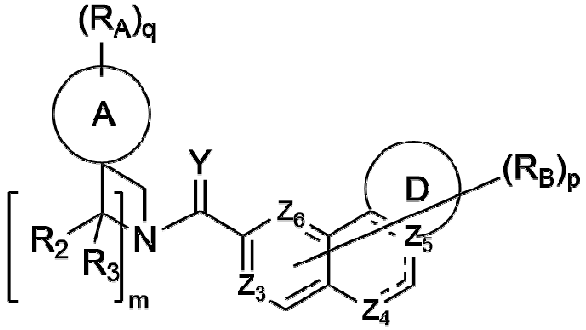
Claims

1. A compound of formula (IC-2) or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of the foregoing that is isotope-labeled:



(IC-2)

wherein ring A, ring D, Y, Z_3, Z_4, Z_5, Z_6, R_2, R_3, R_A, R_B, m, p and q are defined as follows:

Ring A is selected from 8-11 membered fused bicyclic aryl, 8-11 membered fused bicyclic heteroaryl;

Z_3 and Z_6 are N or CR_e;

Z_4 and Z_5 are N, NH, NR_e or CR_e, and at least one of Z_4 and Z_5 is N or NH; wherein ------ is a single bond or a double bond, and the position of the double bond changes when Z_4 or Z_5 is N or NH;

R_e is hydrogen, deuterium, halogen, hydroxyl, cyano, $-NH_2$, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH(C_1-C_6 alkyl) or -N(C_1-C_6 alkyl)(C_1-C_6 alkyl);

Ring D is a 5-6 membered heterocyclyl, a 5-6 membered aryl, or a 5-6 membered heteroaryl which is fused to a 10 membered ring, or is absent;

Y is O or S;

R_2 and R_3 each are independently hydrogen, deuterium, halogen, C_1-C_6 alkyl or C_1-C_6 alkoxy;

each R_A is independently deuterium, halogen, hydroxyl, oxo, cyano, nitro, amine, C_1-C_6 alkyl, cyano C_1-C_6 alkyl, C_1-C_6 alkoxy, -C_1-C_6 alkyl-C_1-C_6 alkoxy, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)(C_1-C_6 alkyl), C_3-C_6 cycloalkyl, C_1-C_6 haloalkyl, -O-(C_1-C_6 haloalkyl), -NH-(C_1-C_6 haloalkyl), -N(C_1-C_6 haloalkyl)(C_1-C_6 haloalkyl), pentafluorosulfur ($-SF_5$), C_1-C_6 haloalkoxy or halocycloalkyl, -S(O)$_2$-(C_1-C_6 alkyl), -S(=O)(C_1-C_6 alkyl)NR_z, -S(=O)(=NR_z)(C_1-C_6 alkyl) , -P(=O)(C_1-C_6 alkyl)$_2$, a 4-8 membered heterocyclyl optionally substituted by 1-3 R_z, a 5-8 membered heteroaryl optionally substituted by 1-3 R_z, a 6-10 membered aryl optionally substituted by 1-3 R_z, a C_3-C_6 cycloalkyl optionally substituted by 1-3 R_z, or

two R_A connected to the same carbon atom form an oxo group, or

two R_A connected to the same carbon atom together with the carbon atom to which they are connected form a C_3-C_8 cycloalkyl;

R_B is deuterium, halogen, hydroxyl, oxo, thioketone, cyano, nitro, amine, C_1-C_6 alkyl, C_1-C_6 alkoxy, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-OH, C_3-C_8 cycloalkyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy or C_3-C_8 halocycloalkyl, or

two R_B connected to the same carbon atom together with the carbon atom to which they are connected form a C_3-C_8 cycloalkyl or 6-7 membered heterocyclyl, or

two R_B connected to different carbon atoms are connected to form a 6-7 membered ring;

R_z is independently selected from deuterium, halogen, C_1-C_6 alkyl, -CN, -OH, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, C_3-C_6 cycloalkyl, -NH_2, -NH(C_1-C_6 alkyl), [[or]]-N(C_1-C_6 alkyl)(C_1-C_6 alkyl), (C_1-C_6 alkyl)C(O)NH-, (C_1-C_6 alkyl)C(O)-, phenyl, pentafluorosulfur, 5-6 membered heteroaryl or 4-6 membered heterocyclyl, or

two R_z connected to the same carbon atom form an oxo group, or

two R_z connected to the same carbon atom together with the carbon atom to which they are connected form a C_3-C_8 cycloalkyl group;

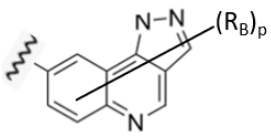
m is 1 or 2;

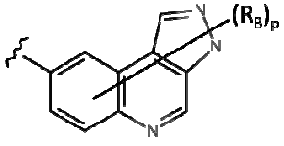
p is 0, 1, 2, 3 or 4; and

q is 0, 1, 2, 3, 4 or 5.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of the foregoing that is isotope-labeled, wherein one of Z_3 and Z_6 is N and the other is CR_e; and Z_4 is N, NH or NR_e and Z_5 is CR_e.

3. The compound according to Claim 1, or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of the foregoing that is isotope-labeled, wherein Z_3 and Z_6 are each independently CR_e; and wherein Z_4 is N, NH or NR_e and Z_5 is CR_e.

4. The compound according to Claim 1, or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of the foregoing that is isotope-labeled, wherein the moiety formed by Ring D fused with the 10-membered ring is selected from 

, 

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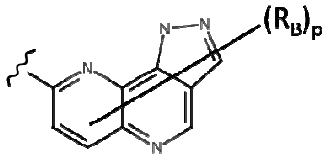
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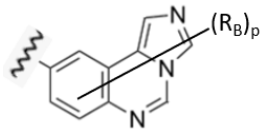
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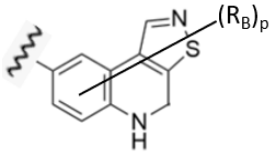
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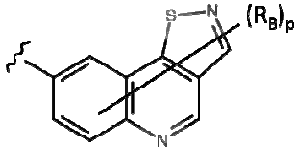
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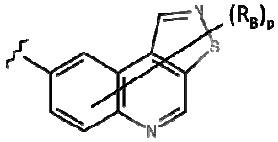
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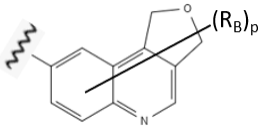
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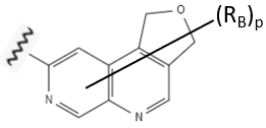
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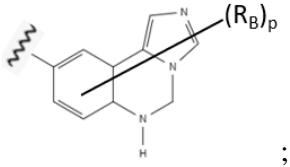
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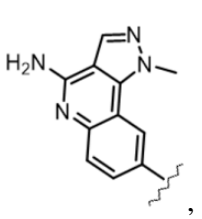
R_B and p are as defined in Claim 1.

5. The compound according to Claim 1, or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of the foregoing that is isotope-labeled, wherein ring D is absent.

6. The compound according to Claim 1, or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of the foregoing that is isotope-labeled, wherein the moiety formed by ring D fused with the 10 membered ring is selected from

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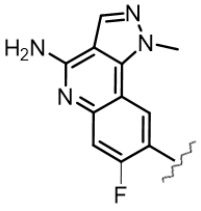
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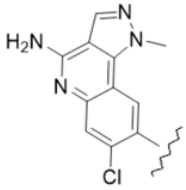
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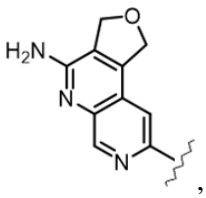
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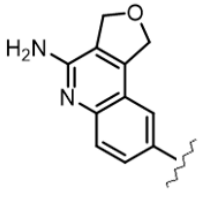
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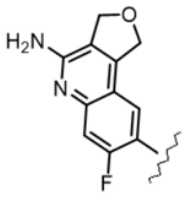
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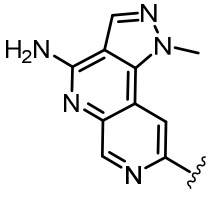
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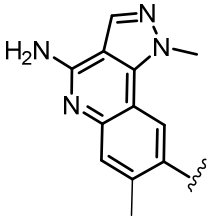
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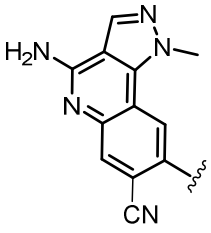
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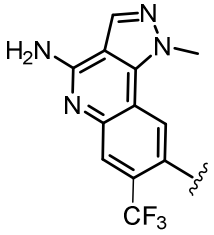
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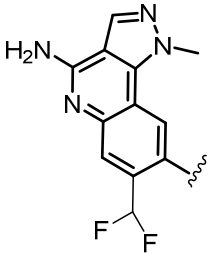
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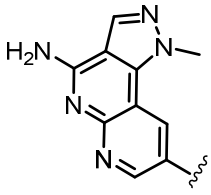
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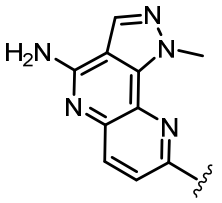
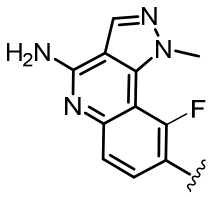
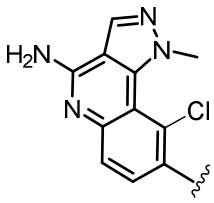
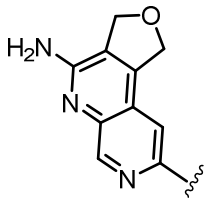
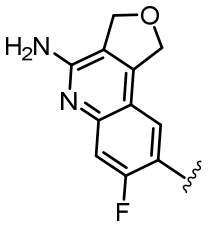
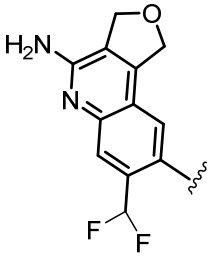
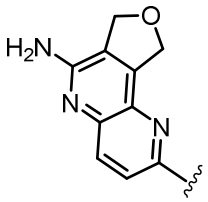
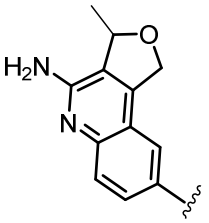
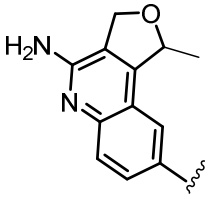
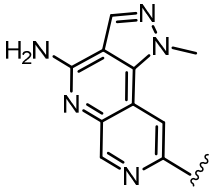
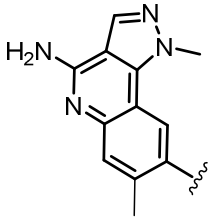
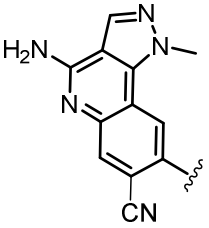
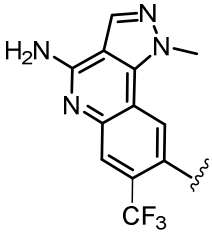
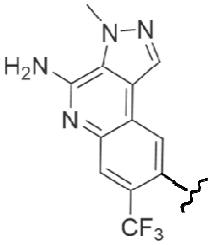
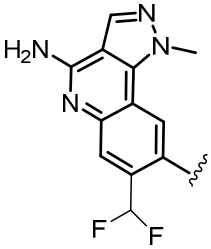
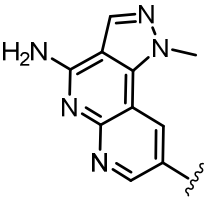
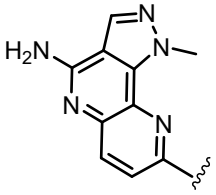
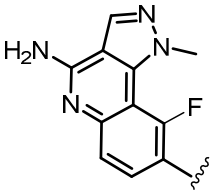
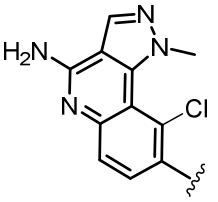
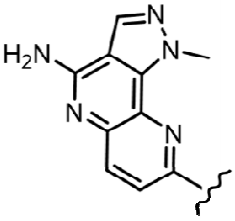
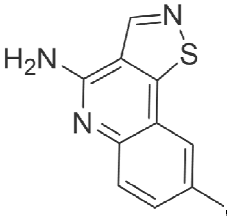
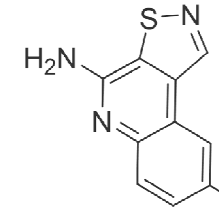
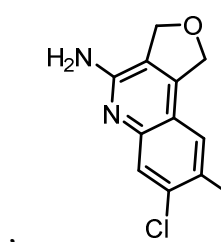
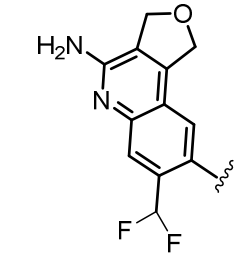
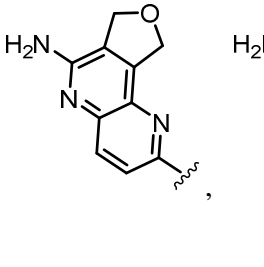
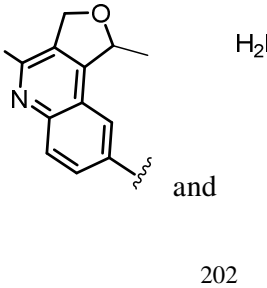
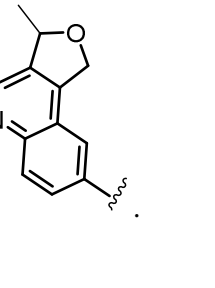
, , , ,
, , , ,
, , , ,
, , , ,
, , , ,
, , , ,
, , , ,
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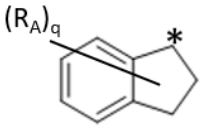
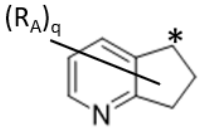
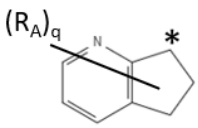
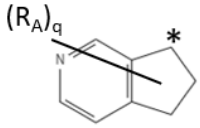
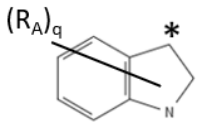
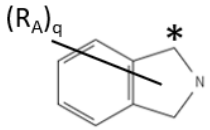
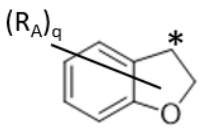
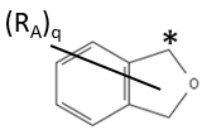
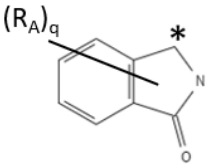
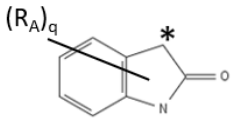
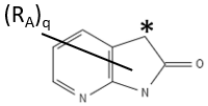
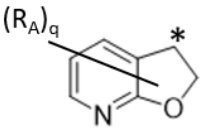
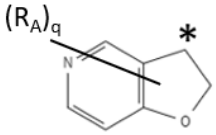
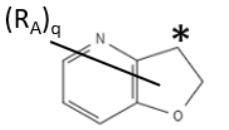
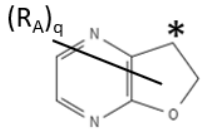
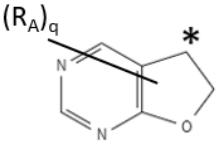
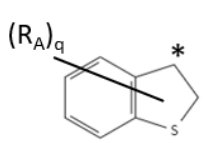
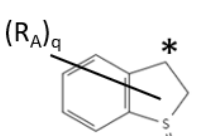
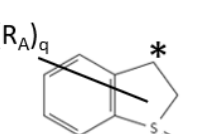
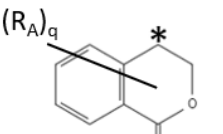
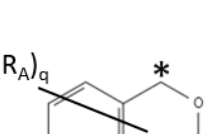
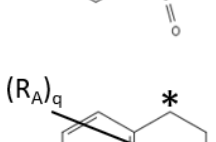
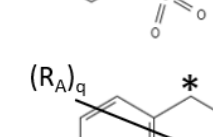
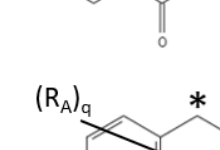
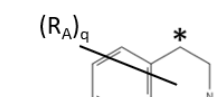
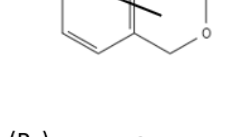
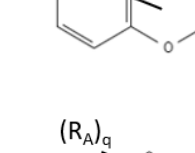
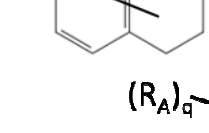
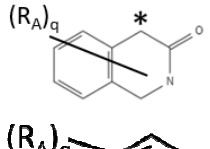
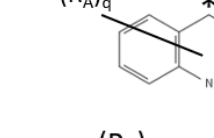
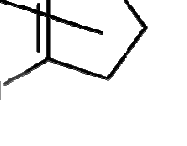
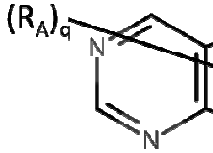
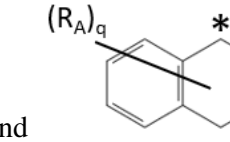
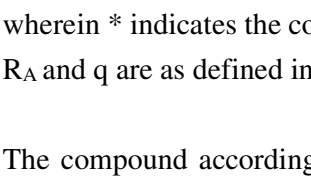
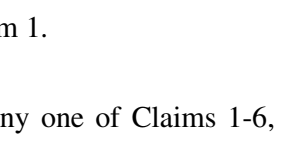
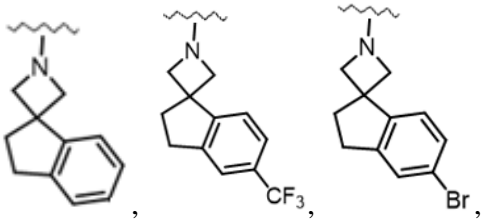
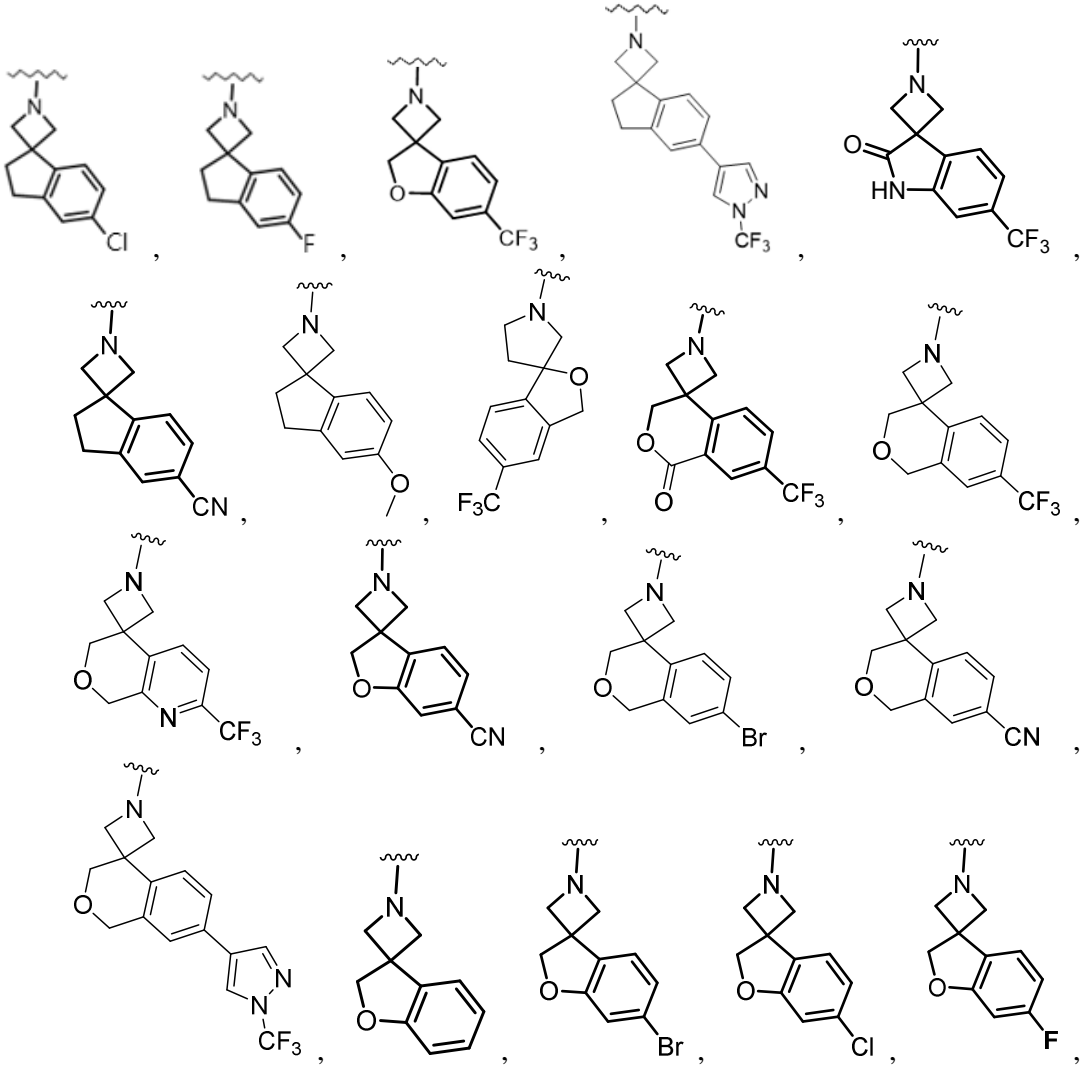
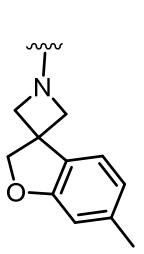
7. The compound according to any one of Claims 1-6, or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of the foregoing that is isotope-labeled, wherein ring A is selected from , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , and wherein * indicates the connecting point of spiral ring; and R_A and q are as defined in Claim 1.

8. The compound according to any one of Claims 1-6, or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of

the foregoing that is isotope-labeled, wherein:

the carbon atom to which R_2 and R_3 are connected, the adjacent nitrogen atom, the adjacent methylene group, and one atom of the ring A form a cyclic moiety, wherein this cyclic moiety and the ring A are connected in the form of sharing such one atom of the ring A to form a spirocyclic structure,

the spirocyclic structure is selected from , 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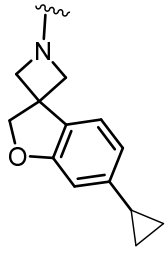
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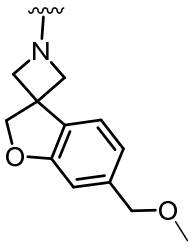
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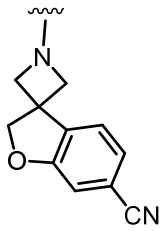
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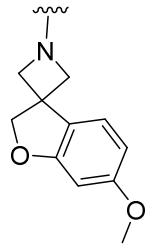
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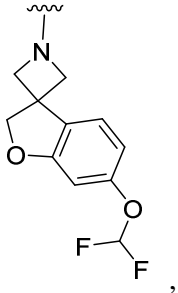
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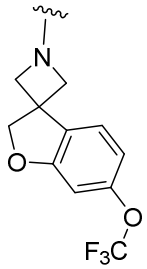
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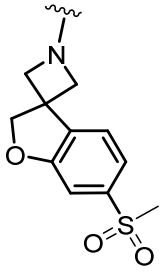
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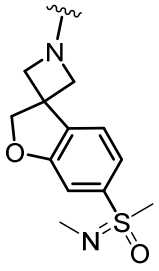
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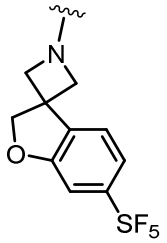
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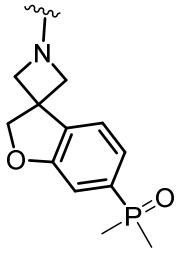
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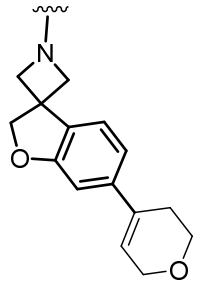
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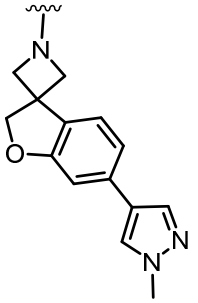
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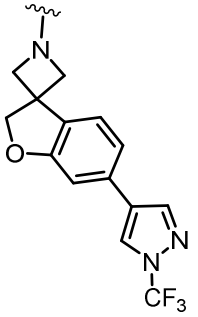
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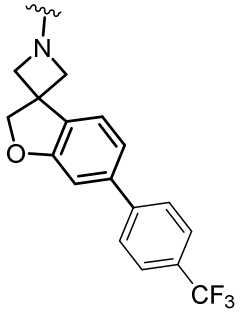
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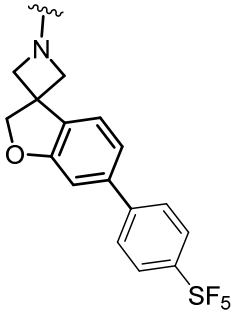
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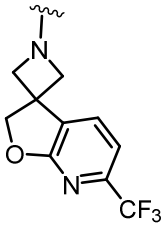
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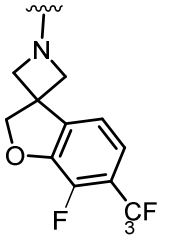
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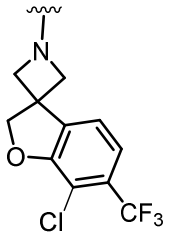
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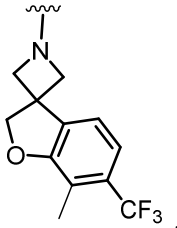
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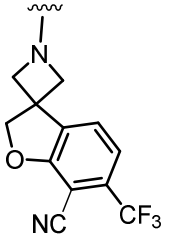
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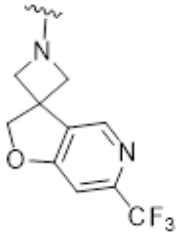
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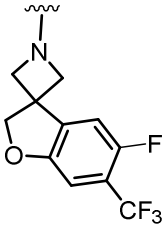
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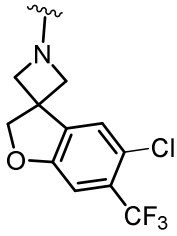
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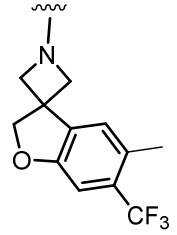
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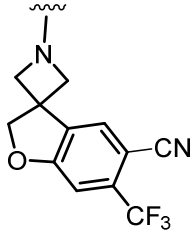
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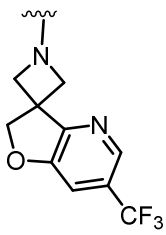
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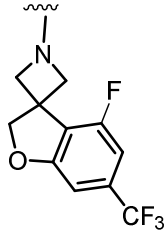
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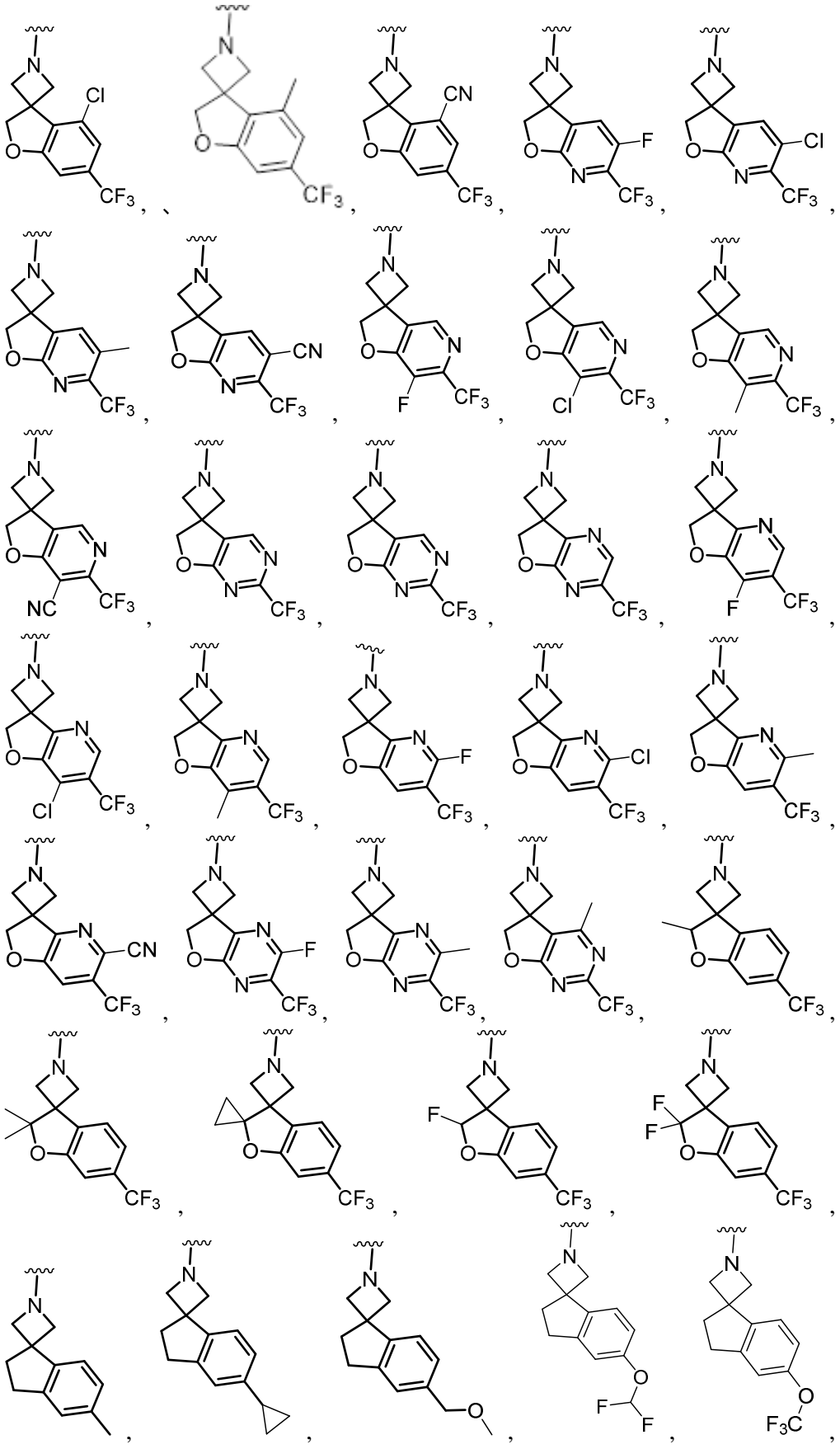
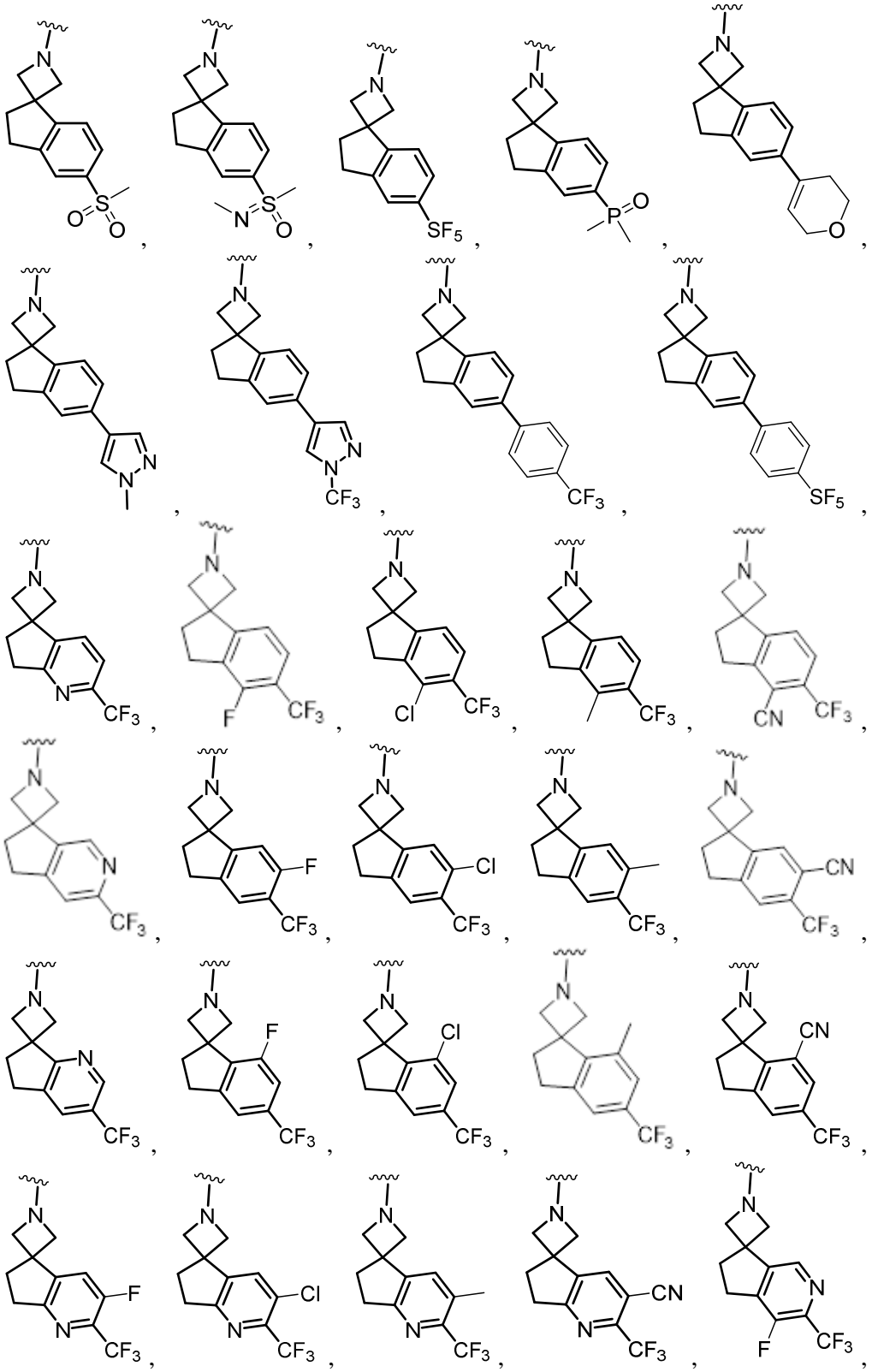
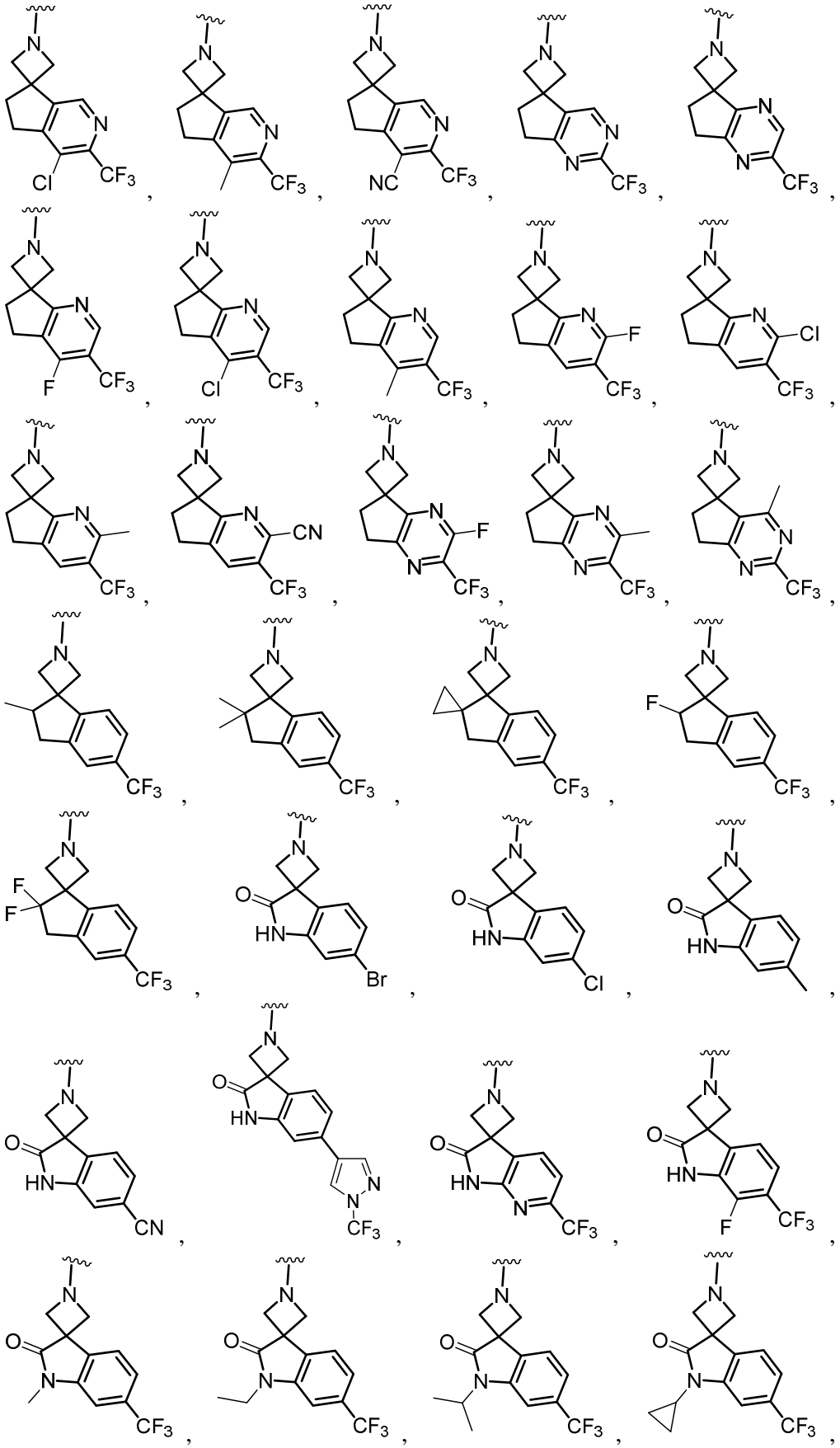
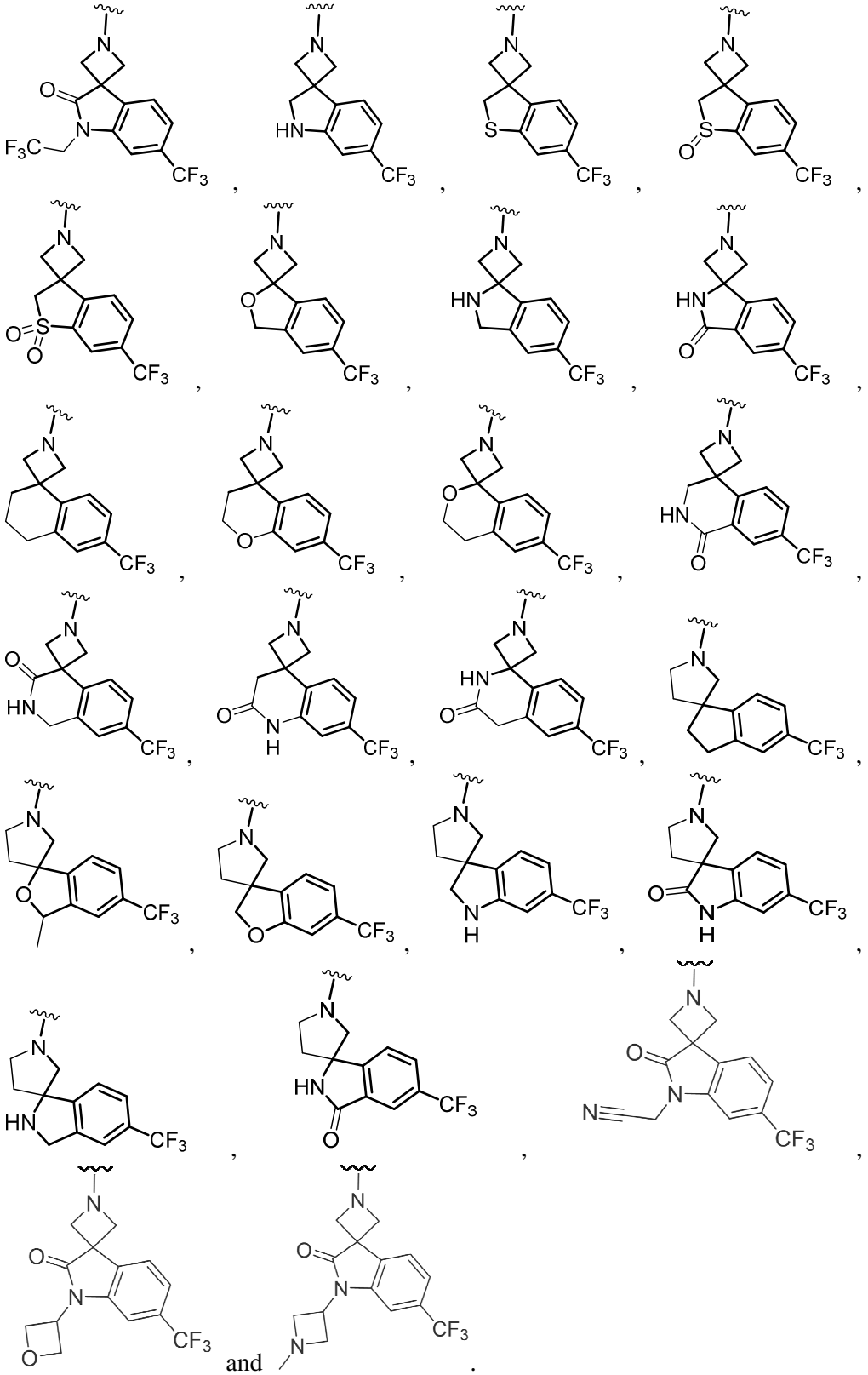


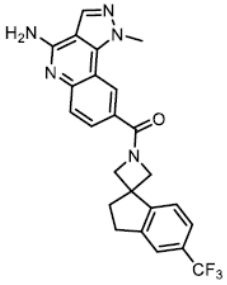






9. The compound according to Claim 1, or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of the foregoing that

is isotope-labeled, which is selected from:



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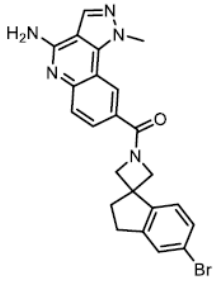

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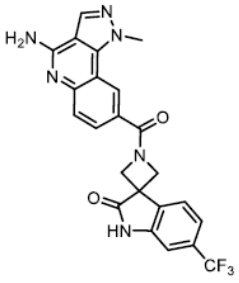

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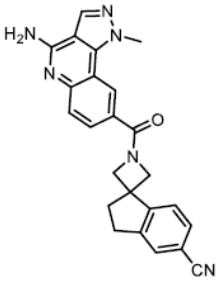

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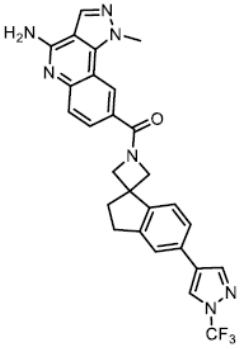

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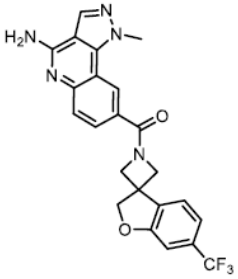

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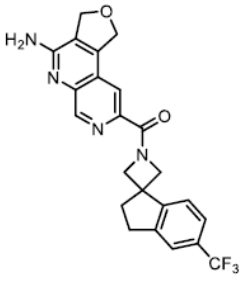

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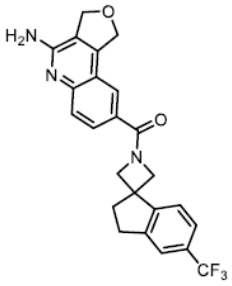

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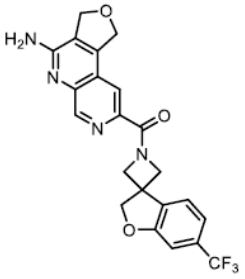

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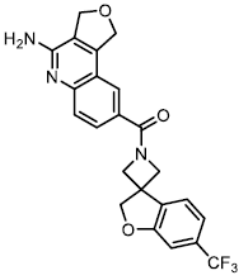

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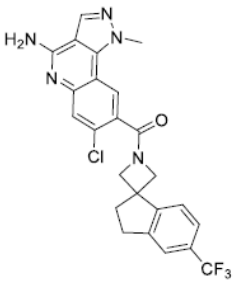

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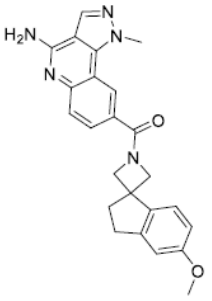

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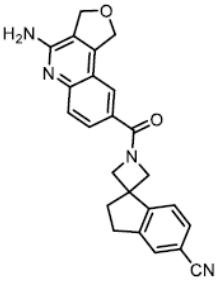

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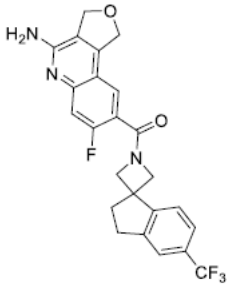

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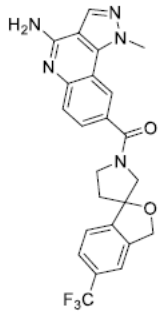

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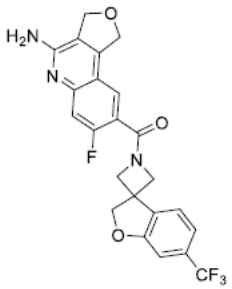

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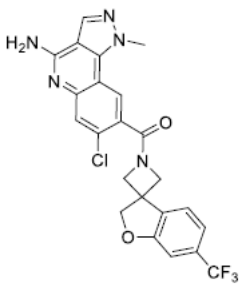

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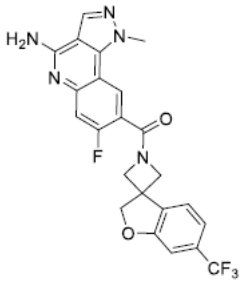

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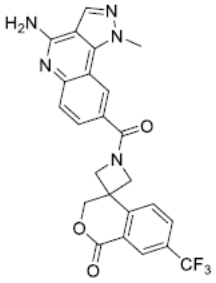

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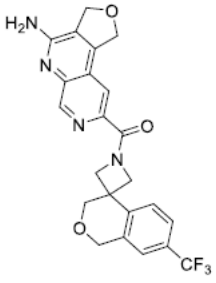

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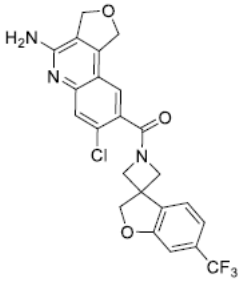

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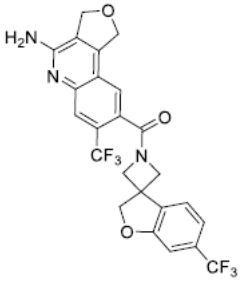

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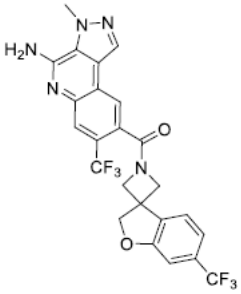

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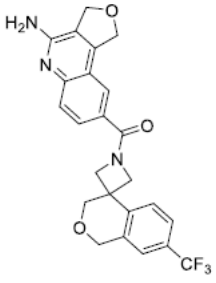

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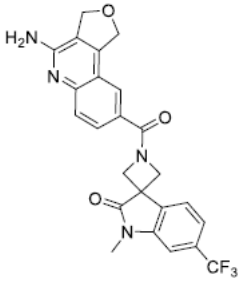

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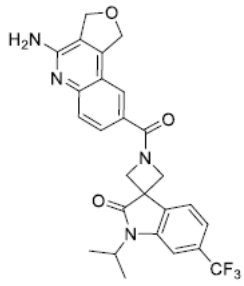

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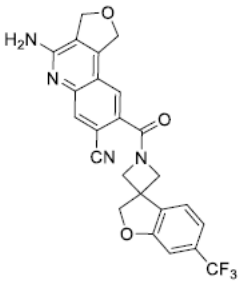

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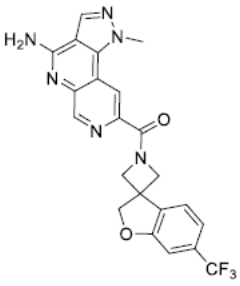

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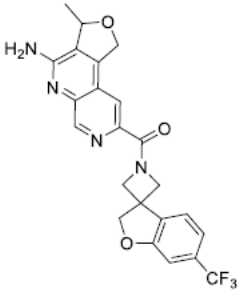

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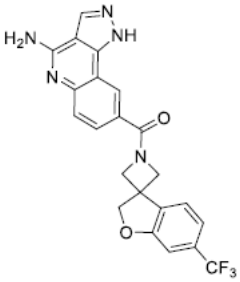

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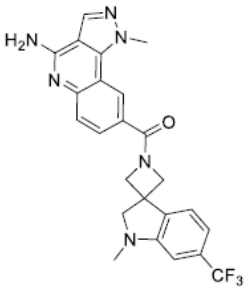

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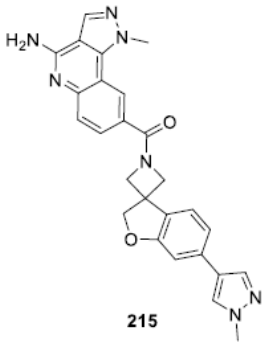

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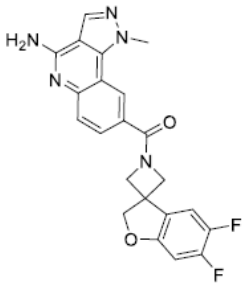

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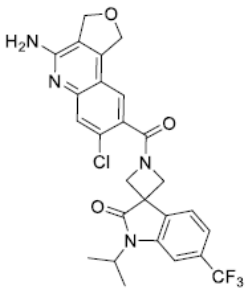

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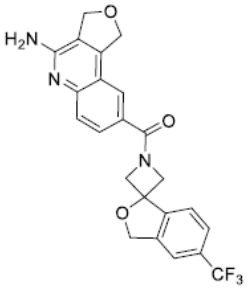

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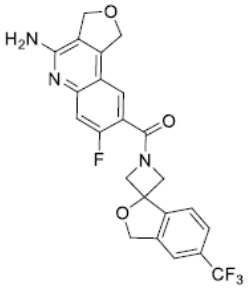

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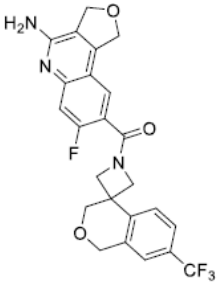

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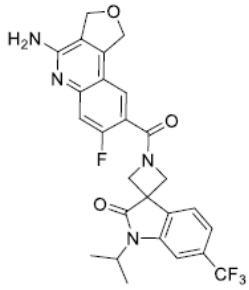

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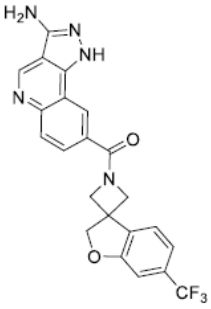

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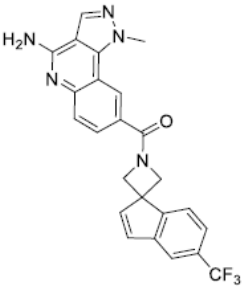

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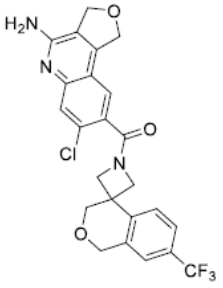

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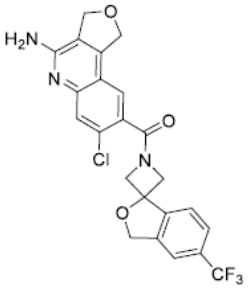

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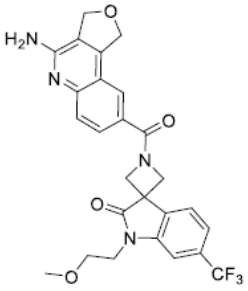

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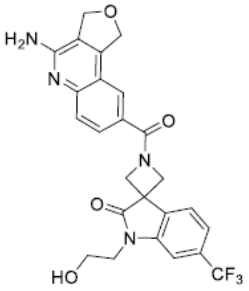

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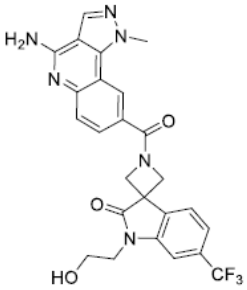

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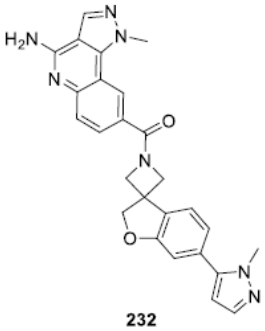

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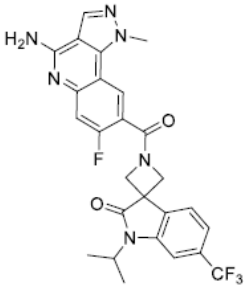

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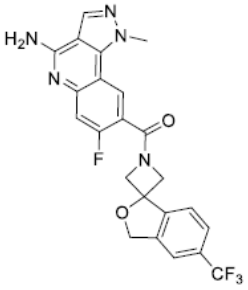

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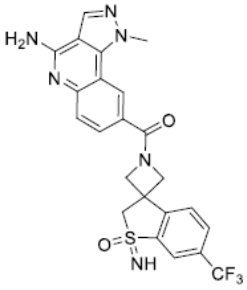

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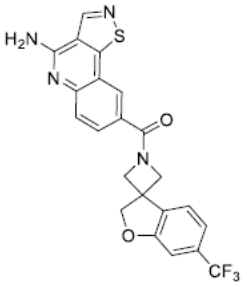

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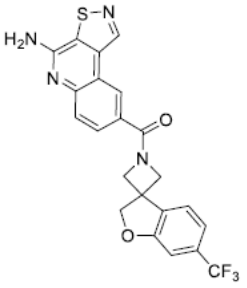

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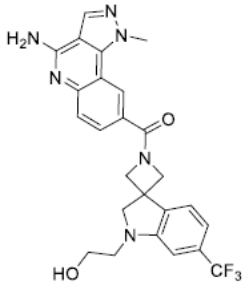

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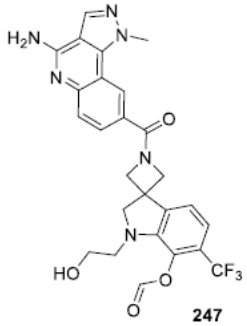

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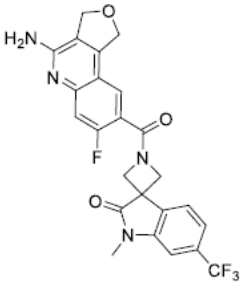

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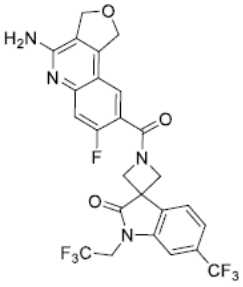

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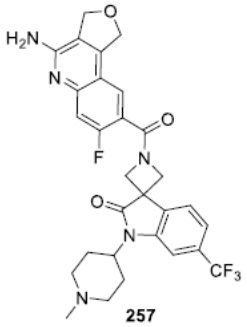

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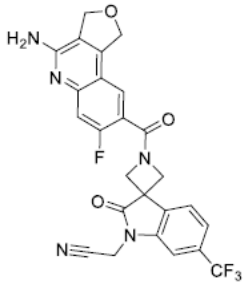

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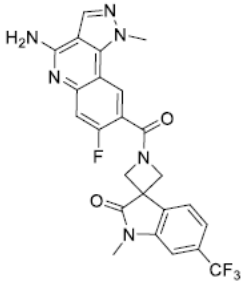

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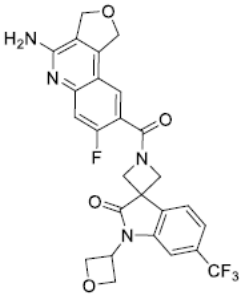

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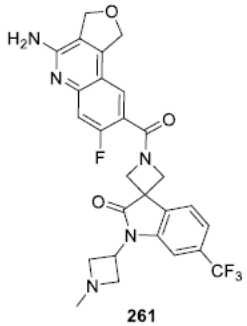

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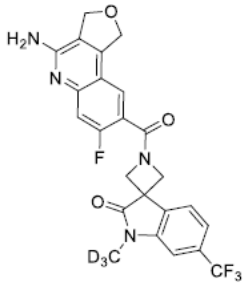

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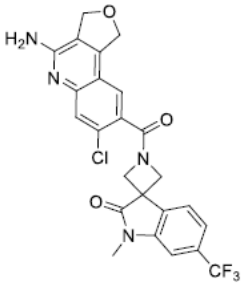

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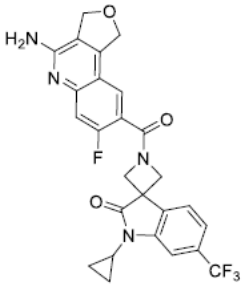

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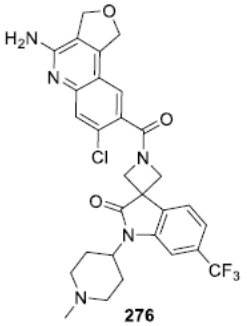

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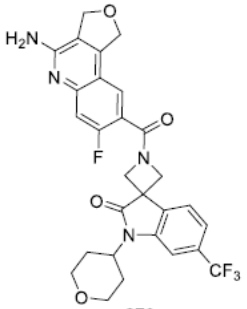

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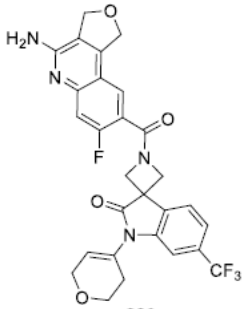

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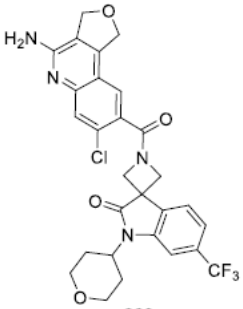

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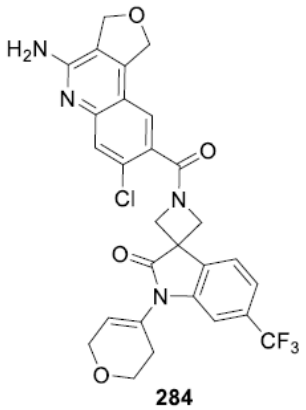

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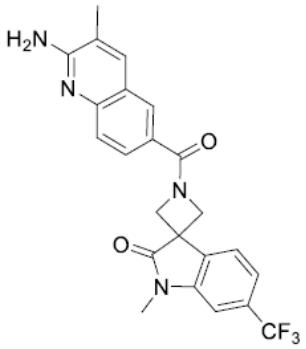

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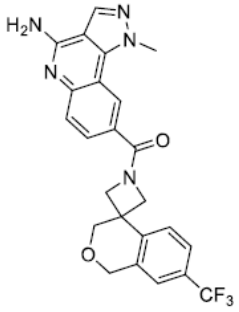

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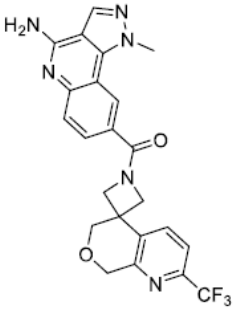

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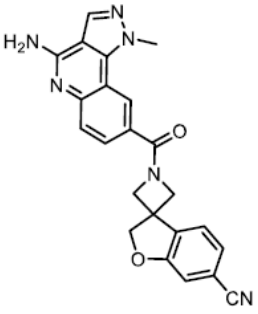

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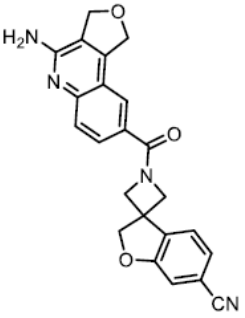

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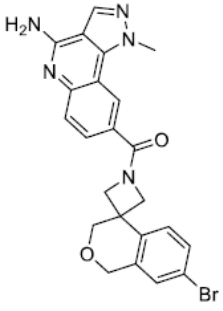

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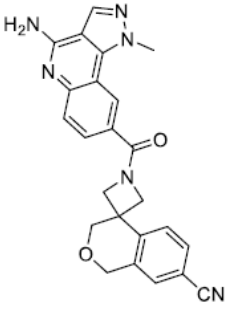

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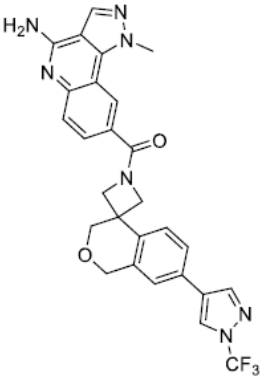

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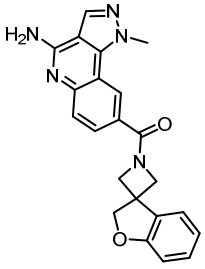

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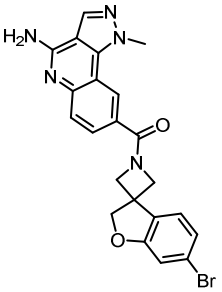

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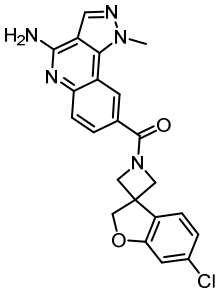

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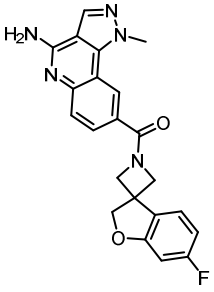

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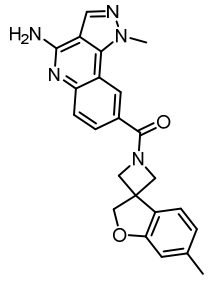

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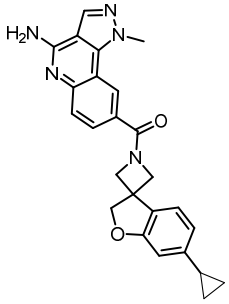

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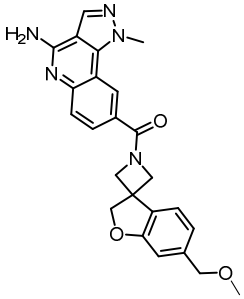

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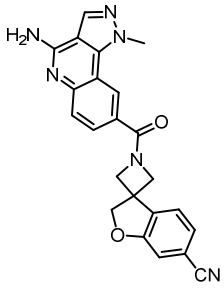

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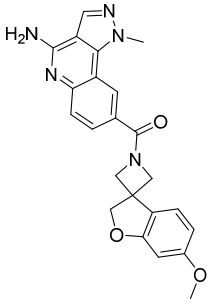

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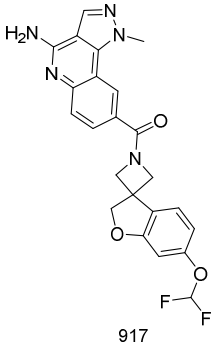

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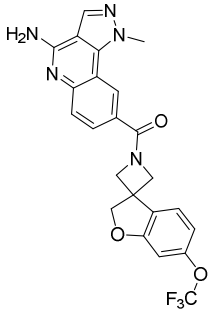

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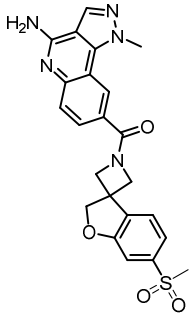

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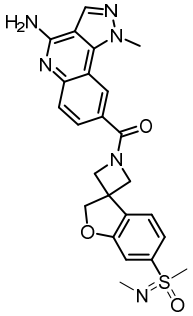

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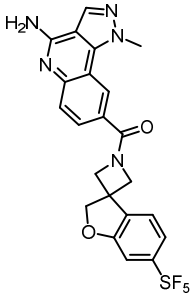

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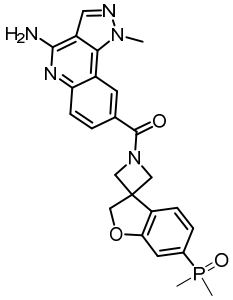

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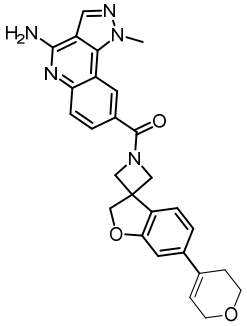

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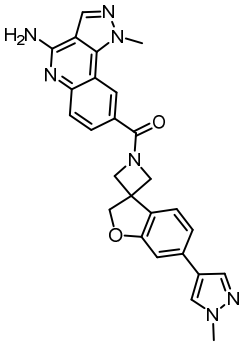

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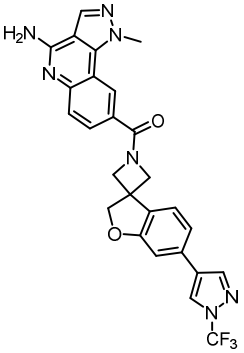

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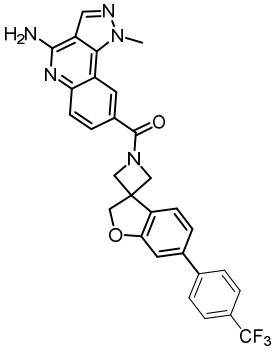

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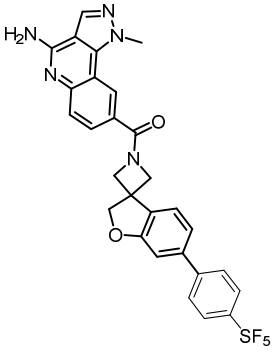

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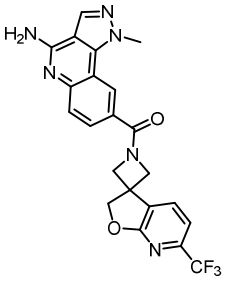

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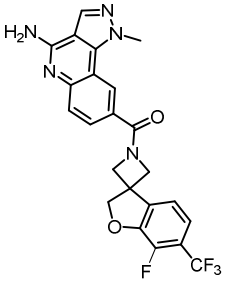

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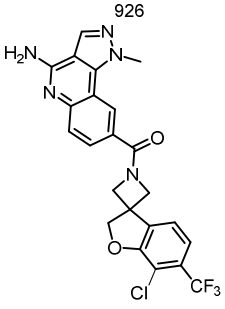

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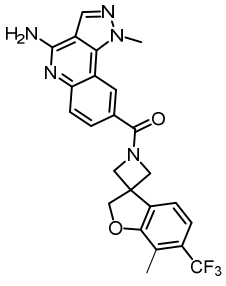

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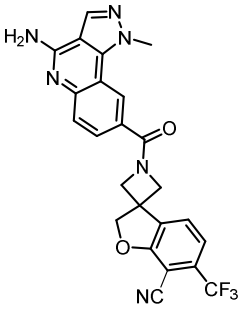

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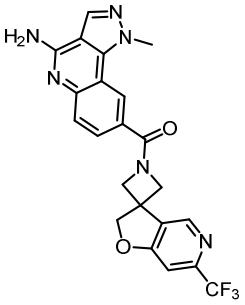

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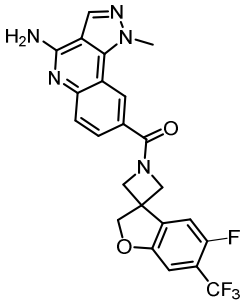

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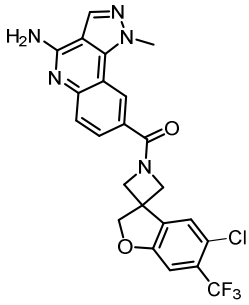

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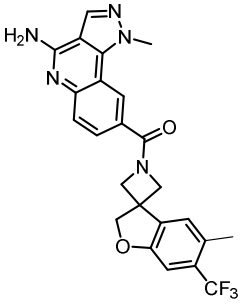

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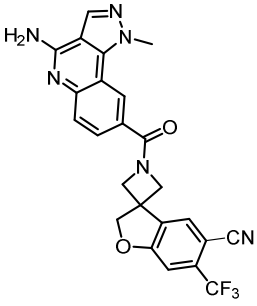

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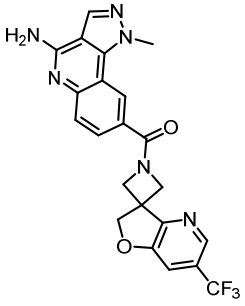

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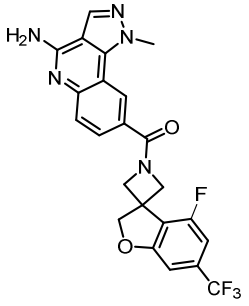

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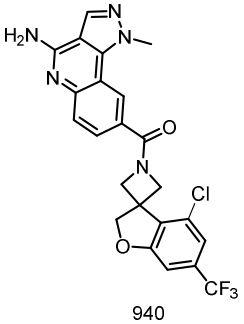

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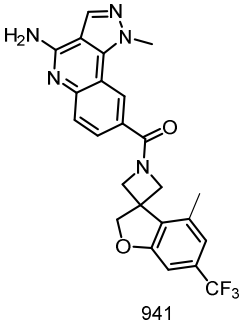

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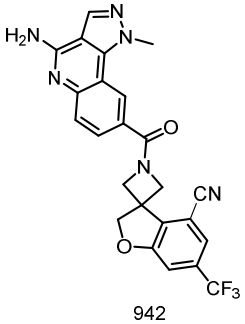

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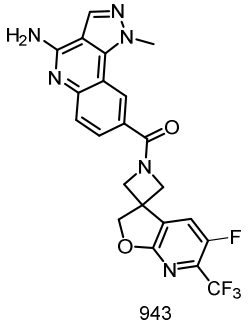

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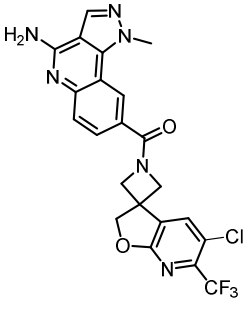

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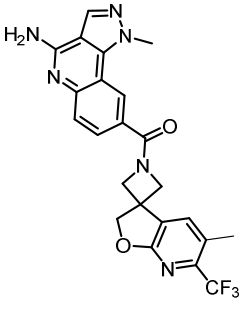

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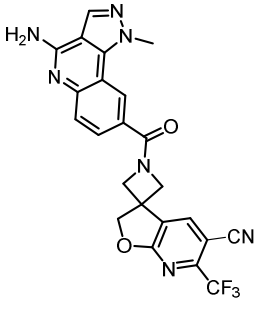

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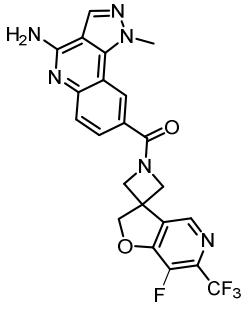

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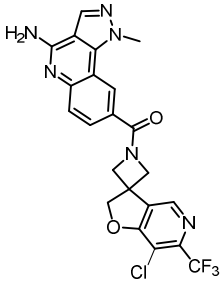

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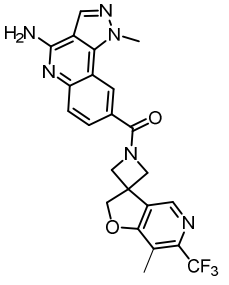

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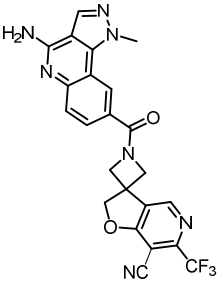

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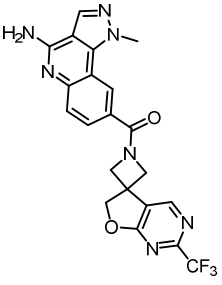

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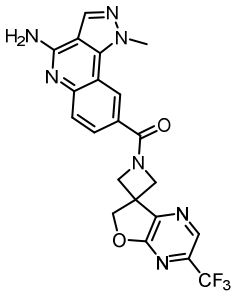

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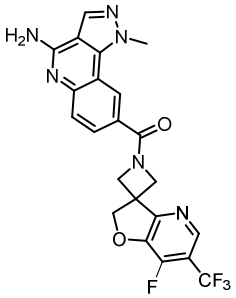

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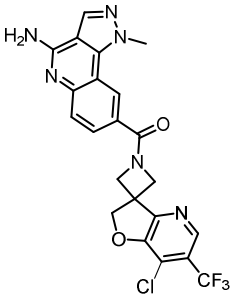

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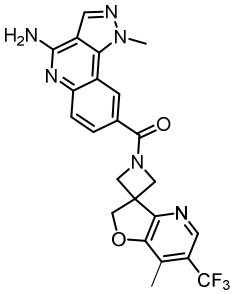

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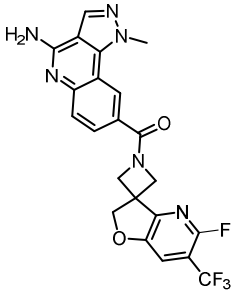

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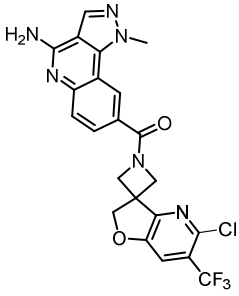

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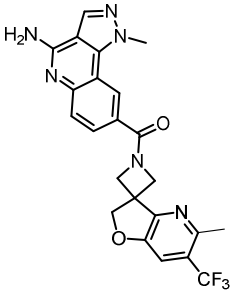

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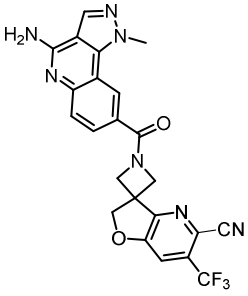

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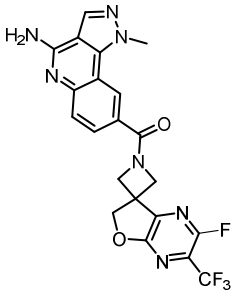

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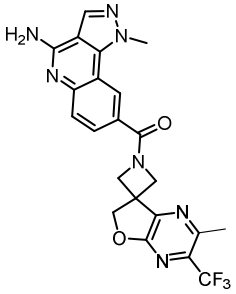

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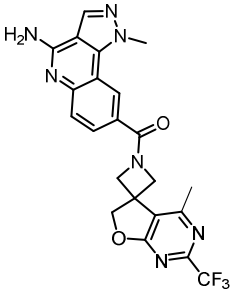

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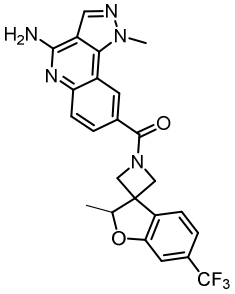

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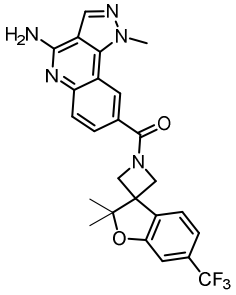

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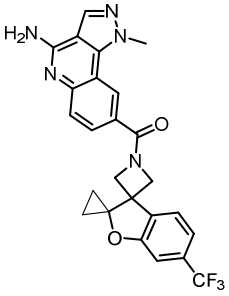

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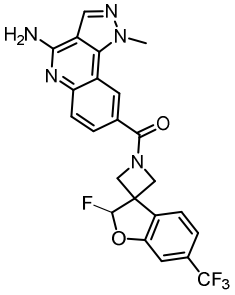

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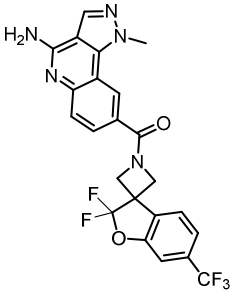

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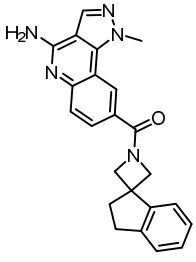

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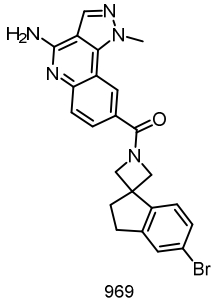

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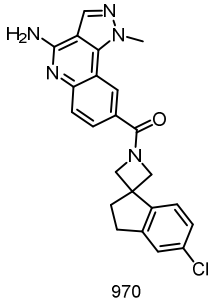

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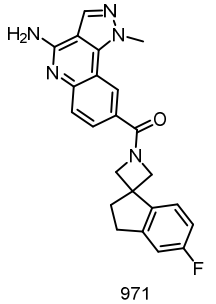

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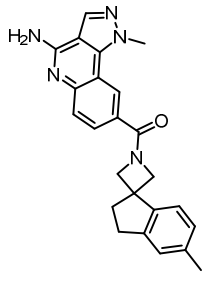

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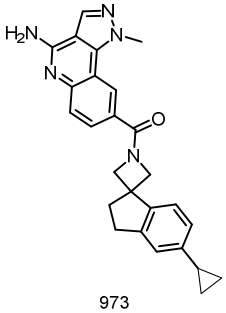

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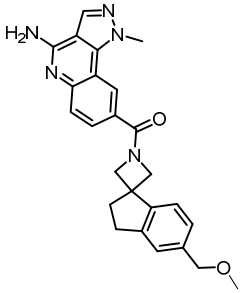

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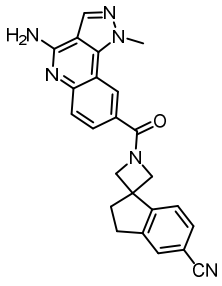

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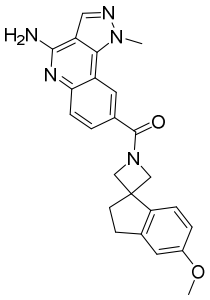

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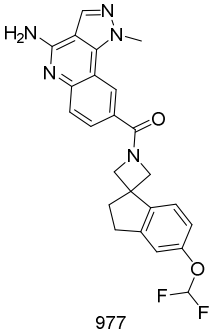

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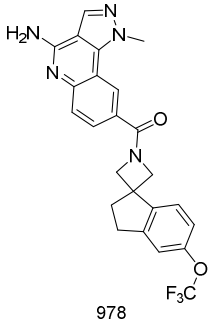

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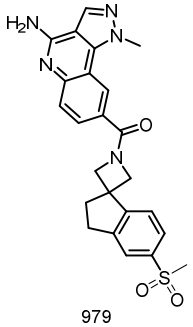

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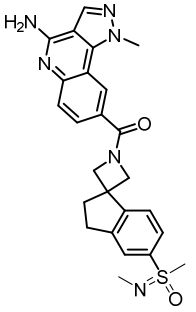

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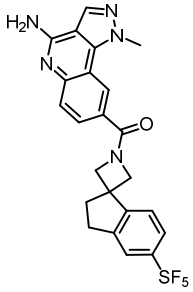

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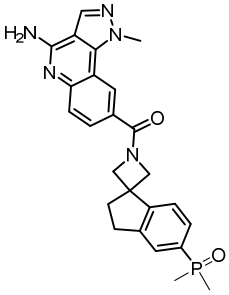

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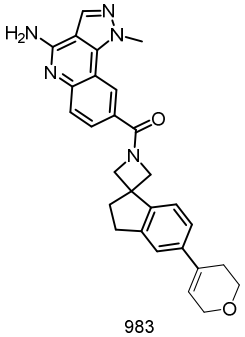

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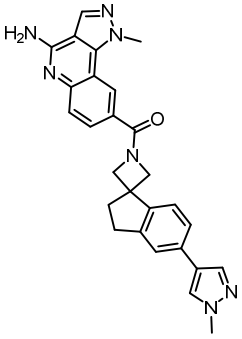

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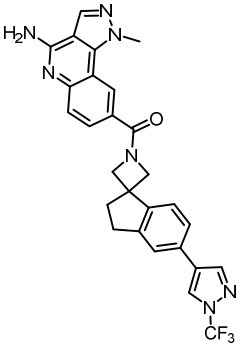

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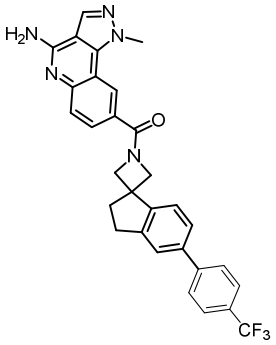

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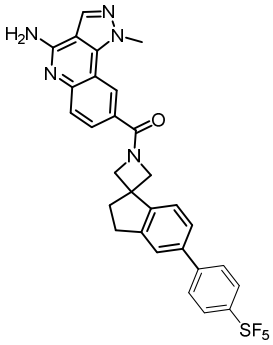

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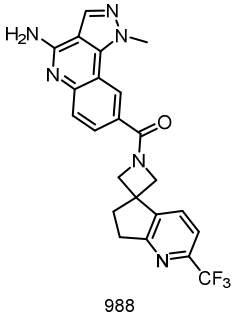

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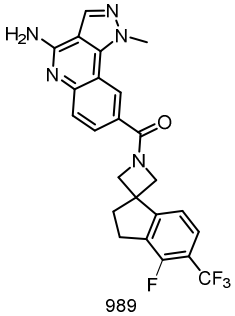

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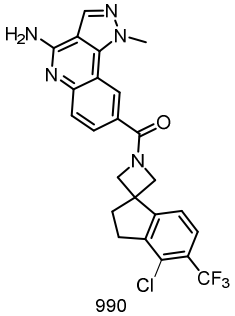

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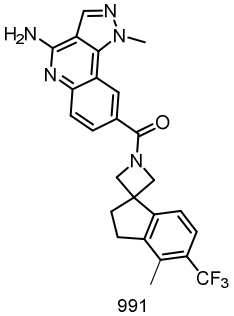

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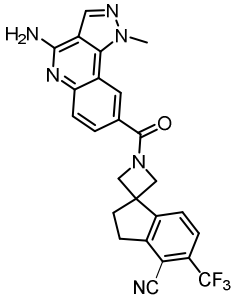
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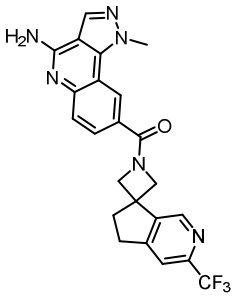
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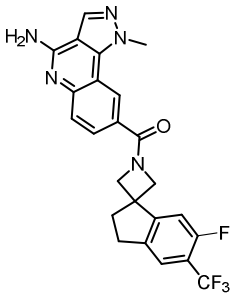
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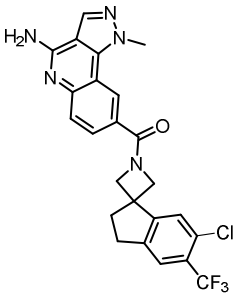
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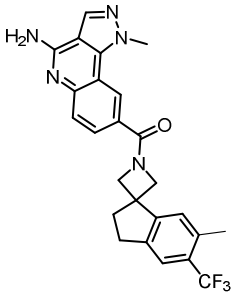
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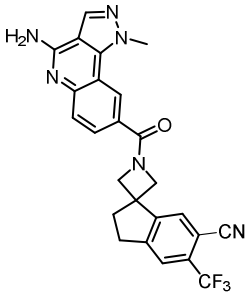
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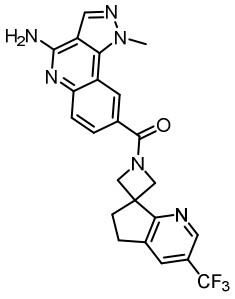
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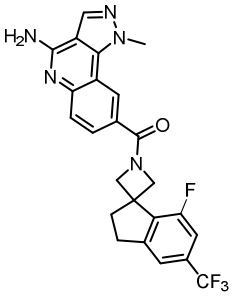
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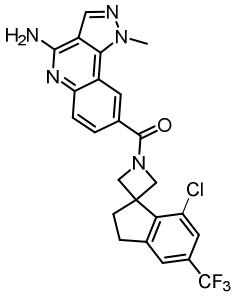
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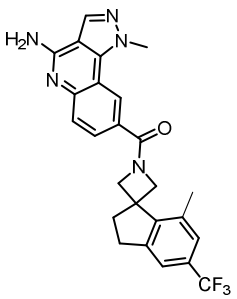
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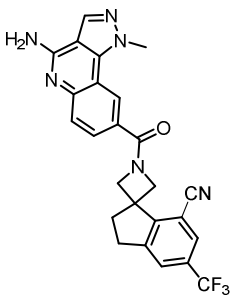
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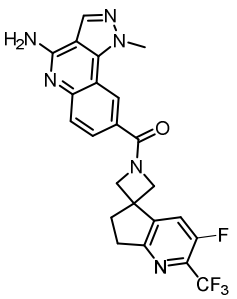
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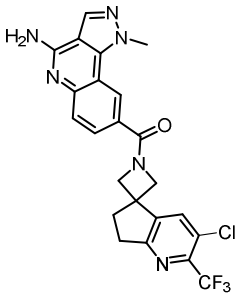
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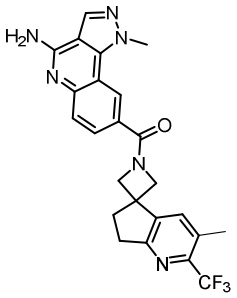
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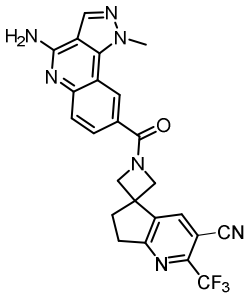
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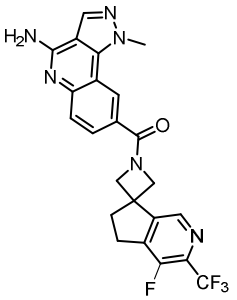
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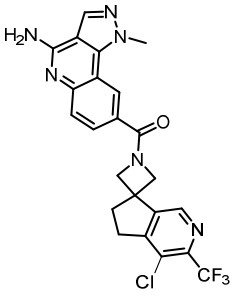
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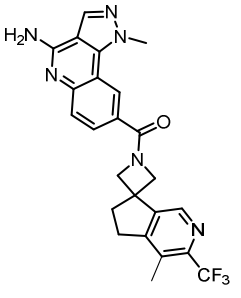
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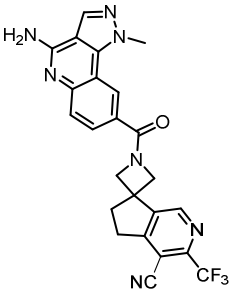
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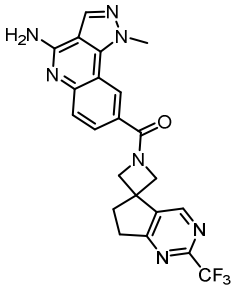
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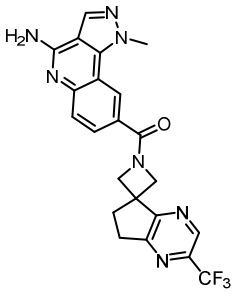
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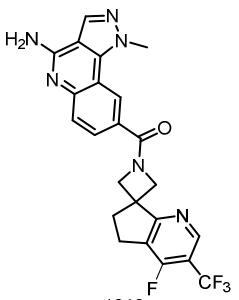
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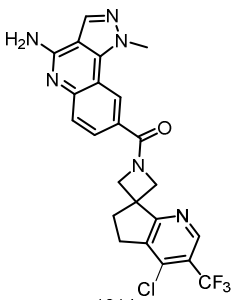
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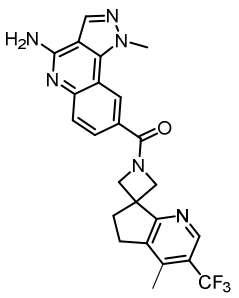
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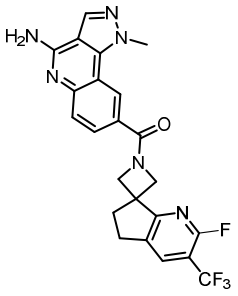
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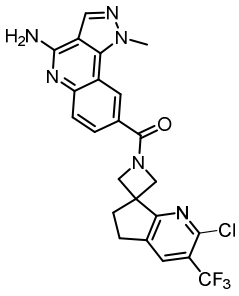
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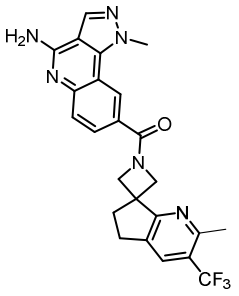
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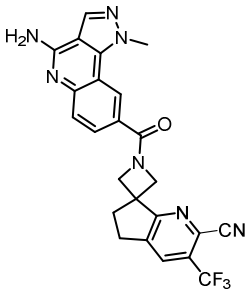
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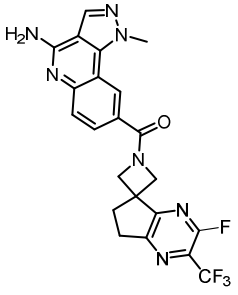
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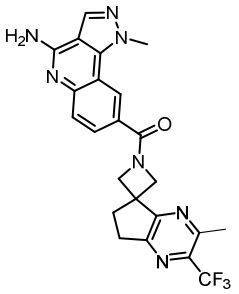
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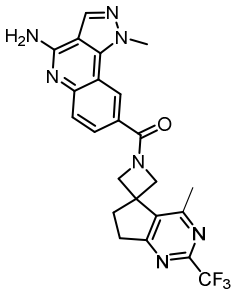
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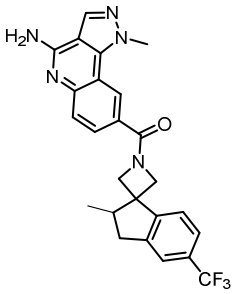
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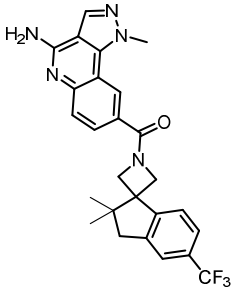
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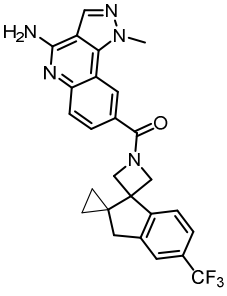
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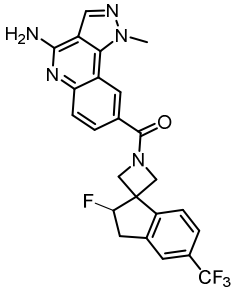
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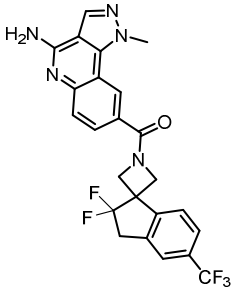
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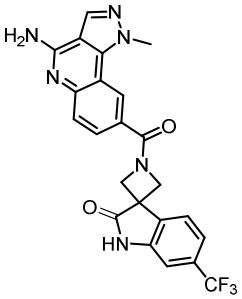
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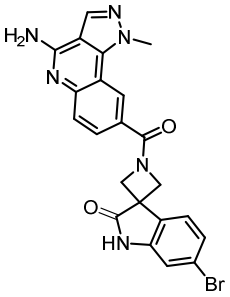
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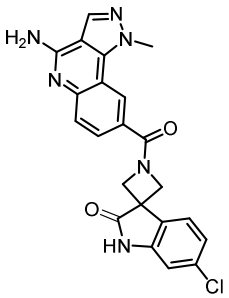
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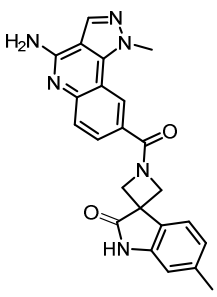
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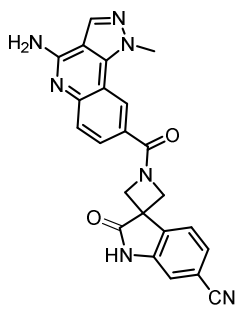
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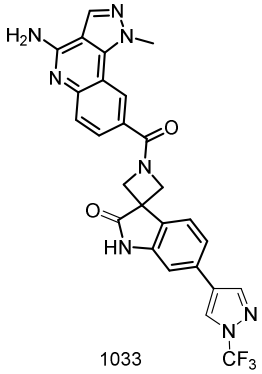
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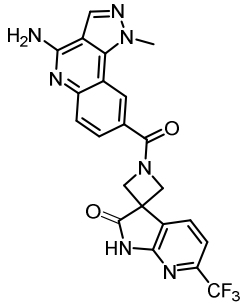
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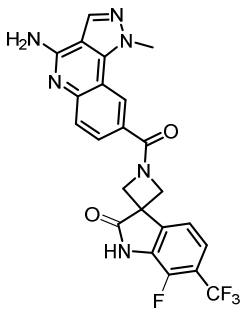
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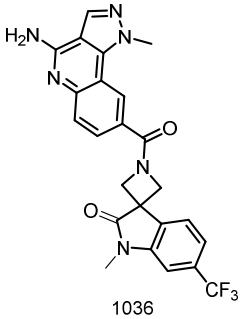
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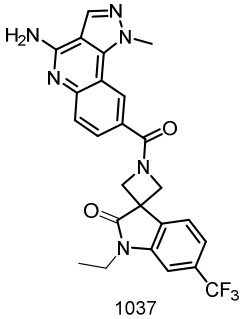
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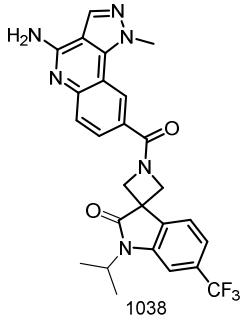
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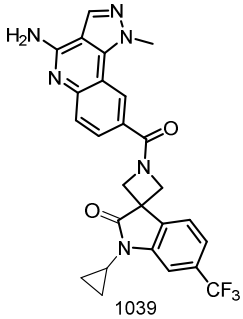
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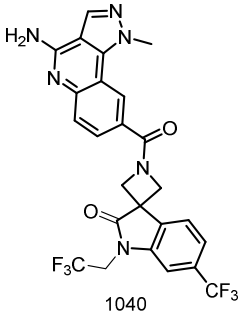
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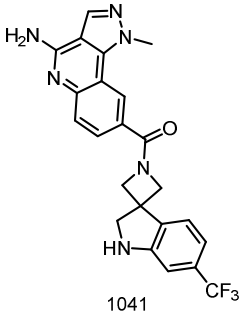
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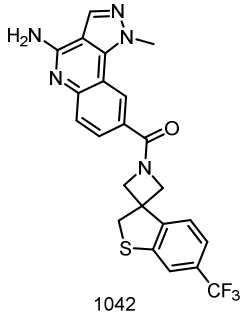
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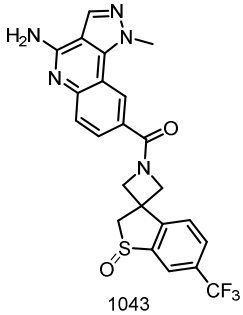
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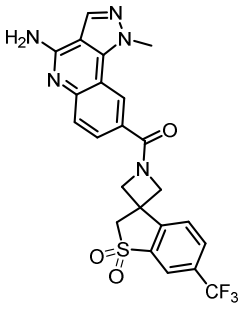
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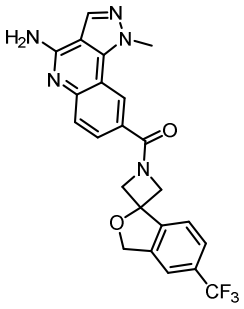
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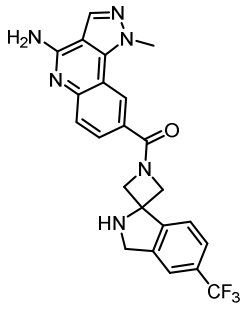
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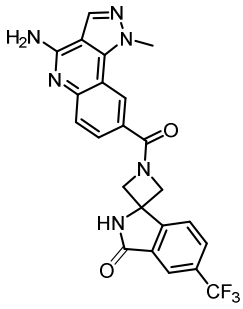
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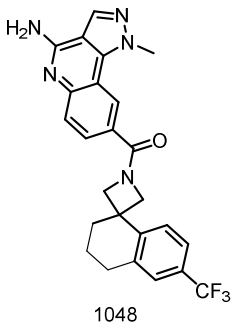
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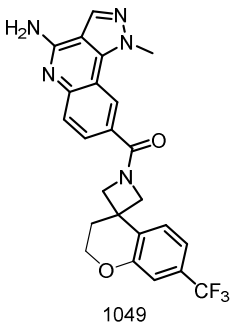
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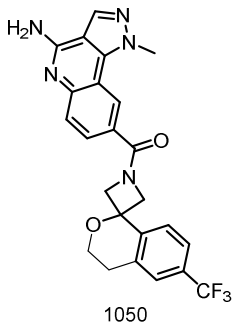
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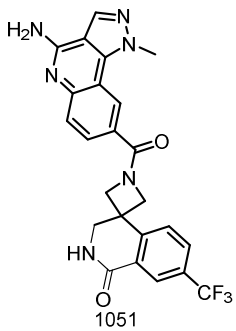
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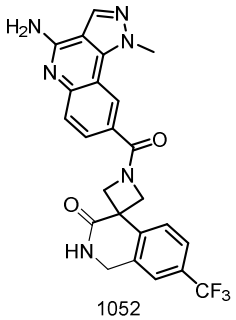
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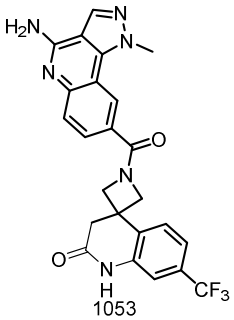
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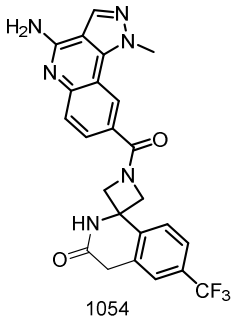
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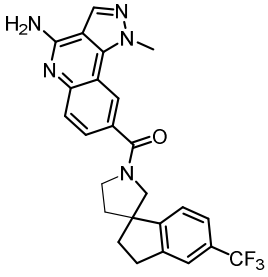
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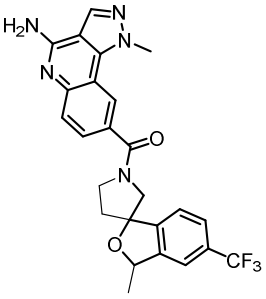
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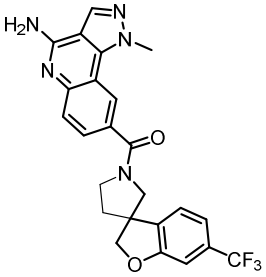
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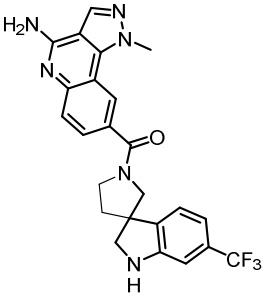
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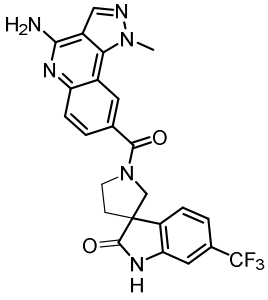
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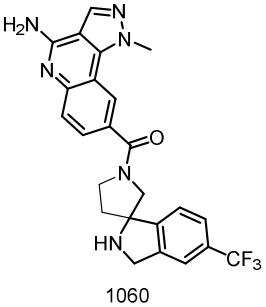
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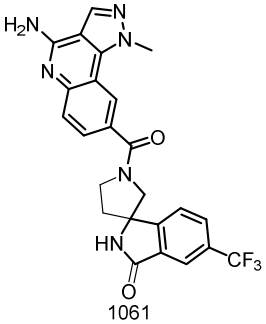
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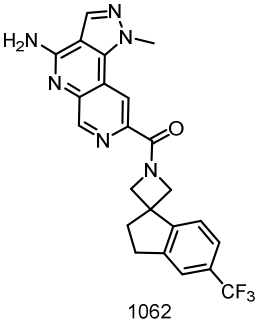
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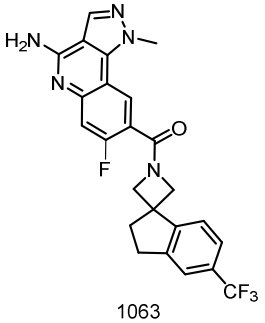
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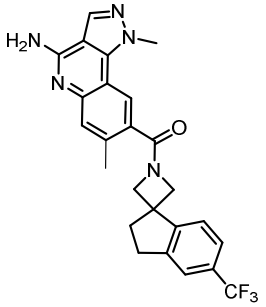
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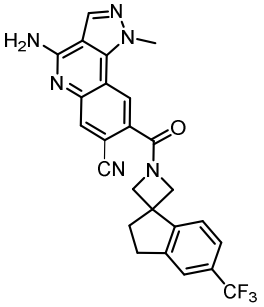
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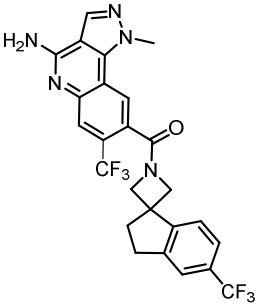
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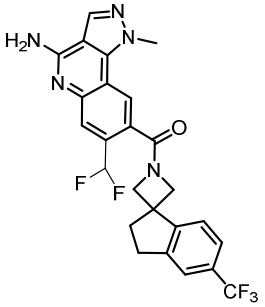
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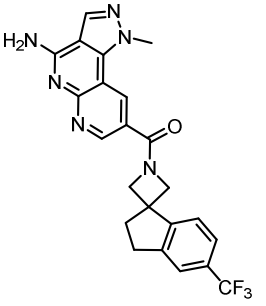
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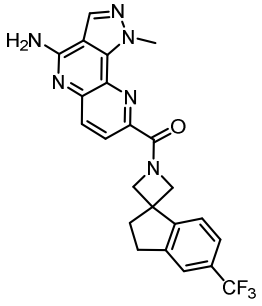
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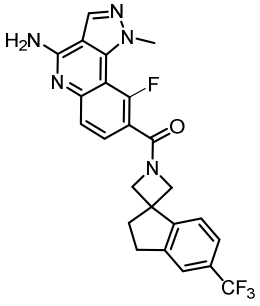
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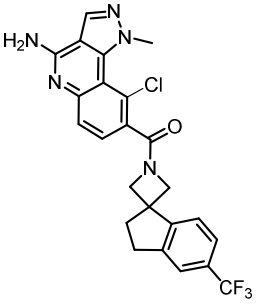
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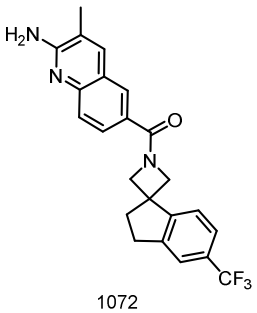
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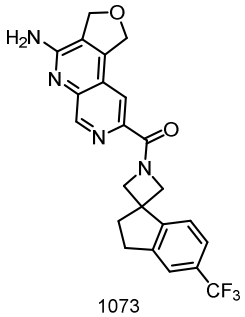
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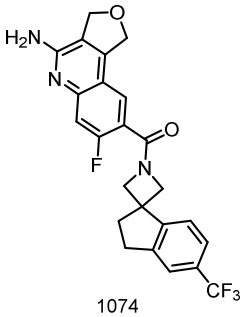
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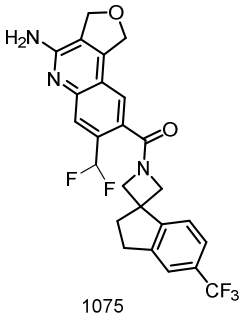
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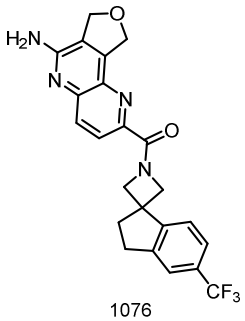
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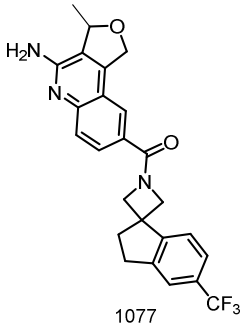
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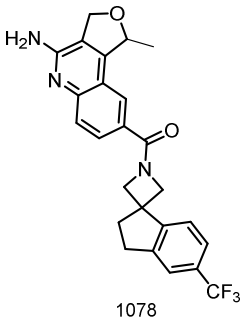
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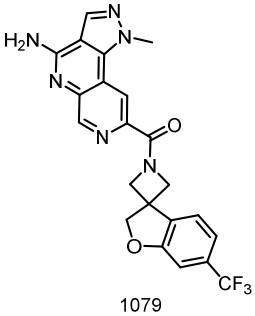
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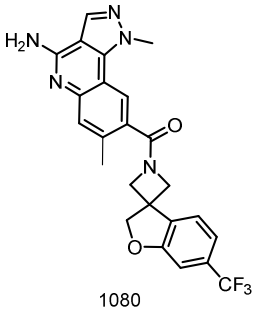
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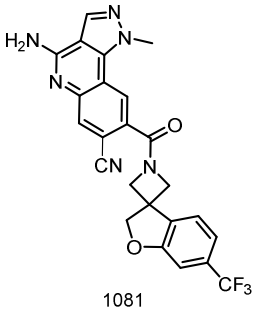
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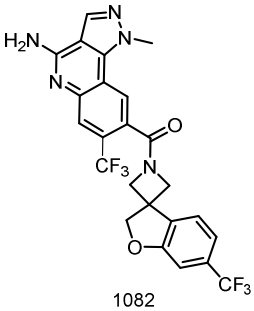
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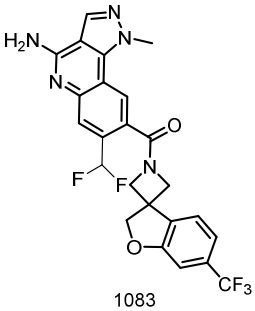
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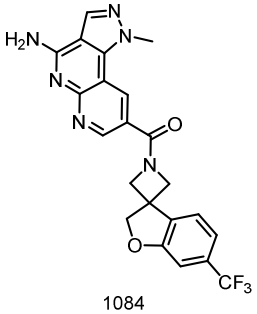
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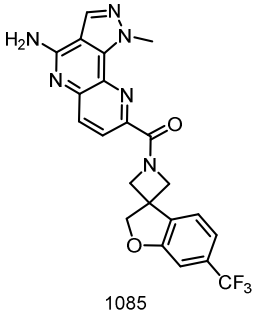
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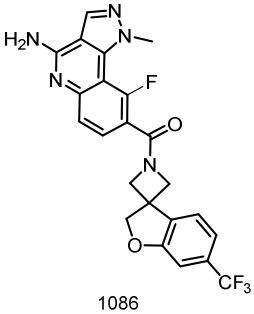
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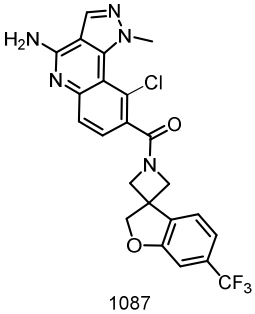
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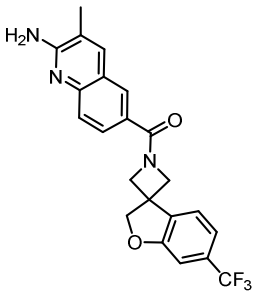
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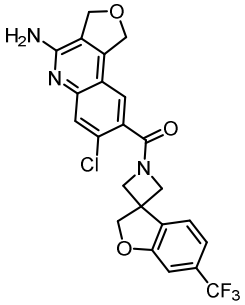
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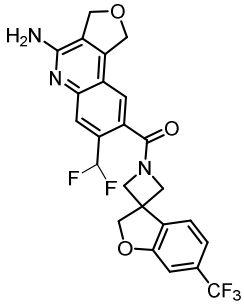
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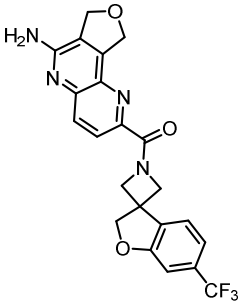
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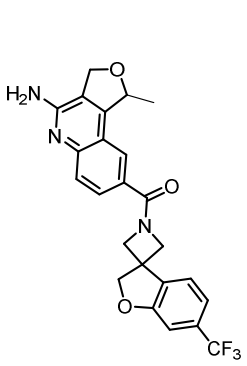

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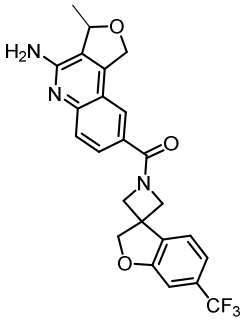

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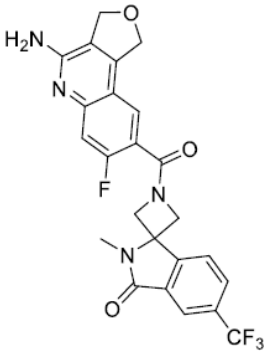

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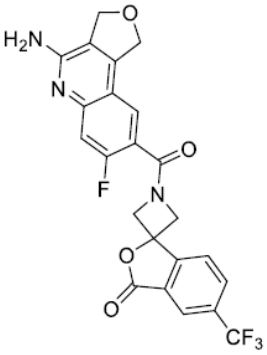

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, or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of the foregoing that is isotope-labeled.

10. A pharmaceutical composition, comprising a compound according to any one of Claims 1-9 or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of the foregoing that is isotope-labeled, and one or more pharmaceutically acceptable carriers or excipients.

11. Use of a compound according to any one of Claims 1-9 or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of the foregoing that is isotope-labeled or a pharmaceutical composition according to Claim 10 in the manufacture of a medicament for treating cancer.

12. Use of a compound according to any one of Claims 1-9 or a pharmaceutically acceptable salt, geometric isomer, enantiomer, diastereomer, racemate, hydrate thereof or any of the foregoing that is isotope-labeled or a pharmaceutical composition according to Claim 10 in the manufacture of a medicament for treating MTAP deficient cancers.