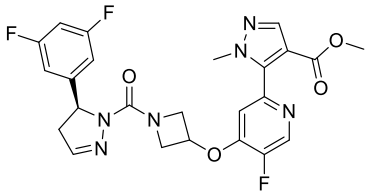

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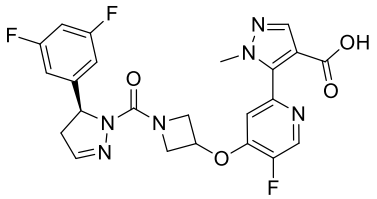

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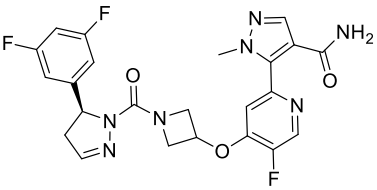

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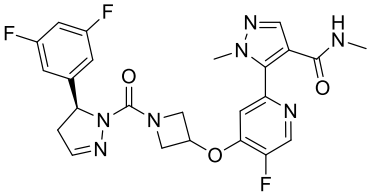

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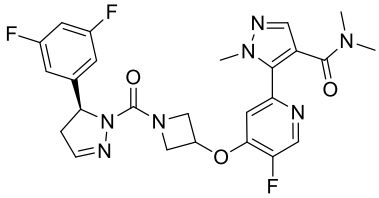

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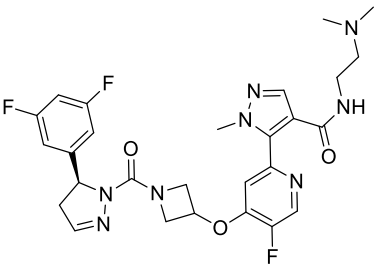

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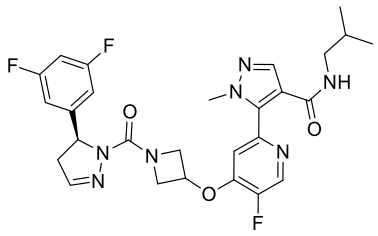

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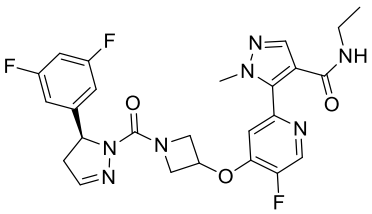

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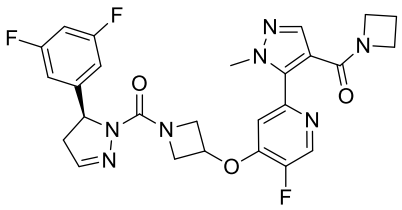

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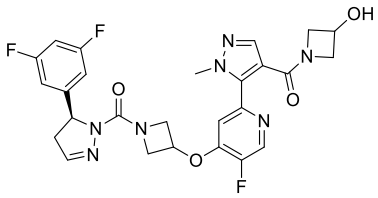

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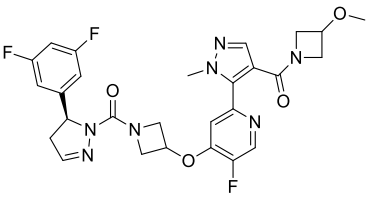

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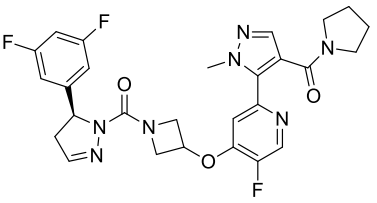

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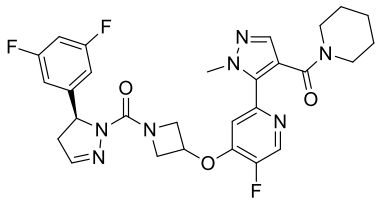

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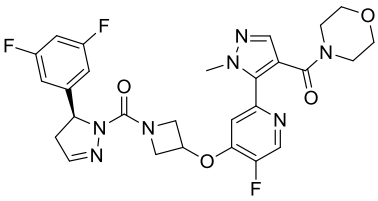

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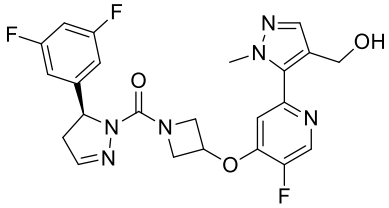

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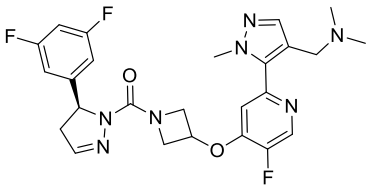

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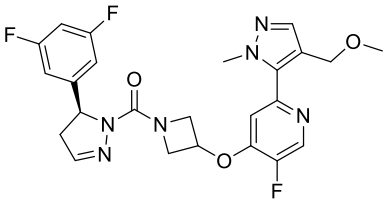

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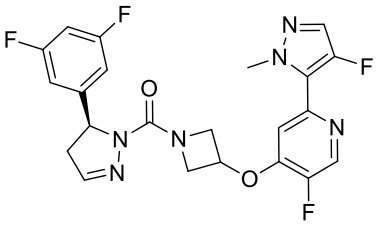

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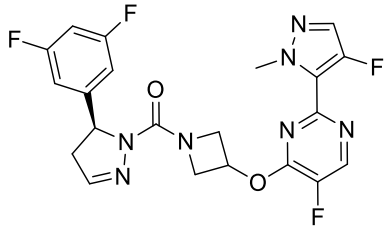

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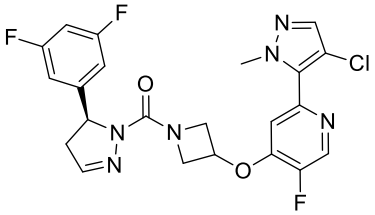

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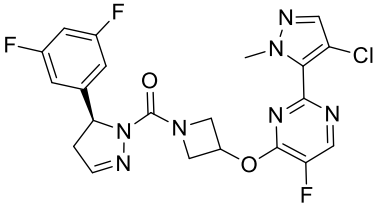

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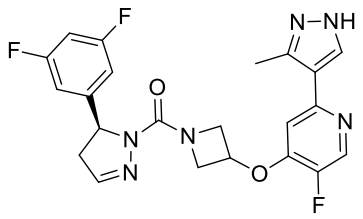

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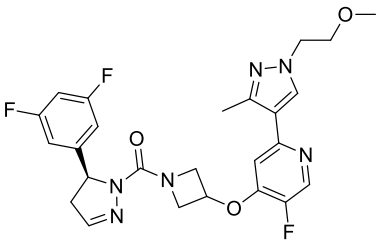

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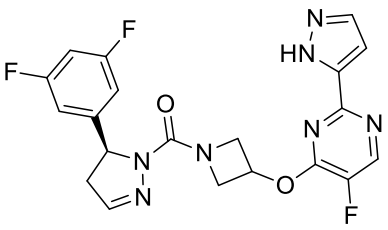

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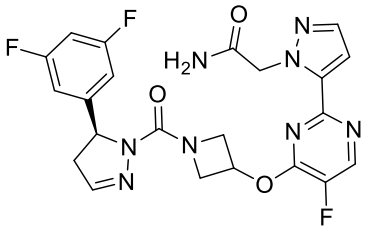

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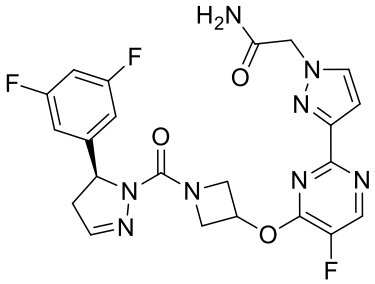

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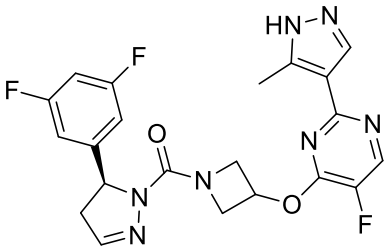

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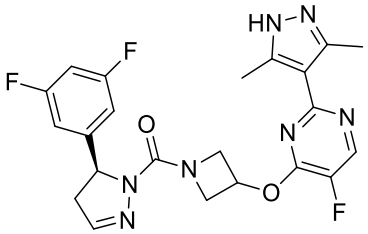

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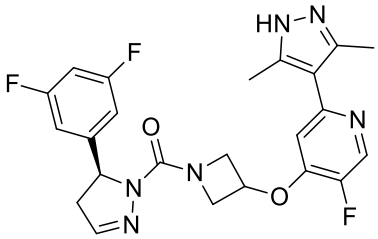

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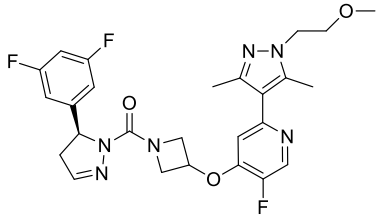

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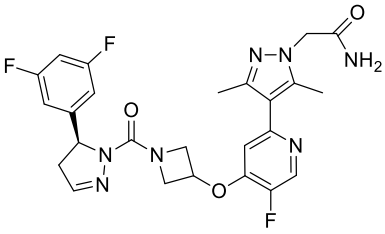

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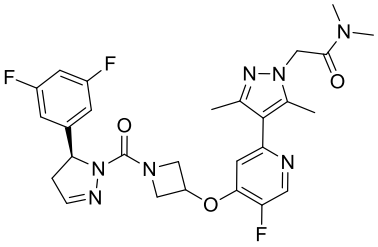

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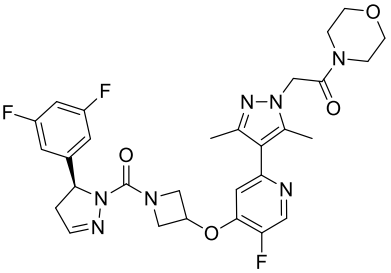

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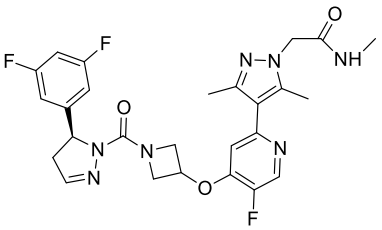

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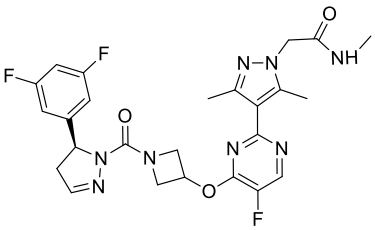

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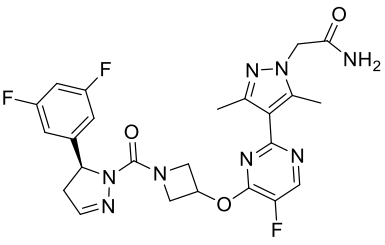

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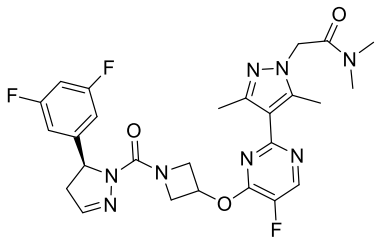

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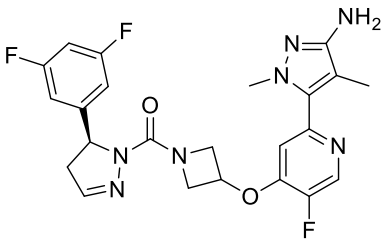

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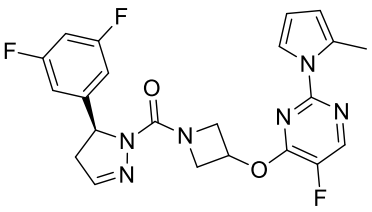

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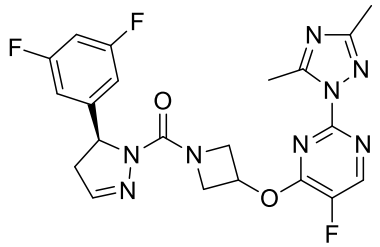

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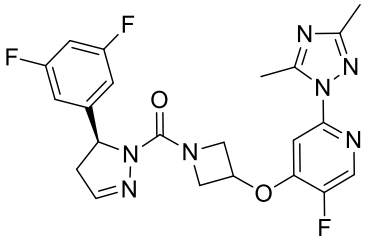

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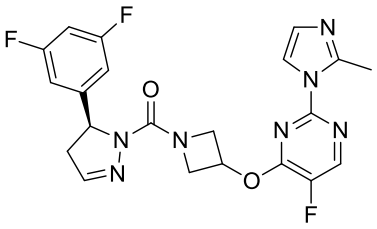

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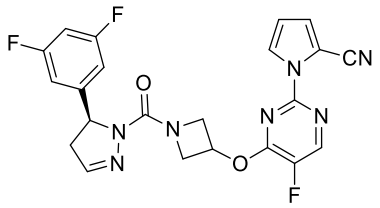

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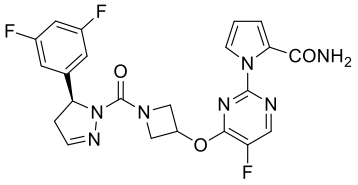

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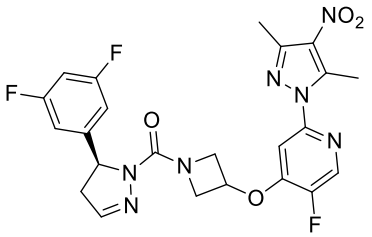

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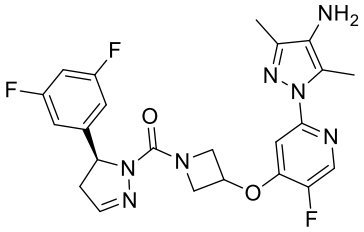

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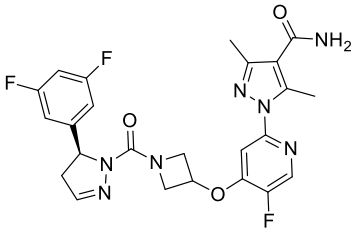

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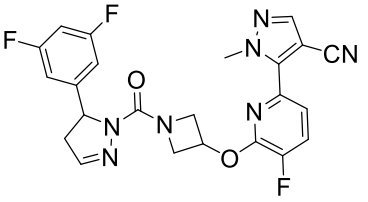

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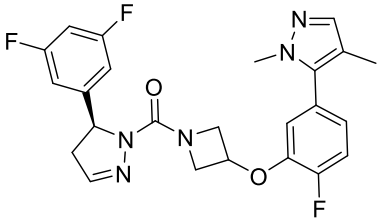

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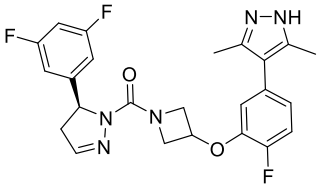

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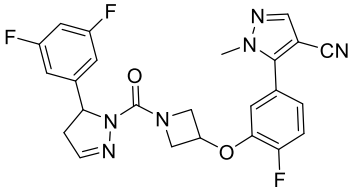

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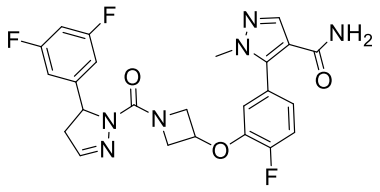

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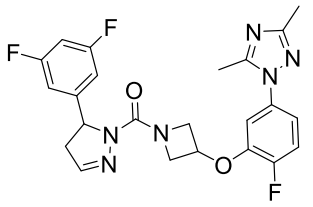

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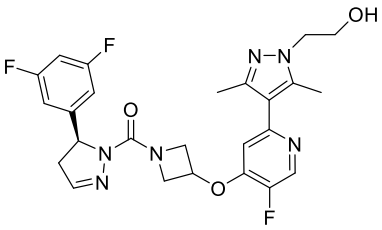

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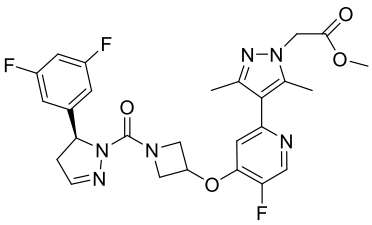

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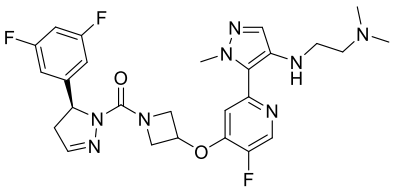

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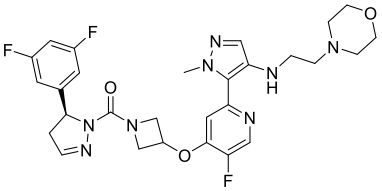

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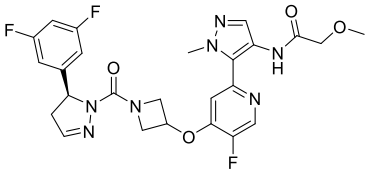

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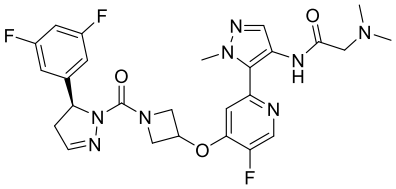

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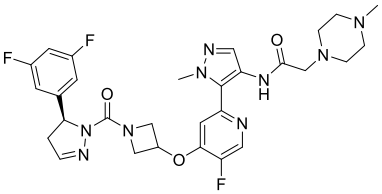

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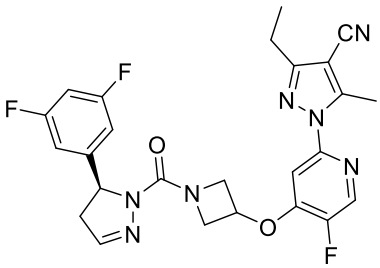

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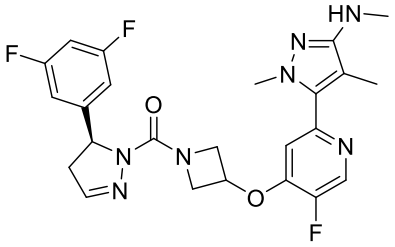

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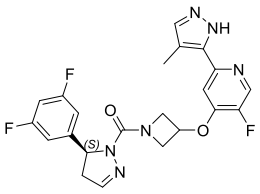

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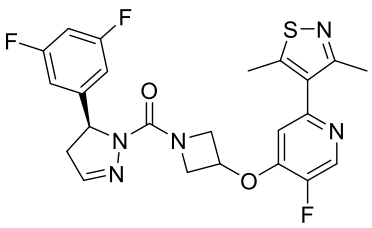

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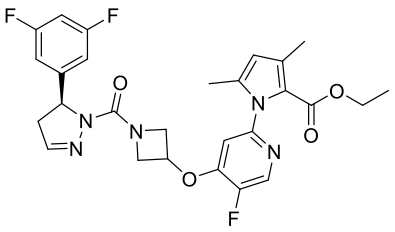

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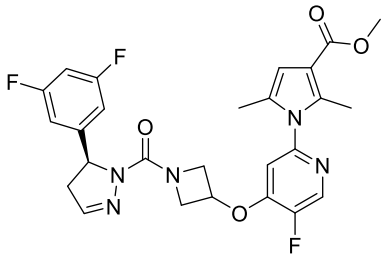

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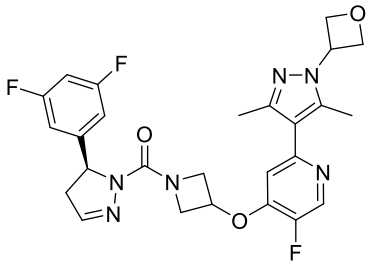

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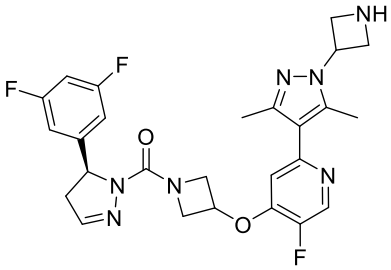

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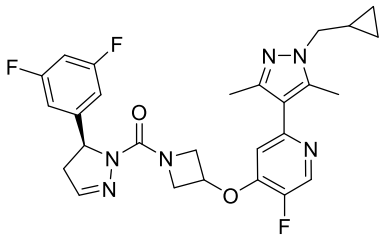

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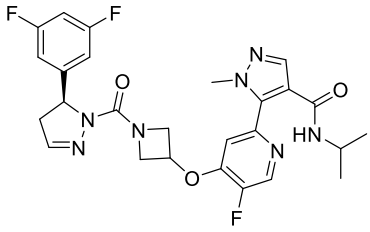

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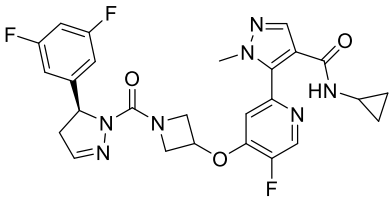

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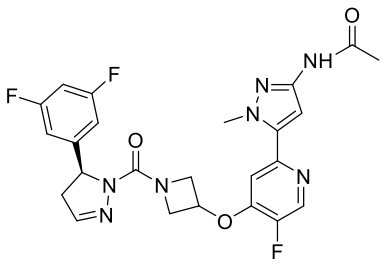

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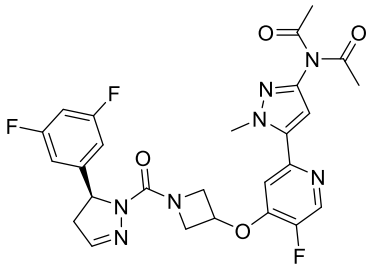

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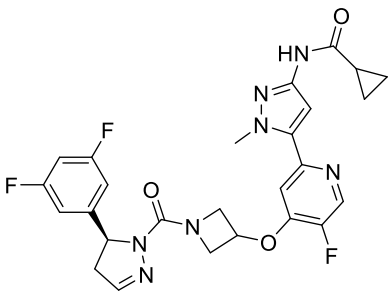

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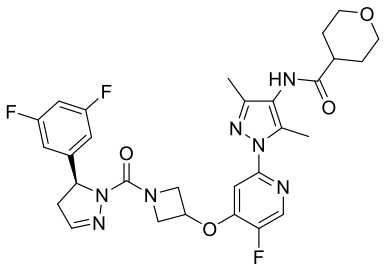

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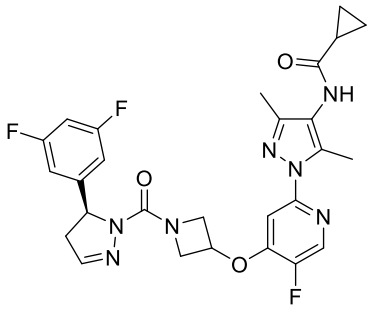

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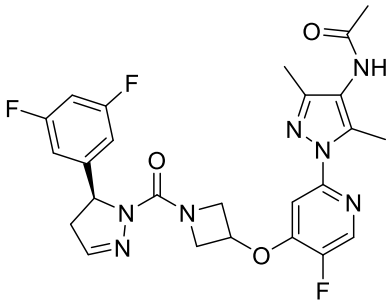

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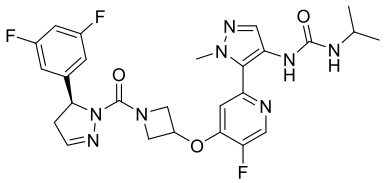

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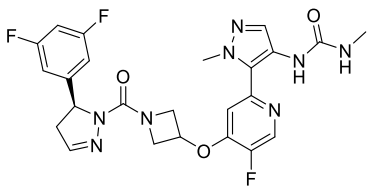

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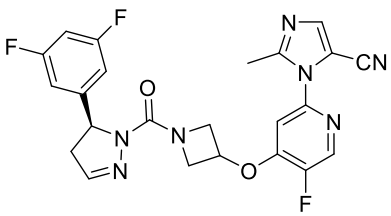

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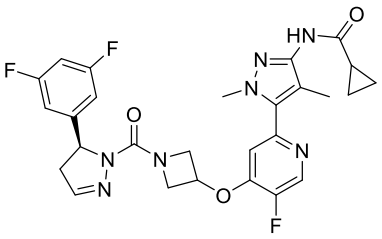

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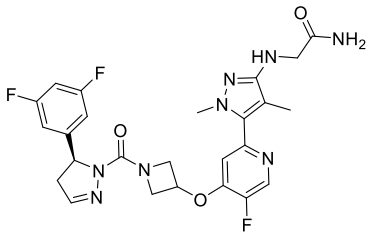

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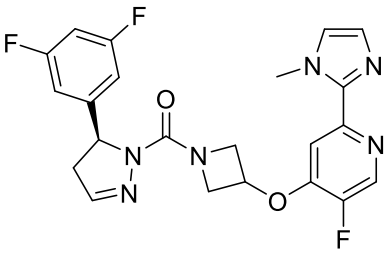

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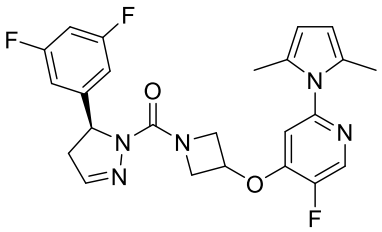

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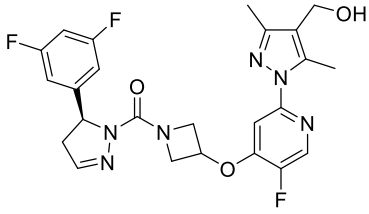

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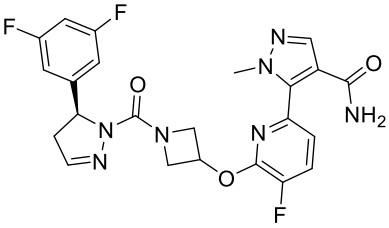

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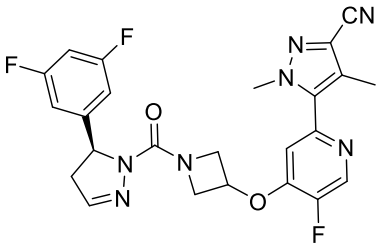

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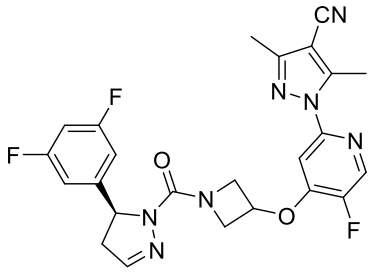

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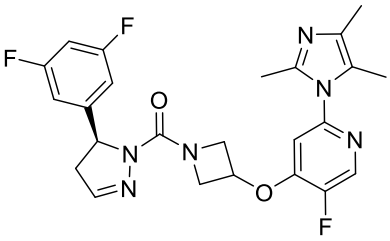

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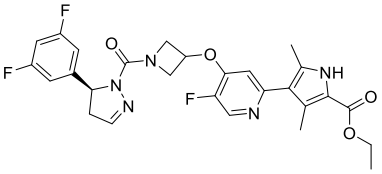

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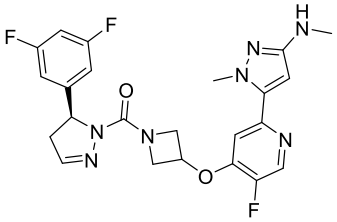

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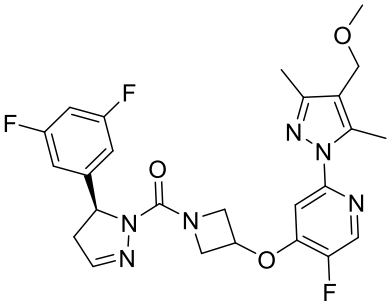

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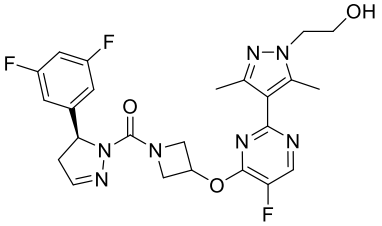

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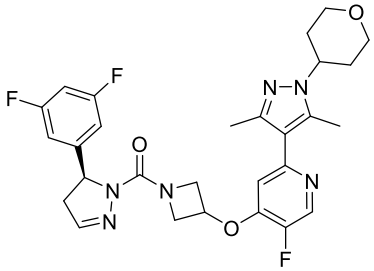

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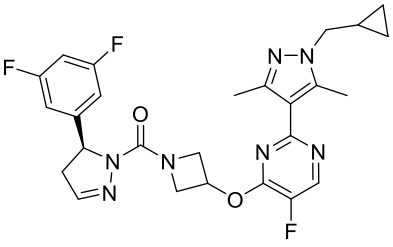

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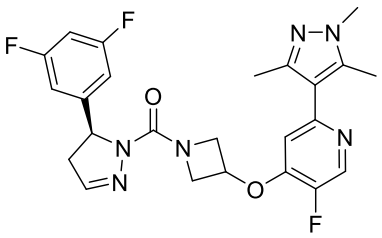

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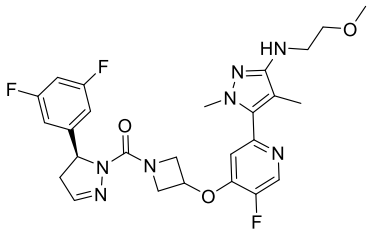

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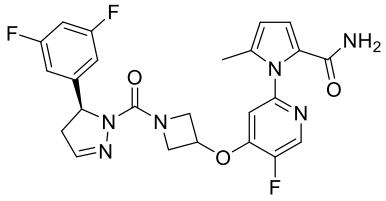

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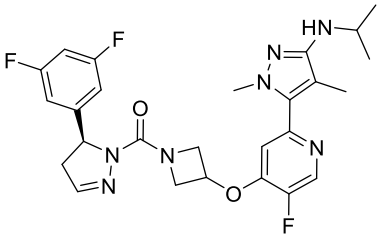

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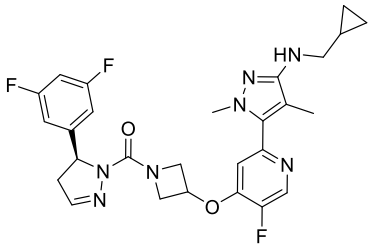

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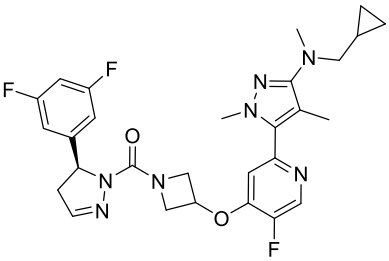

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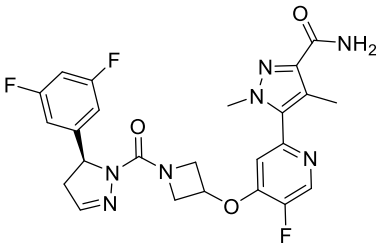

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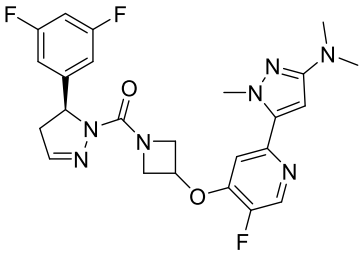

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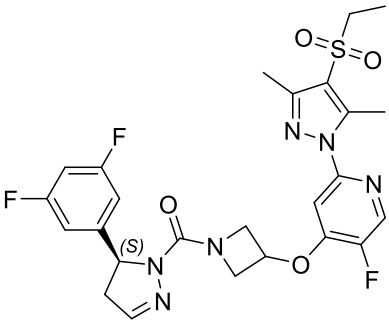

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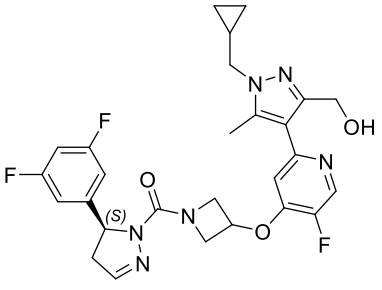

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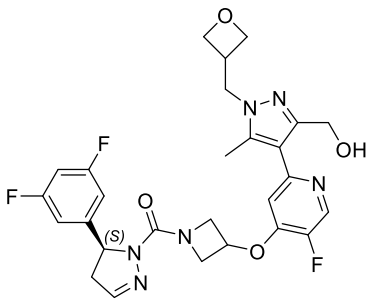

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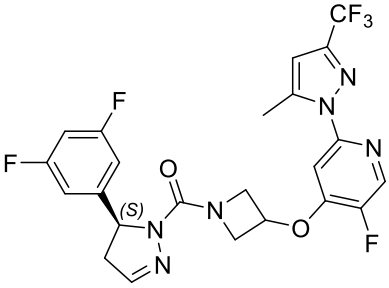

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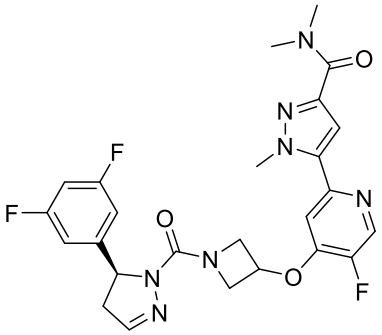

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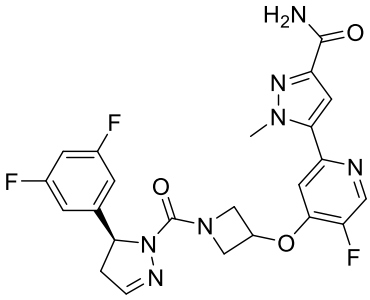

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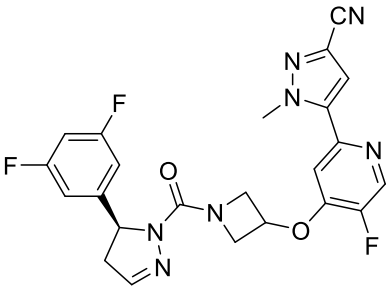

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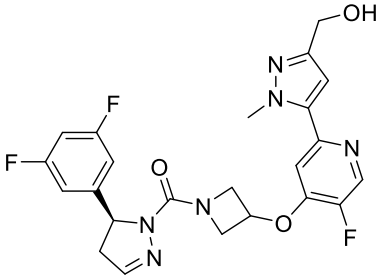

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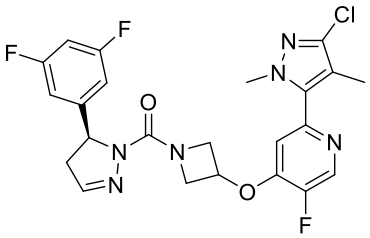

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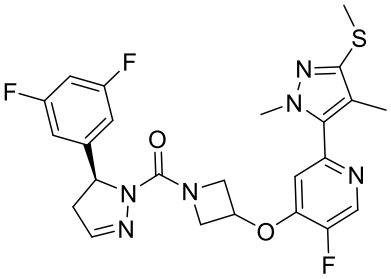

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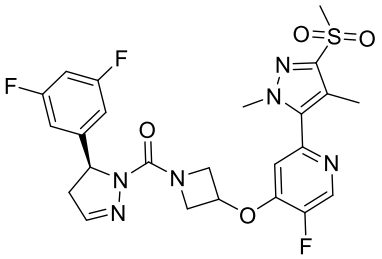

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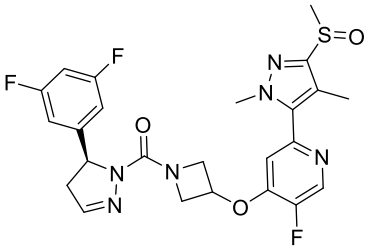

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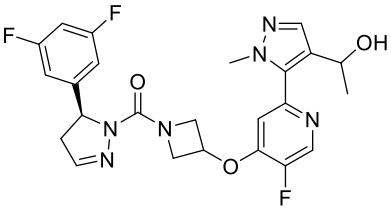

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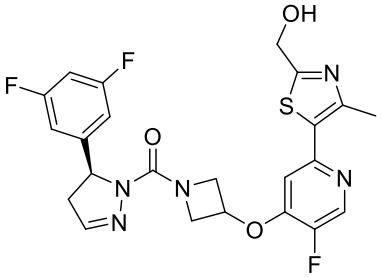

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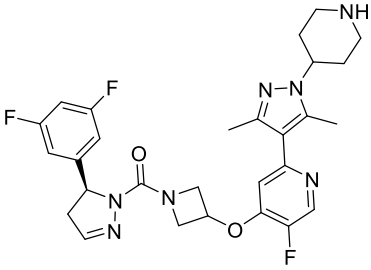

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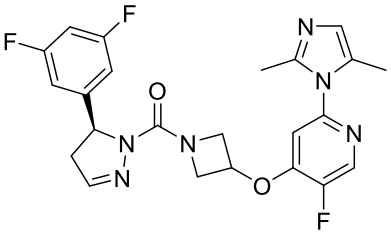

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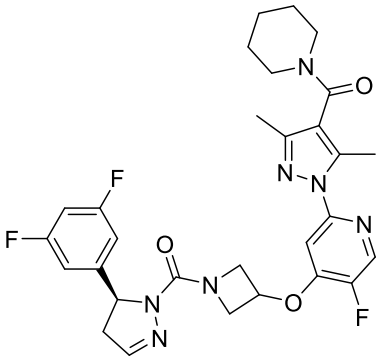

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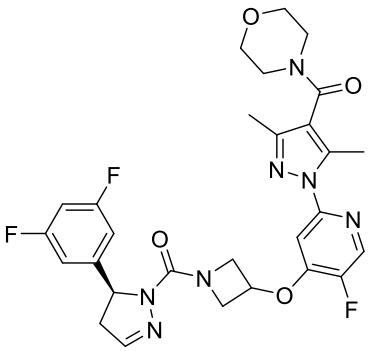

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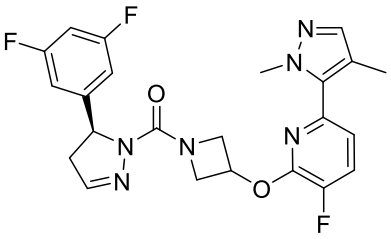

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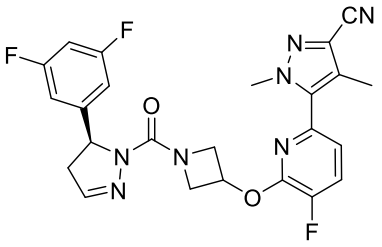

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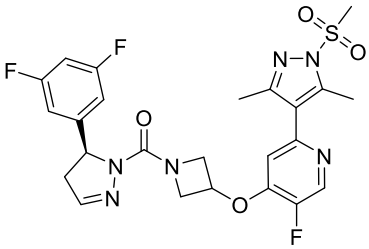

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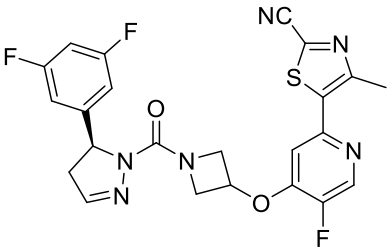

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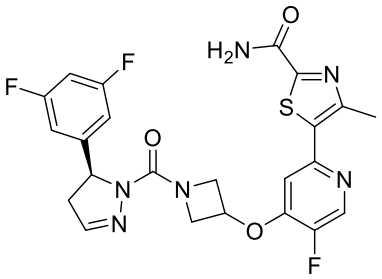

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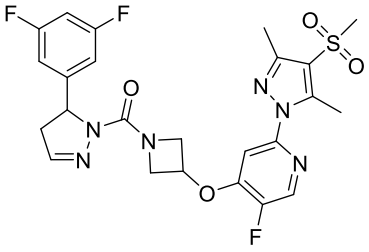

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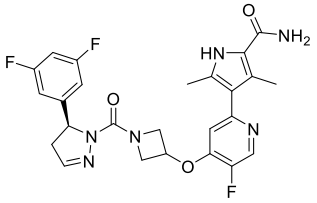

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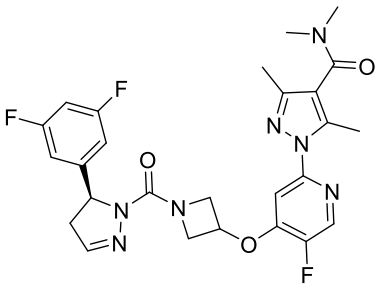

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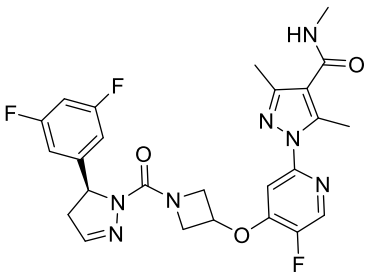

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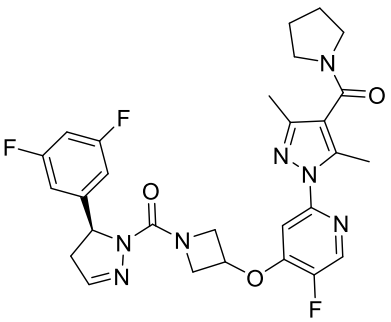

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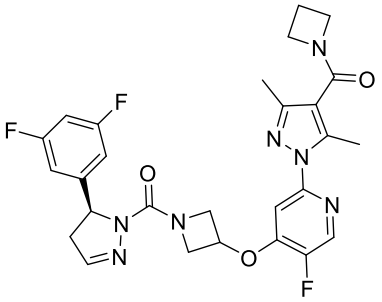

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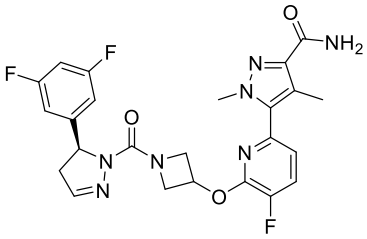

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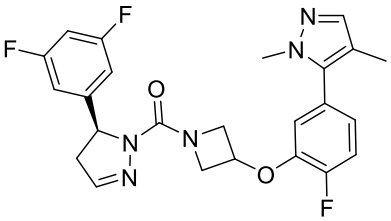

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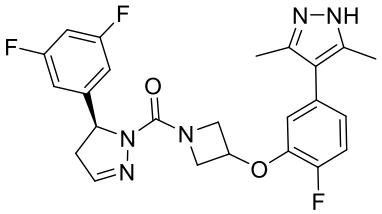

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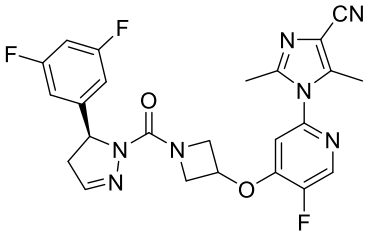

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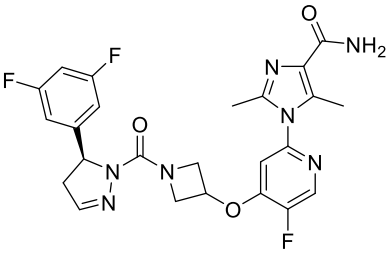

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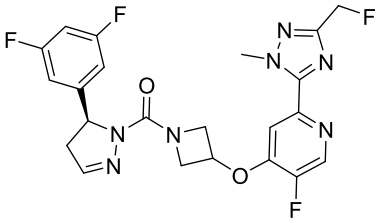

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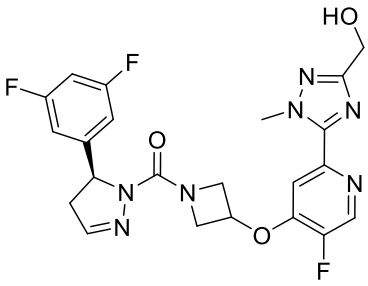

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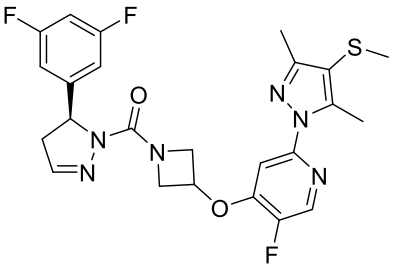

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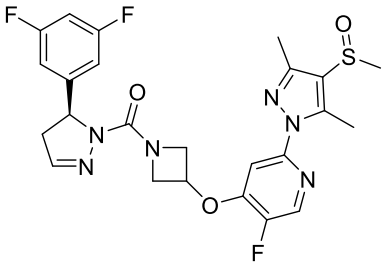

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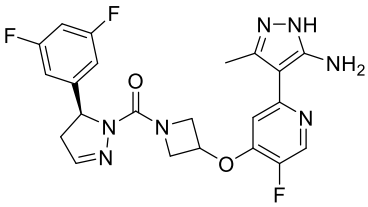

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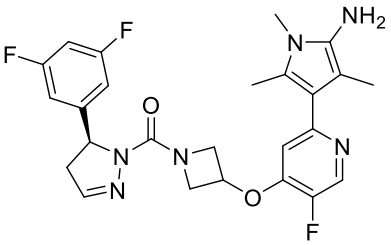

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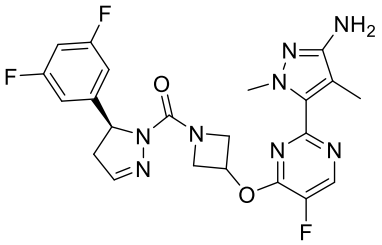

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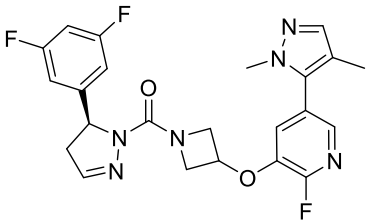

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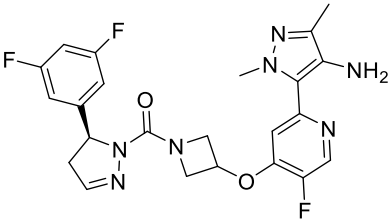

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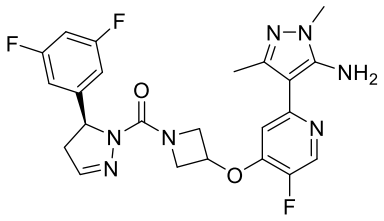

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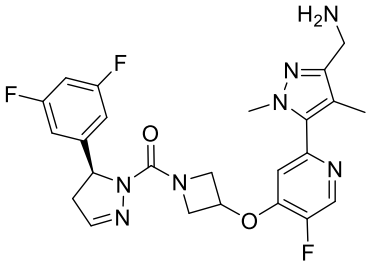

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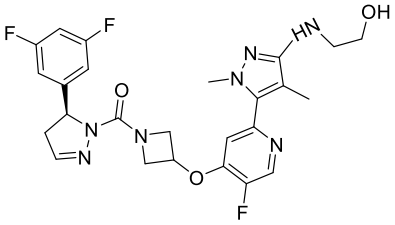

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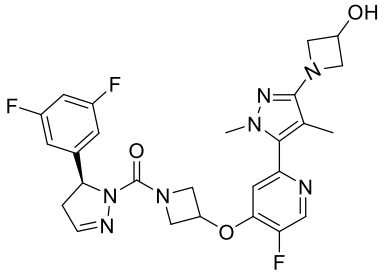

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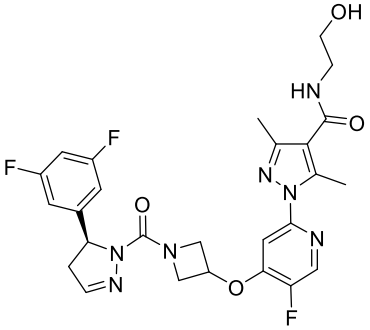

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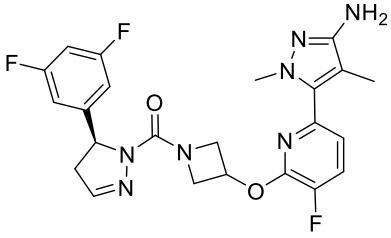

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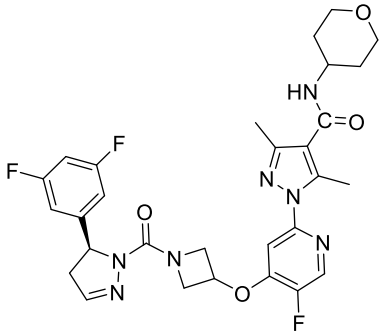

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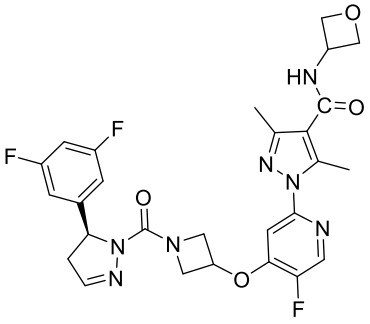

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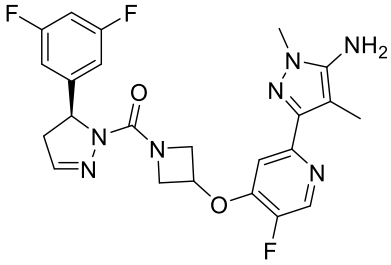

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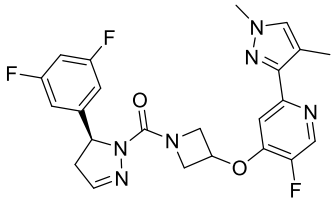

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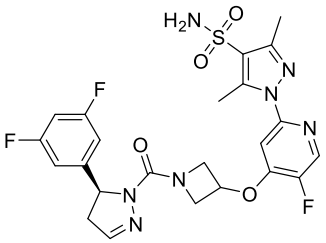

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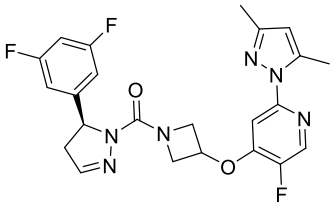

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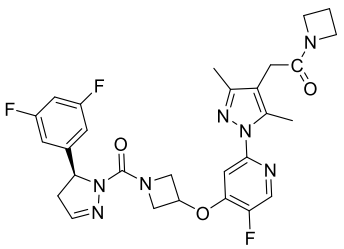

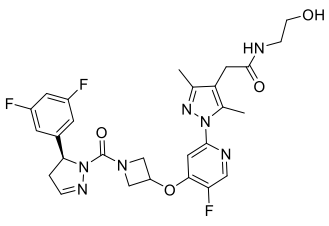

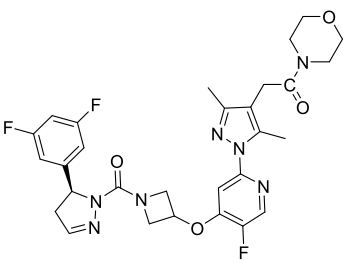

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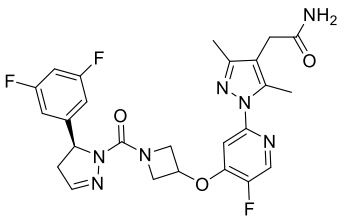

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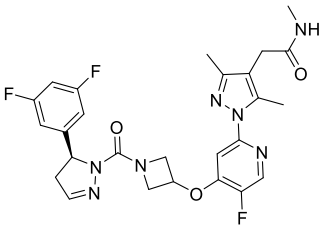

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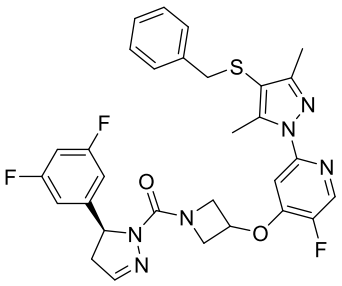

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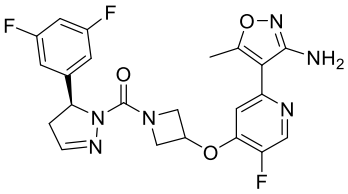

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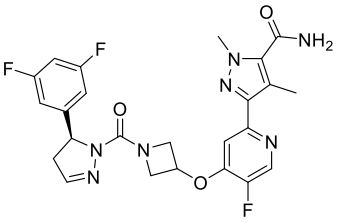

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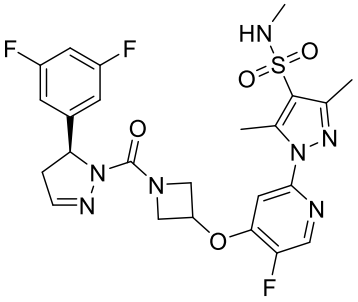

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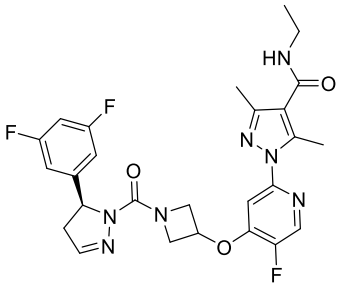

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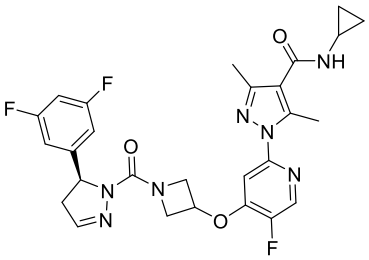

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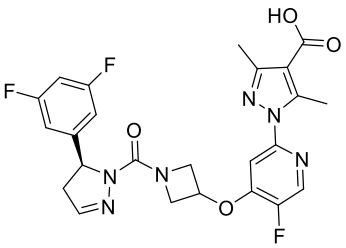

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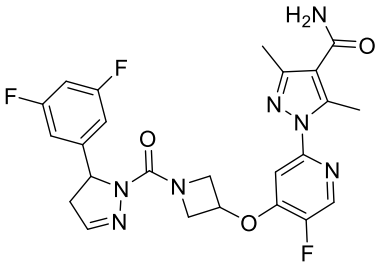

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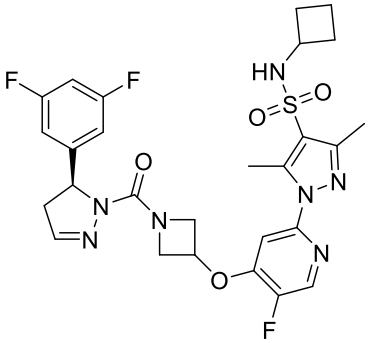

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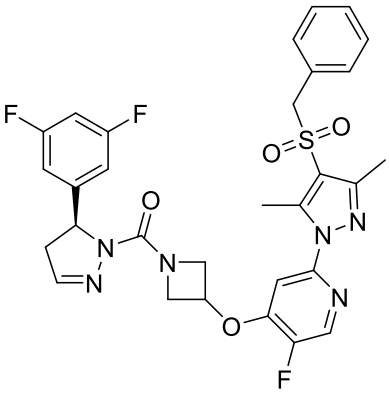

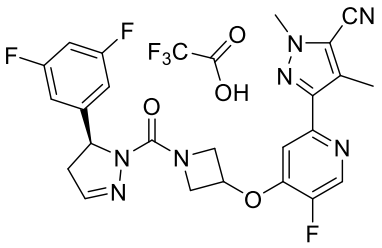

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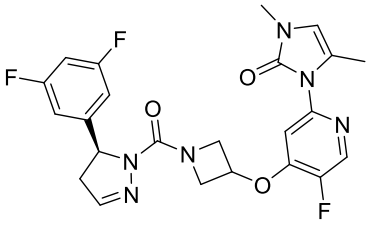

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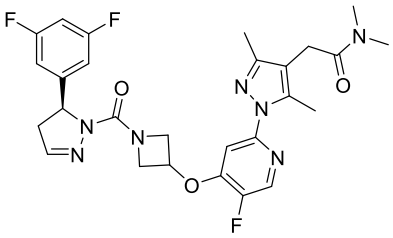

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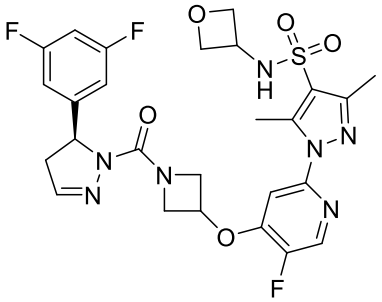

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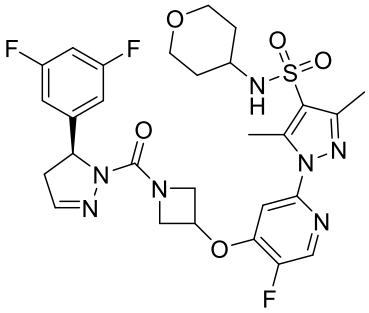

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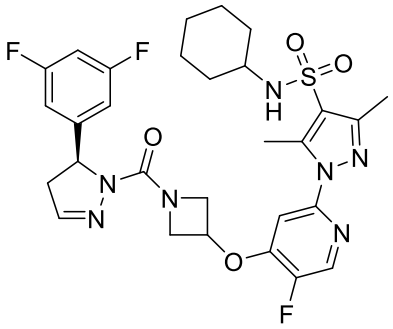

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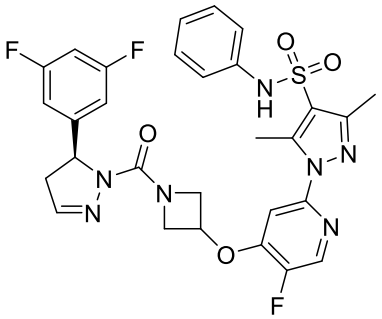

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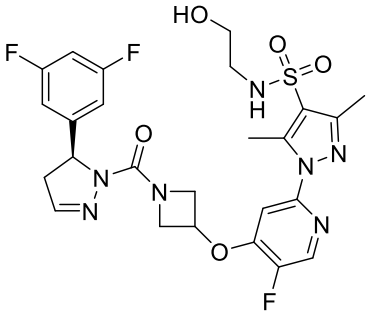

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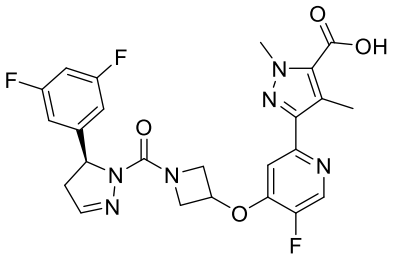

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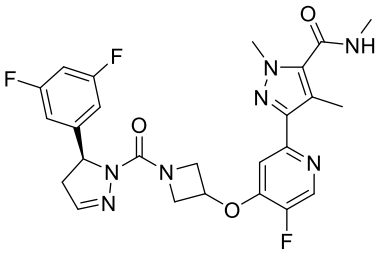

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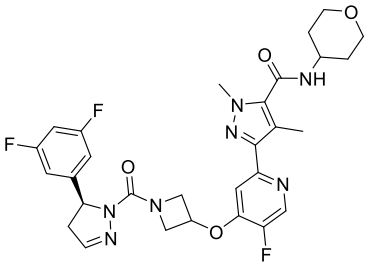

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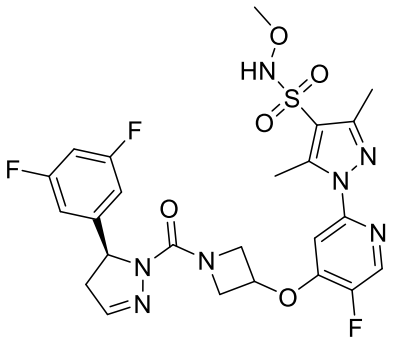

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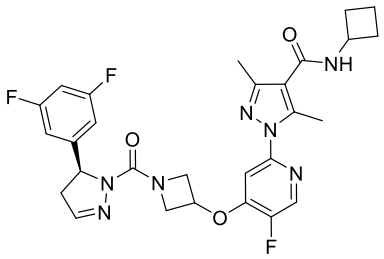

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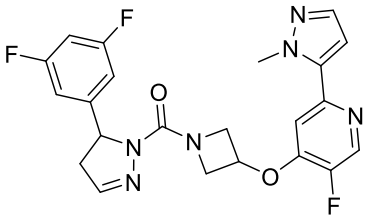

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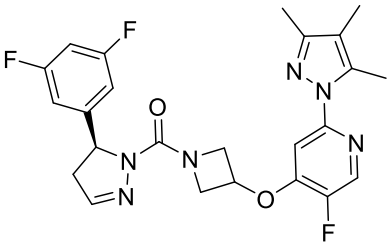

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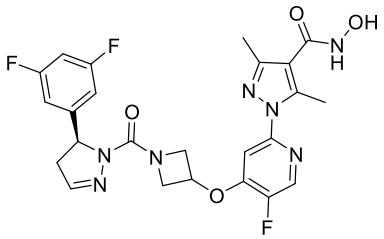

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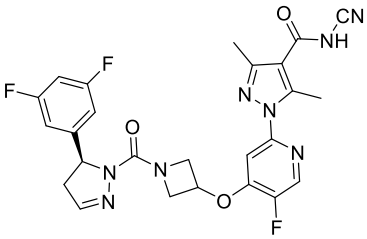

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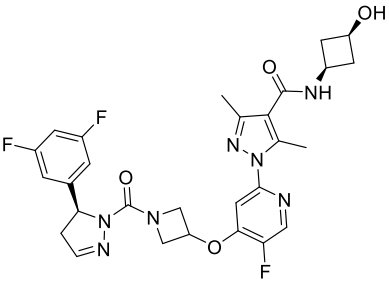

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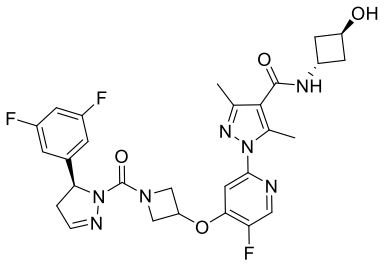

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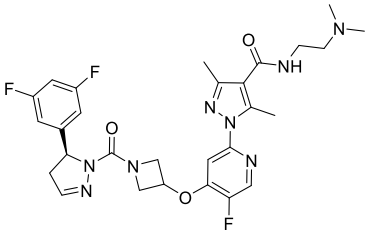

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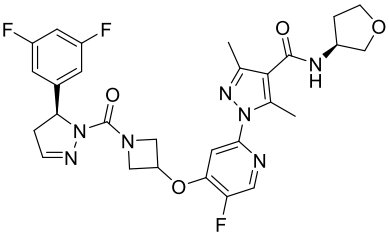

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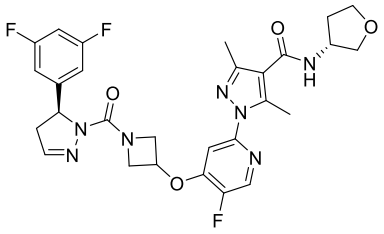

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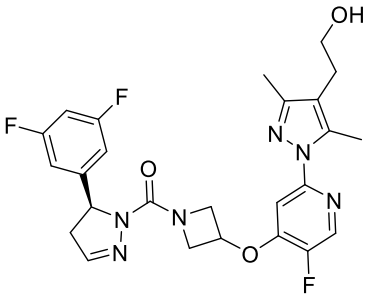

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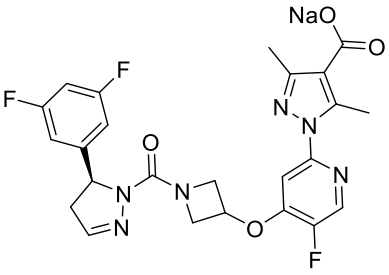

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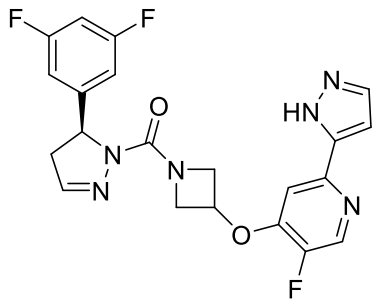

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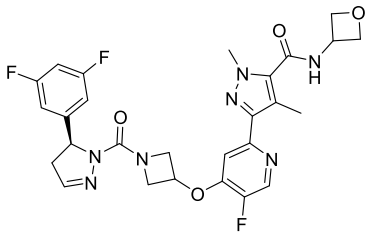

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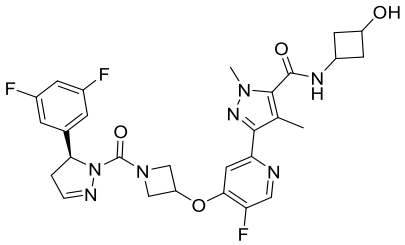

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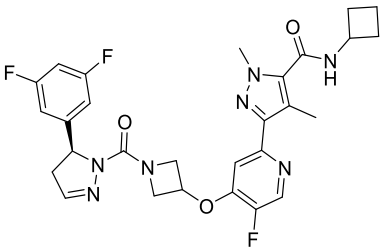

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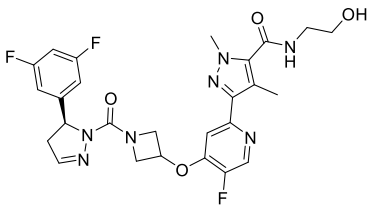

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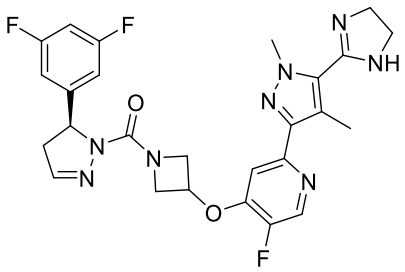

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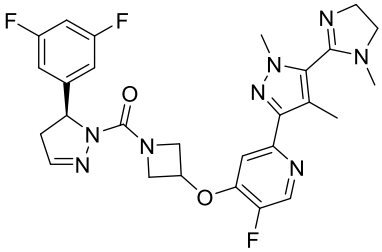

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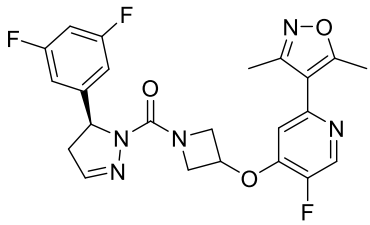

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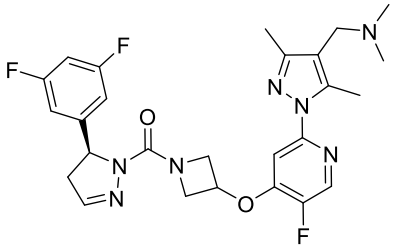

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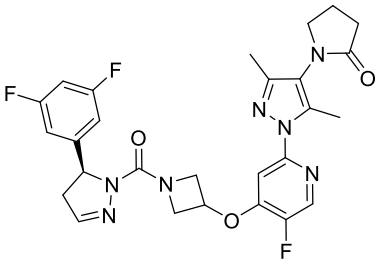

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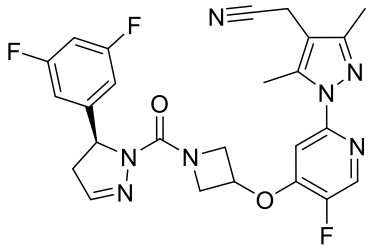

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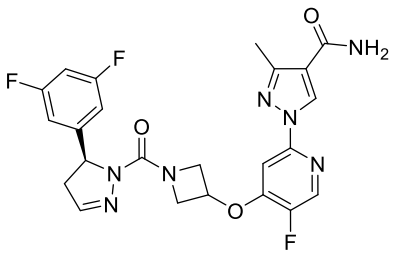

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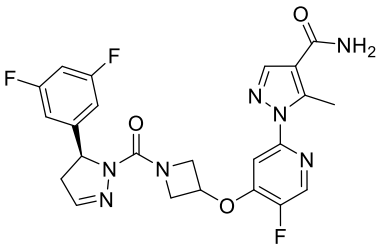

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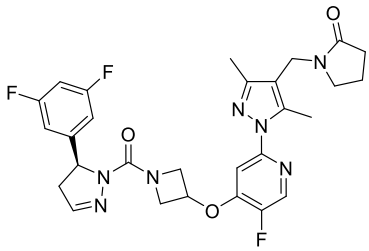

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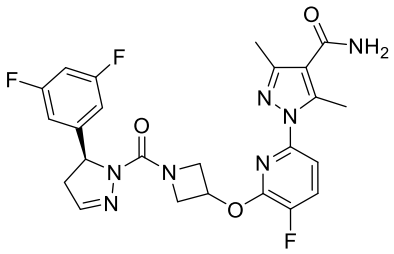

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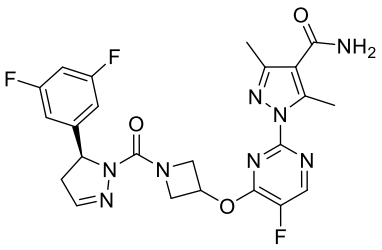

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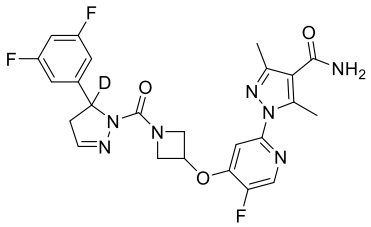

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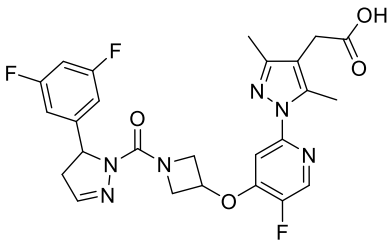

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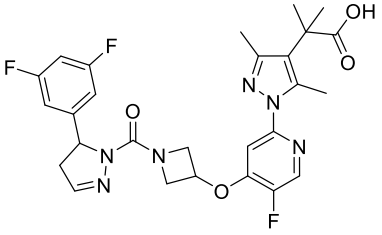
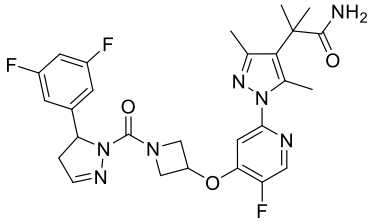
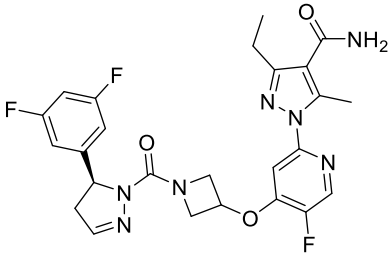


279



280



281.

20. A pharmaceutical composition comprising a therapeutically effective amount of the compound, salt, hydrate, or stereoisomer of any one of claims 1-19 and one or more pharmaceutically acceptable excipients, in predetermined, unit dosage form.

21. Use of the compound, salt, hydrate, or stereoisomer of any one of claims 1-19 or composition of claim 20 in the manufacture of a medicament for treating brain injury, a neurodegenerative disease, viral infection, immune tolerance, or cancer, in a person in need thereof.

22. A compound, salt, hydrate, or stereoisomer of any one of claims 1-19 or composition of claim 20 for use in treating brain injury, a neurodegenerative disease, viral infection, immune tolerance, or cancer in a person in need thereof, or in the manufacture of a medicament thereof in a person in need thereof.