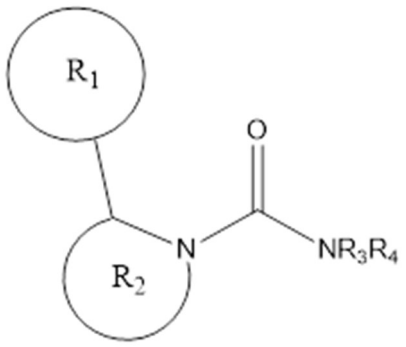
CLAIMS

Claim 1. A compound of structure:



or a pharmaceutically acceptable salt, hydrate or stereoisomer thereof, wherein:

R_1 is substituted or unsubstituted phenyl, or substituted or unsubstituted, 2-, 3-, or 4-, pyrdyl;

R_2 is a dihydro-pyrazole or isoxazolidine; and

R_3 and R_4 are linked, together with the nitrogen atom to which they are bound, to form a 4-6 membered ring with 1-3 heteroatoms: N or N and N/S/O;

wherein the formed 4-6 membered ring is fused to a second ring, or linked through a linker L to R5;

L is a bond, -CH2-, -O-, or =CH

R_5 is substituted or unsubstituted C_3-C_9 cycloalkyl comprising 0-3 heteroatoms, substituted or unsubstituted C_3-C_9 cycloalkenyl comprising 0-3 heteroatoms, substituted or unsubstituted C_3-C_9 cycloalkynyl comprising 0-3 heteroatoms, and substituted or unsubstituted C_5-C_{14} aryl comprising 0-3 heteroatoms;

wherein the substituent(s) are selected from halogen, -R', -OR', =O, =NR', =N-OR', -NR'R", -SR', -SiR'R"R'", -OC(O)R', -C(O)R', -CO_2R', -CONR'R", -OC(O)NR'R", -NR"C(O)R', -NR'-C(O)NR"R'", -NR'-SO_2NR'", -NR"CO_2R', -NH-C(NH_2)=NH, -NR'C(NH_2)=NH, -NH-C(NH_2)=NR', -S(O)R', -SO_2R', -SO_2NR'R", -NR"SO_2R, -CN, -NO_2, -N_3, -CH($Ph)_2$, perfluoro(C_1-C_4) alkoxy and perfluoro(C_1-C_4) alkyl, wherein R', R" and R'" each independently refer to hydrogen, unsubstituted (C_1-C_8) alkyl and heteroalkyl, (C_1-C_8) alkyl and heteroalkyl substituted with one to three halogens, unsubstituted aryl, aryl substituted with one to three halogens, unsubstituted alkyl, alkoxy or thioalkoxy groups, or aryl-(C_1-C_4) alkyl groups, and optionally when R' and R" are attached to the same nitrogen atom, R' and R" form a 5-, 6- or 7-membered ring together with the nitrogen atom to which they are bound.

Claim 2. The compound salt, hydrate or stereoisomer of claim 1 wherein:

R_1 is substituted or unsubstituted phenyl.

Claim 3. The compound salt, hydrate or stereoisomer of claim 1 wherein:
R_1 is fluoro-substituted or unsubstituted phenyl.

Claim 4. The compound salt, hydrate or stereoisomer of claim 1 wherein:
R_2 is a substituted or unsubstituted C3-C6 saturated or unsaturated ring with 1-3 heteroatom (s): N or N and N/S/O.

Claim 5. The compound, salt, hydrate or stereoisomer of any of claims 1-4 wherein:
R_3 and R_4 are linked, together with the nitrogen atom to which they are bound, to form a 4-6 membered N-containing, heterocycloalkyl ring,

Claim 6. The compound, salt, hydrate or stereoisomer of any of claims 1-4 wherein:
R3 and R4 are linked, together with the nitrogen atom to which they are bound, to form a 4-6 membered N-containing, heterocycloalkyl ring, fused to phenyl, to form isoindoline.

Claim 7. The compound, salt, hydrate or stereoisomer of claim 1 wherein L is $-CH_2-$.

Claim 8. The compound, salt, hydrate or stereoisomer of claim 1 wherein L is -O-.

Claim 9. The compound, salt, hydrate or stereoisomer of claim 1 wherein L is =CH-.

Claim 10. The compound, salt, hydrate or stereoisomer of any one of claims 1 to 9 wherein R_5 is:
(a) substituted or unsubstituted phenyl;
(b) substituted or unsubstituted 2-, 3-or 4-pyridine;
(c) substituted or unsubstituted naphthyl or 3-azanaphthyl;
(d) substituted or unsubstituted 0-3 heteroatom cyclohexyl, cyclopentyl; or
(e) substituted or unsubstituted 0-3 heteroatom cyclopentene or cyclopentadiene;

Claim 11. The compound, salt, hydrate or stereoisomer of any one of claims 1 to 9 wherein:
R_5 is substituted or unsubstituted: phenyl, cyclohexyl, furan, thiophene or azole.

Claim 12. The compound, salt, hydrate or stereoisomer of any one claims 1 to 9 wherein:
R_5 is substituted or unsubstituted: phenyl or cyclohexyl.

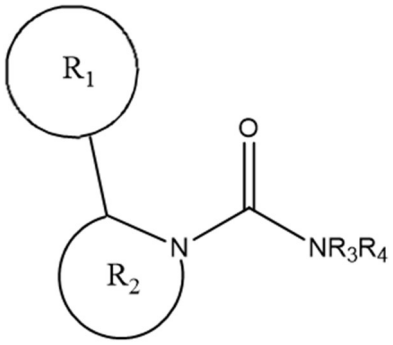
Claim 13. The compound, salt, hydrate or stereoisomer of any one of claims 1 to 9 wherein: R_5 is substituted or unsubstituted phenyl.

Claim 14. The compound, salt, hydrate or stereoisomer of any one of claims 1 to 9 wherein:
R_5 is fluoro-substituted, phenyl, or unsubstituted phenyl.

Claim 15. The compound, salt, hydrate or stereoisomer of any one of claims 1 to 9 wherein:
R5 is 3,5 difluorophenyl.

Claim 16. The compound, salt, hydrate or stereoisomer of any one of claims 1-3 and 5-14 wherein: the substituent(s) of R_1 are selected from halogen and CN; and/or the substituent(s) of R_5 are selected from halogen, -R', -OR', =O, -NR'R", -CO2R', -CONR'R", -NR"C(O)R', and -CN, wherein R' and R" are each independently selected from hydrogen, unsubstituted (C_1-C_4)alkyl, and unsubstituted (C_1-C_4) heteroalkyl, wherein the (C_1-C_4) heteroalkyl has at least one heteroatoms selected from N, O, and S.

Claim 17. A compound of a structure:



or a pharmaceutically acceptable salt, hydrate or stereoisomer thereof wherein:

R_1 is substituted or unsubstituted phenyl or substituted or unsubstituted 2-, 3- or 4-pyridyl, wherein the substitute(s) of R_1 are selected from halogen and CN;

R_2 is dihydro-pyrazole or isoxazolidine; and

R_3 and R_4, together with the nitrogen atom to which they are bound, are linked to form a 4-6 membered N-containing, heterocycloalkyl ring, wherein the formed 4-6 membered heterocycloalkyl ring is fused to phenyl, or linked through a linker to R_5;

wherein the linker is –CH2-, -O-, or =CH-;

R_5 is

(a) substituted or unsubstituted phenyl;

(b) substituted or unsubstituted 2-, 3- or 4-pyridine;

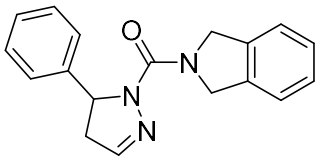
(c) substituted or unsubstituted naphthyl or 3-azanaphthyl;

(d) substituted or unsubstituted 0-3 heteroatom cyclohexyl, cyclopentyl, wherein the heteroatom is selected from N, O, and S; or

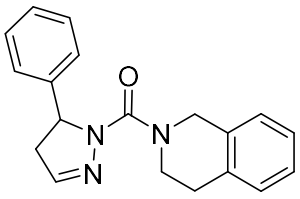
(e) substituted or unsubstituted 0-3 heteroatom cyclopentene or cyclopentadiene, wherein the heteroatom is selected from N, O, and S;

wherein the substituent(s) of R_5 are selected from halogen, -R', -OR', =O, -NR'R", -CO_2R', -CONR'R", -NR"C(O)R', and -CN, wherein R' and R" are each independently selected from hydrogen, unsubstituted (C_1-C^8) alkyl, and unsubstituted (C_1-C_8) heteroalkyl, wherein the (C_1-C_8) heteroalkyl has at least one heteroatoms selected from N, O, and S.

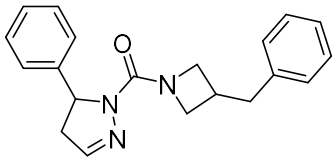
Claim 18. A compound comprising a structure of any one of the following structures:



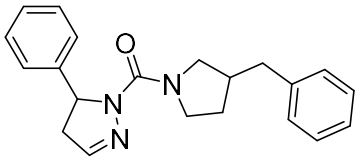
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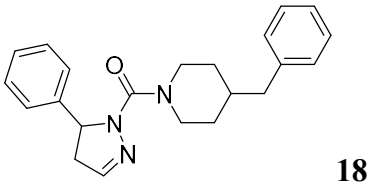
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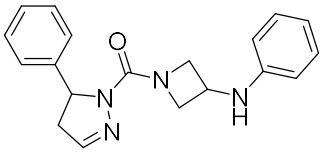
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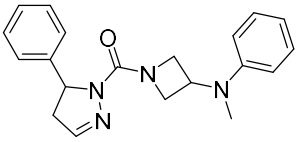
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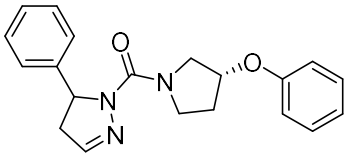
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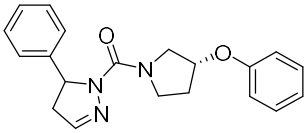
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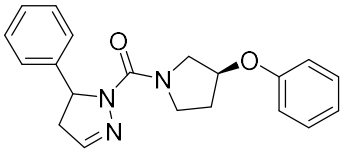
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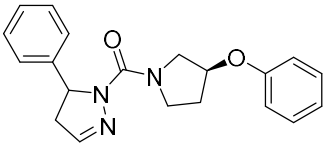
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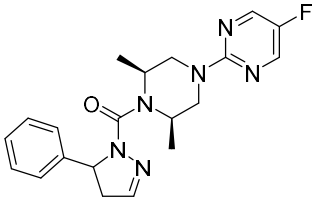
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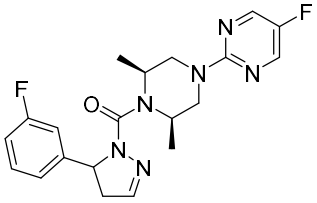
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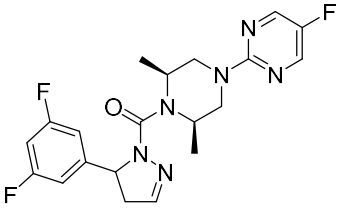
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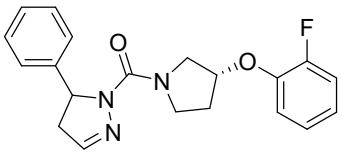
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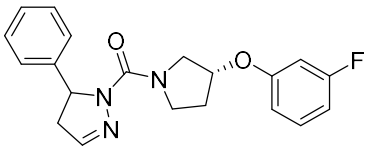
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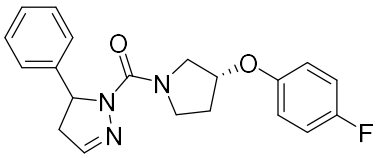
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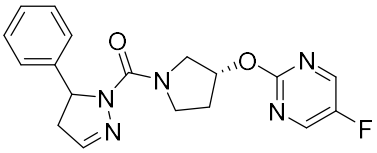
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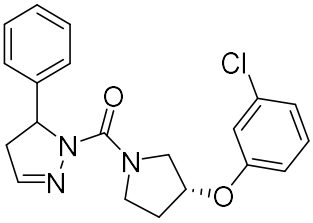
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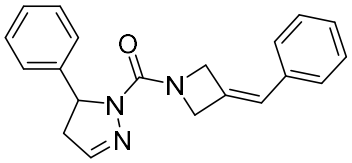
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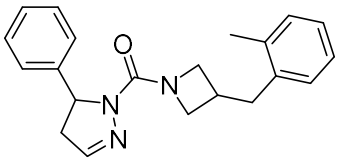
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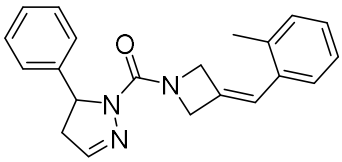
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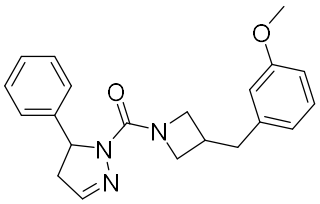
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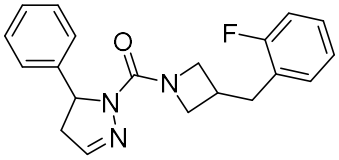
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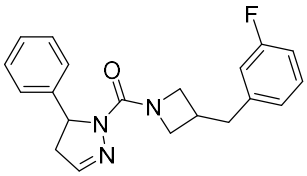
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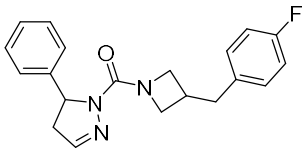
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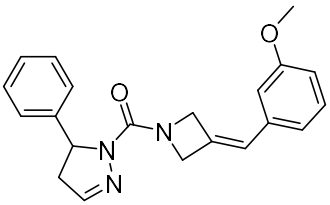
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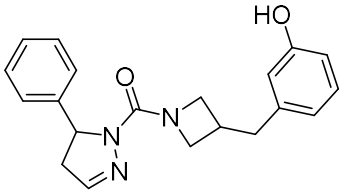
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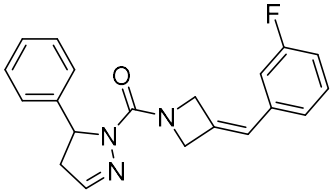
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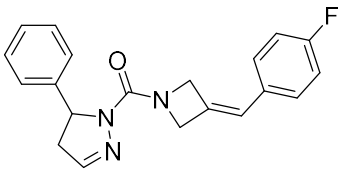
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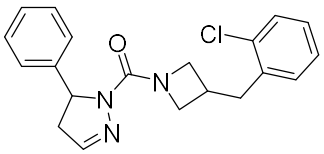
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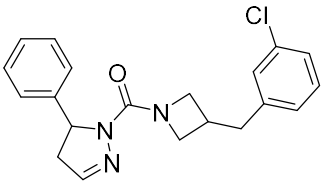
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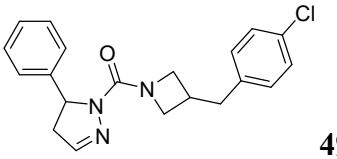
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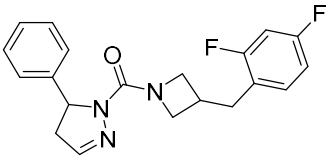
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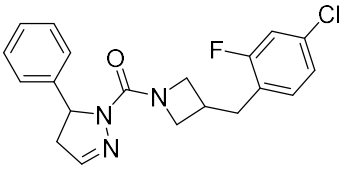
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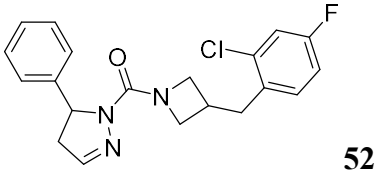
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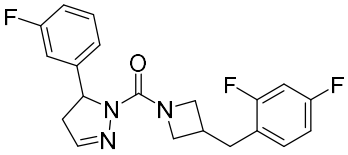
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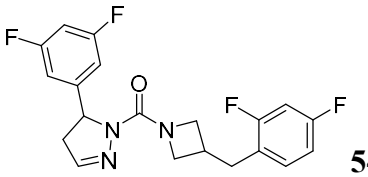
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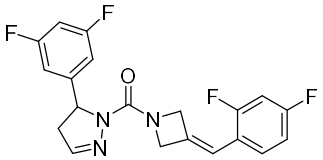
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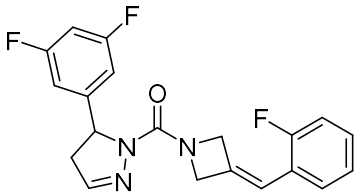
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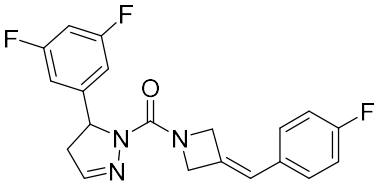
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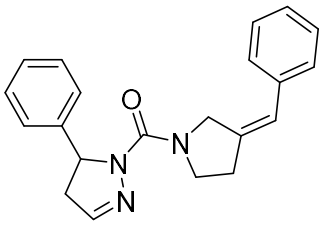
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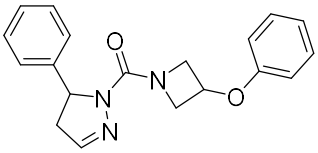
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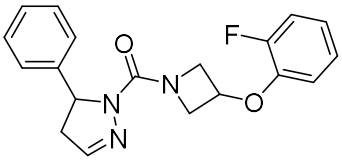
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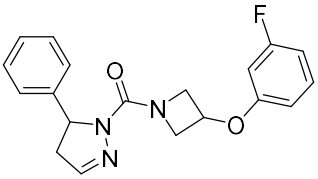
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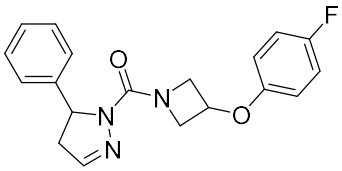
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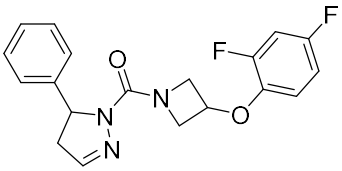
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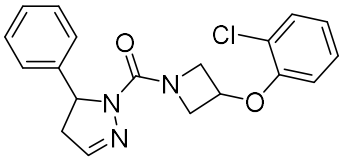
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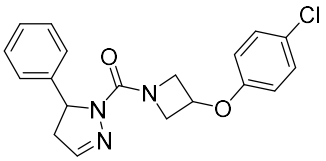
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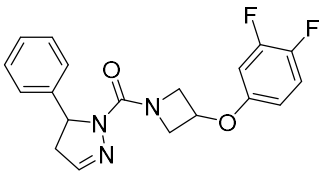
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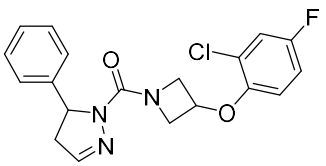
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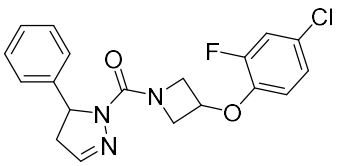
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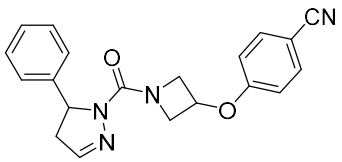
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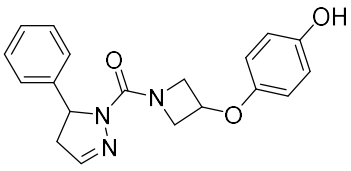
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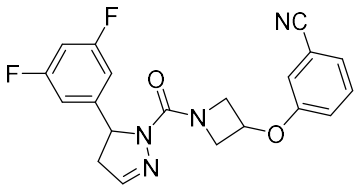
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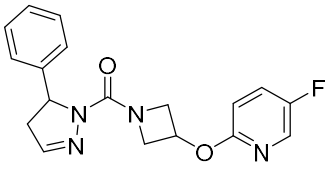
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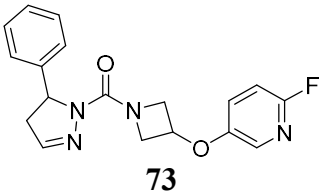
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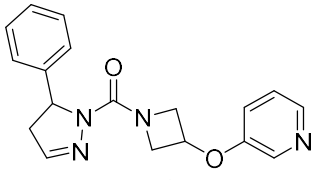
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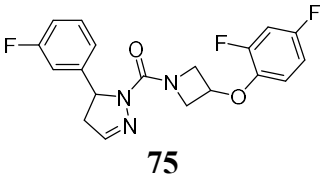
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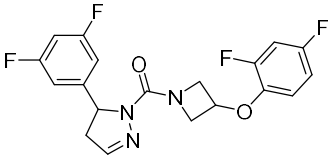
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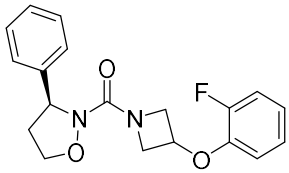
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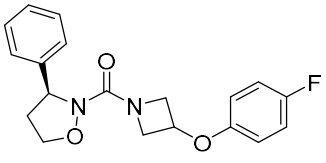
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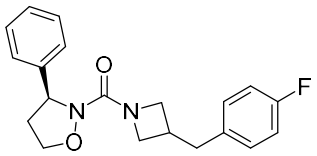
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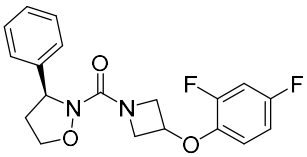
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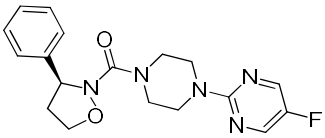
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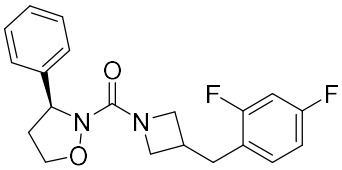
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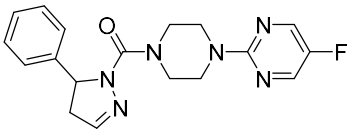
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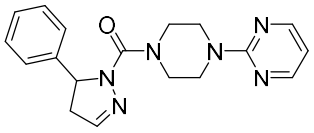
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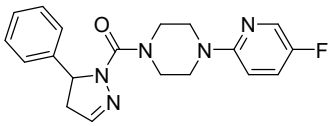
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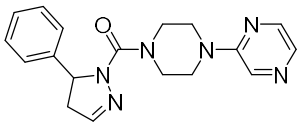
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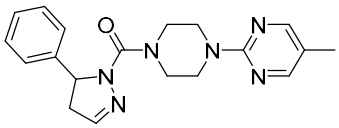
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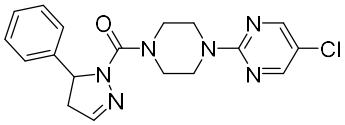
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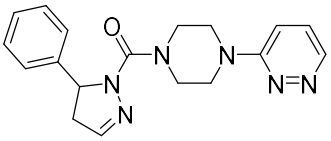
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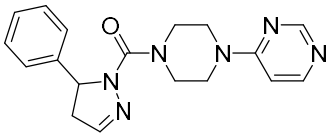
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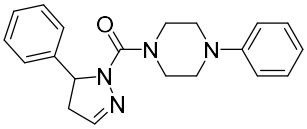
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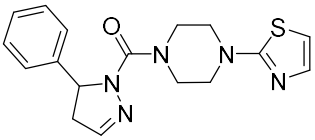
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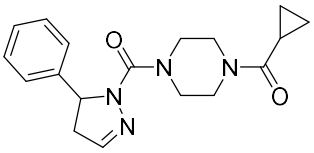
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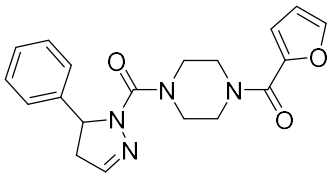
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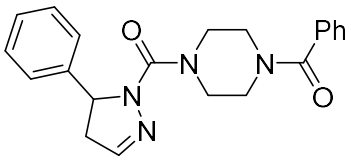
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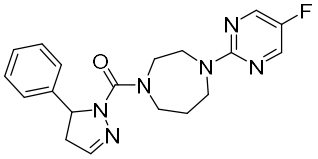
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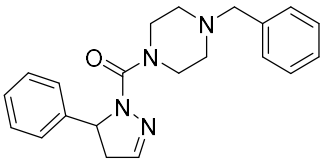
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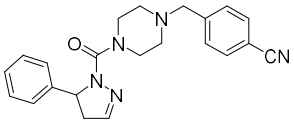
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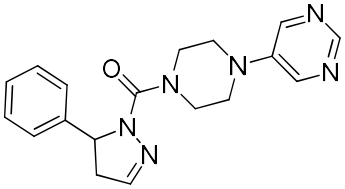
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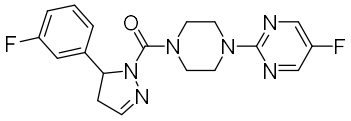
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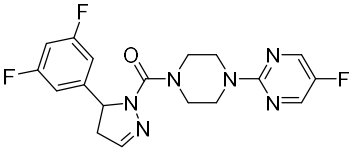
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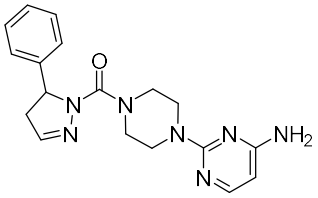
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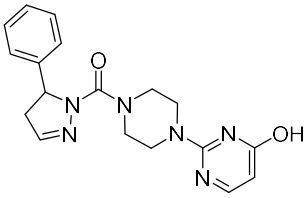
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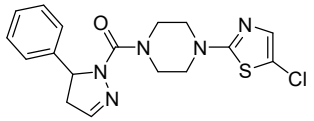
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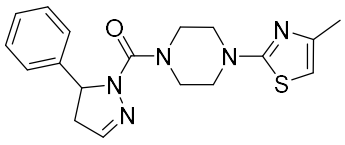
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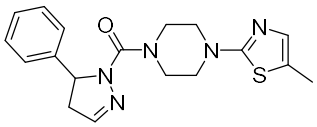
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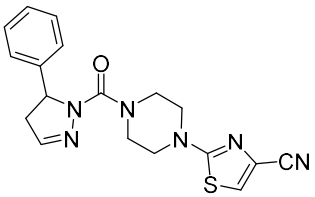
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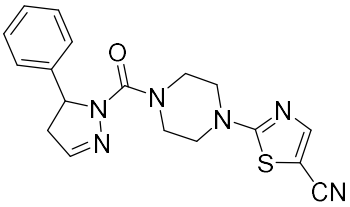
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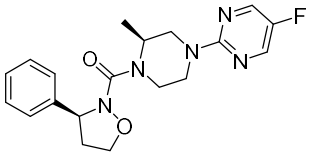
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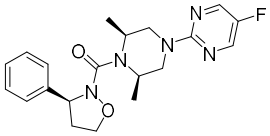
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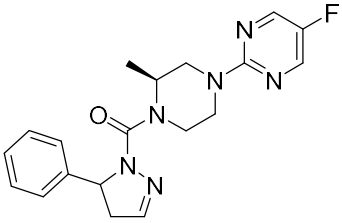
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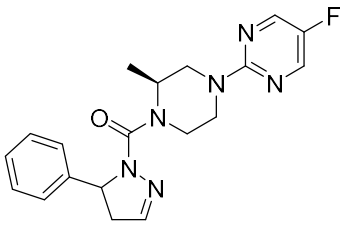
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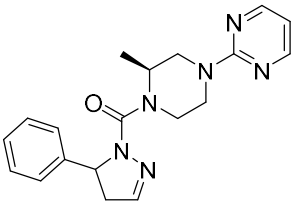
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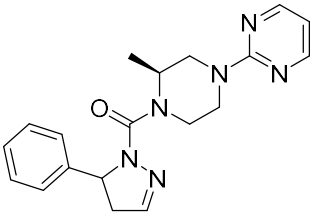
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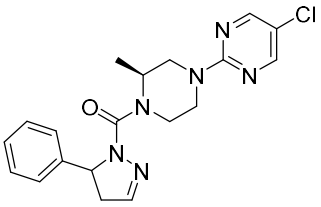
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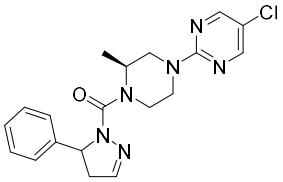
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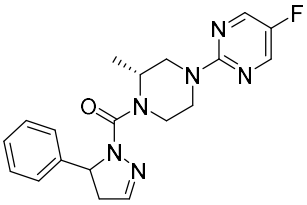
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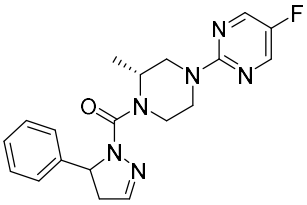
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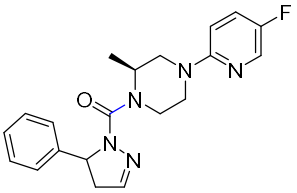
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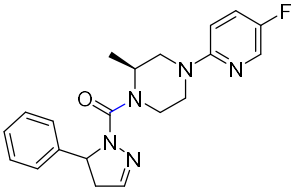
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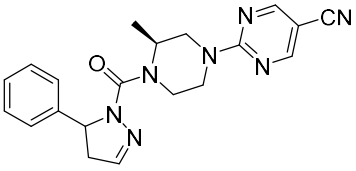
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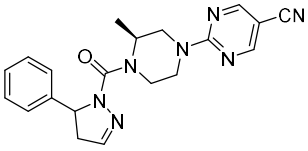
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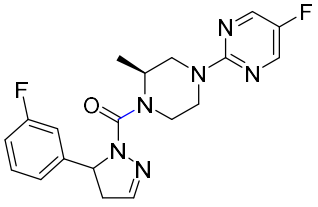
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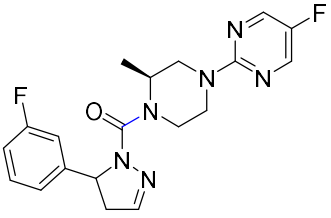
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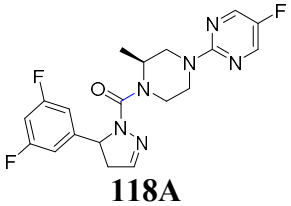
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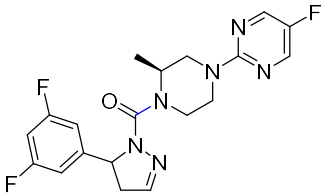
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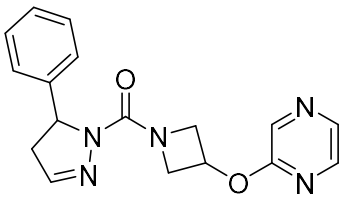
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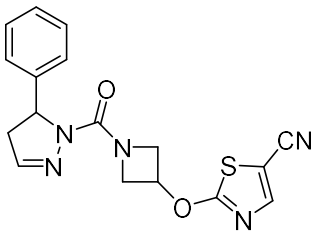
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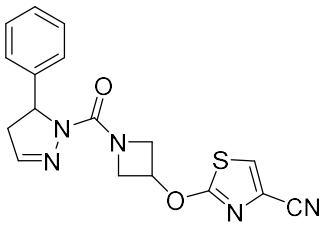
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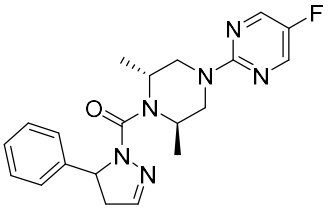
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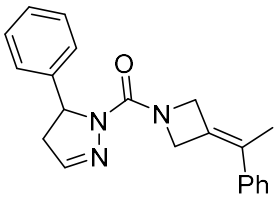
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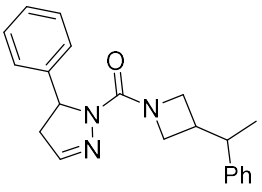
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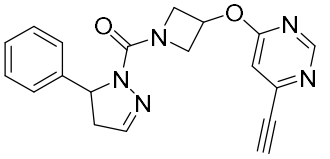
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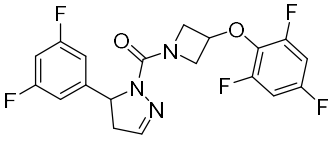
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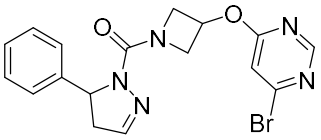
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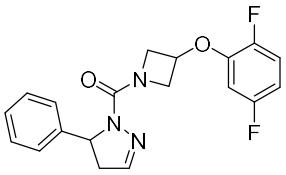
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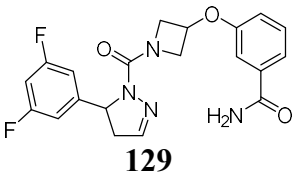
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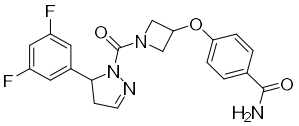
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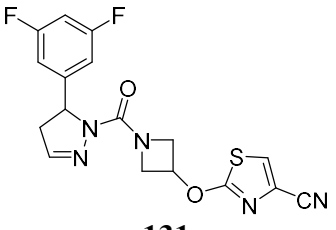
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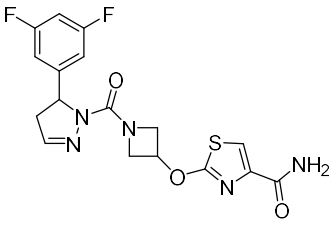
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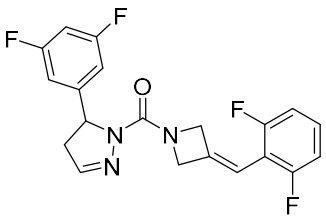
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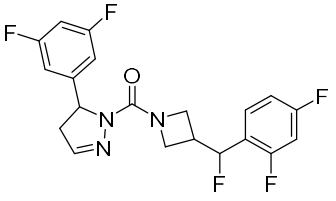
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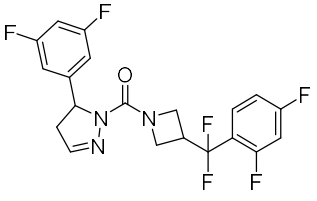
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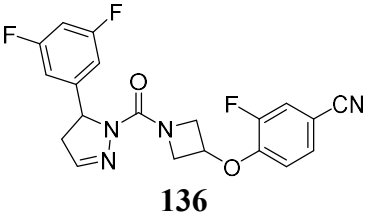
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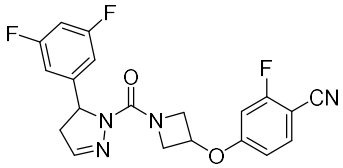
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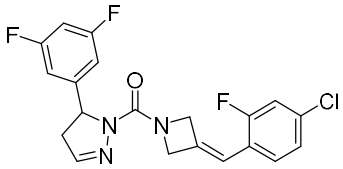
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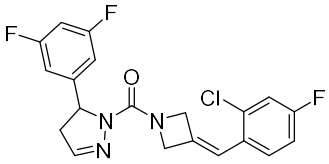
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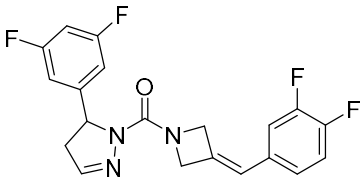
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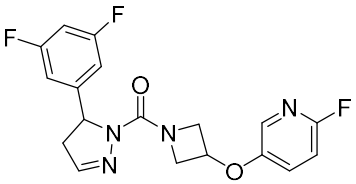
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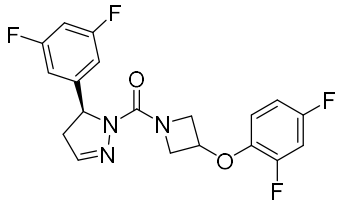
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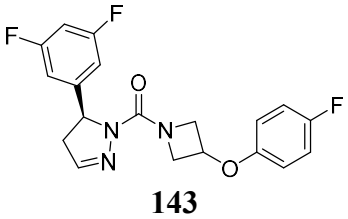
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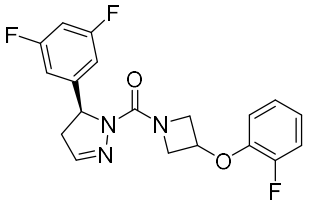
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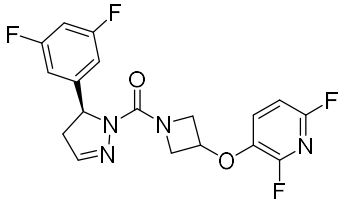
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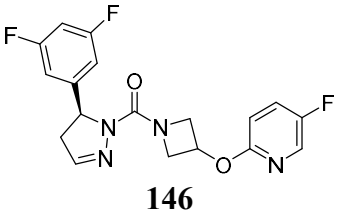
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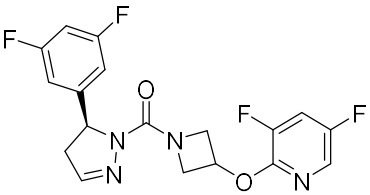
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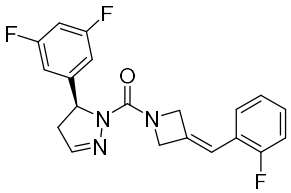
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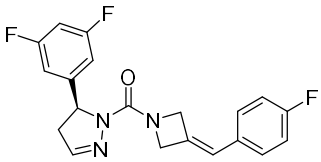
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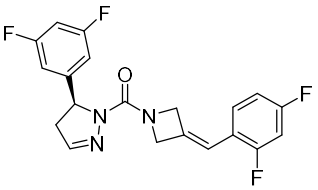
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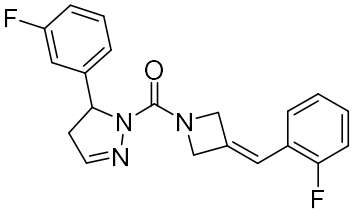
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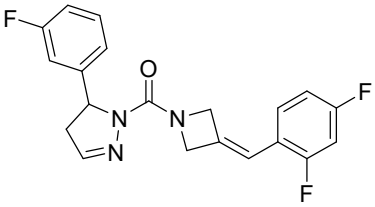
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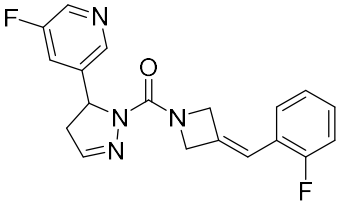
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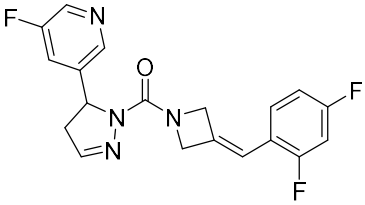
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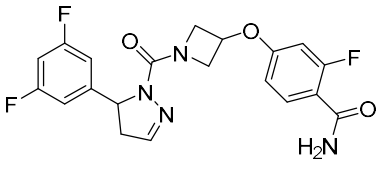
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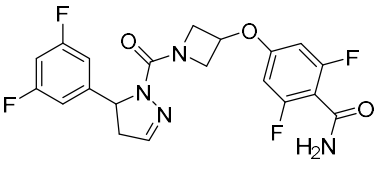
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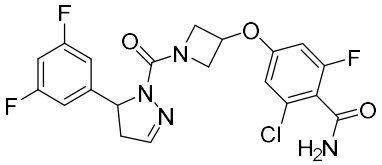
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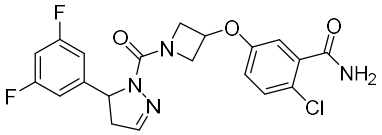
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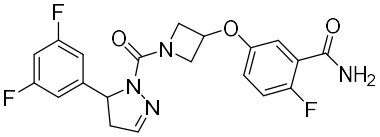
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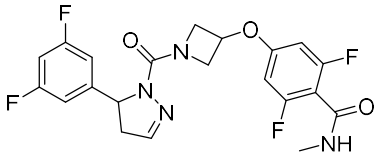
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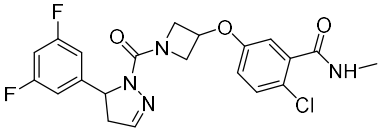
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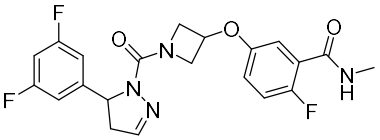
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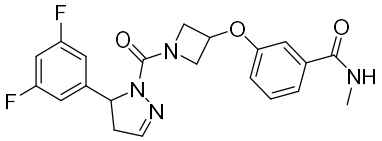
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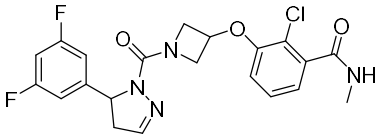
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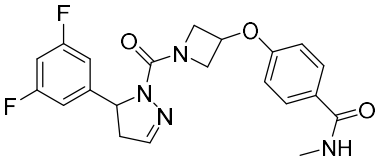
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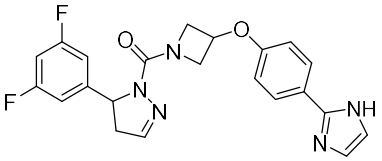
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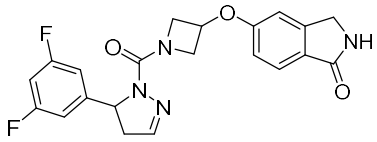
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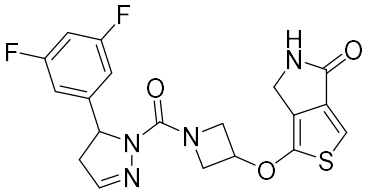
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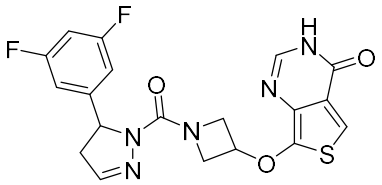
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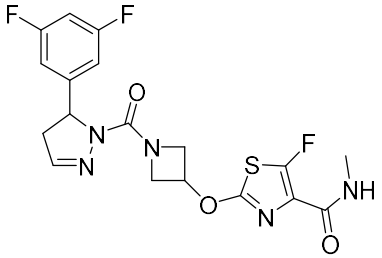
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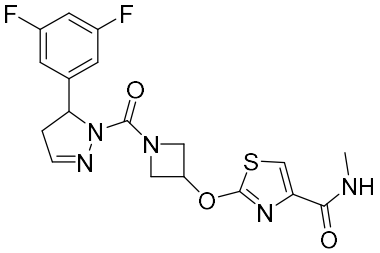
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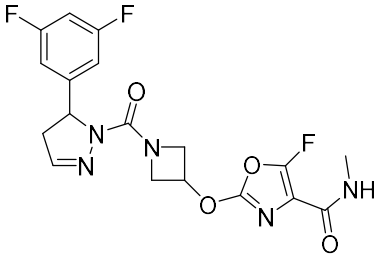
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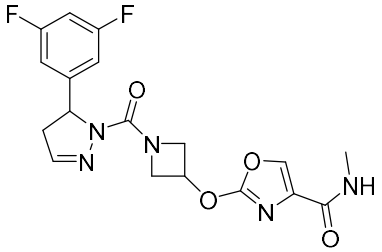
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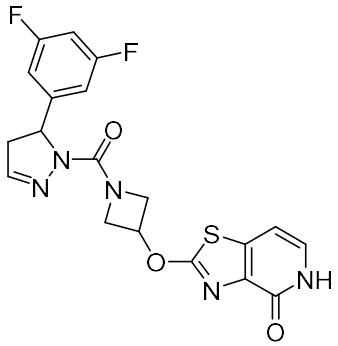
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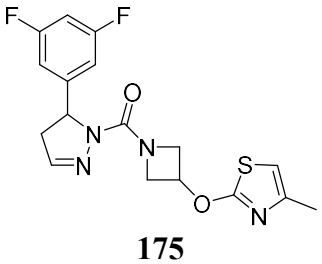
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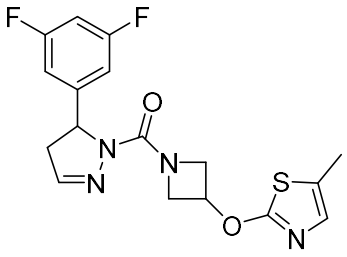
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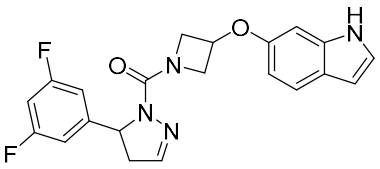
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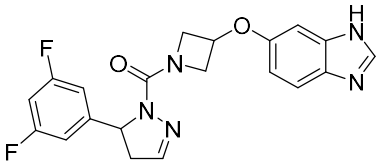
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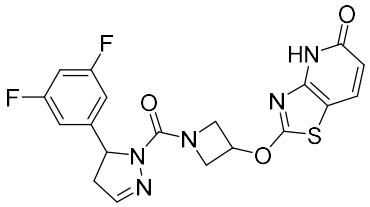
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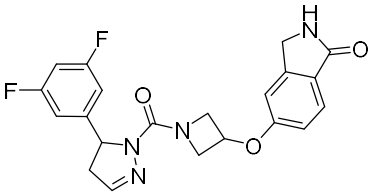
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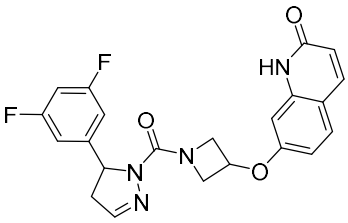
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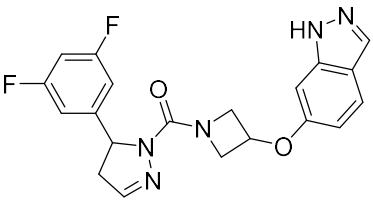
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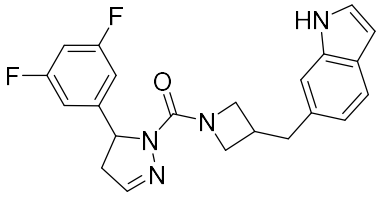
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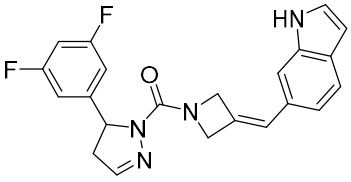
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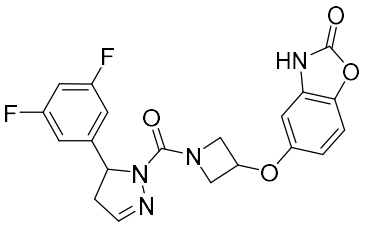
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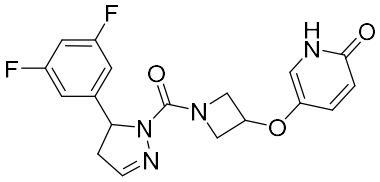
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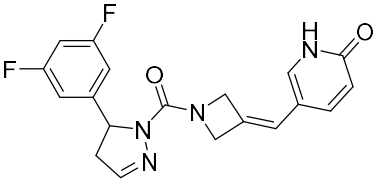
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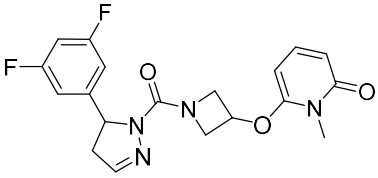
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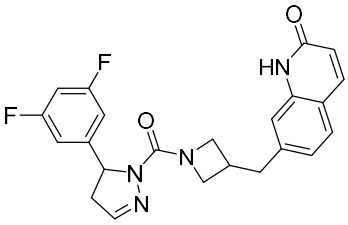
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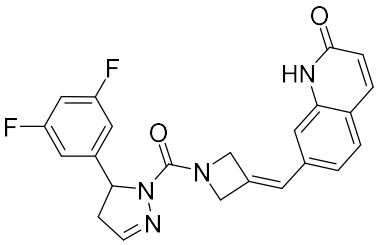
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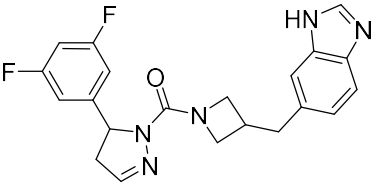
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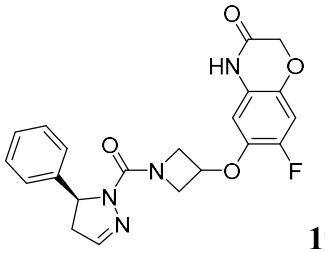
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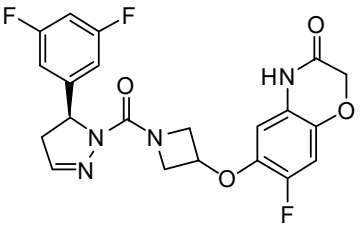
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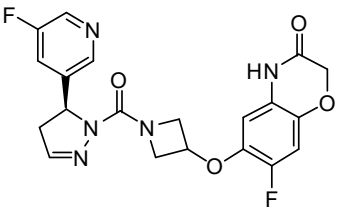
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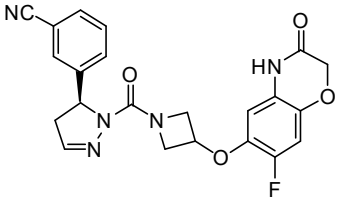
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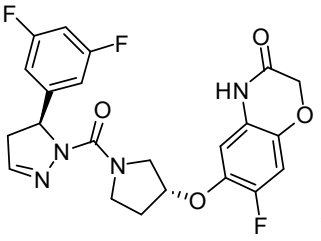
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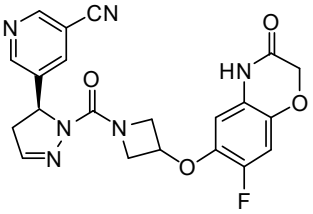
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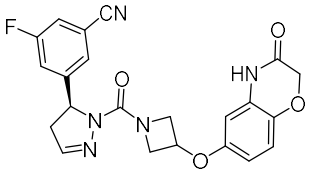
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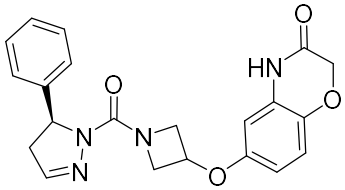
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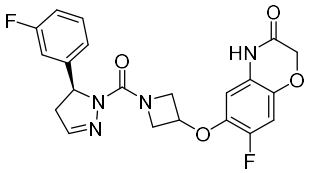
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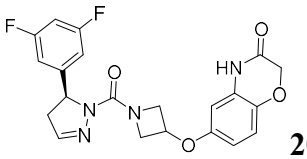
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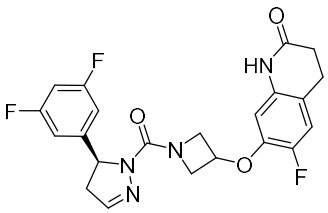
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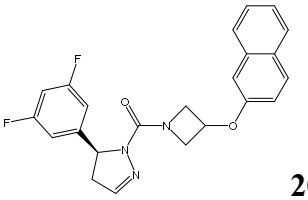
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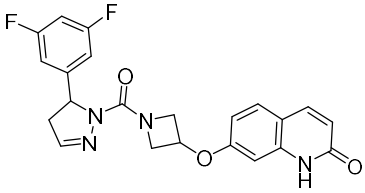
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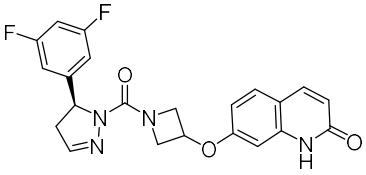
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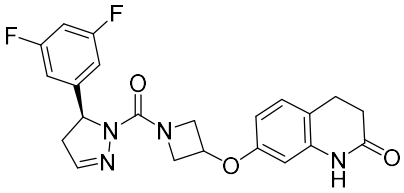
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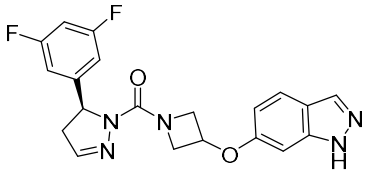
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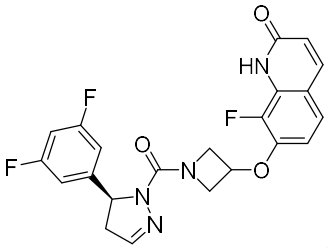
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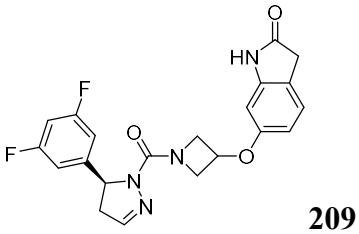
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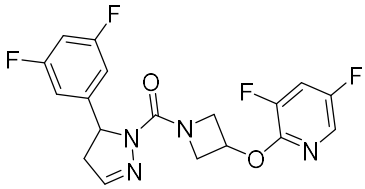
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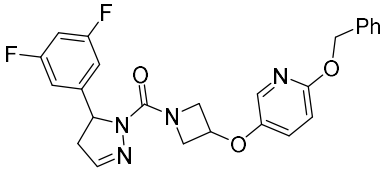
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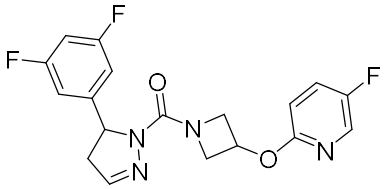
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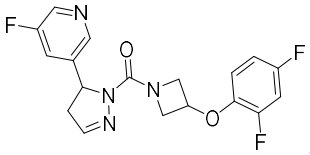
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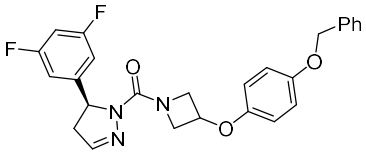
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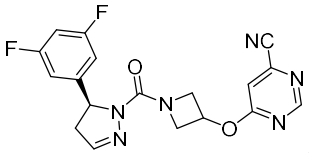
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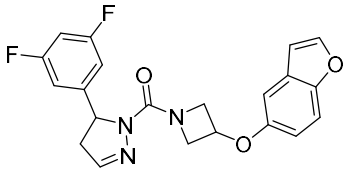
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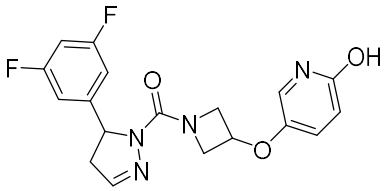
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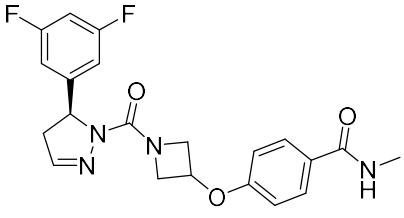
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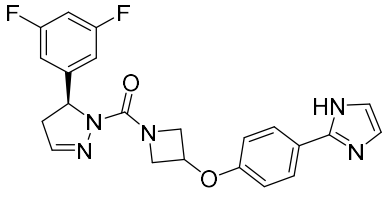
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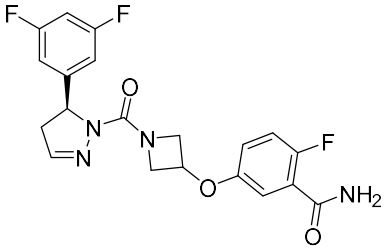
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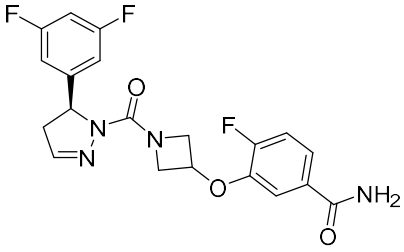
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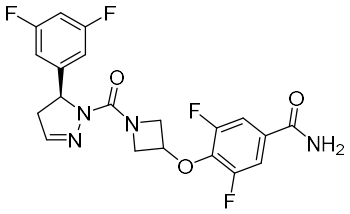
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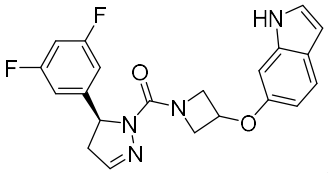
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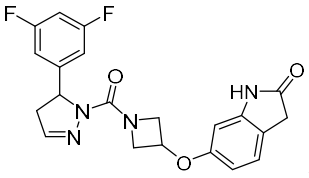
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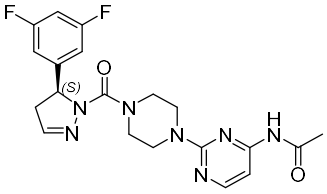
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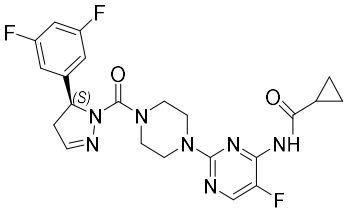
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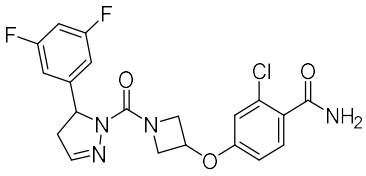
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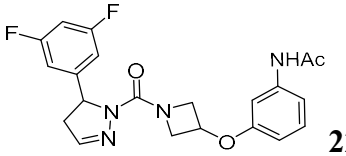
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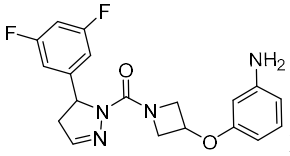
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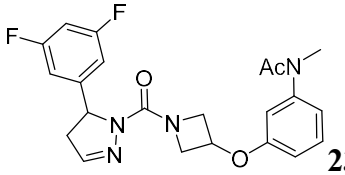
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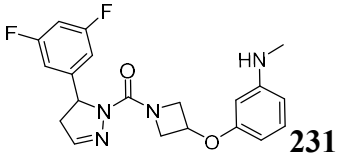
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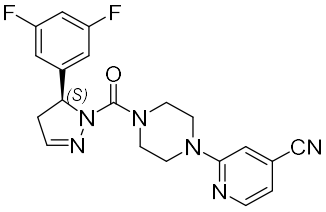
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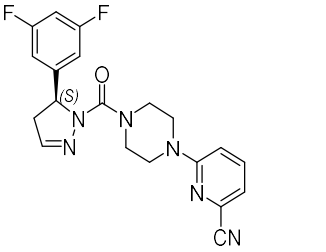
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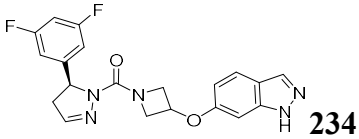
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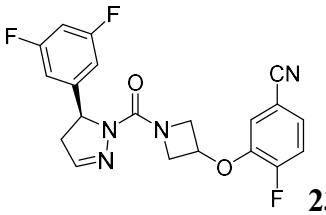
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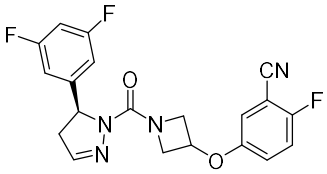
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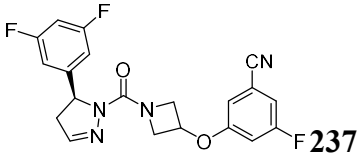
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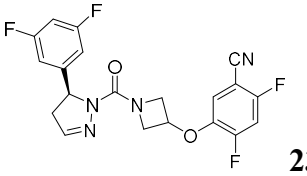
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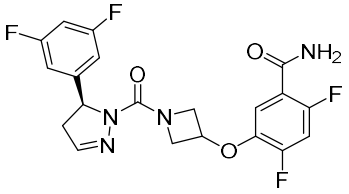
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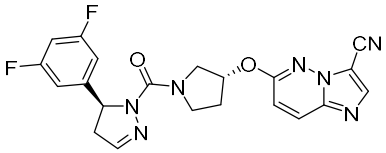
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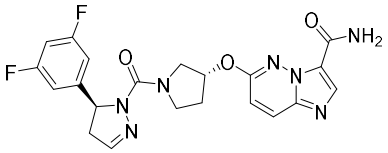
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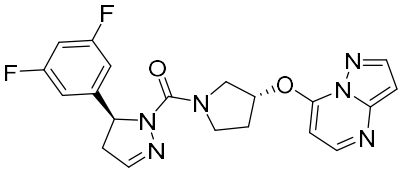
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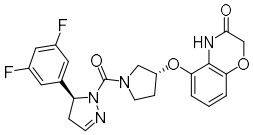
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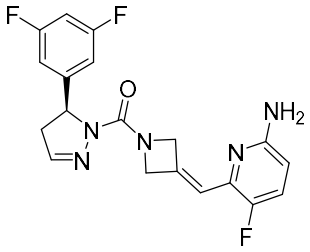
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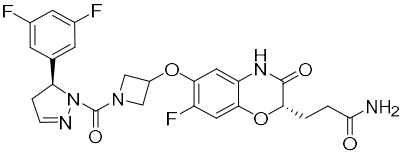
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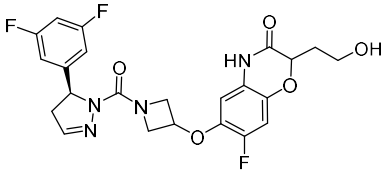
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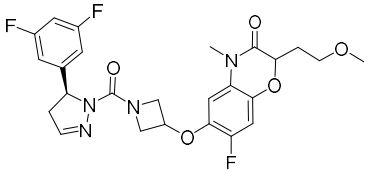
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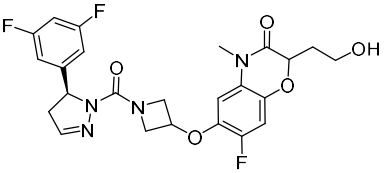
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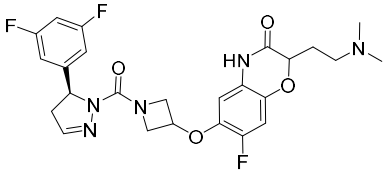
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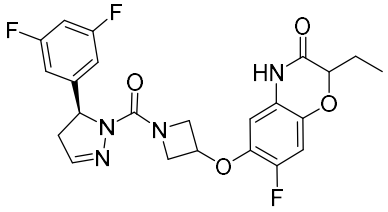
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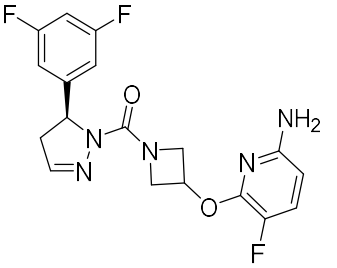
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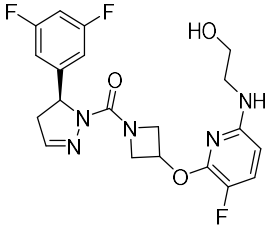
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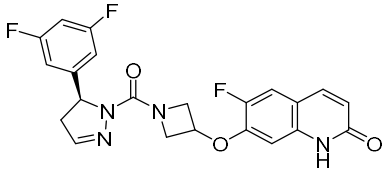
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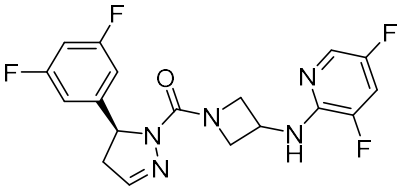
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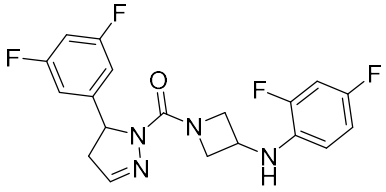
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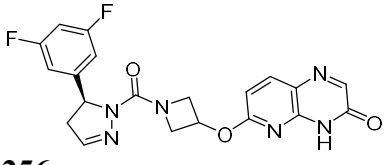
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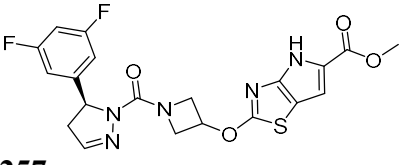
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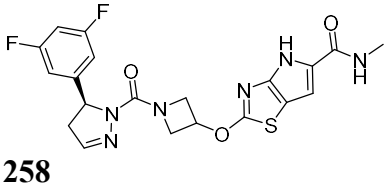
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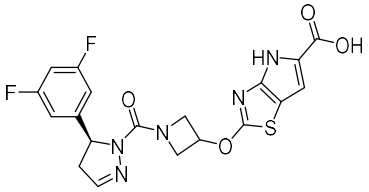
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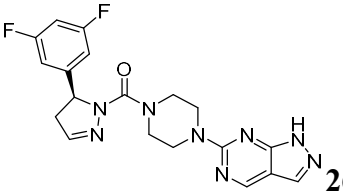
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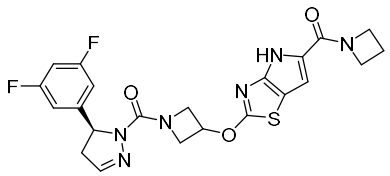
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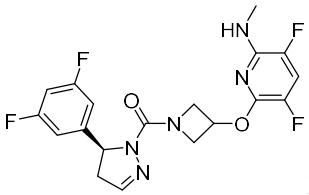
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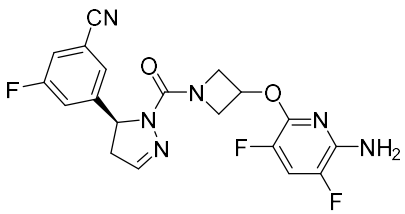
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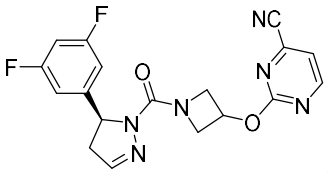
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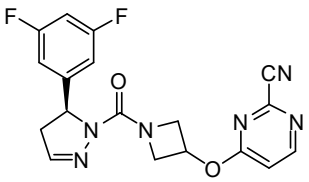
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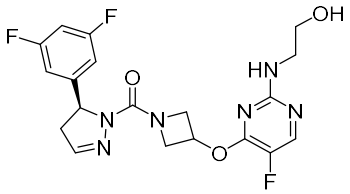
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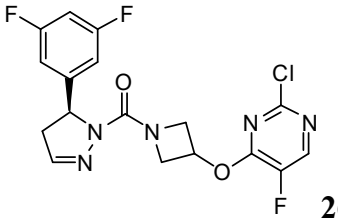
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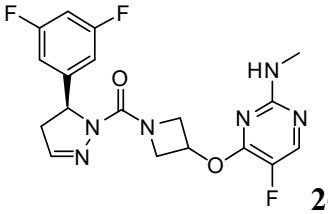
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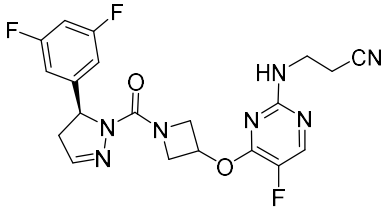
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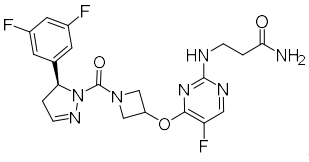
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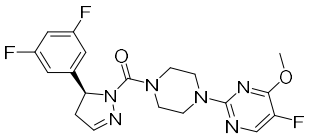
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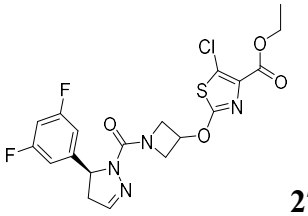
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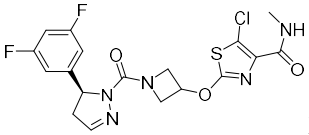
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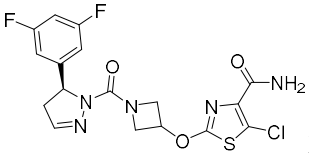
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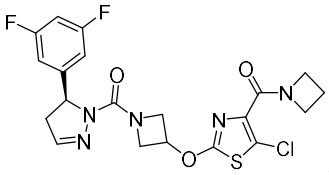
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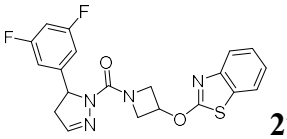
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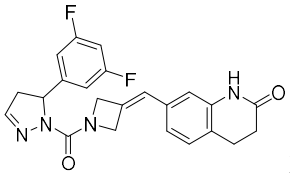
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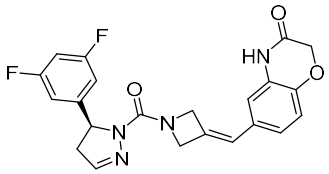
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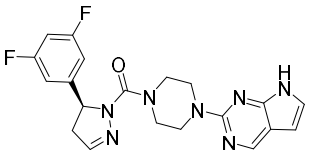
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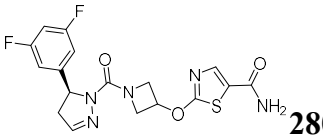
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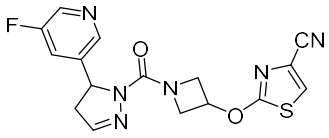
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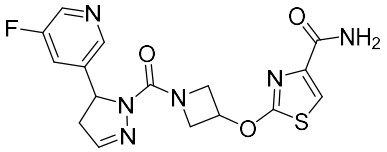
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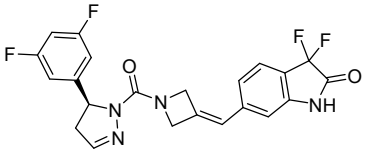
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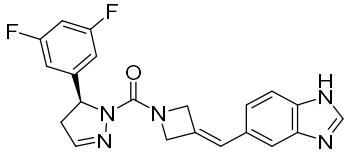
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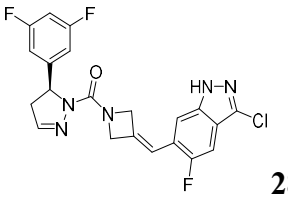
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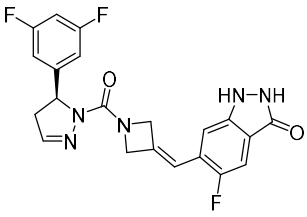
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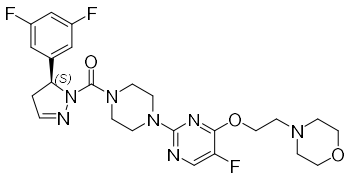
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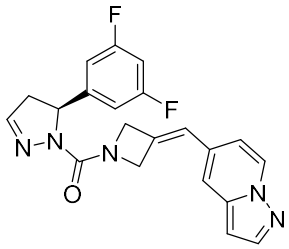
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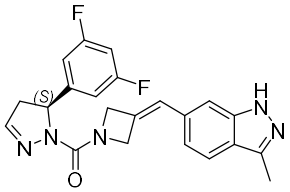
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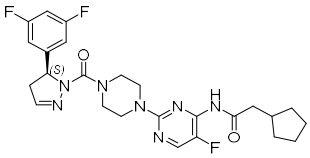
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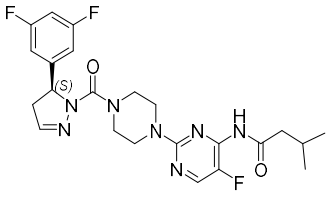
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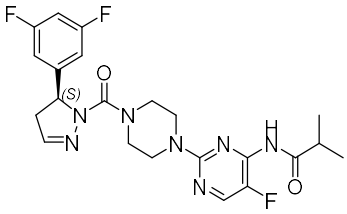
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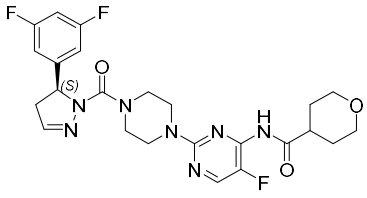
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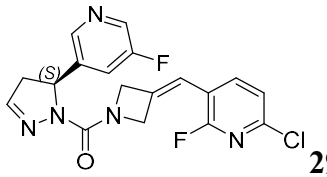
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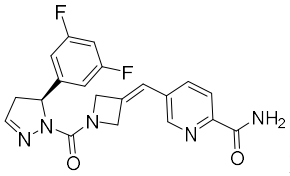
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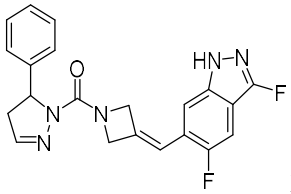
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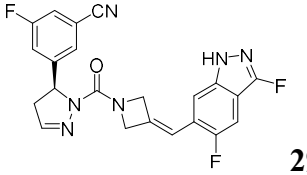
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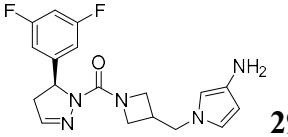
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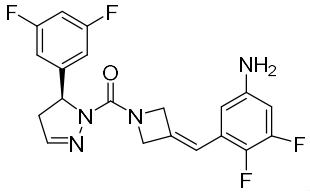
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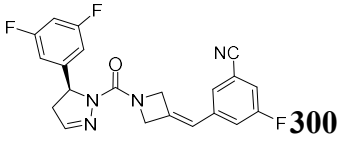
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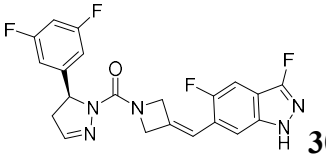
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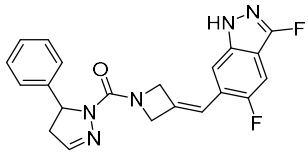
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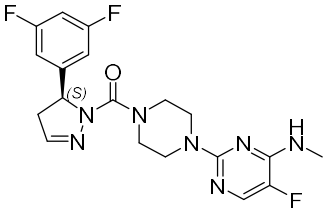
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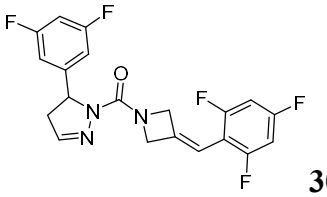
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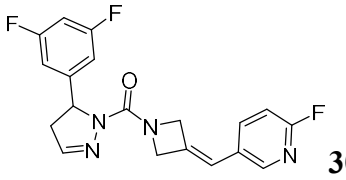
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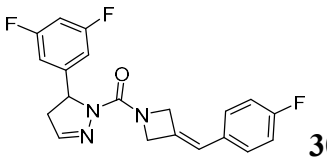
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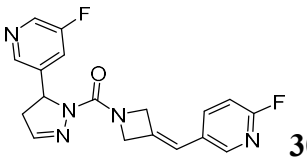
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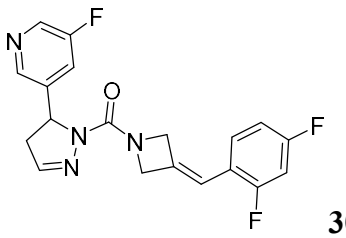
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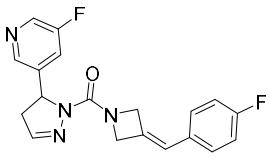
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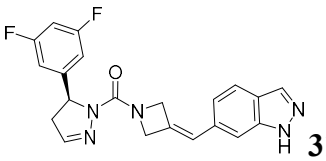
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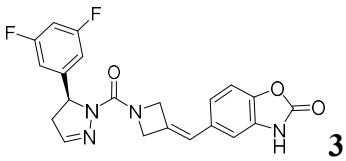
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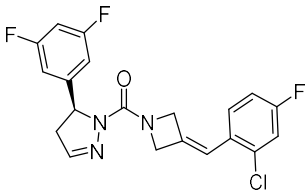
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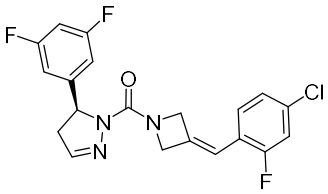
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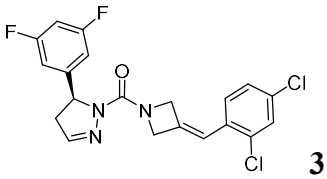
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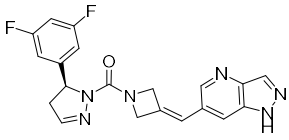
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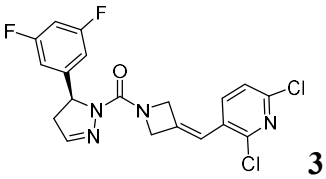
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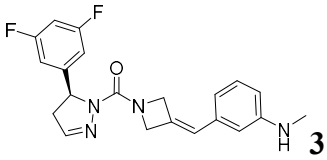
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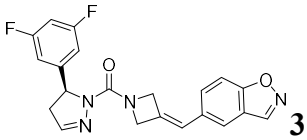
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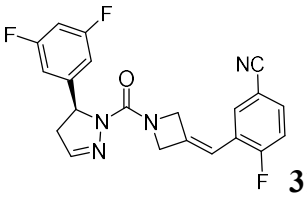
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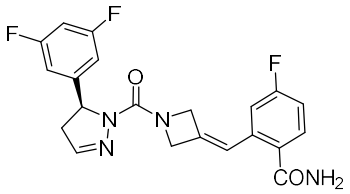
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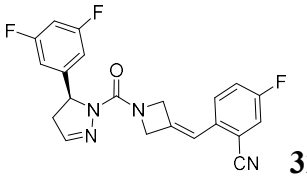
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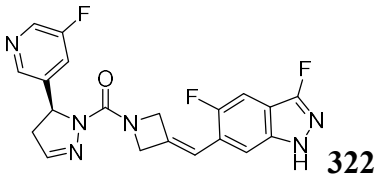
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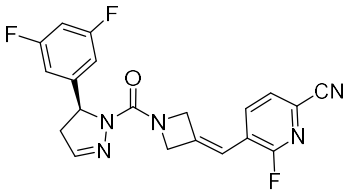
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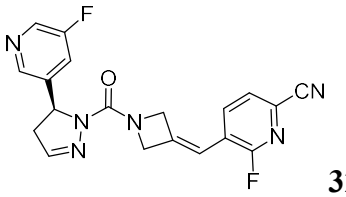
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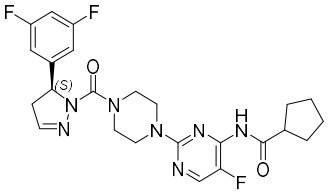
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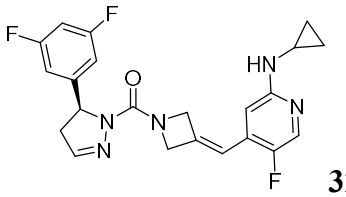
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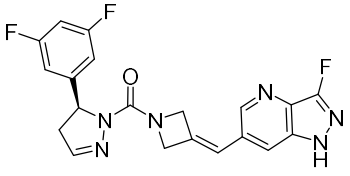
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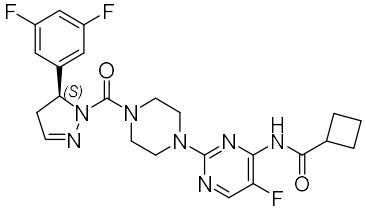
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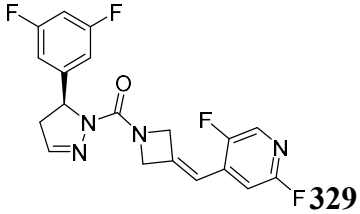
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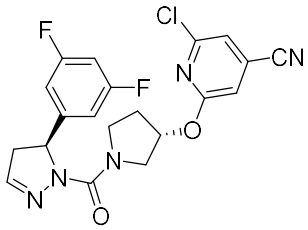
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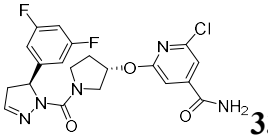
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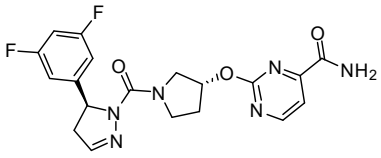
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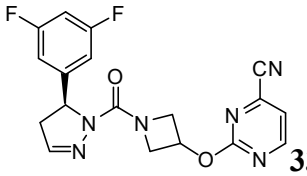
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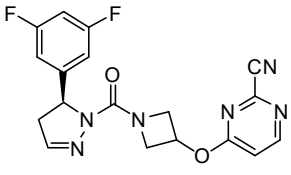
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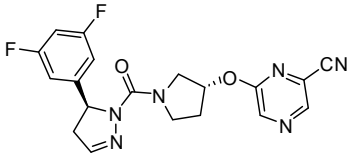
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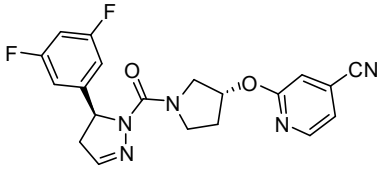
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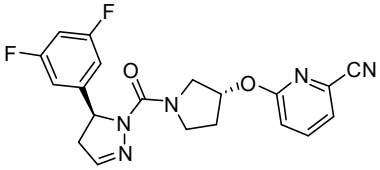
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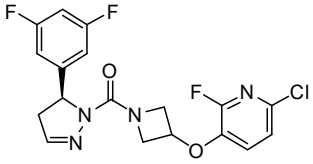
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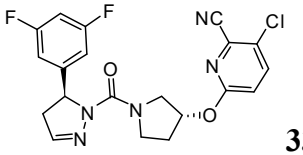
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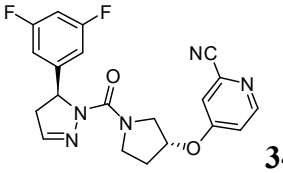
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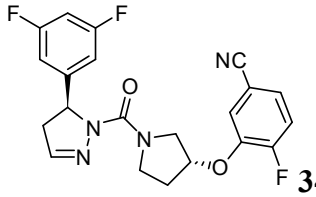
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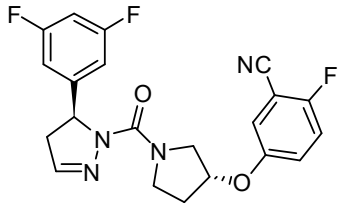
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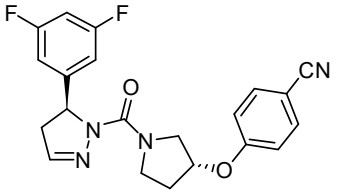
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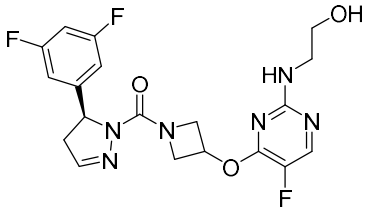
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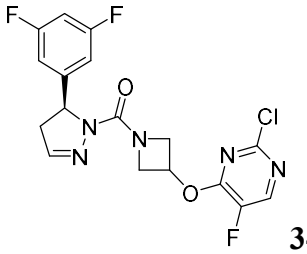
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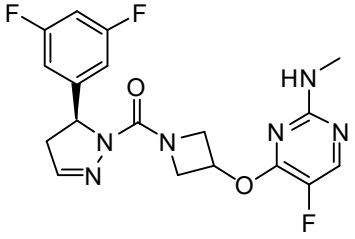
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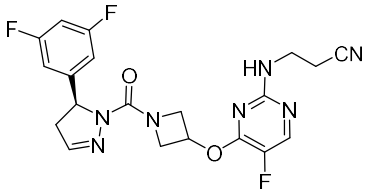
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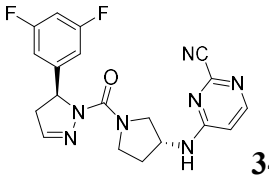
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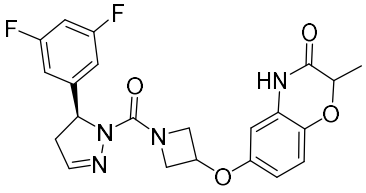
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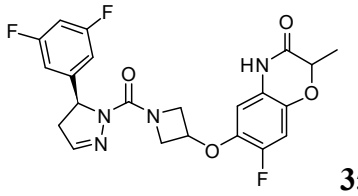
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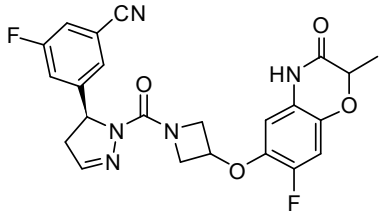
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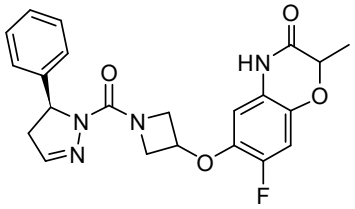
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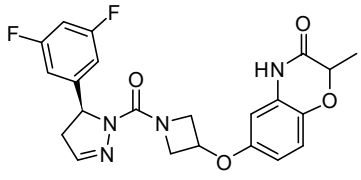
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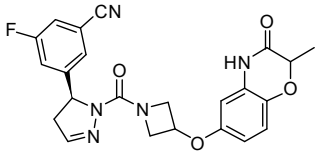
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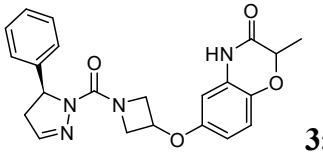
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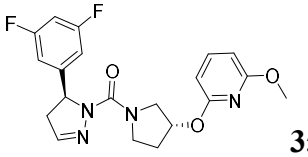
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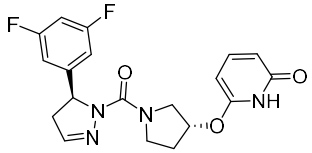
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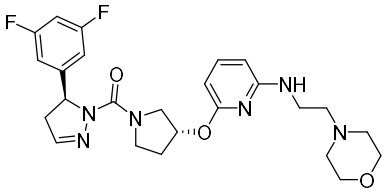
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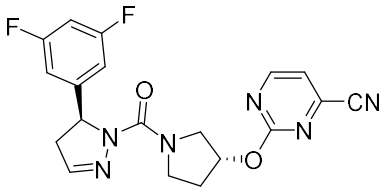
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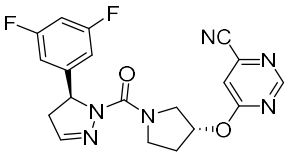
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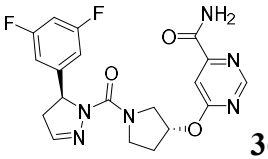
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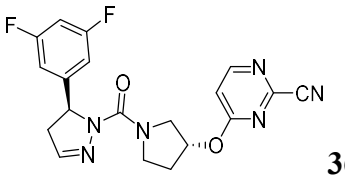
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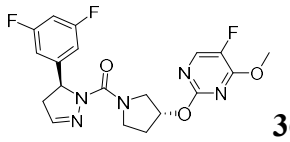
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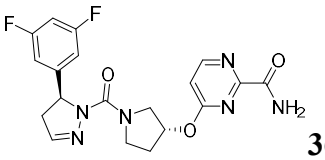
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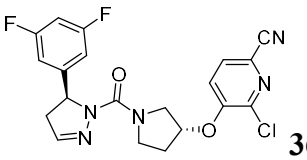
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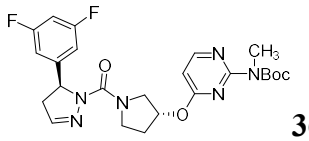
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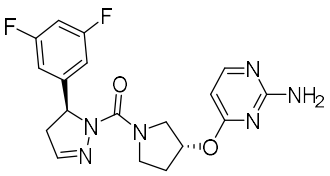
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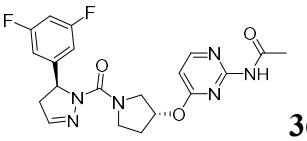
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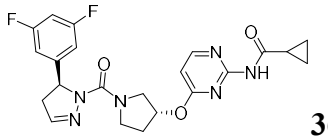
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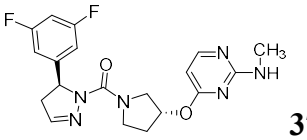
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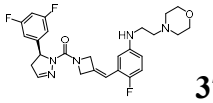
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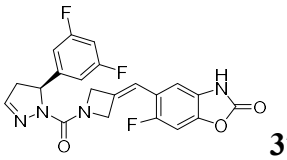
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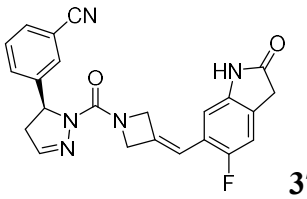
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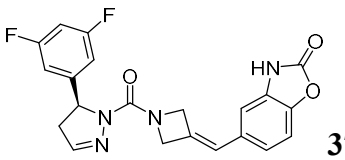
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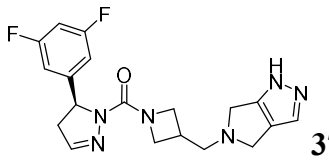
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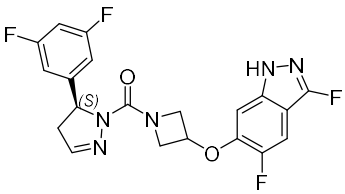
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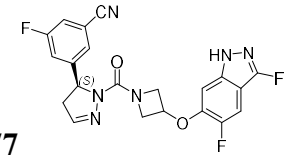
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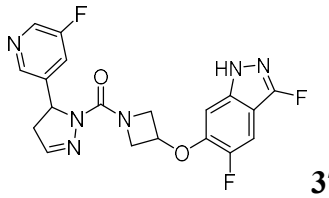
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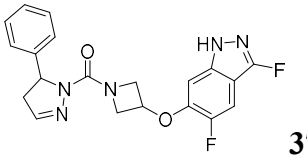
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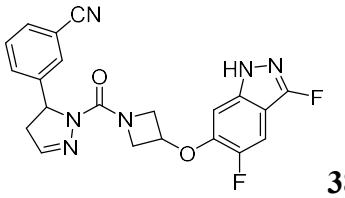
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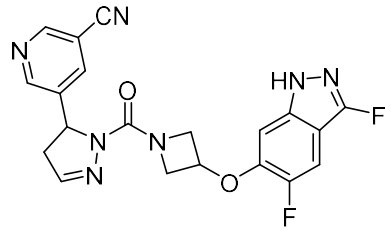
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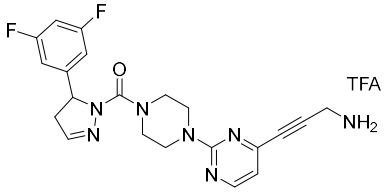
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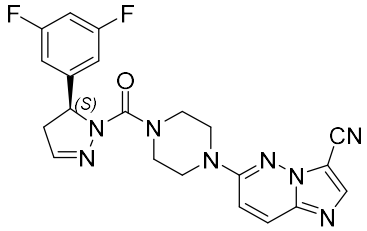
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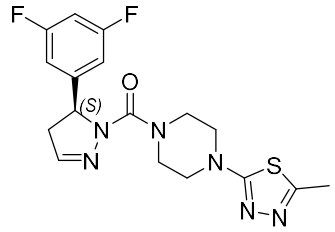
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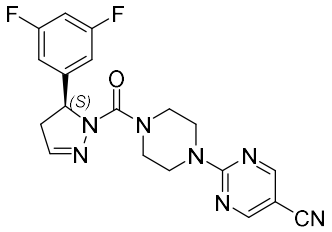
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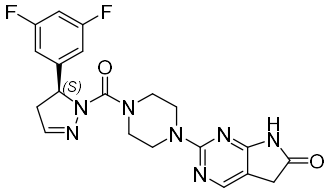
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or a pharmaceutically acceptable salt, hydrate or stereoisomer thereof.

Claim 19. A pharmaceutical composition comprising a therapeutically effective amount of a compound salt, hydrate or stereoisomer of any of claims 1-18 in unit dosage form and one or more pharmaceutically acceptable excipients.

Claim 20. Use of a compound salt, hydrate or stereoisomer of any of claims 1-18 or composition of claim 19 in the manufacture of a medicament for inhibiting necrosis, ferroptosis, human Receptor-Interacting Protein 1 Kinase (RIP 1), or related indications, in a person in need thereof.

Claim 21. A compound salt, hydrate or stereoisomer of any of claims 1-18 or composition of claim 19 for use in inhibiting necrosis, ferroptosis, human Receptor-Interacting Protein 1 Kinase (RIP1), or related indications in a person in need thereof.