

PARG INHIBITOR

[0001] The present application claims priority to Chinese Patent Application No. 2023114041256, filed on October 26, 2023; Chinese Patent Application No. 2023115667661, filed on November 22, 2023; Chinese Patent Application No. 2024100209152, filed on January 5, 2024; Chinese Patent Application No. 2024102516704, filed on March 5, 2024; Chinese Patent Application No. 2024107836041, filed on June 17, 2024; Chinese Patent Application No. 2024112921468, filed on September 13, 2024; and Chinese Patent Application No. 2024114656236, filed on October 18, 2024. The contents of the above Chinese Patent Applications are incorporated herein by reference in their entireties.

TECHNICAL FIELD

[0002] The present disclosure relates to certain compounds for inhibiting the activity of PARG (poly ADP-ribose glycohydrolase). The present disclosure also relates to methods of preparing these compounds, pharmaceutical compositions comprising the same, and the use thereof in the treatment of cancer and other diseases.

BACKGROUND

[0003] Maintaining genomic stability and integrity is essential for normal cellular function in organisms. Since DNA is highly susceptible to damage from external environmental factors or internal factors, organisms possess a series of complex DNA damage repair (DDR)

mechanisms to timely and accurately repair DNA damage. Defects in DNA damage repair mechanisms can easily lead to genomic instability, resulting in cell apoptosis or even carcinogenesis.

[0004] The clinical success of PARP (poly ADP-ribose polymerase) inhibitors has sparked
5 intense interest in the development of drugs targeting DNA damage repair pathways based on the mechanism of synthetic lethality. PARP1/2, as poly(ADP-ribose) polymerases, are key proteins involved in DNA damage repair. Inhibition of the enzymatic activity of PARP1/2 results in the accumulation of a large number of single-strand DNA breaks in cells, which subsequently develop into double-strand breaks. In cancer cells with defective DNA
10 homologous recombination repair, these double-strand DNA breaks cannot be properly repaired, ultimately leading to the death of cancer cells. Therefore, PARP1/2 exhibit a synthetic lethal effect with genes involved in DNA double-strand break repair (primarily homologous recombination repair).

[0005] PARG (poly ADP-ribose glycohydrolase), as the most important poly(ADP-ribose)
15 hydrolase in cells, is responsible for more than 90% of poly(ADP-ribose) hydrolysis and can hydrolyze the poly(ADP-ribose) chains produced by PARP-catalyzed reactions. Although PARG and PARP have opposite functions with respect to their target proteins, both play crucial regulatory roles in DNA damage repair and under replication stress. When DNA damage occurs, PARP is recruited to the damage site to catalyze the formation of poly(ADP-
20 ribose) chains on itself. These branched chains then serve as a platform to recruit other DNA repair factors, facilitating repair at the DNA damage site. After DNA repair, PARG

hydrolyzes these ADP-ribose branched chains, completing the entire repair cycle. On the other hand, the continuous proliferation of cancer cells generates replication stress, which requires stalling of the DNA replication fork to repair DNA damage near the replication fork. During the process, cells also need to recruit PARP to the stalled replication fork. Through rapid synthesis of its own poly(ADP-ribose) branched chains, PARP inhibits the enzymatic activity of RECQ1 that promotes restart of the replication fork while simultaneously recruiting a series of repair factors to complete DNA damage repair. Once repair is completed, PARG rapidly hydrolyzes the poly(ADP-ribose) branched chains, promoting the release of PARP from the stalled replication fork and restoring the enzymatic activity of RECQ1 to restart replication. Since knockout of PARG in cells exacerbates replication stress and DNA damage, PARG has the potential to serve as a synthetic lethal target in tumors with defective DNA damage repair or under replication stress.

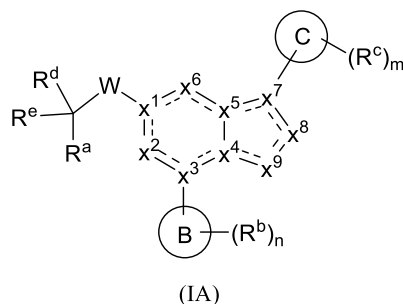
[0006] Given the similarity in biological functions between PARG and PARP, PARG inhibitors, like PARP inhibitors, have the potential to be effective in tumor patients with defects in BRCA genes, or even those with homologous recombination deficiency (HRD). In addition, PARG exhibits synthetic lethal interactions with genes associated with replication stress. Therefore, PARG inhibitors have the potential to be effective in tumors with defects in replication-related genes.

[0007] Currently, few of PARG inhibitors in development have entered clinical stages, with most molecules still in early stages. Therefore, developing a novel class of PARG inhibitors is of significant research importance.

SUMMARY

[0008] The present disclosure aims to provide a class of novel compounds with PARG inhibitory activity, a pharmaceutical composition comprising the compound, a useful intermediate for preparing the compound, and the use of the compound in the manufacture of a medicament for the treatment of cancer.

[0009] The present disclosure provides a compound of formula (IA), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof,



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[0010] wherein

[0011] x^1 is selected from the group consisting of C, CR^{x1} , and N, wherein R^{x1} is selected from the group consisting of H, halogen, hydroxyl, $-NR^{n1}R^{n2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

[0012] x^2 is selected from the group consisting of CR^{x2} , N, $C(=O)$, and $C(=CR^{x2})$, wherein

15 R^{x2} is selected from the group consisting of H, halogen, hydroxyl, amino, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-NR^{n1}R^{n2}$, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$,

wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0013] x³ is selected from the group consisting of C, CR^{x3}, and N, wherein R^{x3} is selected from the group consisting of H, halogen, hydroxyl, -NRⁿ¹Rⁿ², C₁₋₄ alkyl, and -OC₁₋₄ alkyl;

[0014] x⁴ is selected from the group consisting of C, CR^{x4}, and N, wherein R^{x4} is selected from the group consisting of H, halogen, hydroxyl, -NRⁿ¹Rⁿ², C₁₋₄ alkyl, and -OC₁₋₄ alkyl;

[0015] x⁵ is selected from the group consisting of C, CR^{x5}, and N, wherein R^{x5} is selected from the group consisting of H, halogen, hydroxyl, -NRⁿ¹Rⁿ², C₁₋₄ alkyl, and -OC₁₋₄ alkyl;

[0016] x⁶ is selected from the group consisting of CR^{x6}, N, C(=O), and C(=CR^{x6}), wherein R^{x6} is selected from the group consisting of H, halogen, hydroxyl, cyano, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -NRⁿ¹Rⁿ², -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd}; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to

10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd},
 5 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0017] x⁷ is selected from the group consisting of C, CR^{x7}, and N, wherein R^{x7} is selected from the group consisting of H, halogen, hydroxyl, -NRⁿ¹Rⁿ², C₁₋₄ alkyl, and -OC₁₋₄ alkyl;

[0018] x⁸ is selected from the group consisting of N, O, CR^{x8}, CR^{x8}R^{x8}, NR^{x8}, S(O)_p, C(=O),
 10 and C(=CR^{x8}), wherein R^{x8}, at each occurrence, is identical or different, and is independently selected from the group consisting of H, deuterium, halogen, hydroxyl, -NRⁿ¹Rⁿ², cyano, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, -OR^f, -C(O)R^{ba}, -S(O)_pR^{ba}, -N=S(O)R^{ba}, S(O)_pNR^{be}R^{bf}, -
 15 C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd}; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba1}, S(O)_pR^{ba1},
 20 S(O)_pNR^{be1}R^{bf1}, -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, 3- to 8-membered cycloalkyl, 3- to 8-

membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

- [0019]** alternatively, two R^{x8} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl is optionally substituted by one or more
- 5 substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6} deutoalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{bc}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;
- 10 **[0020]** x^9 is selected from the group consisting of CR^{x9} , N, O, NR^{x9} , $S(O)_p$, $CR^{x9}R^{x9}$, and $C(=CR^{x8})$, wherein R^{x9} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, deuterium, halogen, hydroxyl, $-NR^{n1}R^{n2}$, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to
- 15 10-membered heteroaryl, $-OR^f$, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{bc}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba1}$, $S(O)_pR^{ba1}$, $S(O)_pNR^{be1}R^{bf1}$,
- 20

$-\text{C}(\text{O})\text{OR}^{\text{bb1}}$, $-\text{C}(\text{O})\text{NR}^{\text{bc1}}\text{R}^{\text{bd1}}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0021] alternatively, two R^{x9} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl and 3- to 8-membered heterocyclyl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6} deuterioalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-\text{NR}^{\text{a1}}\text{R}^{\text{a2}}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-\text{C}(\text{O})\text{R}^{\text{ba}}$, $\text{S}(\text{O})\text{R}^{\text{ba}}$, $\text{S}(\text{O})\text{pNR}^{\text{bc}}\text{R}^{\text{bf}}$, $-\text{C}(\text{O})\text{OR}^{\text{bb}}$, $-\text{C}(\text{O})\text{NR}^{\text{bc}}\text{R}^{\text{bd}}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0022] alternatively, R^{x8} and R^{x9} , together with the atom to which they are attached, form a 3- to 7-membered ring; wherein the 3- to 7-membered ring is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6} deuterioalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-\text{NR}^{\text{a1}}\text{R}^{\text{a2}}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-\text{OR}^{\text{f}}$, $-\text{C}(\text{O})\text{R}^{\text{ba}}$, $\text{S}(\text{O})\text{R}^{\text{ba}}$, $\text{S}(\text{O})\text{pNR}^{\text{bc}}\text{R}^{\text{bf}}$, $-\text{C}(\text{O})\text{OR}^{\text{bb}}$, $-\text{C}(\text{O})\text{NR}^{\text{bc}}\text{R}^{\text{bd}}$, C_{1-6} deuterioalkoxy, $-\text{C}_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl,

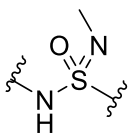
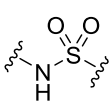
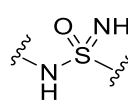
C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NRⁿ¹Rⁿ², nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{be1}R^{bfl}, -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

5 [0023]  is a single bond or a double bond;

[0024] R^a, R^d, and R^e are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, halogen, C₁₋₆ alkyl, cyano, -NRⁿ¹Rⁿ², hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{be1}R^{bfl}, -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

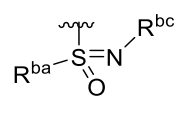
[0025] alternatively, any two of R^a, R^d, and R^e, together with the atom to which they are attached, form a 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, or 5- to 10-membered heteroaryl ring; wherein the 3- to 8-membered

cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, C₁₋₆ deutoalkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0026] W is selected from the group consisting of , , and ;

[0027] ring B is selected from the group consisting of 3- to 10-membered cycloalkyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

[0028] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, deuterium, halogen, C₁₋₆ alkyl, cyano, hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -NRⁿ¹Rⁿ², -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered

heteroaryl, , -OR^f, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, S(O)_pNR^{be}R^{bf}, and S(O)_pR^{ba}; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents

selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{be1}R^{bfl}, -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 5- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, -C(O)R^{ba2}, S(O)_pR^{ba2}, S(O)_pNR^{be2}R^{bfl}, -C(O)OR^{bb2}, -C(O)NR^{bc2}R^{bd2}, and C₁₋₆ hydroxyalkyl;

[0029] Rⁿ¹, Rⁿ², R^{a1}, and R^{a2} are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, C₁₋₆ alkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, -OR^f, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bfl}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deutoalkoxy, C₁₋₆ deutoalkyl, cyano, amino, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

[0030] R^{ba} , R^{bb} , R^{bc} , R^{bd} , R^{be} , and R^{bf} are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, C_{1-6} alkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} deutoalkoxy, C_{1-6} alkoxy, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6-
5 to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6}
10 deutoalkoxy, C_{1-6} deutoalkyl, $-OR^f$, $-C(O)R^{ba1}$, $S(O)_pR^{ba1}$, $S(O)_pNR^{be1}R^{bfl}$, $-C(O)OR^{bb1}$, $-C(O)NR^{bc1}R^{bd1}$, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, and C_{1-6} hydroxyalkyl;

[0031] alternatively, R^{n1} and R^{n2} , R^{a1} and R^{a2} , R^{bc} and R^{bd} , or R^{be} and R^{bf} , together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring; wherein the 3- to 7-membered heterocyclyl is optionally substituted by one or more
15 substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6} deutoalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0032] ring C is selected from the group consisting of 3- to 10-membered cycloalkyl, 3- to 10-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0033] each R^c is identical or different, and is independently selected from the group consisting of hydrogen, deuterium, halogen, C_{1-6} alkyl, cyano, $-NR^{n1}R^{n2}$, hydroxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba1}$, $S(O)_pR^{ba1}$, $S(O)_pNR^{be1}R^{bf1}$, $-C(O)OR^{bb1}$, $-C(O)NR^{bc1}R^{bd1}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, $-C(O)R^{ba2}$, $S(O)_pR^{ba2}$, $S(O)_pNR^{be2}R^{bf2}$, $-C(O)OR^{bb2}$, $-C(O)NR^{bc2}R^{bd2}$, and C_{1-6} hydroxyalkyl;

[0034] R^{ba1} , R^{bb1} , R^{bc1} , R^{bd1} , R^{be1} , R^{bf1} , R^{ba2} , R^{bb2} , R^{bc2} , R^{bd2} , R^{be2} , and R^{bf2} are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, C_{1-6} alkyl, C_{1-6} haloalkoxy, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, C_{2-6} alkenyl, C_{2-6}

alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ deuteroalkoxy, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or
 5 more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deuteroalkoxy, C₁₋₆ deuteroalkyl, cyano, -NR^{a1}R^{a2}, -OR^f, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

[0035] R^f is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and
 10 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆
 15 haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deuteroalkyl, C₁₋₆ deuteroalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

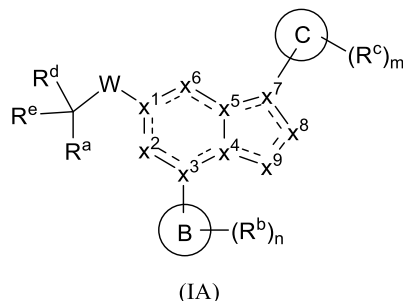
[0036] n is selected from the group consisting of 0, 1, 2, and 3;

[0037] m is selected from the group consisting of 0, 1, 2, and 3;

[0038] p is selected from the group consisting of 0, 1, and 2.

20 **[0039]** The present disclosure provides a compound of formula (IA), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a

solvate thereof, or an isotopic derivative thereof,



[0040] wherein

[0041] x^1 is selected from the group consisting of C, CR^{x1} , and N, wherein R^{x1} is selected

5 from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

[0042] x^2 is selected from the group consisting of CR^{x2} , N, $C(=O)$, and $C(=CR^{x2})$, wherein

R^{x2} is selected from the group consisting of H, halogen, hydroxyl, amino, cyano, C_{2-6} alkenyl,

C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-NR^{b1}R^{b2}$, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3-

to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to

10 10-membered heteroaryl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$,

wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to

8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to

10-membered heteroaryl are optionally substituted by one or more substituents selected from

the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl,

15 C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro,

hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$,

3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and

5- to 10-membered heteroaryl;

- [0043] x^3 is selected from the group consisting of C, CR^{x3} , and N, wherein R^{x3} is selected from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;
- [0044] x^4 is selected from the group consisting of C, CR^{x4} , and N, wherein R^{x4} is selected from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;
- 5 [0045] x^5 is selected from the group consisting of C, CR^{x5} , and N, wherein R^{x5} is selected from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;
- [0046] x^6 is selected from the group consisting of CR^{x6} , N, $C(=O)$, and $C(=CR^{x6})$, wherein R^{x6} is selected from the group consisting of H, halogen, hydroxyl, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-NR^{b1}R^{b2}$, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to
- 10 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{bc}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from
- 15 the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{bc}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;
- 20 [0047] x^7 is selected from the group consisting of C, CR^{x7} , and N, wherein R^{x7} is selected from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

- [0048] x^8 is selected from the group consisting of N, O, CR^{x8} , $CR^{x8}R^{x8}$, NR^{x8} , $S(O)_p$, $C(=O)$, and $C(=CR^{x8})$, wherein R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, deuterium, halogen, hydroxyl, $-NR^{b1}R^{b2}$, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-OR^f$, $-C(O)R^{ba}$, $-S(O)_pR^{ba}$, $-N=S(O)R^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba1}$, $S(O)_pR^{ba1}$, $S(O)_pNR^{be1}R^{bf1}$, $-C(O)OR^{bb1}$, $-C(O)NR^{bc1}R^{bd1}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;
- [0049] alternatively, two R^{x8} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6} deuterioalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl,

3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0050] x^9 is selected from the group consisting of CR^{x9} , N, O, NR^{x9} , $S(O)_p$, $CR^{x9}R^{x9}$, and $C(=CR^{x8})$, wherein R^{x9} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, deuterium, halogen, hydroxyl, $-NR^{b1}R^{b2}$, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-OR^f$, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{bc}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba1}$, $S(O)_pR^{ba1}$, $S(O)_pNR^{bc1}R^{bf1}$, $-C(O)OR^{bb1}$, $-C(O)NR^{bc1}R^{bd1}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0051] alternatively, two R^{x9} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl and 3- to 8-membered heterocyclyl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6} deutoalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, -

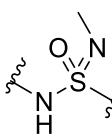
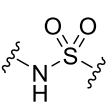
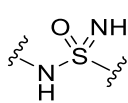
$C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{bc}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl,
 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;
[0052] alternatively, R^{x8} and R^{x9} , together with the atom to which they are attached, form a
 3- to 7-membered ring; wherein the 3- to 7-membered ring is optionally substituted by one
 5 or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl,
 C_{1-6} deuterioalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6}
 alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl,
 $-OR^f$, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{bc}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, C_{1-6} deuterioalkoxy, -
 C_{1-6} alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to
 10 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered
 cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered
 heteroaryl are optionally substituted by one or more substituents selected from the group
 consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl,
 C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{n1}R^{n2}$, nitro,
 15 hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba1}$, $S(O)_pR^{ba1}$, $S(O)_pNR^{bc1}R^{bf1}$, $-C(O)OR^{bb1}$, -
 $C(O)NR^{bc1}R^{bd1}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-
 membered aryl, and 5- to 10-membered heteroaryl;

[0053] $\diagup$ is a single bond or a double bond;

[0054] R^a , R^d , and R^e are identical or different, and are each independently selected from the
 20 group consisting of hydrogen, deuterium, halogen, C_{1-6} alkyl, cyano, $-NR^{b1}R^{b2}$, hydroxyl,
 C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, $-C(O)R^{ba}$,

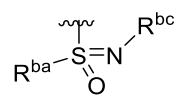
$S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba1}$, $S(O)_pR^{ba1}$, $S(O)_pNR^{be1}R^{bf1}$, $-C(O)OR^{bb1}$, $-C(O)NR^{bc1}R^{bd1}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0055] alternatively, any two of R^a , R^d , and R^e , together with the atom to which they are attached, form a 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, or 5- to 10-membered heteroaryl ring; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6} deuterioalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0056] W is selected from the group consisting of , , and ;

[0057] ring B is selected from the group consisting of 3- to 10-membered cycloalkyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

[0058] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, deuterium, halogen, C_{1-6} alkyl, cyano, hydroxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-NR^{b1}R^{b2}$, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered

heteroaryl, , $-OR^f$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, $S(O)_pNR^{be}R^{bf}$, and $S(O)_pR^{ba}$; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba1}$, $S(O)_pR^{ba1}$, $S(O)_pNR^{be1}R^{bf1}$, $-C(O)OR^{bb1}$, $-C(O)NR^{bc1}R^{bd1}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group

consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, -C(O)R^{ba2}, S(O)_pR^{ba2}, S(O)_pNR^{bc2}R^{bf2}, -C(O)OR^{bb2}, -C(O)NR^{bc2}R^{bd2}, and C₁₋₆ hydroxyalkyl;

- 5 **[0059]** R^{b1}, R^{b2}, R^{a1}, and R^{a2} are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, C₁₋₆ alkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, -OR^f, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{bc}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-
- 10 membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deutoalkoxy, C₁₋₆ deutoalkyl, cyano, amino, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;
- 15 **[0060]** R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, C₁₋₆ alkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ deutoalkoxy, C₁₋₆ alkoxy, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-
- 20 membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from

the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deutoalkoxy, C₁₋₆ deutoalkyl, -OR^f, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{be1}R^{bfl}, -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

- 5 **[0061]** alternatively, R^{b1} and R^{b2}, R^{a1} and R^{a2}, R^{bc} and R^{bd}, or R^{be} and R^{bf}, together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring; wherein the 3- to 7-membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, C₁₋₆ deutoalkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0062] ring C is selected from the group consisting of 3- to 10-membered cycloalkyl, 3- to 10-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

- 15 **[0063]** each R^c is identical or different, and is independently selected from the group consisting of hydrogen, deuterium, halogen, C₁₋₆ alkyl, cyano, -NR^{b1}R^{b2}, hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{bc}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein
- 20 the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more

substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{be1}R^{bfl}, -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, -C(O)R^{ba2}, S(O)_pR^{ba2}, S(O)_pNR^{be2}R^{bfl}, -C(O)OR^{bb2}, -C(O)NR^{bc2}R^{bd2}, and C₁₋₆ hydroxyalkyl;

[0064] R^{ba1}, R^{bb1}, R^{bc1}, R^{bd1}, R^{be1}, R^{bfl}, R^{ba2}, R^{bb2}, R^{bc2}, R^{bd2}, R^{be2}, and R^{bfl} are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, C₁₋₆ alkyl, C₁₋₆ haloalkoxy, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ deutoalkoxy, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deutoalkoxy, C₁₋₆ deutoalkyl, cyano, -NR^{a1}R^{a2}, -OR^f, nitro, hydroxyl,

and C₁₋₆ hydroxyalkyl;

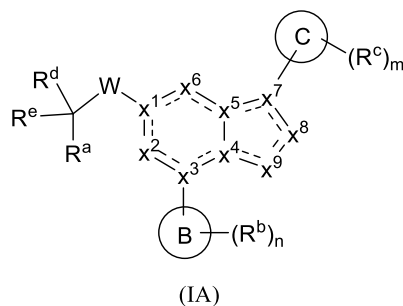
[0065] R^f is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deuterioalkyl, C₁₋₆ deuterioalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

10 [0066] n is selected from the group consisting of 0, 1, 2, and 3;

[0067] m is selected from the group consisting of 0, 1, 2, and 3;

[0068] p is selected from the group consisting of 0, 1, and 2.

[0069] The present disclosure provides a compound of formula (IA), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a
15 solvate thereof, or an isotopic derivative thereof,



[0070] wherein

[0071] x¹ is selected from the group consisting of C, CR^{x1}, and N, wherein R^{x1} is selected

from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

[0072] x^2 is selected from the group consisting of CR^{x2} , N, $C(=O)$, and $C(=CR^{x2})$, wherein

R^{x2} is selected from the group consisting of H, halogen, hydroxyl, amino, cyano, C_{2-6} alkenyl,

C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-NR^{b1}R^{b2}$, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3-

5 to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to

10-membered heteroaryl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$;

wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to

8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to

10-membered heteroaryl are optionally substituted by one or more substituents selected from

10 the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl,

C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro,

hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$,

3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and

5- to 10-membered heteroaryl;

15 **[0073]** x^3 is selected from the group consisting of C, CR^{x3} , and N, wherein R^{x3} is selected

from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

[0074] x^4 is selected from the group consisting of C, CR^{x4} , and N, wherein R^{x4} is selected

from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

[0075] x^5 is selected from the group consisting of C, CR^{x5} , and N, wherein R^{x5} is selected

20 from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

[0076] x^6 is selected from the group consisting of CR^{x6} , N, $C(=O)$, and $C(=CR^{x6})$, wherein

R^{x6} is selected from the group consisting of H, halogen, hydroxyl, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-NR^{b1}R^{b2}$, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$;
 5 wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$,
 10 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0077] x^7 is selected from the group consisting of C, CR^{x7} , and N, wherein R^{x7} is selected from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

[0078] x^8 is selected from the group consisting of N, O, CR^{x8} , $CR^{x8}R^{x8}$, NR^{x8} , $S(O)_p$, $C(=O)$, and $C(=CR^{x8})$, wherein R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, deuterium, halogen, hydroxyl, $-NR^{b1}R^{b2}$, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-OR^f$, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$;
 20 wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy-

C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{be1}R^{bf1}, -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0079] alternatively, two R^{x8} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, C₁₋₆ deuterioalkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{bc}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0080] x⁹ is selected from the group consisting of CR^{x9}, N, O, NR^{x9}, S(O)_p, CR^{x9}R^{x9}, and C(=CR^{x8}), wherein R^{x9}, at each occurrence, is identical or different, and is independently selected from the group consisting of H, deuterium, halogen, hydroxyl, -NR^{b1}R^{b2}, cyano, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, -OR^f, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{bc}R^{bf}, -C(O)OR^{bb}, and -

$C(O)NR^{bc}R^{bd}$; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy-
 C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered
 aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents
 selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6}
 5 alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy,
 cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba1}$, $S(O)_pR^{ba1}$, $S(O)_pNR^{be1}R^{bf1}$,
 $-C(O)OR^{bb1}$, $-C(O)NR^{bc1}R^{bd1}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl,
 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0081] alternatively, two R^{x9} attached to the same carbon atom together form a 3- to 8-
 10 membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered
 cycloalkyl and 3- to 8-membered heterocyclyl are optionally substituted by one or more
 substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6}
 deuteroalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy,
 C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, -
 15 $C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl,
 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0082] alternatively, R^{x8} and R^{x9} , together with the atom to which they are attached, form a
 3- to 7-membered ring; wherein the 3- to 7-membered ring is optionally substituted by one
 or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl,
 20 C_{1-6} deuteroalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6}
 alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl,

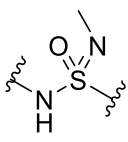
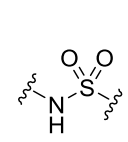
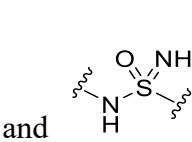
-OR^f, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, C₁₋₆ deuteroalkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0083] $\diagup$ is a single bond or a double bond;

- 5 **[0084]** R^a, R^d, and R^e are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, halogen, C₁₋₆ alkyl, cyano, -NR^{b1}R^{b2}, hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein
- 10 the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2},
- 15 nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{be1}R^{bf1}, -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

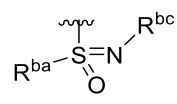
- [0085]** alternatively, any two of R^a, R^d, and R^e, together with the atom to which they are attached, form a 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, or 5- to 10-membered heteroaryl ring; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered
- 20

heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, C₁₋₆ deuterioalkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb},
 5 -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0086] W is selected from the group consisting of , , and ;

[0087] ring B is selected from the group consisting of 3- to 10-membered cycloalkyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, 5- to 7-membered monocyclic
 10 heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

[0088] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, deuterium, halogen, C₁₋₆ alkyl, cyano, hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -NR^{b1}R^{b2}, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered
 15 cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered

heteroaryl, , -OR^f, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, S(O)_pNR^{be}R^{bf}, and S(O)_pR^{ba}; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents

20 selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆

alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{be1}R^{bf1}, -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, -C(O)R^{ba2}, S(O)_pR^{ba2}, S(O)_pNR^{be2}R^{bf2}, -C(O)OR^{bb2}, -C(O)NR^{bc2}R^{bd2}, and C₁₋₆ hydroxyalkyl;

[0089] R^{b1}, R^{b2}, R^{a1}, and R^{a2} are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, C₁₋₆ alkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, -OR^f, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deutoalkoxy, C₁₋₆ deutoalkyl, cyano, amino, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

[0090] R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are identical or different, and are each independently

selected from the group consisting of hydrogen, deuterium, C₁₋₆ alkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ deuterioalkoxy, C₁₋₆ alkoxy, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deuterioalkoxy, C₁₋₆ deuterioalkyl, -OR^f, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{be1}R^{bfl}, -C(O)OR^{bb1},
 10 -C(O)NR^{bc1}R^{bd1}, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

[0091] alternatively, R^{b1} and R^{b2}, R^{a1} and R^{a2}, R^{bc} and R^{bd}, or R^{be} and R^{bf}, together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring; wherein the 3- to 7-membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, C₁₋₆ deuterioalkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0092] ring C is selected from the group consisting of 3- to 10-membered cycloalkyl, 3- to 10-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0093] each R^c is identical or different, and is independently selected from the group

consisting of hydrogen, deuterium, halogen, C₁₋₆ alkyl, cyano, -NR^{b1}R^{b2}, hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein

5 the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba1}, S(O)_pR^{ba1},

10 S(O)_pNR^{be1}R^{bfl}, -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy,

15 cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, -C(O)R^{ba2}, S(O)_pR^{ba2}, S(O)_pNR^{be2}R^{bfl2}, -C(O)OR^{bb2}, -C(O)NR^{bc2}R^{bd2}, and C₁₋₆ hydroxyalkyl;

[0094] R^{ba1}, R^{bb1}, R^{bc1}, R^{bd1}, R^{be1}, R^{bfl}, R^{ba2}, R^{bb2}, R^{bc2}, R^{bd2}, R^{be2}, and R^{bfl2} are identical or different, and are each independently selected from the group consisting of hydrogen,

20 deuterium, C₁₋₆ alkyl, C₁₋₆ haloalkoxy, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ deutoalkoxy, 3- to 8-membered cycloalkyl,

3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;
 wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to
 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or
 more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo,
 5 C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆
 haloalkoxy, C₁₋₆ deuterioalkoxy, C₁₋₆ deuterioalkyl, cyano, -NR^{a1}R^{a2}, -OR^f, nitro, hydroxyl,
 and C₁₋₆ hydroxyalkyl;

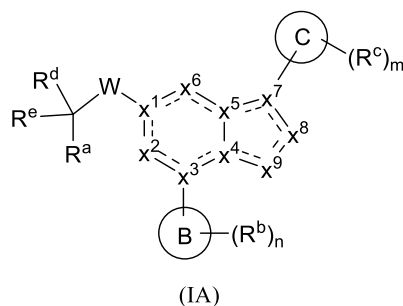
[0095] R^f is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl,
 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and
 10 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-
 membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are
 optionally substituted by one or more substituents selected from the group consisting of
 deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆
 haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deuterioalkyl, C₁₋₆
 15 deuterioalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

[0096] n is selected from the group consisting of 0, 1, 2, and 3;

[0097] m is selected from the group consisting of 0, 1, 2, and 3;

[0098] p is selected from the group consisting of 0, 1, and 2.

[0099] The present disclosure provides a compound of formula (IA), a pharmaceutically
 20 acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a
 solvate thereof, or an isotopic derivative thereof,



[0100] wherein

[0101] x^1 is selected from the group consisting of C, CR^{x1} , and N, wherein R^{x1} is selected from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

- 5 **[0102]** x^2 is selected from the group consisting of CR^{x2} , N, $C(=O)$, and $C(=CR^{x2})$, wherein R^{x2} is selected from the group consisting of H, halogen, hydroxyl, amino, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-NR^{b1}R^{b2}$, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{be}R^{bd}$,
- 10 wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{be}R^{bd}$,
- 15 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0103] x^3 is selected from the group consisting of C, CR^{x3} , and N, wherein R^{x3} is selected

from the group consisting of H, halogen, hydroxyl, $-\text{NR}^{\text{b1}}\text{R}^{\text{b2}}$, C_{1-4} alkyl, and $-\text{OC}_{1-4}$ alkyl;

[0104] x^4 is selected from the group consisting of C, CR^{x4} , and N, wherein R^{x4} is selected from the group consisting of H, halogen, hydroxyl, $-\text{NR}^{\text{b1}}\text{R}^{\text{b2}}$, C_{1-4} alkyl, and $-\text{OC}_{1-4}$ alkyl;

[0105] x^5 is selected from the group consisting of C, CR^{x5} , and N, wherein R^{x5} is selected
5 from the group consisting of H, halogen, hydroxyl, $-\text{NR}^{\text{b1}}\text{R}^{\text{b2}}$, C_{1-4} alkyl, and $-\text{OC}_{1-4}$ alkyl;

[0106] x^6 is selected from the group consisting of CR^{x6} , N, $\text{C}(=\text{O})$, and $\text{C}(=\text{CR}^{\text{x6}})$, wherein R^{x6} is selected from the group consisting of H, halogen, hydroxyl, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-\text{NR}^{\text{b1}}\text{R}^{\text{b2}}$, $-\text{C}_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-
10 membered heteroaryl, $-\text{C}(\text{O})\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{NR}^{\text{be}}\text{R}^{\text{bf}}$, $-\text{C}(\text{O})\text{OR}^{\text{bb}}$, and $-\text{C}(\text{O})\text{NR}^{\text{be}}\text{R}^{\text{bd}}$, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-\text{C}_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-\text{NR}^{\text{a1}}\text{R}^{\text{a2}}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-\text{C}(\text{O})\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{NR}^{\text{be}}\text{R}^{\text{bf}}$, $-\text{C}(\text{O})\text{OR}^{\text{bb}}$, $-\text{C}(\text{O})\text{NR}^{\text{be}}\text{R}^{\text{bd}}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0107] x^7 is selected from the group consisting of C, CR^{x7} , and N, wherein R^{x7} is selected
20 from the group consisting of H, halogen, hydroxyl, $-\text{NR}^{\text{b1}}\text{R}^{\text{b2}}$, C_{1-4} alkyl, and $-\text{OC}_{1-4}$ alkyl;

[0108] x^8 is selected from the group consisting of N, O, CR^{x8} , $\text{CR}^{\text{x8}}\text{R}^{\text{x8}}$, NR^{x8} , $\text{S}(\text{O})_{\text{p}}$, $\text{C}(=\text{O})$,

and $C(=CR^{x8})$, wherein R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, deuterium, halogen, hydroxyl, $-NR^{b1}R^{b2}$, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0109] alternatively, two R^{x8} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6} deutoalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

- [0110] x^9 is selected from the group consisting of CR^{x9} , N, O, NR^{x9} , $S(O)_p$, $CR^{x9}R^{x9}$, and $C(=CR^{x8})$, wherein R^{x9} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, deuterium, halogen, hydroxyl, $-NR^{b1}R^{b2}$, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;
- [0111] alternatively, two R^{x9} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl and 3- to 8-membered heterocyclyl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6} deuteroalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl,

3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0112] alternatively, R^{x8} and R^{x9} , together with the atom to which they are attached, form a

3- to 7-membered ring; wherein the 3- to 7-membered ring is optionally substituted by one

or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl,

5 C_{1-6} deuterioalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6}

alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl,

$-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl,

3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0113]  is a single bond or a double bond;

10 **[0114]** R^a , R^d , and R^e are identical or different, and are each independently selected from the

group consisting of hydrogen, deuterium, halogen, C_{1-6} alkyl, cyano, $-NR^{b1}R^{b2}$, hydroxyl,

C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, $-C(O)R^{ba}$,

$S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-

membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein

15 the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-

membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-

membered heteroaryl are optionally substituted by one or more substituents selected from

the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6}

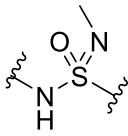
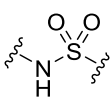
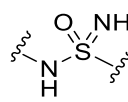
haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$,

20 nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, -

$C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-

membered aryl, and 5- to 10-membered heteroaryl;

[0115] alternatively, any two of R^a , R^d , and R^e , together with the atom to which they are attached, form a 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, or 5- to 10-membered heteroaryl ring; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6} deuterioalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, - $NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, - $C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, - $C(O)OR^{bb}$, - $C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0116] W is selected from the group consisting of , , and ;

[0117] ring B is selected from the group consisting of 3- to 10-membered cycloalkyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

[0118] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, deuterium, halogen, C_{1-6} alkyl, cyano, hydroxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, - $NR^{b1}R^{b2}$, - C_{1-6} alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered

heteroaryl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, $S(O)_pNR^{be}R^{bf}$, and $S(O)_pR^{ba}$; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, and C_{1-6} hydroxyalkyl;

[0119] R^{b1} , R^{b2} , R^{a1} , R^{a2} , R^{ba} , R^{bb} , R^{bc} , R^{bd} , R^{be} , and R^{bf} are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, C_{1-6} alkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6}

alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

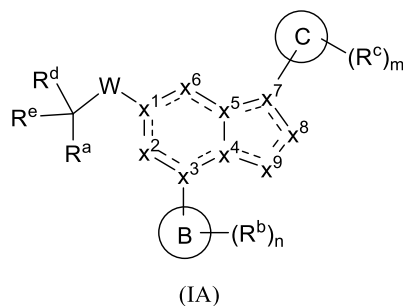
[0120] alternatively, R^{b1} and R^{b2}, R^{a1} and R^{a2}, R^{bc} and R^{bd}, or R^{be} and R^{bf}, together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring;

5 wherein the 3- to 7-membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, C₁₋₆ deutoalkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0121] ring C is selected from the group consisting of 3- to 10-membered cycloalkyl, 3- to 10-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0122] each R^c is identical or different, and is independently selected from the group consisting of hydrogen, deuterium, halogen, C₁₋₆ alkyl, cyano, -NR^{b1}R^{b2}, hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆

- haloalkoxy, cyano, $-\text{NR}^{\text{a1}}\text{R}^{\text{a2}}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-\text{C}(\text{O})\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{NR}^{\text{be}}\text{R}^{\text{bf}}$, $-\text{C}(\text{O})\text{OR}^{\text{bb}}$, $-\text{C}(\text{O})\text{NR}^{\text{bc}}\text{R}^{\text{bd}}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-\text{NR}^{\text{a1}}\text{R}^{\text{a2}}$, nitro, hydroxyl, $-\text{C}(\text{O})\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{NR}^{\text{be}}\text{R}^{\text{bf}}$, $-\text{C}(\text{O})\text{OR}^{\text{bb}}$, $-\text{C}(\text{O})\text{NR}^{\text{bc}}\text{R}^{\text{bd}}$, and C_{1-6} hydroxyalkyl;
- 10 **[0123]** n is selected from the group consisting of 0, 1, 2, and 3;
- [0124]** m is selected from the group consisting of 0, 1, 2, and 3;
- [0125]** p is selected from the group consisting of 0, 1, and 2.
- [0126]** The present disclosure provides a compound of formula (IA), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a
- 15 solvate thereof, or an isotopic derivative thereof,



[0127] wherein

[0128] x^1 is selected from the group consisting of C, CR^{x1} , and N, wherein R^{x1} is selected

from the group consisting of H, halogen, hydroxyl, $-\text{NR}^{\text{b1}}\text{R}^{\text{b2}}$, C_{1-4} alkyl, and $-\text{OC}_{1-4}$ alkyl;

[0129] x^2 is selected from the group consisting of CR^{x2} , N, $\text{C}(=\text{O})$, and $\text{C}(=\text{CR}^{\text{x2}})$, wherein

R^{x2} is selected from the group consisting of H, halogen, hydroxyl, amino, cyano, C_{2-6} alkenyl,

C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-\text{NR}^{\text{b1}}\text{R}^{\text{b2}}$, $-\text{C}_{1-6}$ alkoxy- C_{1-6} alkyl, 3-

5 to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to

10-membered heteroaryl, $-\text{C}(\text{O})\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{NR}^{\text{be}}\text{R}^{\text{bf}}$, $-\text{C}(\text{O})\text{OR}^{\text{bb}}$, and $-\text{C}(\text{O})\text{NR}^{\text{bc}}\text{R}^{\text{bd}}$;

wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-\text{C}_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to

8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to

10-membered heteroaryl are optionally substituted by one or more substituents selected from

10 the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl,

C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-\text{NR}^{\text{a1}}\text{R}^{\text{a2}}$, nitro,

hydroxyl, C_{1-6} hydroxyalkyl, $-\text{C}(\text{O})\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{NR}^{\text{be}}\text{R}^{\text{bf}}$, $-\text{C}(\text{O})\text{OR}^{\text{bb}}$, $-\text{C}(\text{O})\text{NR}^{\text{bc}}\text{R}^{\text{bd}}$,

3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and

5- to 10-membered heteroaryl;

15 **[0130]** x^3 is selected from the group consisting of C, CR^{x3} , and N, wherein R^{x3} is selected

from the group consisting of H, halogen, hydroxyl, $-\text{NR}^{\text{b1}}\text{R}^{\text{b2}}$, C_{1-4} alkyl, and $-\text{OC}_{1-4}$ alkyl;

[0131] x^4 is selected from the group consisting of C, CR^{x4} , and N, wherein R^{x4} is selected

from the group consisting of H, halogen, hydroxyl, $-\text{NR}^{\text{b1}}\text{R}^{\text{b2}}$, C_{1-4} alkyl, and $-\text{OC}_{1-4}$ alkyl;

[0132] x^5 is selected from the group consisting of C, CR^{x5} , and N, wherein R^{x5} is selected

20 from the group consisting of H, halogen, hydroxyl, $-\text{NR}^{\text{b1}}\text{R}^{\text{b2}}$, C_{1-4} alkyl, and $-\text{OC}_{1-4}$ alkyl;

[0133] x^6 is selected from the group consisting of CR^{x6} , N, $\text{C}(=\text{O})$, and $\text{C}(=\text{CR}^{\text{x6}})$, wherein

R^{x6} is selected from the group consisting of H, halogen, hydroxyl, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-NR^{b1}R^{b2}$, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{be}R^{bd}$;
 5 wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{be}R^{bd}$,
 10 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0134] x^7 is selected from the group consisting of C, CR^{x7} , and N, wherein R^{x7} is selected from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

15 **[0135]** x^8 is selected from the group consisting of N, O, CR^{x8} , $CR^{x8}R^{x8}$, NR^{x8} , $S(O)_p$, $C(=O)$, and $C(=CR^{x8})$, wherein R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{be}R^{bd}$;
 20 wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to

8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0136] alternatively, two R^{x8} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0137] x⁹ is selected from the group consisting of CR^{x9}, N, O, NR^{x9}, S(O)_p, CR^{x9}R^{x9}, and C(=CR^{x8}), wherein R^{x9}, at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, hydroxyl, -NR^{b1}R^{b2}, cyano, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd};

wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{bc}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0138] alternatively, two R^{x9} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl and 3- to 8-membered heterocyclyl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{bc}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0139] alternatively, R^{x8} and R^{x9}, together with the atom to which they are attached, form a 3- to 7-membered ring; wherein the 3- to 7-membered ring is optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba},

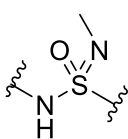
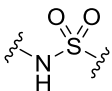
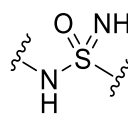
$S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0140] $\diagup$ is a single bond or a double bond;

[0141] R^a , R^d , and R^e are identical or different, and are each independently selected from the group consisting of hydrogen, halogen, C_{1-6} alkyl, cyano, $-NR^{b1}R^{b2}$, hydroxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0142] alternatively, any two of R^a , R^d , and R^e , together with the atom to which they are attached, form a 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, or 5- to 10-membered heteroaryl ring; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group

consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{bc}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0143] W is selected from the group consisting of , , and ;

[0144] ring B is selected from the group consisting of 3- to 10-membered cycloalkyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

[0145] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, halogen, C₁₋₆ alkyl, cyano, hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -NR^{b1}R^{b2}, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, S(O)_pNR^{bc}R^{bf}, and S(O)_pR^{ba}; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl,

-C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, and C₁₋₆ hydroxyalkyl;

[0146] R^{b1}, R^{b2}, R^{a1}, R^{a2}, R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are identical or different, and are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

[0147] alternatively, R^{b1} and R^{b2}, R^{a1} and R^{a2}, R^{bc} and R^{bd}, or R^{be} and R^{bf}, together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring; wherein the 3- to 7-membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋

₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0148] ring C is selected from the group consisting of 3- to 10-membered cycloalkyl, 3- to 10-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0149] each R^c is identical or different, and is independently selected from the group consisting of hydrogen, halogen, C₁₋₆ alkyl, cyano, -NR^{b1}R^{b2}, hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{bc}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{bc}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, -C(O)R^{ba}, S(O)_pR^{ba},

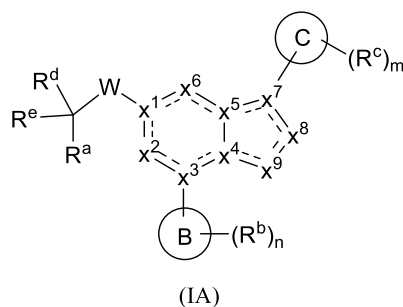
$S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, and C_{1-6} hydroxyalkyl;

[0150] n is selected from the group consisting of 0, 1, 2, and 3;

[0151] m is selected from the group consisting of 0, 1, 2, and 3;

[0152] p is selected from the group consisting of 0, 1, and 2.

- 5 **[0153]** The present disclosure provides a compound of formula (IA), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof,



[0154] wherein

- 10 **[0155]** x^1 is selected from the group consisting of C, CR^{x1} , and N, wherein R^{x1} is selected from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;
- [0156]** x^2 is selected from the group consisting of CR^{x2} , N, $C(=O)$, and $C(=CR^{x2})$, wherein R^{x2} is selected from the group consisting of H, halogen, hydroxyl, amino, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-NR^{b1}R^{b2}$, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl

are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0157] x³ is selected from the group consisting of C, CR^{x3}, and N, wherein R^{x3} is selected from the group consisting of H, halogen, hydroxyl, -NR^{b1}R^{b2}, C₁₋₄ alkyl, and -OC₁₋₄ alkyl;

[0158] x⁴ is selected from the group consisting of C, CR^{x4}, and N, wherein R^{x4} is selected from the group consisting of H, halogen, hydroxyl, -NR^{b1}R^{b2}, C₁₋₄ alkyl, and -OC₁₋₄ alkyl;

[0159] x⁵ is selected from the group consisting of C, CR^{x5}, and N, wherein R^{x5} is selected from the group consisting of H, halogen, hydroxyl, -NR^{b1}R^{b2}, C₁₋₄ alkyl, and -OC₁₋₄ alkyl;

[0160] x⁶ is selected from the group consisting of CR^{x6}, N, C(=O), and C(=CR^{x6}), wherein R^{x6} is selected from the group consisting of H, halogen, hydroxyl, cyano, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -NR^{b1}R^{b2}, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, -C(O)R^{ba}, -C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd}; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl,

3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0161] x^7 is selected from the group consisting of C, CR^{x7} , and N, wherein R^{x7} is selected from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

5 **[0162]** x^8 is selected from the group consisting of N, O, CR^{x8} , $CR^{x8}R^{x8}$, NR^{x8} , $S(O)_p$, $C(=O)$, and $C(=CR^{x8})$, wherein R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, hydroxyl, $-NR^{b1}R^{b2}$, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0163] alternatively, two R^{x8} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-}

⁶ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0164] x⁹ is selected from the group consisting of CR^{x9}, N, O, NR^{x9}, S(O)_p, CR^{x9}R^{x9}, and
 5 C(=CR^{x8}), wherein R^{x9}, at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, hydroxyl, -NR^{b1}R^{b2}, cyano, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, -C(O)R^{ba}, -C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd}; wherein the C₁₋₆ alkyl, C₂₋₆
 10 ⁶ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl,
 15 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0165] alternatively, two R^{x9} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl and 3- to 8-membered heterocyclyl are optionally substituted by one or more
 20 substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy,

cyano, $\text{-NR}^{\text{a1}}\text{R}^{\text{a2}}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

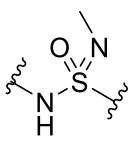
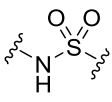
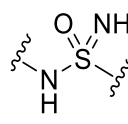
[0166] alternatively, R^{x8} and R^{x9} , together with the atom to which they are attached, form a 3- to 7-membered ring; wherein the 3- to 7-membered ring is optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $\text{-NR}^{\text{a1}}\text{R}^{\text{a2}}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0167] --- is a single bond or a double bond;

[0168] R^{a} , R^{d} , and R^{e} are identical or different, and are each independently selected from the group consisting of hydrogen, halogen, C_{1-6} alkyl, cyano, $\text{-NR}^{\text{b1}}\text{R}^{\text{b2}}$, hydroxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $\text{-C}_{1-6}\text{ alkoxy-C}_{1-6}\text{ alkyl}$, $\text{-C(O)R}^{\text{ba}}$, $\text{-C(O)OR}^{\text{bb}}$, $\text{-C(O)NR}^{\text{bc}}\text{R}^{\text{bd}}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $\text{-C}_{1-6}\text{ alkoxy-C}_{1-6}\text{ alkyl}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $\text{-NR}^{\text{a1}}\text{R}^{\text{a2}}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and

5- to 10-membered heteroaryl;

[0169] alternatively, any two of R^a , R^d , and R^e , together with the atom to which they are attached, form a 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, or 5- to 10-membered heteroaryl ring; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0170] W is selected from the group consisting of , , and ;

[0171] ring B is selected from the group consisting of 3- to 10-membered cycloalkyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

[0172] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, halogen, C_{1-6} alkyl, cyano, hydroxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-NR^{b1}R^{b2}$, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, and $S(O)_2NR^{be}R^{bf}$, wherein the C_{1-6} alkyl, C_{2-6} alkenyl,

C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

[0173] R^{b1}, R^{b2}, R^{a1}, R^{a2}, R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are identical or different, and are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

[0174] alternatively, R^{b1} and R^{b2}, R^{a1} and R^{a2}, R^{bc} and R^{bd}, or R^{be} and R^{bf}, together with the

nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring; wherein the 3- to 7-membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0175] ring C is selected from the group consisting of 3- to 10-membered cycloalkyl, 3- to 10-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

[0176] each R^c is identical or different, and is independently selected from the group consisting of hydrogen, halogen, C₁₋₆ alkyl, cyano, -NR^{b1}R^{b2}, hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of

halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

[0177] n is selected from the group consisting of 0, 1, 2, and 3;

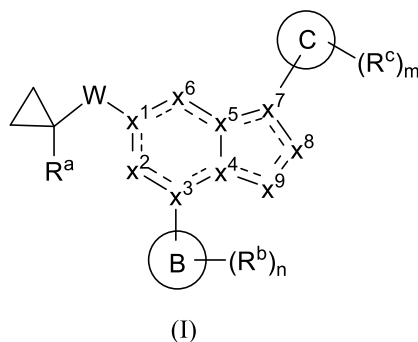
5 **[0178]** m is selected from the group consisting of 0, 1, 2, and 3;

[0179] p is selected from the group consisting of 0, 1, and 2.

[0180] In some embodiments of the present disclosure, in the compound of formula (IA), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^d and R^e, together
10 with the atom to which they are attached, form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring, preferably a 3- to 6-membered cycloalkyl or 3- to 6-membered heterocyclyl ring, more preferably a cyclopropyl ring.

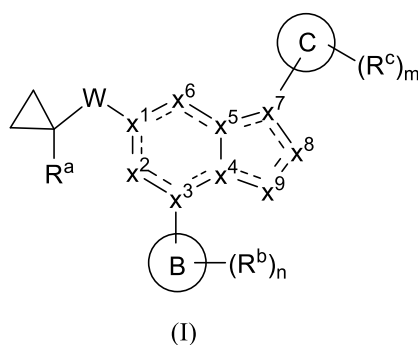
[0181] In some embodiments of the present disclosure, in the compound of formula (IA), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof,
15 the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^d and R^e, together with the atom to which they are attached, form an oxetanyl ring.

[0182] In some embodiments of the present disclosure, the compound of formula (IA), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof is a compound of
20 formula (I), a pharmaceutically acceptable salt thereof, or a stereoisomer thereof,



[0183] wherein $\diagup$, ring B, ring C, R^b , R^a , R^c , m , n , W , and x^1 to x^9 are as defined in any embodiment of formula (IA).

[0184] The present disclosure provides a compound of formula (I), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof,



[0185] wherein

[0186] x^1 is selected from the group consisting of C, CR^{x1} , and N, wherein R^{x1} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0187] x^2 is selected from the group consisting of CR^{x2} , N, and $C(=O)$, wherein R^{x2} is selected from the group consisting of H, halogen, hydroxyl, amino, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} aminoalkyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} haloalkyl, C_{1-6}

₆ haloalkoxy, -OC₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, -NHC₁₋₆ alkyl, and -N(C₁₋₆ alkyl)₂;

[0188] x³ is selected from the group consisting of C, CR^{x3}, and N, wherein R^{x3} is selected from the group consisting of H, halogen, hydroxyl, amino, C₁₋₄ alkyl, -OC₁₋₄ alkyl, -NHC₁₋₄ alkyl, and -N(C₁₋₄ alkyl)₂;

5 **[0189]** x⁴ is selected from the group consisting of C, CR^{x4}, and N, wherein R^{x4} is selected from the group consisting of H, halogen, hydroxyl, amino, C₁₋₄ alkyl, -OC₁₋₄ alkyl, -NHC₁₋₄ alkyl, and -N(C₁₋₄ alkyl)₂;

[0190] x⁵ is selected from the group consisting of C, CR^{x5}, and N, wherein R^{x5} is selected from the group consisting of H, halogen, hydroxyl, amino, C₁₋₄ alkyl, -OC₁₋₄ alkyl, -NHC₁₋₄ alkyl, and -N(C₁₋₄ alkyl)₂;

[0191] x⁶ is selected from the group consisting of CR^{x6}, N, and C(=O), wherein R^{x6} is selected from the group consisting of H, halogen, hydroxyl, amino, cyano, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkyl, C₁₋₆ aminoalkyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, -OC₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, -NHC₁₋₆ alkyl, and -N(C₁₋₆ alkyl)₂;

15 **[0192]** x⁷ is selected from the group consisting of C, CR^{x7}, and N, wherein R^{x7} is selected from the group consisting of H, halogen, hydroxyl, amino, C₁₋₄ alkyl, -OC₁₋₄ alkyl, -NHC₁₋₄ alkyl, and -N(C₁₋₄ alkyl)₂;

[0193] x⁸ is selected from the group consisting of N, O, CR^{x8}, CR^{x8}R^{x8}, NR^{x8}, S(O)_p, and C(=O), wherein R^{x8}, at each occurrence, is identical or different, and is independently
20 selected from the group consisting of H, halogen, hydroxyl, amino, cyano, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkyl, C₁₋₆ aminoalkyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ haloalkyl, C₁₋

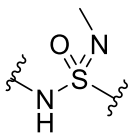
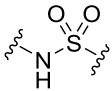
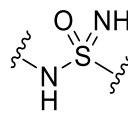
₆ haloalkoxy, -OC₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, -NHC₁₋₆ alkyl, and -N(C₁₋₆ alkyl)₂;

[0194] x⁹ is selected from the group consisting of CR^{x9}, N, O, NR^{x9}, S(O)_p, and CR^{x9}R^{x9}, wherein R^{x9}, at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, hydroxyl, amino, cyano, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkyl, C₁₋₆ aminoalkyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, -OC₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, -NHC₁₋₆ alkyl, and -N(C₁₋₆ alkyl)₂; alternatively, two R^{x9} attached to the same carbon atom together form a C₃₋₆ cycloalkyl ring;

[0195] alternatively, R^{x8} and R^{x9}, together with the atom to which they are attached, form a 3- to 7-membered ring;

[0196]  is a single bond or a double bond;

[0197] R^a is selected from the group consisting of hydrogen, halogen, C₁₋₆ alkyl, cyano, amino, hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, C₁₋₆ aminoalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, -C(O)R^{ba}, -C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd};

[0198] W is selected from the group consisting of , , and ;

[0199] ring B is selected from the group consisting of 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

[0200] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, halogen, C₁₋₆ alkyl, cyano, amino, hydroxyl, C₂₋₆ alkenyl, C₂₋₆

alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, C₁₋₆ aminoalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, and S(O)₂NR^{be}R^{bf},

[0201] R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are identical or different, and are each independently
 5 selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, and C₁₋₆ aminoalkyl; alternatively, R^{bc} and R^{bd}, or R^{be} and R^{bf}, together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring;

[0202] ring C is 5- to 6-membered heteroaryl;

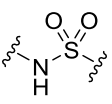
[0203] each R^c is identical or different, and is independently selected from the group
 10 consisting of hydrogen, halogen, C₁₋₆ alkyl, cyano, amino, hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, C₁₋₆ aminoalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, -C(O)R^{ba}, -C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd},

[0204] n is selected from the group consisting of 0, 1, 2, and 3;

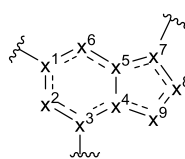
15 [0205] m is selected from the group consisting of 0, 1, 2, and 3;

[0206] p is selected from the group consisting of 0, 1, and 2;

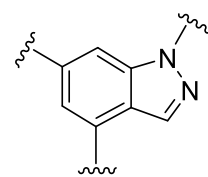
[0207] and,

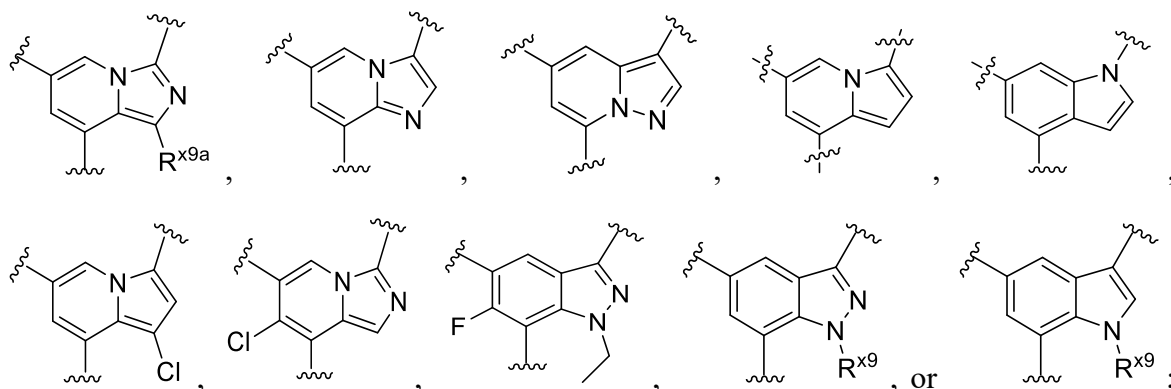
[0208] when W is , and R^a is selected from the group consisting of -CH₃, cyano, -

CH₂F, and -CONH₂; the structural moiety



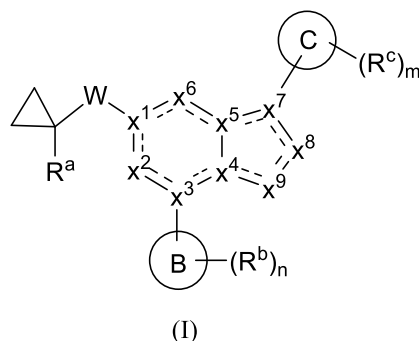
is not





wherein R^{x9} is selected from the group consisting of H and C_{1-4} alkyl, and R^{x9a} is selected from the group consisting of H, $-CH_3$, F, and Cl.

- 5 [0209] The present disclosure provides a compound of formula (I), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof,



[0210] wherein

- 10 [0211] x^1 is selected from the group consisting of C, CR^{x1} , and N, wherein R^{x1} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

- [0212] x^2 is selected from the group consisting of CR^{x2} , N, and $C(=O)$, wherein R^{x2} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;
- 15

[0213] x^3 is selected from the group consisting of C, CR^{x3} , and N, wherein R^{x3} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0214] x^4 is selected from the group consisting of C, CR^{x4} , and N, wherein R^{x4} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0215] x^5 is selected from the group consisting of C, CR^{x5} , and N, wherein R^{x5} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0216] x^6 is selected from the group consisting of CR^{x6} , N, and $C(=O)$, wherein R^{x6} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0217] x^7 is selected from the group consisting of C, CR^{x7} , and N, wherein R^{x7} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0218] x^8 is selected from the group consisting of N, O, CR^{x8} , $CR^{x8}R^{x8}$, NR^{x8} , $S(O)_p$, and $C(=O)$, wherein R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, $C\equiv CH$, CN, halogen, and C_{1-4} alkyl; alternatively, two R^{x8} attached to the same carbon atom together form a C_{3-6} cycloalkyl ring;

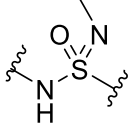
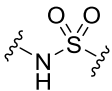
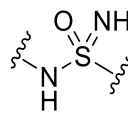
[0219] x^9 is selected from the group consisting of CR^{x9} , N, O, NR^{x9} , $S(O)_p$, and $CR^{x9}R^{x9}$, wherein R^{x9} , at each occurrence, is identical or different, and is independently selected from

the group consisting of H, halogen, and C₁₋₄ alkyl; alternatively, two R^{x9} attached to the same carbon atom together form a C₃₋₆ cycloalkyl ring;

[0220] alternatively, R^{x8} and R^{x9}, together with the atom to which they are attached, form a 3- to 7-membered ring;

5 [0221]  is a single bond or a double bond;

[0222] R^a is selected from the group consisting of hydrogen, cyano, formyl, -CONH₂, -CH₂OH, -CH₂OC₁₋₄ alkyl, C₁₋₄ alkyl, and C₁₋₄ haloalkyl;

[0223] W is selected from the group consisting of , , and ;

[0224] ring B is selected from the group consisting of 5- to 7-membered monocyclic
10 heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

[0225] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, hydroxyl, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, C₁₋₆ aminoalkyl, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, and
15 S(O)₂NR^{be}R^{bf}, wherein R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, and C₁₋₆ aminoalkyl; alternatively, R^{bc} and R^{bd}, or R^{be} and R^{bf}, together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring;

[0226] ring C is 5- to 6-membered heteroaryl;

20 [0227] each R^c is identical or different, and is independently selected from the group

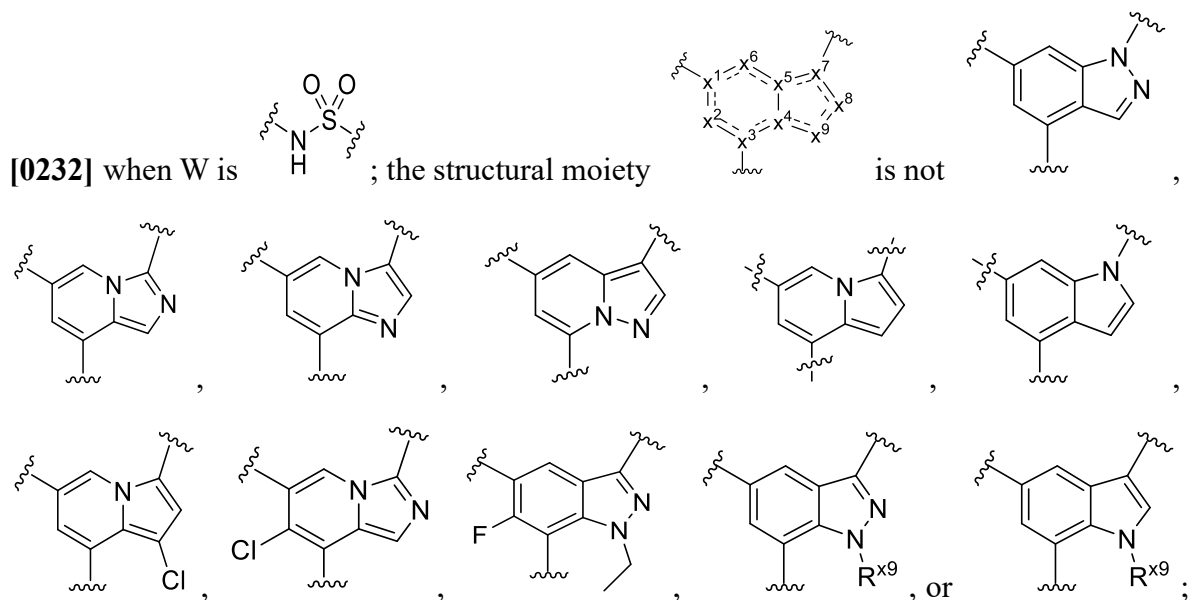
consisting of hydrogen, halogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, and C₁₋₆ haloalkoxy;

[0228] n is selected from the group consisting of 0, 1, 2, and 3;

[0229] m is selected from the group consisting of 0, 1, 2, and 3;

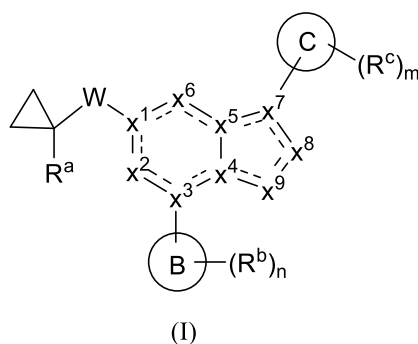
5 [0230] p is selected from the group consisting of 0, 1, and 2;

[0231] and,



10 wherein R^{x9} is selected from the group consisting of H and C₁₋₄ alkyl.

[0233] The present disclosure provides a compound of formula (I), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof,



[0234] wherein

[0235] x^1 is selected from the group consisting of C and N;

[0236] x^2 is selected from the group consisting of CR^{x2} , N, and $C(=O)$, wherein R^{x2} is
 5 selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0237] x^3 is selected from the group consisting of C and N;

[0238] x^4 is selected from the group consisting of C and N;

[0239] x^5 is selected from the group consisting of C and N;

10 [0240] x^6 is selected from the group consisting of CR^{x6} , N, and $C(=O)$, wherein R^{x6} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0241] x^7 is selected from the group consisting of C and N;

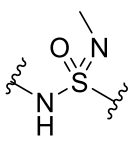
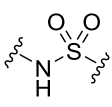
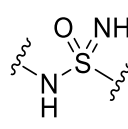
[0242] x^8 is selected from the group consisting of N, O, CR^{x8} , $CR^{x8}R^{x8}$, NR^{x8} , $S(O)_2$, and
 15 $C(=O)$, wherein R^{x8} is selected from the group consisting of H, $C\equiv CH$, CN, halogen, and C_{1-4} alkyl; alternatively, two R^{x8} attached to the same carbon atom together form a C_{3-6} cycloalkyl ring;

[0243] x^9 is selected from the group consisting of CR^{x9} , N, O, NR^{x9} , and $CR^{x9}R^{x9}$, wherein

R^{x9} is selected from the group consisting of H, halogen, and C_{1-4} alkyl; alternatively, two R^{x9} attached to the same carbon atom together form a C_{3-6} cycloalkyl ring;

[0244] alternatively, R^{x8} and R^{x9} , together with the atom to which they are attached, form a 3- to 7-membered ring;

- 5 [0245] R^a is selected from the group consisting of hydrogen, cyano, formyl, $-CONH_2$, $-CH_2OH$, $-CH_2OC_{1-4}$ alkyl, C_{1-4} alkyl, and C_{1-4} haloalkyl;

[0246] W is selected from the group consisting of , , and ;

- [0247] ring B is selected from the group consisting of 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl,
10 and 6- to 10-membered fused heterocyclyl;

- [0248] R^b is selected from the group consisting of hydrogen, hydroxyl, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, and $S(O)_2NR^{be}R^{bf}$, wherein R^{ba} , R^{bb} , R^{bc} , R^{bd} , R^{be} , and R^{bf} are each independently selected from the group consisting of hydrogen and C_{1-4} alkyl; alternatively, R^{bc} and R^{bd} , or R^{be} and R^{bf} ,
15 together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring;

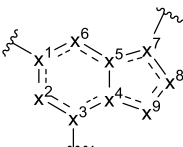
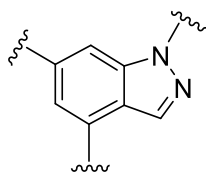
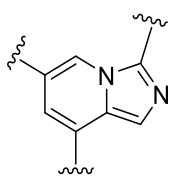
[0249] ring C is 5- to 6-membered heteroaryl;

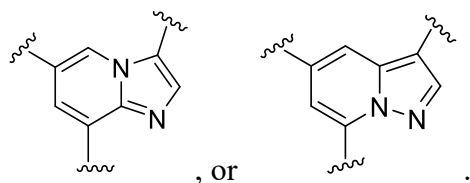
[0250] R^c is selected from the group consisting of hydrogen, halogen, hydroxyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, and C_{1-6} haloalkoxy;

- 20 [0251] n is selected from the group consisting of 0, 1, 2, and 3;

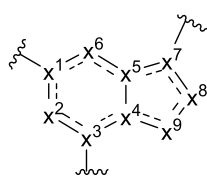
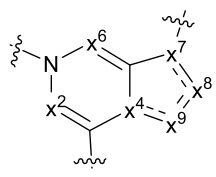
[0252] m is selected from the group consisting of 0, 1, 2, and 3;

[0253] and,

[0254] the structural moiety  is not , ,

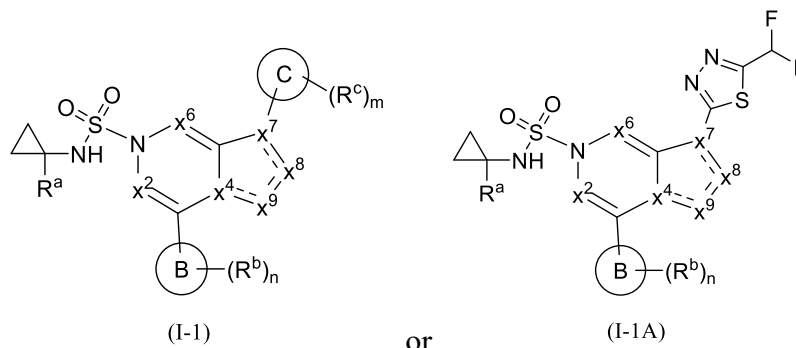


5 [0255] In some embodiments of the present disclosure, the structural moiety

 is ; wherein , x^2 , x^4 , x^6 , x^7 , x^8 , and x^9 are as defined in any embodiment of formula (I) or any embodiment of formula (IA).

[0256] The present disclosure provides a compound of formula (I-1) or formula (I-1A), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:

10



[0257] wherein , x^2 , x^4 , x^6 , x^7 , x^8 , x^9 , R^a , R^b , R^c , ring B, ring C, n, m, and p are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0258] In some embodiments of the present disclosure, in the compound of formula (I-1) or formula (I-1A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,

[0259] x^2 is selected from the group consisting of CR^{x^2} and N, wherein R^{x^2} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0260] x^4 is selected from the group consisting of C, CR^{x^4} , and N, wherein R^{x^4} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0261] x^6 is selected from the group consisting of CR^{x^6} and N, wherein R^{x^6} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0262] x^7 is selected from the group consisting of C, CR^{x^7} , and N, wherein R^{x^7} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0263] x^8 is selected from the group consisting of N, O, CR^{x^8} , $CR^{x^8}R^{x^8}$, NR^{x^8} , $S(O)_p$, and $C(=O)$, wherein R^{x^8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, $C\equiv CH$, CN, halogen, and C_{1-4} alkyl; alternatively, two R^{x^8} attached to the same carbon atom together form a C_{3-6} cycloalkyl ring;

[0264] x^9 is selected from the group consisting of CR^{x^9} , N, O, NR^{x^9} , $S(O)_p$, and $CR^{x^9}R^{x^9}$, wherein R^{x^9} , at each occurrence, is identical or different, and is independently selected from

the group consisting of H, halogen, and C₁₋₄ alkyl; alternatively, two R^{x9} attached to the same carbon atom together form a C₃₋₆ cycloalkyl ring;

[0265] alternatively, R^{x8} and R^{x9}, together with the atom to which they are attached, form a 3- to 7-membered ring;

5 **[0266]**  is a single bond or a double bond;

[0267] R^a is selected from the group consisting of hydrogen, cyano, formyl, -CONH₂, -CH₂OH, -CH₂OC₁₋₄ alkyl, C₁₋₄ alkyl, and C₁₋₄ haloalkyl;

[0268] ring B is selected from the group consisting of 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl,
10 and 6- to 10-membered fused heterocyclyl;

[0269] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, hydroxyl, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, C₁₋₆ aminoalkyl, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, and S(O)₂NR^{be}R^{bf};

15 **[0270]** R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, and C₁₋₆ aminoalkyl; alternatively, R^{bc} and R^{bd}, or R^{be} and R^{bf}, together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring;

[0271] ring C is 5- to 6-membered heteroaryl;

20 **[0272]** each R^c is identical or different, and is independently selected from the group consisting of hydrogen, halogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, and C₁₋₆

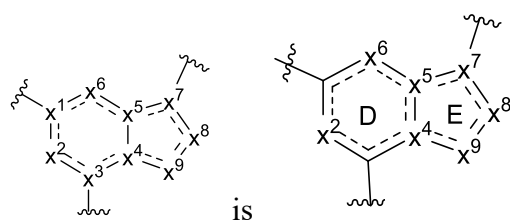
haloalkoxy;

[0273] n is selected from the group consisting of 0, 1, 2, and 3;

[0274] m is selected from the group consisting of 0, 1, 2, and 3;

[0275] p is selected from the group consisting of 0, 1, and 2.

5 **[0276]** In some embodiments of the present disclosure, the structural moiety

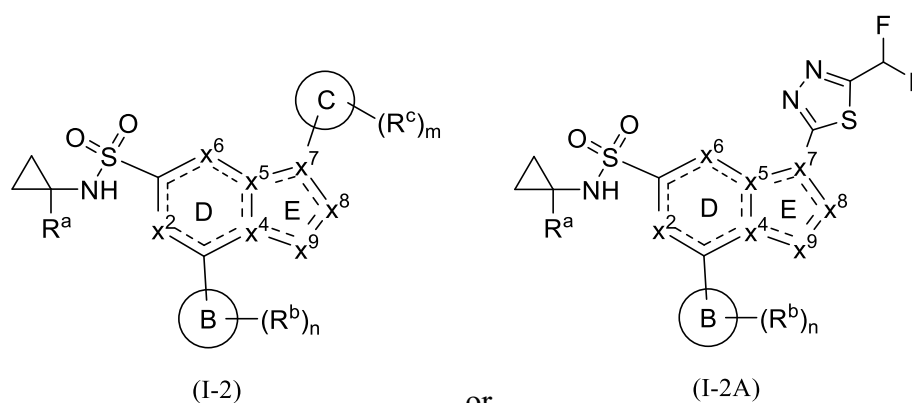


; wherein both ring D and ring E are aromatic rings;

--- , x^2 , x^4 , x^5 , x^6 , x^7 , x^8 , and x^9 are as defined in any embodiment of formula (I) or any embodiment of formula (IA).

[0277] The present disclosure provides a compound of formula (I-2) or formula (I-2A), a

10 pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-
oxide thereof, a solvate thereof, or an isotopic derivative thereof:



or

[0278] wherein $\not\sim$, x^2 , x^4 , x^5 , x^6 , x^7 , x^8 , x^9 , R^a , R^b , R^c , ring B, ring C, n, m, and p are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

15 **[0279]** In some embodiments of the present disclosure, in the compound of formula (I-2) or

formula (I-2A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,

[0280] x^2 is selected from the group consisting of CR^{x2} , N, and $C(=O)$, wherein R^{x2} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl,
5 $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0281] x^4 is selected from the group consisting of C, CR^{x4} , and N, wherein R^{x4} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0282] x^5 is selected from the group consisting of C, CR^{x5} , and N, wherein R^{x5} is selected
10 from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0283] x^6 is selected from the group consisting of CR^{x6} , N, and $C(=O)$, wherein R^{x6} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0284] x^7 is selected from the group consisting of C, CR^{x7} , and N, wherein R^{x7} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0285] x^8 is selected from the group consisting of N, O, CR^{x8} , $CR^{x8}R^{x8}$, NR^{x8} , $S(O)_p$, and $C(=O)$, wherein R^{x8} , at each occurrence, is identical or different, and is independently
20 selected from the group consisting of H, $C\equiv CH$, CN, halogen, and C_{1-4} alkyl; alternatively, two R^{x8} attached to the same carbon atom together form a C_{3-6} cycloalkyl ring;

[0286] x^9 is selected from the group consisting of CR^{x9} , N, O, NR^{x9} , $S(O)_p$, and $CR^{x9}R^{x9}$, wherein R^{x9} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, and C_{1-4} alkyl; alternatively, two R^{x9} attached to the same carbon atom together form a C_{3-6} cycloalkyl ring;

- 5 [0287] alternatively, R^{x8} and R^{x9} , together with the atom to which they are attached, form a 3- to 7-membered ring;

[0288] $\diagup$ is a single bond or a double bond;

[0289] R^a is selected from the group consisting of hydrogen, cyano, formyl, $-CONH_2$, $-CH_2OH$, $-CH_2OC_{1-4}$ alkyl, C_{1-4} alkyl, and C_{1-4} haloalkyl;

- 10 [0290] ring B is selected from the group consisting of 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

- [0291] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, hydroxyl, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, and $S(O)_2NR^{be}R^{bf}$, wherein R^{ba} , R^{bb} , R^{bc} , R^{bd} , R^{be} , and R^{bf} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, and C_{1-6} aminoalkyl; alternatively, R^{bc} and R^{bd} , or R^{be} and R^{bf} , together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring;

- 20 [0292] ring C is 5- to 6-membered heteroaryl;

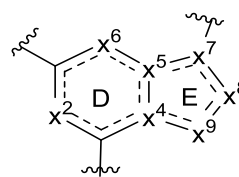
[0293] each R^c is identical or different, and is independently selected from the group

consisting of hydrogen, halogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, and C₁₋₆ haloalkoxy;

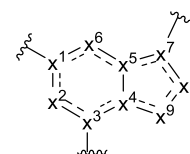
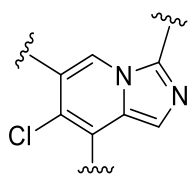
[0294] n is selected from the group consisting of 0, 1, 2, and 3;

[0295] m is selected from the group consisting of 0, 1, 2, and 3;

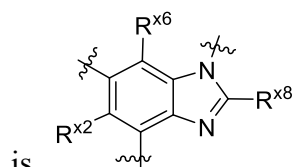
5 **[0296]** p is selected from the group consisting of 0, 1, and 2; provided that both ring D and



ring E are aromatic rings; x² and x⁶ are not both CH, and is not

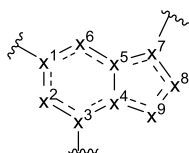


[0297] In some embodiments of the present disclosure, the structural moiety

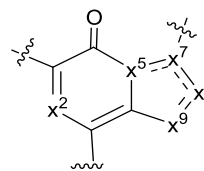


is , wherein R^{x2}, R^{x6}, and R^{x8} are as defined in any embodiment of
10 formula (IA) or any embodiment of formula (I).

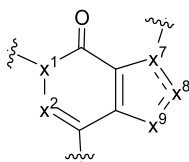
[0298] In some embodiments of the present disclosure, the structural moiety



is selected from the group consisting of



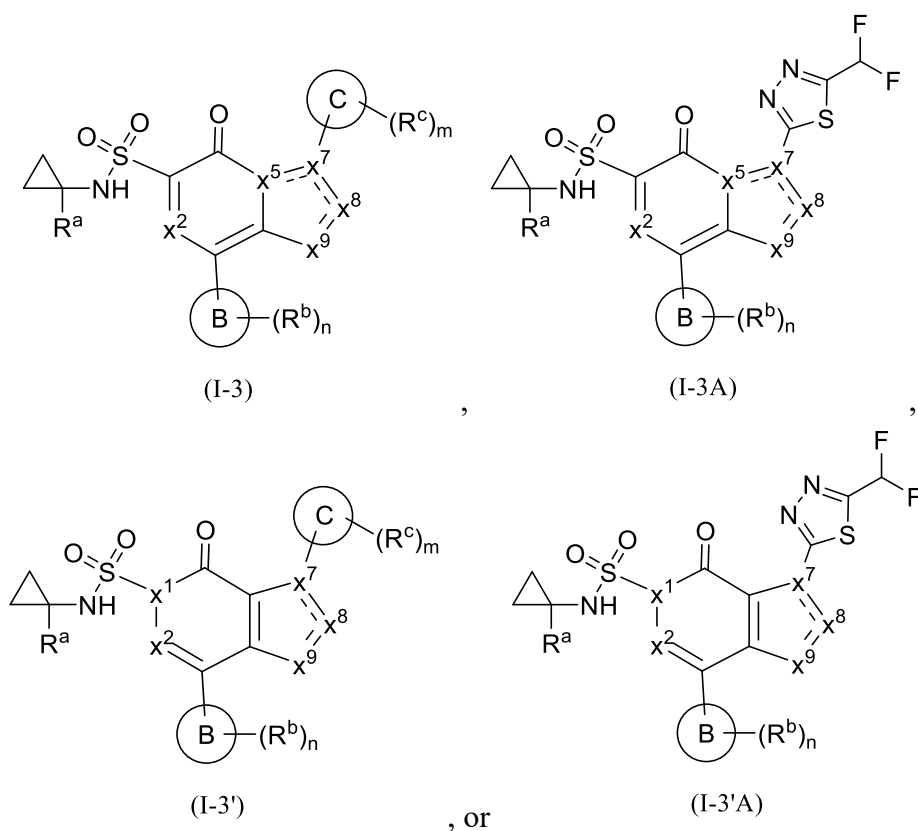
and



; wherein , x¹, x², x⁵, x⁷, x⁸, and x⁹ are as defined in any embodiment of

formula (IA) or any embodiment of formula (I).

[0299] The present disclosure provides a compound of formula (I-3), formula (I-3A), formula (I-3'), or formula (I-3'A), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:



[0300] wherein --- , x^1 , x^2 , x^5 , x^7 , x^8 , x^9 , R^a , R^b , R^c , ring B, ring C, n , m , and p are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

10 [0301] In some embodiments of the present disclosure, in the compound of formula (I-3), formula (I-3A), formula (I-3'), or formula (I-3'A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,

[0302] x^1 is selected from the group consisting of CR^{x1} and N, wherein R^{x1} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0303] x^2 is selected from the group consisting of CR^{x2} and N, wherein R^{x2} is selected from
 5 the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0304] x^5 is selected from the group consisting of C, CR^{x5} , and N, wherein R^{x5} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0305] x^7 is selected from the group consisting of C, CR^{x7} , and N, wherein R^{x7} is selected
 10 from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0306] x^8 is selected from the group consisting of N, O, CR^{x8} , $CR^{x8}R^{x8}$, NR^{x8} , $S(O)_p$, and $C(=O)$, wherein R^{x8} , at each occurrence, is identical or different, and is independently
 15 selected from the group consisting of H, $C\equiv CH$, CN, halogen, and C_{1-4} alkyl; alternatively, two R^{x8} attached to the same carbon atom together form a C_{3-6} cycloalkyl ring;

[0307] x^9 is selected from the group consisting of CR^{x9} , N, O, NR^{x9} , $S(O)_p$, and $CR^{x9}R^{x9}$, wherein R^{x9} , at each occurrence, is identical or different, and is independently selected from
 20 the group consisting of H, halogen, and C_{1-4} alkyl; alternatively, two R^{x9} attached to the same carbon atom together form a C_{3-6} cycloalkyl ring;

[0308] alternatively, R^{x8} and R^{x9} , together with the atom to which they are attached, form a

3- to 7-membered ring;

[0309] $\diagup$ is a single bond or a double bond;

[0310] R^a is selected from the group consisting of hydrogen, cyano, formyl, $-\text{CONH}_2$, $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OC}_{1-4}$ alkyl, C_{1-4} alkyl, and C_{1-4} haloalkyl;

5 [0311] ring B is selected from the group consisting of 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

[0312] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, hydroxyl, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, $-\text{C}(\text{O})\text{R}^{ba}$, $-\text{C}(\text{O})\text{OR}^{bb}$, $-\text{C}(\text{O})\text{NR}^{bc}\text{R}^{bd}$, and $\text{S}(\text{O})_2\text{NR}^{be}\text{R}^{bf}$, wherein R^{ba} , R^{bb} , R^{bc} , R^{bd} , R^{be} , and R^{bf} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, and C_{1-6} aminoalkyl; alternatively, R^{bc} and R^{bd} , or R^{be} and R^{bf} , together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring;

15 [0313] ring C is 5- to 6-membered heteroaryl;

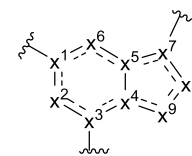
[0314] each R^c is identical or different, and is independently selected from the group consisting of hydrogen, halogen, hydroxyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, and C_{1-6} haloalkoxy;

[0315] n is selected from the group consisting of 0, 1, 2, and 3;

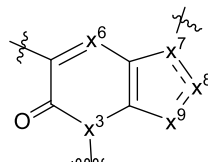
20 [0316] m is selected from the group consisting of 0, 1, 2, and 3;

[0317] p is selected from the group consisting of 0, 1, and 2.

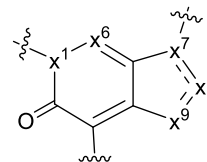
[0318] In some embodiments of the present disclosure, the structural moiety



is selected from the group consisting of



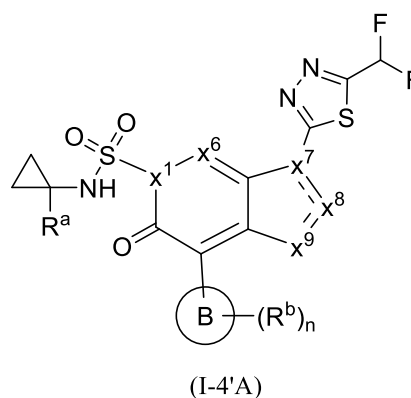
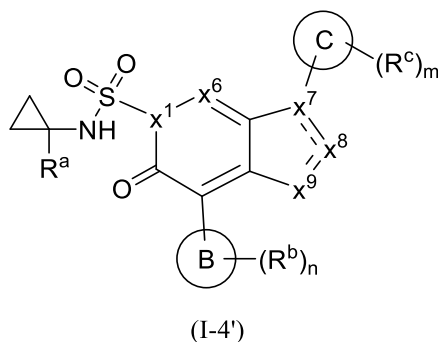
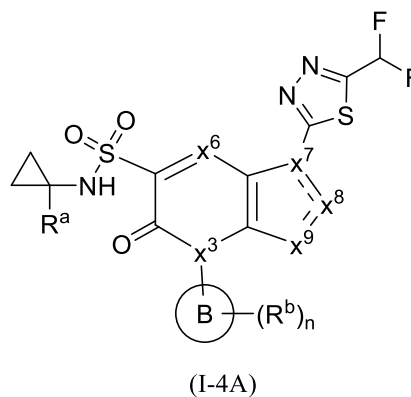
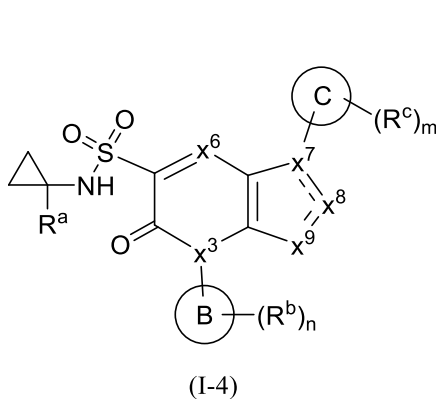
and



; wherein

$\diagup$, x^1 , x^3 , x^6 , x^7 , x^8 , and x^9 are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

- 5 [0319] The present disclosure provides a compound of formula (I-4), formula (I-4A), formula (I-4'), or formula (I-4'A), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:



10

[0320] wherein $\diagup$, x^1 , x^3 , x^6 , x^7 , x^8 , x^9 , R^a , R^b , R^c , ring B, ring C, n, m, and p are as defined

in any embodiment of formula (IA) or any embodiment of formula (I).

[0321] In some embodiments of the present disclosure, in the compound of formula (I-4), formula (I-4A), formula (I-4'), or formula (I-4'A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,

[0322] x^1 is selected from the group consisting of C, CR^{x^1} , and N, wherein R^{x^1} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0323] x^3 is selected from the group consisting of C, CR^{x^3} , and N, wherein R^{x^3} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0324] x^6 is selected from the group consisting of CR^{x^6} , N, and $C(=O)$, wherein R^{x^6} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0325] x^7 is selected from the group consisting of C, CR^{x^7} , and N, wherein R^{x^7} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

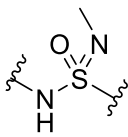
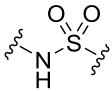
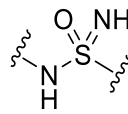
[0326] x^8 is selected from the group consisting of N, O, CR^{x^8} , $CR^{x^8}R^{x^8}$, NR^{x^8} , $S(O)_p$, and $C(=O)$, wherein R^{x^8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, $C\equiv CH$, CN, halogen, and C_{1-4} alkyl; alternatively, two R^{x^8} attached to the same carbon atom together form a C_{3-6} cycloalkyl ring;

[0327] x^9 is selected from the group consisting of CR^{x9} , N, O, NR^{x9} , $S(O)_p$, and $CR^{x9}R^{x9}$, wherein R^{x9} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, and C_{1-4} alkyl; alternatively, two R^{x9} attached to the same carbon atom together form a C_{3-6} cycloalkyl ring;

- 5 [0328] alternatively, R^{x8} and R^{x9} , together with the atom to which they are attached, form a 3- to 7-membered ring;

[0329]  is a single bond or a double bond;

[0330] R^a is selected from the group consisting of hydrogen, cyano, formyl, $-CONH_2$, $-CH_2OH$, $-CH_2OC_{1-4}$ alkyl, C_{1-4} alkyl, and C_{1-4} haloalkyl;

- 10 [0331] W is selected from the group consisting of , , and ;

[0332] ring B is selected from the group consisting of 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

- [0333] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, hydroxyl, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, and $S(O)_2NR^{be}R^{bf}$, wherein R^{ba} , R^{bb} , R^{bc} , R^{bd} , R^{be} , and R^{bf} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, and C_{1-6} aminoalkyl; alternatively, R^{bc} and R^{bd} , or R^{be} and R^{bf} , together with the nitrogen atom to
- 20 which they are attached, form a 3- to 7-membered heterocyclyl ring;

[0334] ring C is 5- to 6-membered heteroaryl;

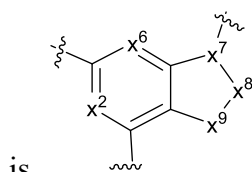
[0335] each R^c is identical or different, and is independently selected from the group consisting of hydrogen, halogen, hydroxyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, and C_{1-6} haloalkoxy;

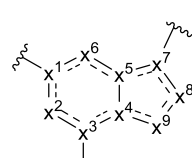
5 [0336] n is selected from the group consisting of 0, 1, 2, and 3;

[0337] m is selected from the group consisting of 0, 1, 2, and 3;

[0338] p is selected from the group consisting of 0, 1, and 2.

[0339] In some embodiments of the present disclosure, the structural moiety

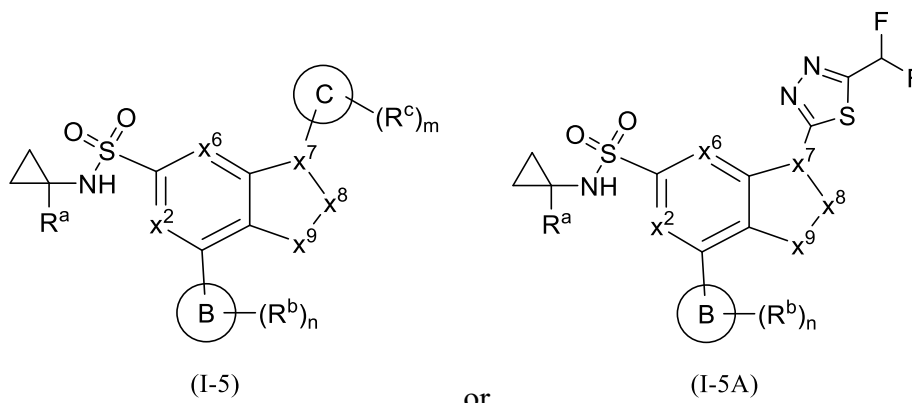


is ; wherein , x^2 , x^6 , x^7 , x^8 , and x^9 are as defined in any embodiment of

10 formula (IA) or any embodiment of formula (I).

[0340] In some embodiments of the present disclosure, the compound of formula (I), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof is a compound of formula (I-5) or formula (I-5A), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:

15



[0341] wherein $\diagup$, x^2 , x^6 , x^7 , x^8 , x^9 , R^a , R^b , R^c , ring B, ring C, n , m , and p are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0342] In some embodiments of the present disclosure, in the compound of formula (I-5) or
 5 formula (I-5A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,

[0343] x^2 is selected from the group consisting of CR^{x2} , N, and $C(=O)$, wherein R^{x2} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

10 [0344] x^6 is selected from the group consisting of CR^{x6} , N, and $C(=O)$, wherein R^{x6} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0345] x^7 is selected from the group consisting of CR^{x7} and N, wherein R^{x7} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl,
 15 and $-N(C_{1-4} \text{ alkyl})_2$;

[0346] x^8 is selected from the group consisting of O, $CR^{x8}R^{x8}$, NR^{x8} , $S(O)_p$, and $C(=O)$, wherein R^{x8} , at each occurrence, is identical or different, and is independently selected from

the group consisting of H, C≡CH, CN, halogen, and C₁₋₄ alkyl; alternatively, two R^{x8} attached to the same carbon atom together form a C₃₋₆ cycloalkyl ring;

[0347] x⁹ is selected from the group consisting of O, NR^{x9}, S(O)_p, and CR^{x9}R^{x9}, wherein R^{x9}, at each occurrence, is identical or different, and is independently selected from the group
 5 consisting of H, halogen, and C₁₋₄ alkyl; alternatively, two R^{x9} attached to the same carbon atom together form a C₃₋₆ cycloalkyl ring;

[0348] alternatively, R^{x8} and R^{x9}, together with the atom to which they are attached, form a 3- to 7-membered ring;

[0349]  is a single bond or a double bond;

10 [0350] R^a is selected from the group consisting of hydrogen, cyano, formyl, -CONH₂, -CH₂OH, -CH₂OC₁₋₄ alkyl, C₁₋₄ alkyl, and C₁₋₄ haloalkyl;

[0351] ring B is selected from the group consisting of 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

15 [0352] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, hydroxyl, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, C₁₋₆ aminoalkyl, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, and S(O)₂NR^{be}R^{bf}, wherein R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, and C₁₋₆
 20 aminoalkyl; alternatively, R^{bc} and R^{bd}, or R^{be} and R^{bf}, together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring;

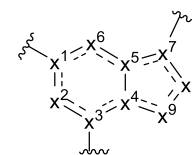
[0353] ring C is 5- to 6-membered heteroaryl;

[0354] each R^c is identical or different, and is independently selected from the group consisting of hydrogen, halogen, hydroxyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, and C_{1-6} haloalkoxy;

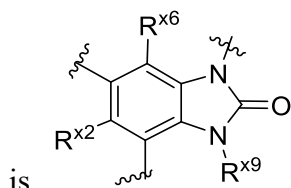
5 [0355] n is selected from the group consisting of 0, 1, 2, and 3;

[0356] m is selected from the group consisting of 0, 1, 2, and 3;

[0357] p is selected from the group consisting of 0, 1, and 2.

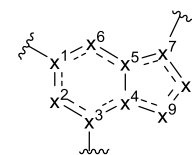


[0358] In some embodiments of the present disclosure, the structural moiety

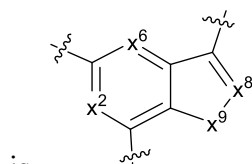


is R^{x2} , R^{x6} , and R^{x9} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

10



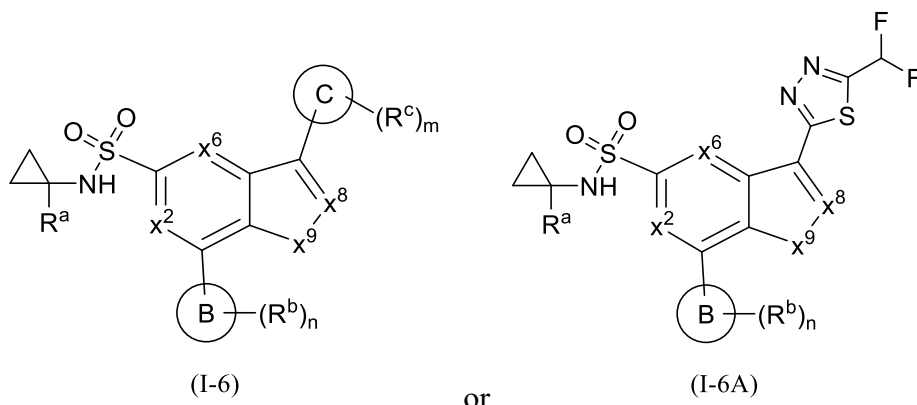
[0359] In some embodiments of the present disclosure, the structural moiety



is x^2 , x^6 , x^8 , and x^9 are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0360] The present disclosure provides a compound of formula (I-6) or formula (I-6A), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:

15



[0361] wherein --- , x^2 , x^6 , x^8 , x^9 , R^a , R^b , R^c , ring B, ring C, n, m, and p are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0362] In some embodiments of the present disclosure, in the compound of formula (I-6) or

5 formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, x^2 is selected from the group consisting of CR^{x2} and N, wherein R^{x2} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

10 **[0363]** x^6 is selected from the group consisting of CR^{x6} and N, wherein R^{x6} is selected from the group consisting of H, halogen, hydroxyl, amino, C_{1-4} alkyl, $-OC_{1-4}$ alkyl, $-NHC_{1-4}$ alkyl, and $-N(C_{1-4} \text{ alkyl})_2$;

[0364] x^8 is selected from the group consisting of N and CR^{x8} , wherein R^{x8} is selected from the group consisting of H, $C\equiv CH$, CN, halogen, and C_{1-4} alkyl;

15 **[0365]** x^9 is selected from the group consisting of O and S;

[0366] alternatively, R^{x8} and R^{x9}, together with the atom to which they are attached, form a 3- to 7-membered ring;

[0367] $\diagup$ is a single bond or a double bond;

[0368] R^a is selected from the group consisting of hydrogen, cyano, formyl, $-\text{CONH}_2$, $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OC}_{1-4}$ alkyl, C_{1-4} alkyl, and C_{1-4} haloalkyl;

[0369] ring B is selected from the group consisting of 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

[0370] each R^b is identical or different, and is independently selected from the group consisting of hydrogen, hydroxyl, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, C_{1-6} aminoalkyl, $-\text{C}(\text{O})\text{R}^{ba}$, $-\text{C}(\text{O})\text{OR}^{bb}$, $-\text{C}(\text{O})\text{NR}^{bc}\text{R}^{bd}$, and $\text{S}(\text{O})_2\text{NR}^{be}\text{R}^{bf}$, wherein R^{ba} , R^{bb} , R^{bc} , R^{bd} , R^{be} , and R^{bf} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, and C_{1-6} aminoalkyl; alternatively, R^{bc} and R^{bd} , or R^{be} and R^{bf} , together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring;

[0371] ring C is 5- to 6-membered heteroaryl;

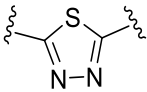
[0372] each R^c is identical or different, and is independently selected from the group consisting of hydrogen, halogen, hydroxyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, and C_{1-6} haloalkoxy;

[0373] n is selected from the group consisting of 0, 1, 2, and 3;

[0374] m is selected from the group consisting of 0, 1, 2, and 3;

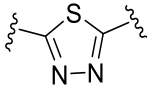
[0375] p is selected from the group consisting of 0, 1, and 2.

[0376] In some embodiments of the present disclosure, in the above formula containing ring

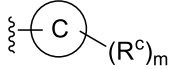
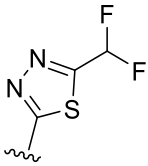
C, ring C is 5-membered heteroaryl, preferably .

[0377] In some embodiments of the present disclosure, in the above formula containing R^c , each R^c is identical or different, and is independently C_{1-6} haloalkyl; preferably, R^c is $-CHF_2$.

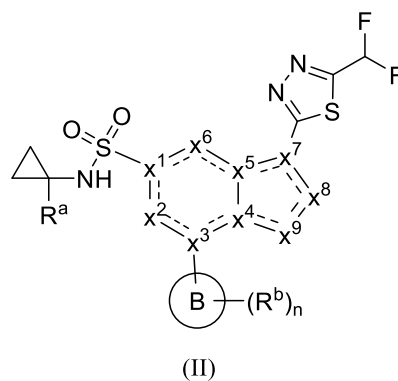
[0378] In some embodiments of the present disclosure, in the above formula containing ring C and R^c , ring C is 5-membered heteroaryl; each R^c is identical or different, and is

independently C_{1-6} haloalkyl; preferably, ring C is , and R^c is $-CHF_2$.

[0379] In some embodiments of the present disclosure, in the above formula containing ring

C and R^c ,  is .

[0380] In some embodiments of the present disclosure, the compound of formula (IA) or formula (I), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof is a compound of formula (II), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:



[0381] wherein , x^1 , x^2 , x^3 , x^4 , x^5 , x^6 , x^7 , x^8 , x^9 , ring B, R^b , R^a , and n are as defined in any embodiment of formula (I) or any embodiment of formula (IA).

[0382] In some embodiments of the present disclosure, in the above formula containing R^a , R^a is selected from the group consisting of $-CH_3$, $-CH_2F$, $-CN$, and $-CH_2=CHF$; preferably,

5 R^a is selected from the group consisting of $-CH_3$, $-CH_2F$, and $-CN$.

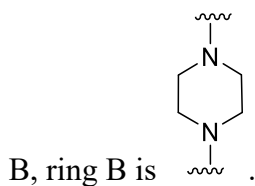
[0383] In some embodiments of the present disclosure, in the above formula containing R^a , R^a is selected from the group consisting of $-CHF_2$ and $-CHF_3$.

[0384] In some embodiments of the present disclosure, in the above formula containing R^a , R^a is $-CD_3$.

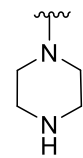
10 [0385] In some embodiments of the present disclosure, in the above formula containing R^b , each R^b is identical or different, and is independently selected from the group consisting of hydrogen, C_{1-6} alkyl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; wherein R^{ba} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I); preferably, each R^b is identical or different, and is independently selected from the group

15 consisting of hydrogen, C_{1-6} alkyl, $-C(O)R^{ba}$, and $-C(O)NR^{bc}R^{bd}$; wherein R^{ba} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0386] In some embodiments of the present disclosure, in the above formula containing ring

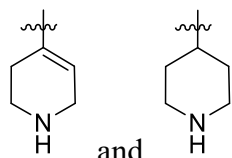


[0387] In some embodiments of the present disclosure, ring B is 6-membered heterocyclyl.



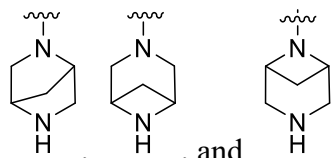
[0388] In some embodiments of the present disclosure, ring B is

[0389] In some embodiments of the present disclosure, ring B is selected from the group



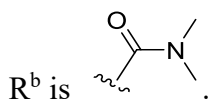
consisting of and .

[0390] In some embodiments of the present disclosure, ring B is selected from the group

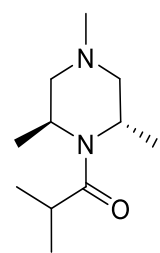
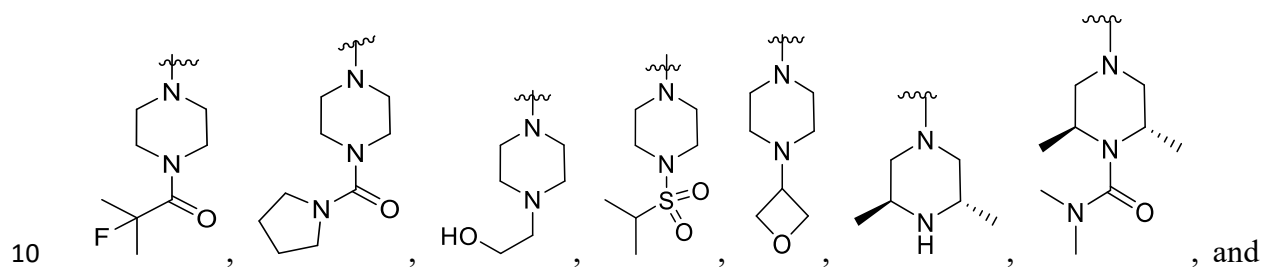
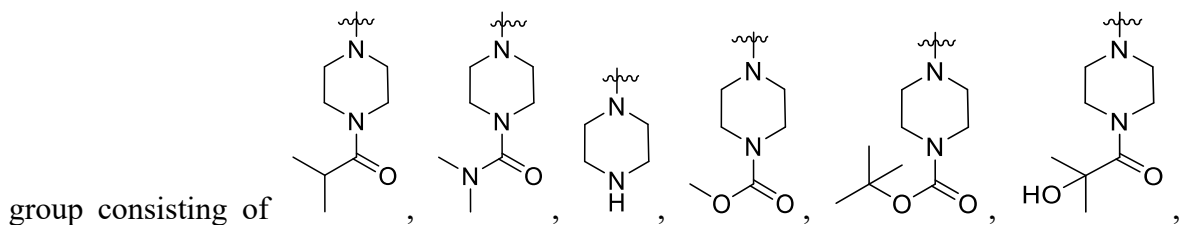


5 consisting of , , and .

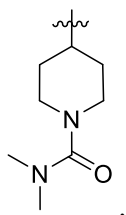
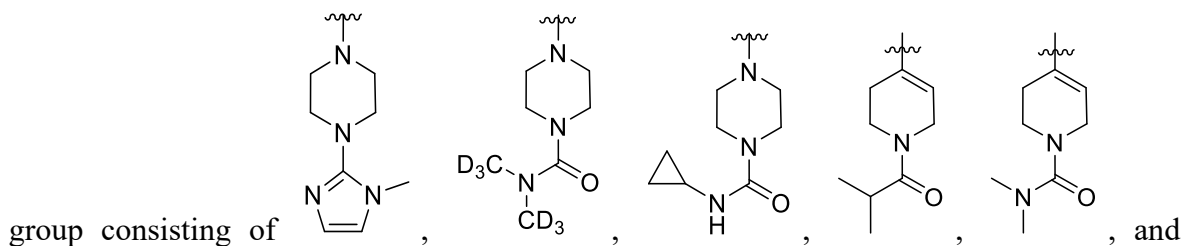
[0391] In some embodiments of the present disclosure, in the above formula containing R^b ,



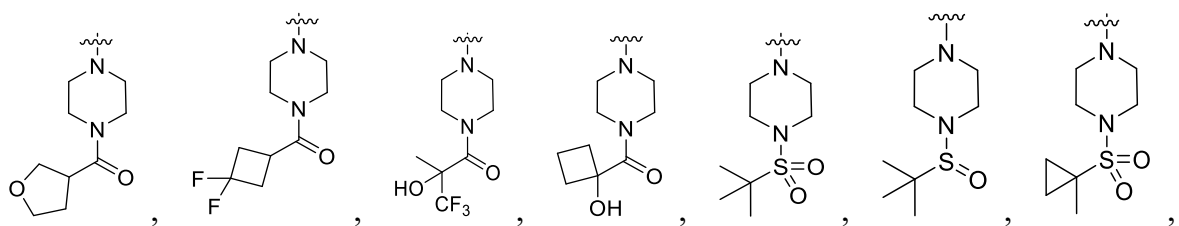
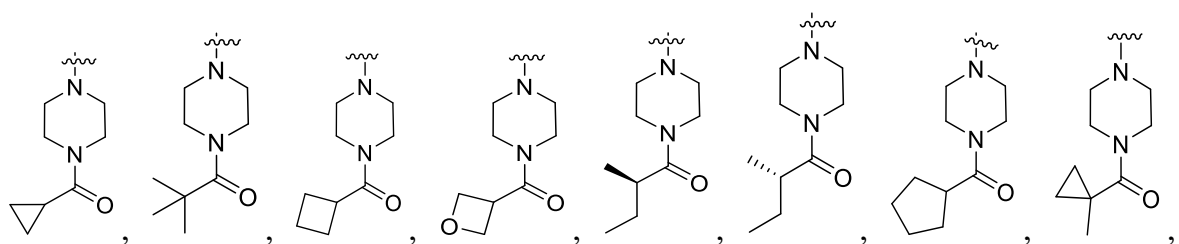
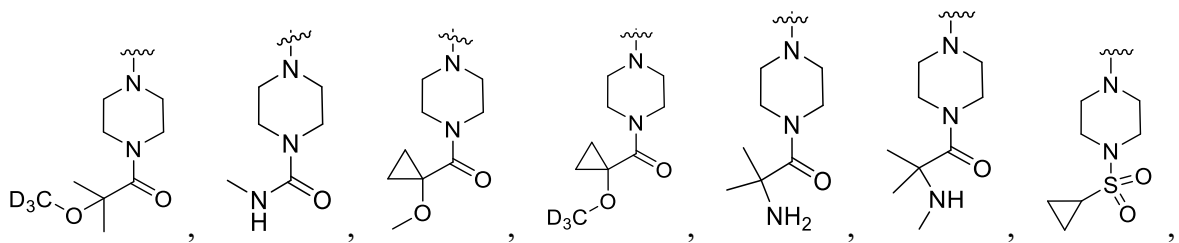
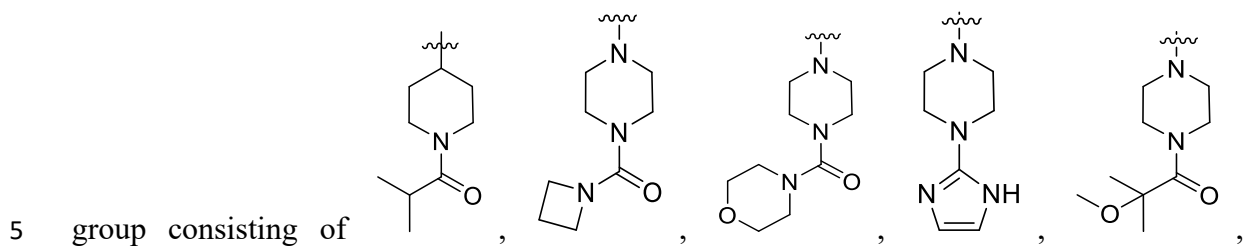
[0392] In some embodiments of the present disclosure, $\text{---} \text{B} \text{---} (R^b)_n$ is selected from the

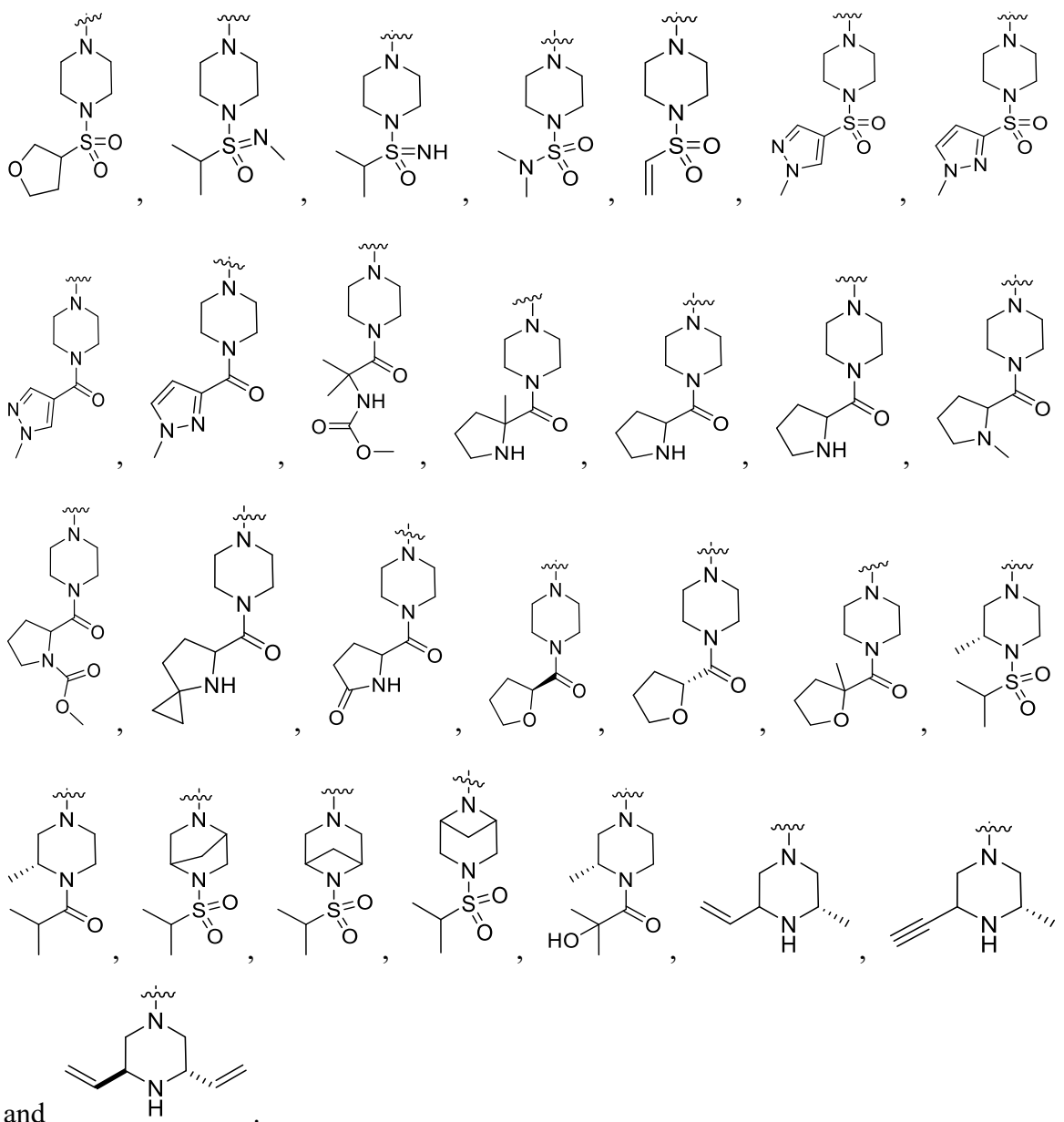


[0393] In some embodiments of the present disclosure, $\text{---}\text{B}\text{---}(\text{R}^b)_n$ is selected from the



[0394] In some embodiments of the present disclosure, $\text{---}\text{B}\text{---}(\text{R}^b)_n$ is selected from the





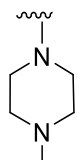
[0395] In some embodiments of the present disclosure, $\text{---}(\text{B})\text{---}(\text{R}^b)_n$ is .

[0396] In some embodiments of the present disclosure, in the above formula containing ring

B and R^b , $\text{---}(\text{B})\text{---}(\text{R}^b)_n$ is ; R^b is selected from the group consisting of C₁₋₆

hydroxyalkyl, 3- to 8-membered heterocyclyl, and $-S(O)_2R^{ba}$; R^{ba} is as defined in any

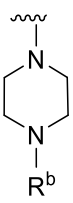
embodiment of formula (IA) or any embodiment of formula (I); preferably, $\text{---} \bigcirc \text{B} \text{---} (R^b)_n$



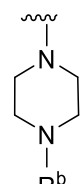
is R^b ; R^b is selected from the group consisting of C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, and $-S(O)_2R^{ba}$; R^{ba} is selected from the group consisting of hydrogen, C_{1-6} alkyl,

5 3- to 8-membered heterocyclyl, C_{1-6} haloalkyl, and C_{1-6} hydroxyalkyl.

[0397] In some embodiments of the present disclosure, in the above formula containing ring

B and R^b , $\text{---} \bigcirc \text{B} \text{---} (R^b)_n$ is ; R^b is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, and 5- to 6-membered heteroaryl optionally substituted by C_{1-6}

10 alkyl; R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in claims 1 to 11; preferably, $\text{---} \bigcirc \text{B} \text{---} (R^b)_n$ is

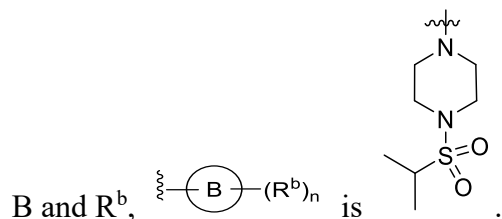


R^b ; R^b is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, and 5- to

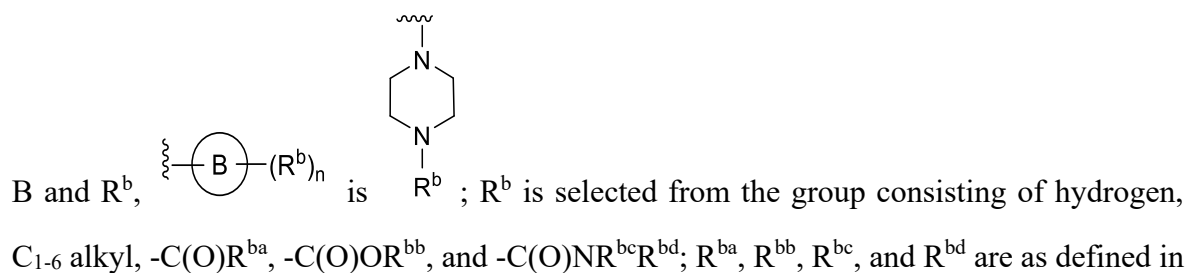
6-membered heteroaryl optionally substituted by C_{1-6} alkyl; R^{ba} , R^{bb} , R^{bc} , and R^{bd} are identical or different, and are each independently selected from the group consisting of

15 hydrogen, C_{1-6} alkyl, 3- to 8-membered heterocyclyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} deuterioalkyl, and 3- to 8-membered cycloalkyl.

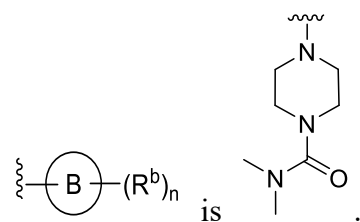
[0398] In some embodiments of the present disclosure, in the above formula containing ring



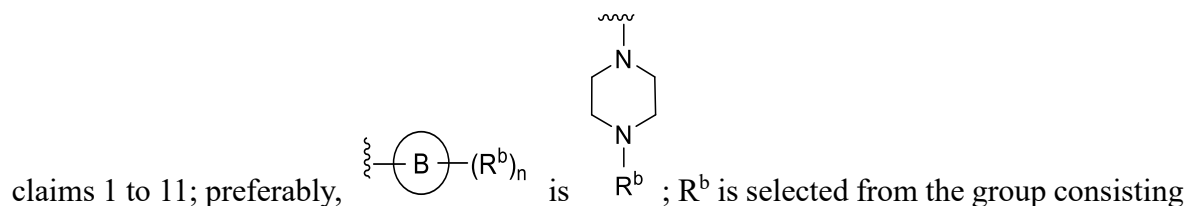
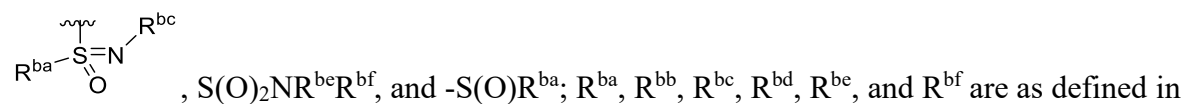
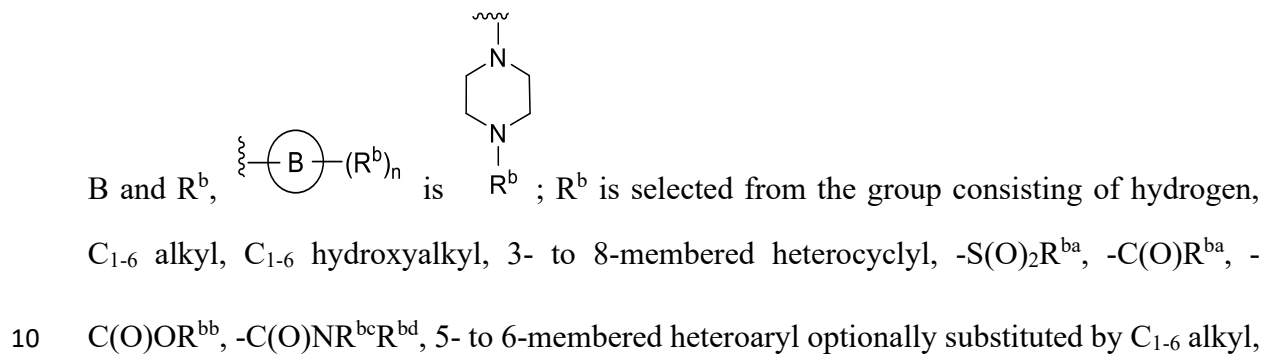
[0399] In some embodiments of the present disclosure, in the above formula containing ring

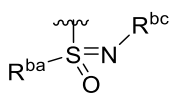


5 any embodiment of formula (IA) or any embodiment of formula (I); preferably,

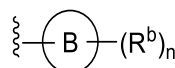
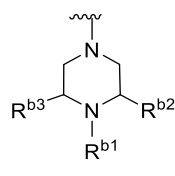
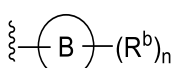
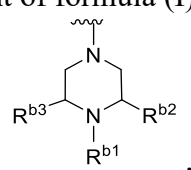
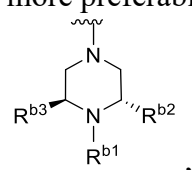
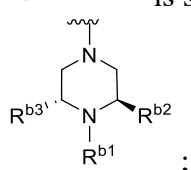


[0400] In some embodiments of the present disclosure, in the above formula containing ring

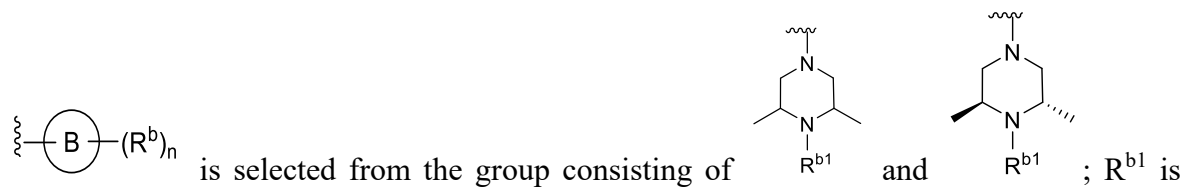


of hydrogen, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered heterocyclyl, -S(O)₂R^{ba}, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{be}R^{bd}, 5- to 6-membered heteroaryl optionally substituted by C₁₋₆ alkyl, , S(O)₂NR^{be}R^{bf}, and -S(O)R^{ba}; R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are identical or different, and are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, 3- to 8-membered heterocyclyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ deuterioalkyl, 3- to 8-membered cycloalkyl, C₁₋₆ alkoxy, C₂₋₆ alkenyl, and 5- to 6-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered heterocyclyl, 3- to 8-membered cycloalkyl, and 5- to 6-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of C₁₋₆ alkyl, halogen, C₁₋₆ deuterioalkyl, C₁₋₆ haloalkyl, hydroxyl, C₁₋₆ alkoxy, C₁₋₆ deuterioalkoxy, -C(O)OR^{bb1}, and -NR^{a1}R^{a2}; R^{bb1}, R^{a1}, and R^{a2} are as defined in claims 1 to 11.

[0401] In some embodiments of the present disclosure, in the above formula containing ring

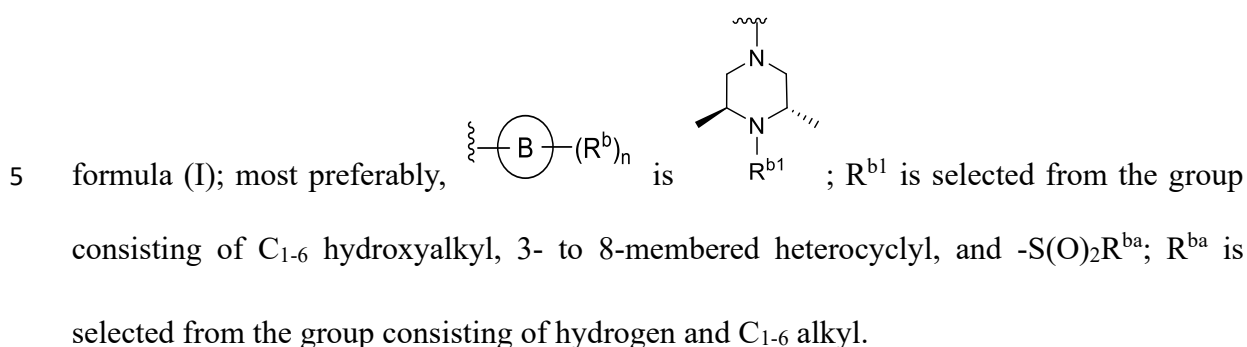
B and R^b,  is ; R^{b1} is selected from the group consisting of C₁₋₆ hydroxyalkyl, 3- to 8-membered heterocyclyl, and -S(O)₂R^{ba}; R^{b2} and R^{b3} are identical or different, and are each independently C₁₋₆ alkyl; R^{ba} is as defined in any embodiment of formula (IA) or any embodiment of formula (I); more preferably,  is selected from the group consisting of , , and ; R^{b1} is selected from the group consisting of C₁₋₆ hydroxyalkyl, 3- to 8-membered heterocyclyl, and -S(O)₂R^{ba}; R^{b2} and R^{b3} are identical, and are both C₁₋₆ alkyl; R^{ba} is as defined in any

embodiment of formula (IA) or any embodiment of formula (I); further preferably,

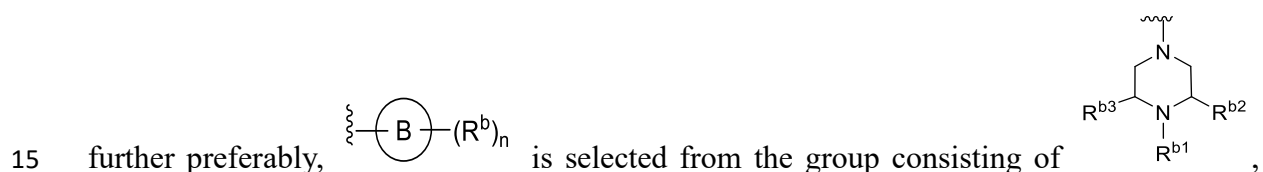
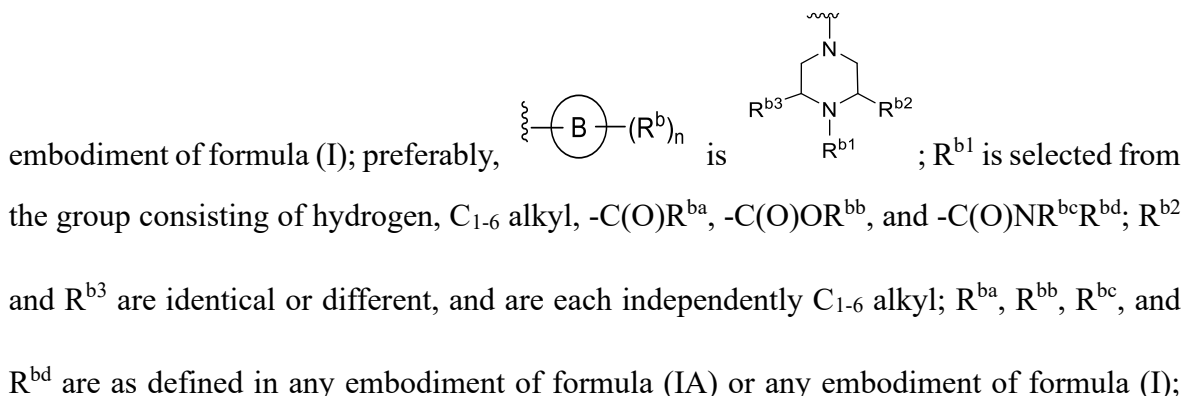
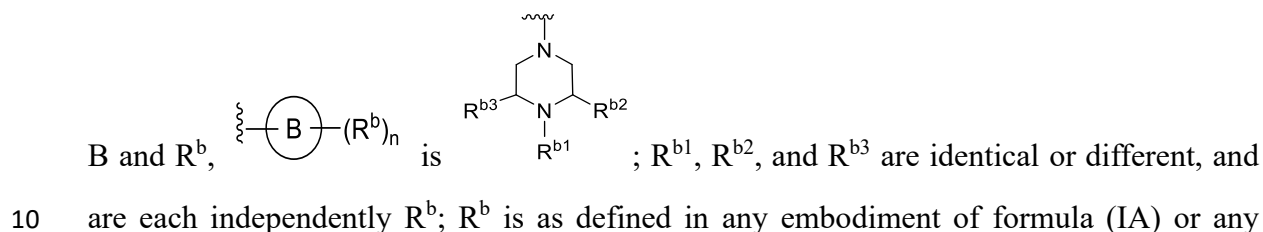


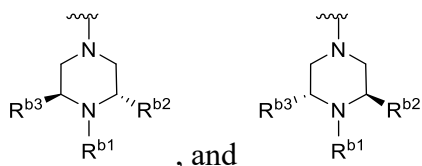
selected from the group consisting of C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, and

$-\text{S}(\text{O})_2\text{R}^{ba}$; R^{ba} is as defined in any embodiment of formula (IA) or any embodiment of



[0402] In some embodiments of the present disclosure, in the above formula containing ring





, and ; R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; R^{b2} and R^{b3} are identical, and are both C_{1-6} alkyl; R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any

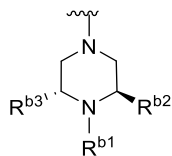
embodiment of formula (I); most preferably, is selected from the group

consisting of and ; R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

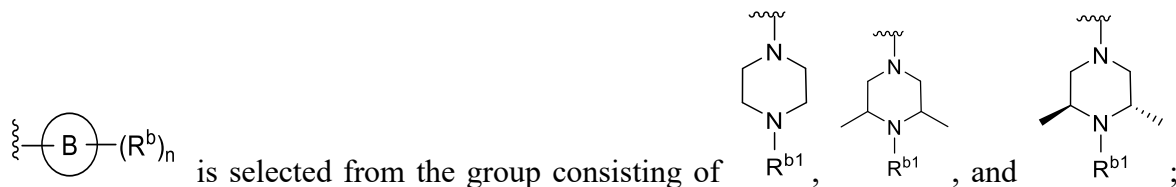
[0403] In some embodiments of the present disclosure, in the above formula containing ring

B and R^b , is ; R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, and 5- to 6-membered heteroaryl optionally substituted by C_{1-6} alkyl; R^{b2} and R^{b3} are identical or different, and are each independently selected from the group consisting of hydrogen and C_{1-6} alkyl; R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I); more preferably,

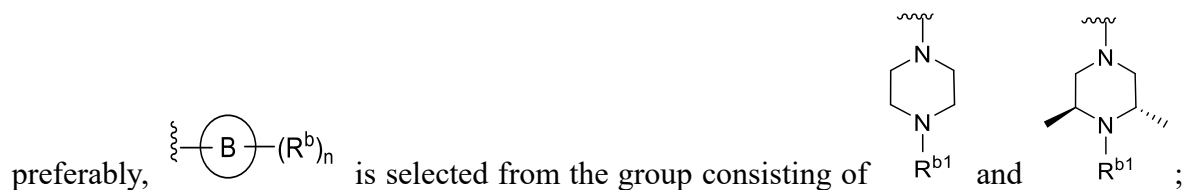
is selected from the group consisting of , , ,



and ; R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, and 5- to 6-membered heteroaryl optionally substituted by C_{1-6} alkyl; R^{b2} and R^{b3} are identical, and are both C_{1-6} alkyl; R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any
5 embodiment of formula (IA) or any embodiment of formula (I); further preferably,

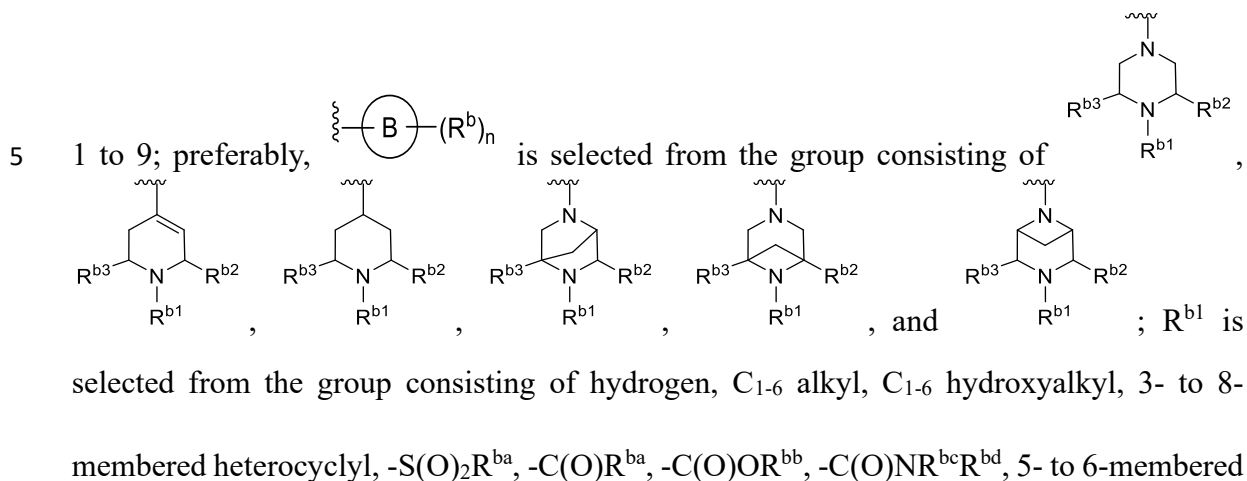
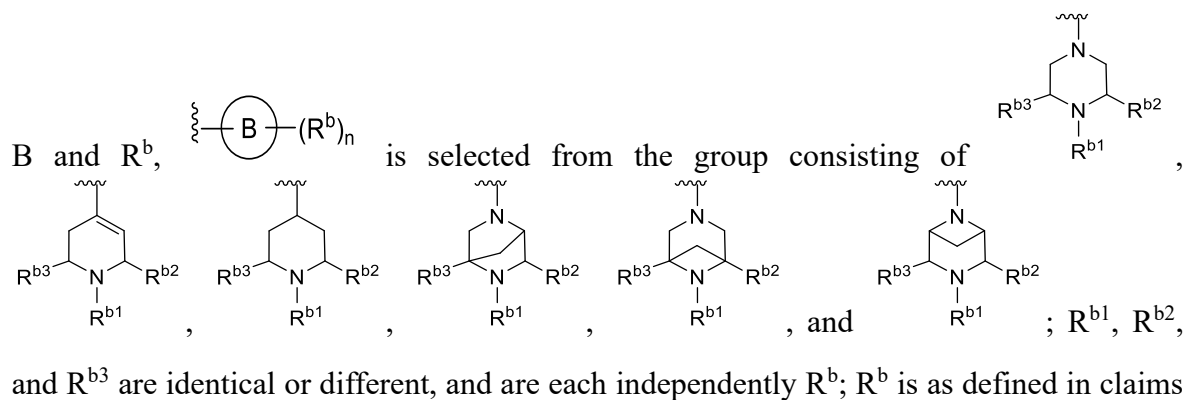


R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, and 5- to 6-membered heteroaryl optionally substituted by C_{1-6} alkyl; R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as
10 defined in any embodiment of formula (IA) or any embodiment of formula (I); most



R^{b1} is selected from the group consisting of hydrogen, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, and 5- to 6-membered heteroaryl optionally substituted by C_{1-6} alkyl; R^{ba} , R^{bb} , R^{bc} , and R^{bd} are identical or different,
15 and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, 3- to 8-membered heterocyclyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} deuterioalkyl, and 3- to 8-membered cycloalkyl.

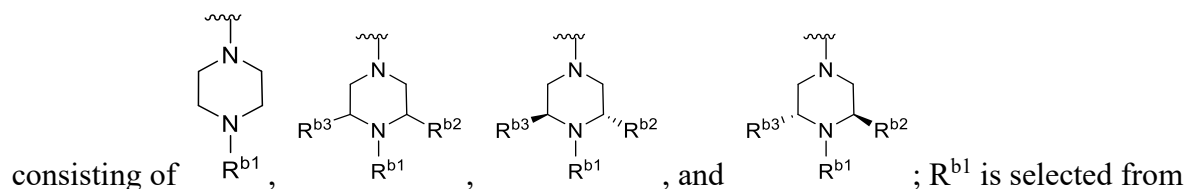
[0404] In some embodiments of the present disclosure, in the above formula containing ring



membered heterocyclyl, $-\text{S}(\text{O})_2\text{R}^{ba}$, $-\text{C}(\text{O})\text{R}^{ba}$, $-\text{C}(\text{O})\text{OR}^{bb}$, $-\text{C}(\text{O})\text{NR}^{bc}\text{R}^{bd}$, 5- to 6-membered

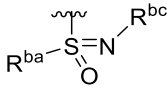
heteroaryl optionally substituted by C_{1-6} alkyl, $\text{R}^{ba}-\text{S}(\text{O})_2-\text{N}(\text{R}^{bc})$, $\text{S}(\text{O})_2\text{NR}^{be}\text{R}^{bf}$, and $-\text{S}(\text{O})\text{R}^{ba}$;

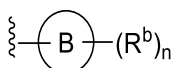
R^{b2} and R^{b3} are identical or different, and are each independently selected from the group

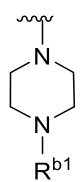
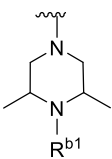
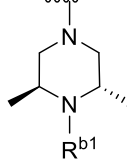
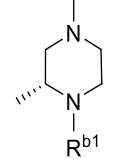
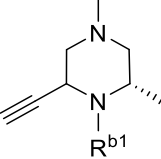
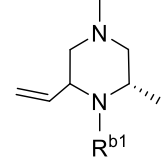


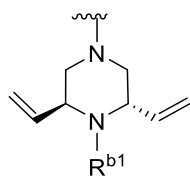
the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered

heterocyclyl, $-\text{S}(\text{O})_2\text{R}^{ba}$, $-\text{C}(\text{O})\text{R}^{ba}$, $-\text{C}(\text{O})\text{OR}^{bb}$, $-\text{C}(\text{O})\text{NR}^{bc}\text{R}^{bd}$, 5- to 6-membered heteroaryl

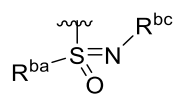
optionally substituted by C₁₋₆ alkyl, , S(O)₂NR^{be}R^{bf}, and -S(O)R^{ba}; R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are identical or different, and are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl; R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are as

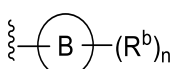
defined in claims 1 to 9; further preferably,  is selected from the group

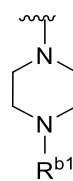
5 consisting of , , , , , , and

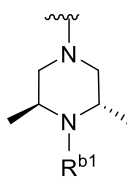


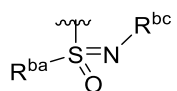
; R^{b1} is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered heterocyclyl, -S(O)₂R^{ba}, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 5- to 6-membered heteroaryl optionally substituted by C₁₋₆ alkyl,

, S(O)₂NR^{be}R^{bf}, and -S(O)R^{ba}; R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are as defined in

10 claims 1 to 9; most preferably,  is selected from the group consisting of

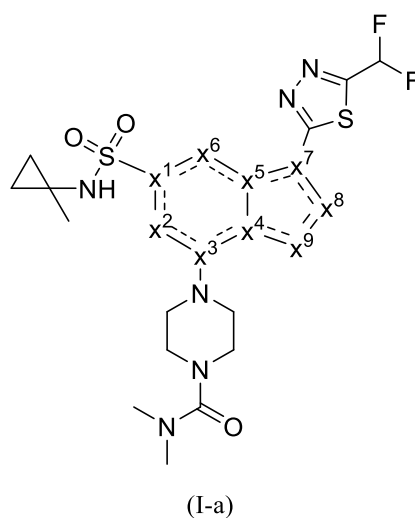


and ; R^{b1} is selected from the group consisting of hydrogen, C₁₋₆ hydroxyalkyl, 3- to 8-membered heterocyclyl, -S(O)₂R^{ba}, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 5- to 6-

membered heteroaryl optionally substituted by C₁₋₆ alkyl, , S(O)₂NR^{be}R^{bf}, and -S(O)R^{ba}; R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are identical or different, and are each independently

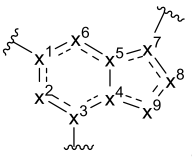
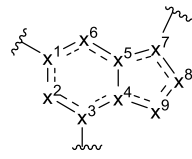
selected from the group consisting of hydrogen, C₁₋₆ alkyl, 3- to 8-membered heterocyclyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ deutoalkyl, 3- to 8-membered cycloalkyl, C₁₋₆ alkoxy, C₂₋₆ alkenyl, and 5- to 6-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered heterocyclyl, 3- to 8-membered cycloalkyl, and 5- to 6-membered heteroaryl are
 5 optionally substituted by one or more substituents selected from the group consisting of C₁₋₆ alkyl, halogen, C₁₋₆ deutoalkyl, C₁₋₆ haloalkyl, hydroxyl, C₁₋₆ alkoxy, C₁₋₆ deutoalkoxy, -C(O)OR^{bb1}, and -NR^{a1}R^{a2}; R^{bb1}, R^{a1}, and R^{a2} are as defined in claims 1 to 9.

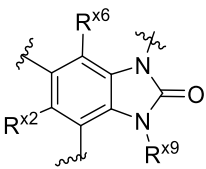
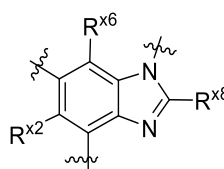
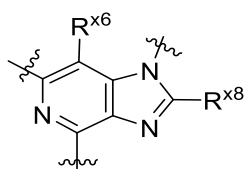
[0405] In some embodiments of the present disclosure, the compound of formula (IA), formula (I), or formula (II), the pharmaceutically acceptable salt thereof, the stereoisomer
 10 thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof is a compound of formula (I-a), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:

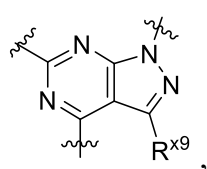
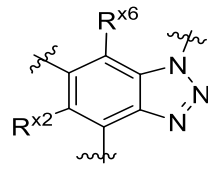
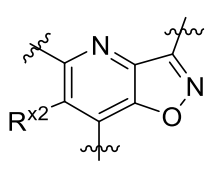
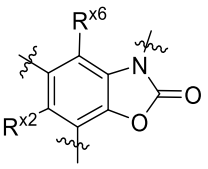
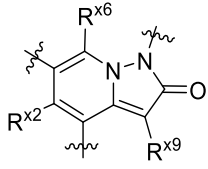


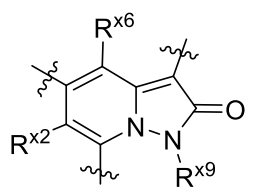
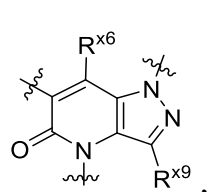
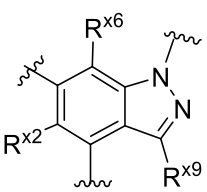
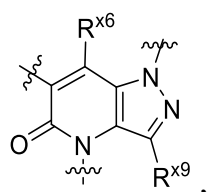
15 **[0406]** wherein , x¹, x², x³, x⁴, x⁵, x⁶, x⁷, x⁸, and x⁹ are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

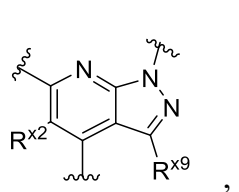
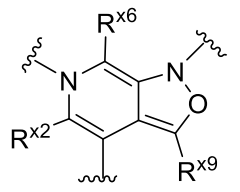
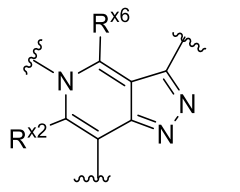
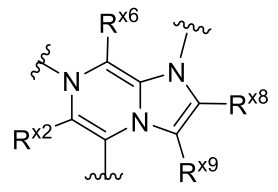
[0407] In some embodiments of the present disclosure, in the above formula containing the

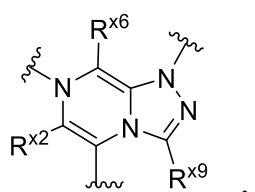
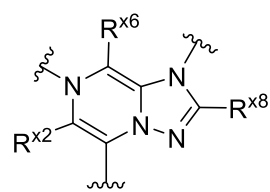
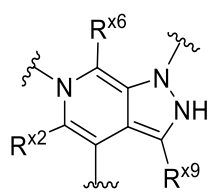
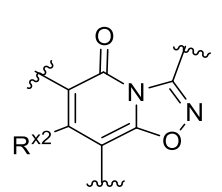
structural moiety , the structural moiety  is selected from the

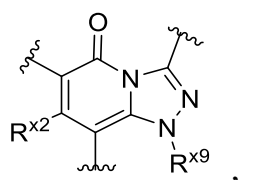
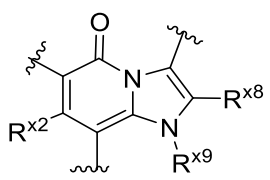
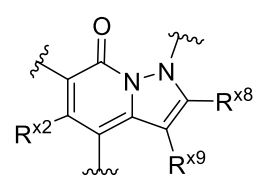
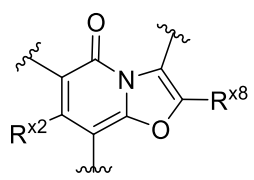
group consisting of , , ,

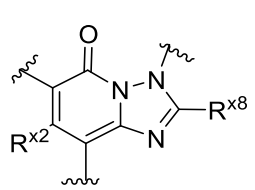
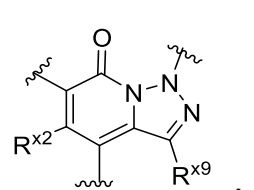
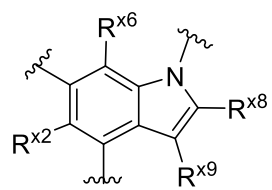
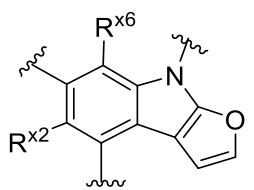
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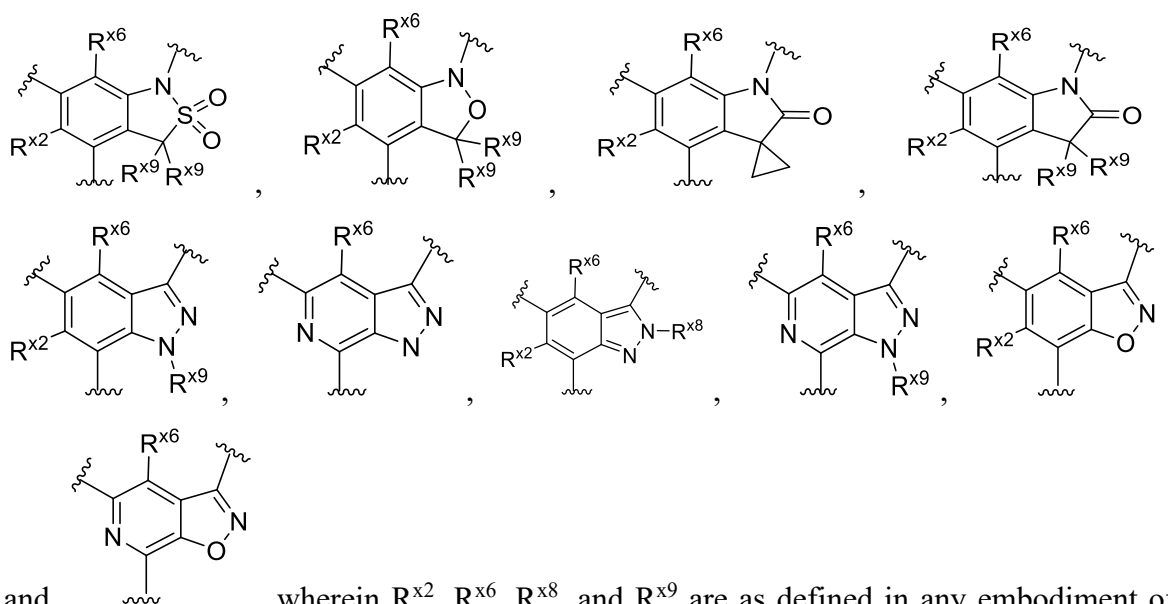
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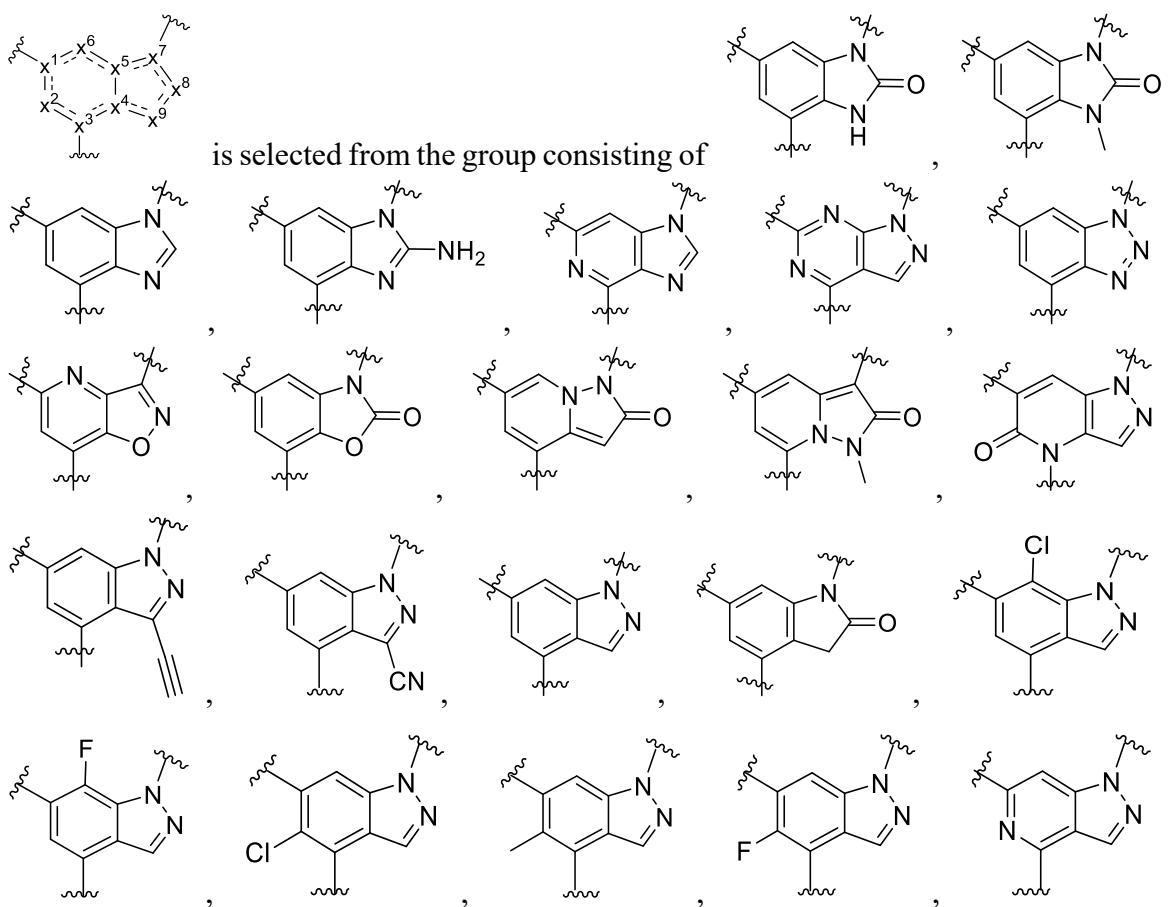
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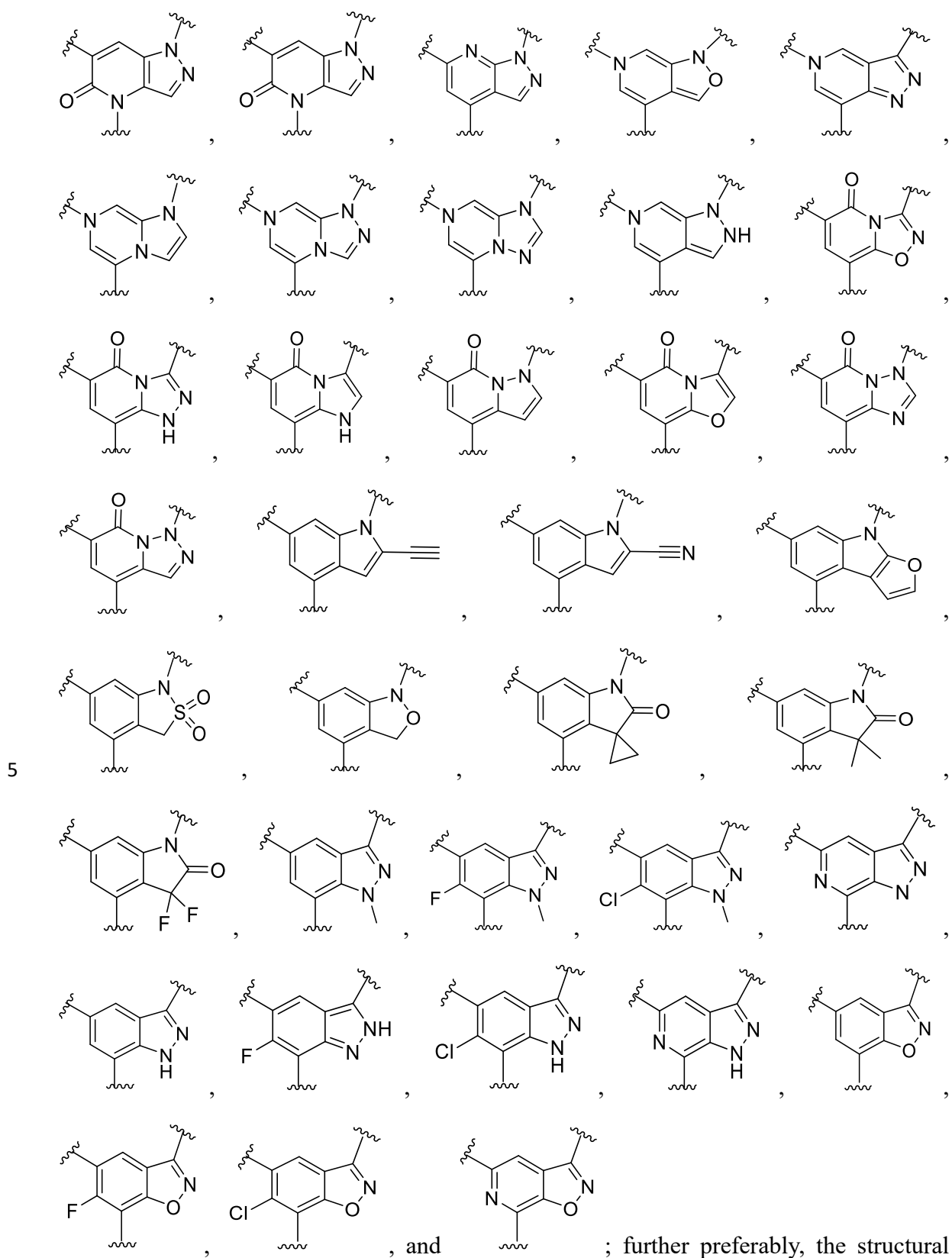
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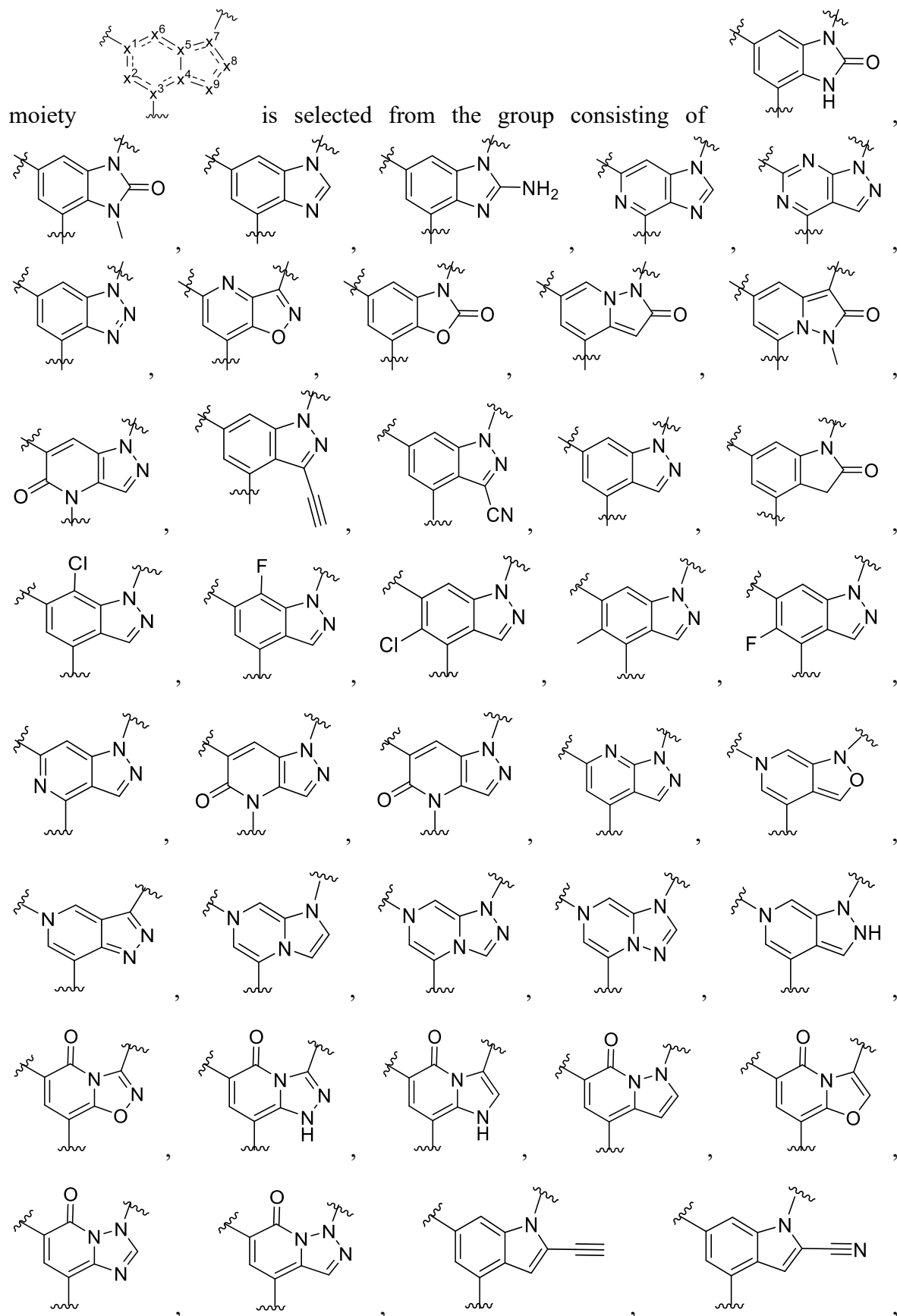
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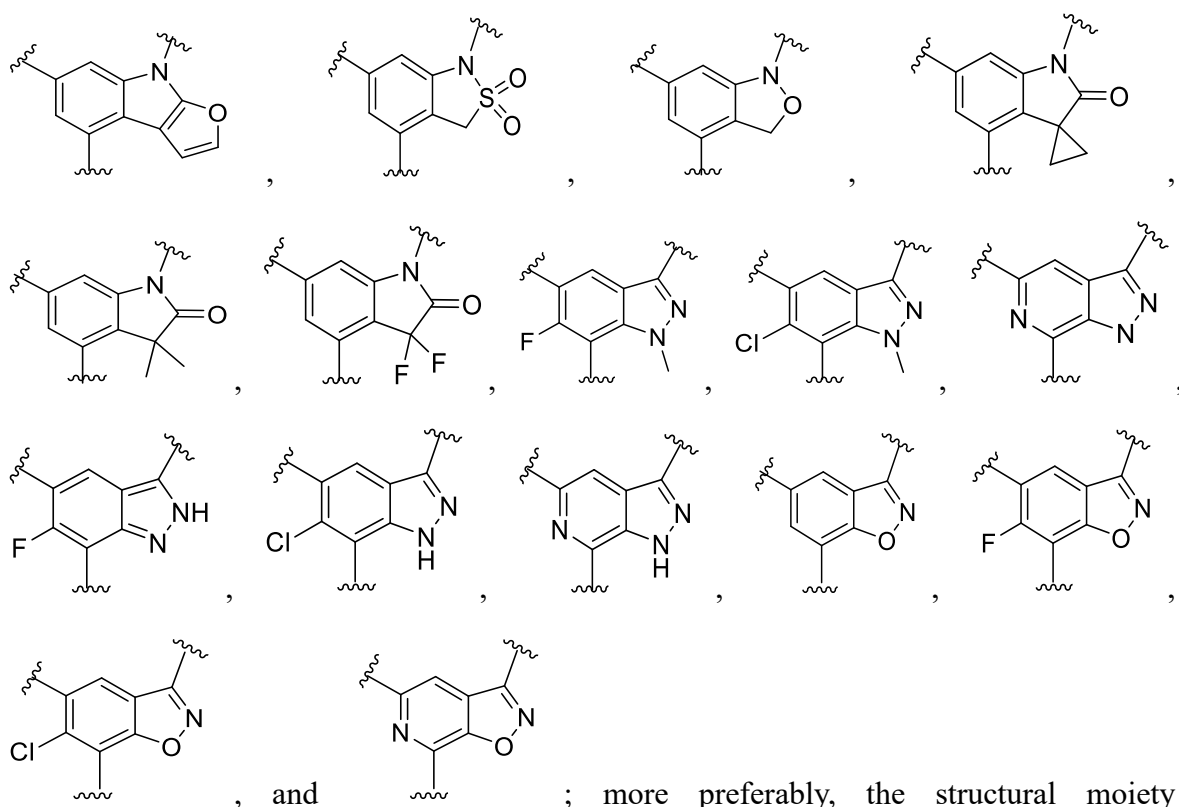


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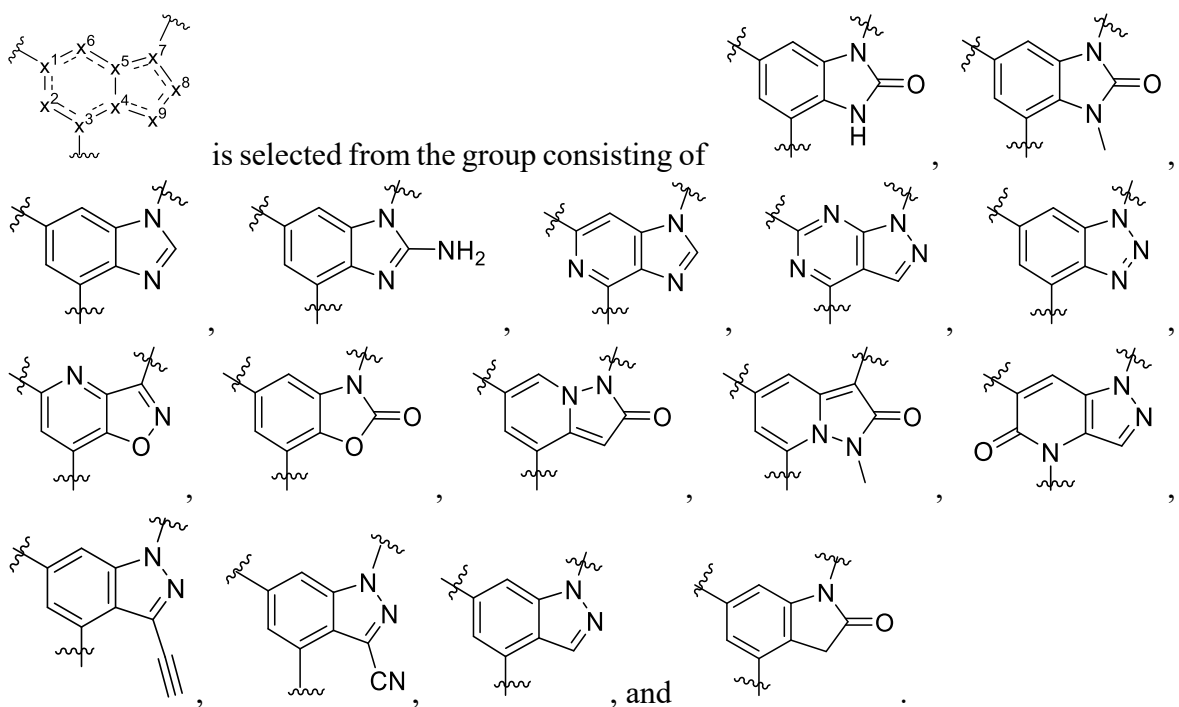








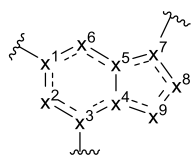
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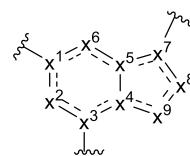
[0408] In some embodiments of the present disclosure, in the above formula containing the

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structural moiety

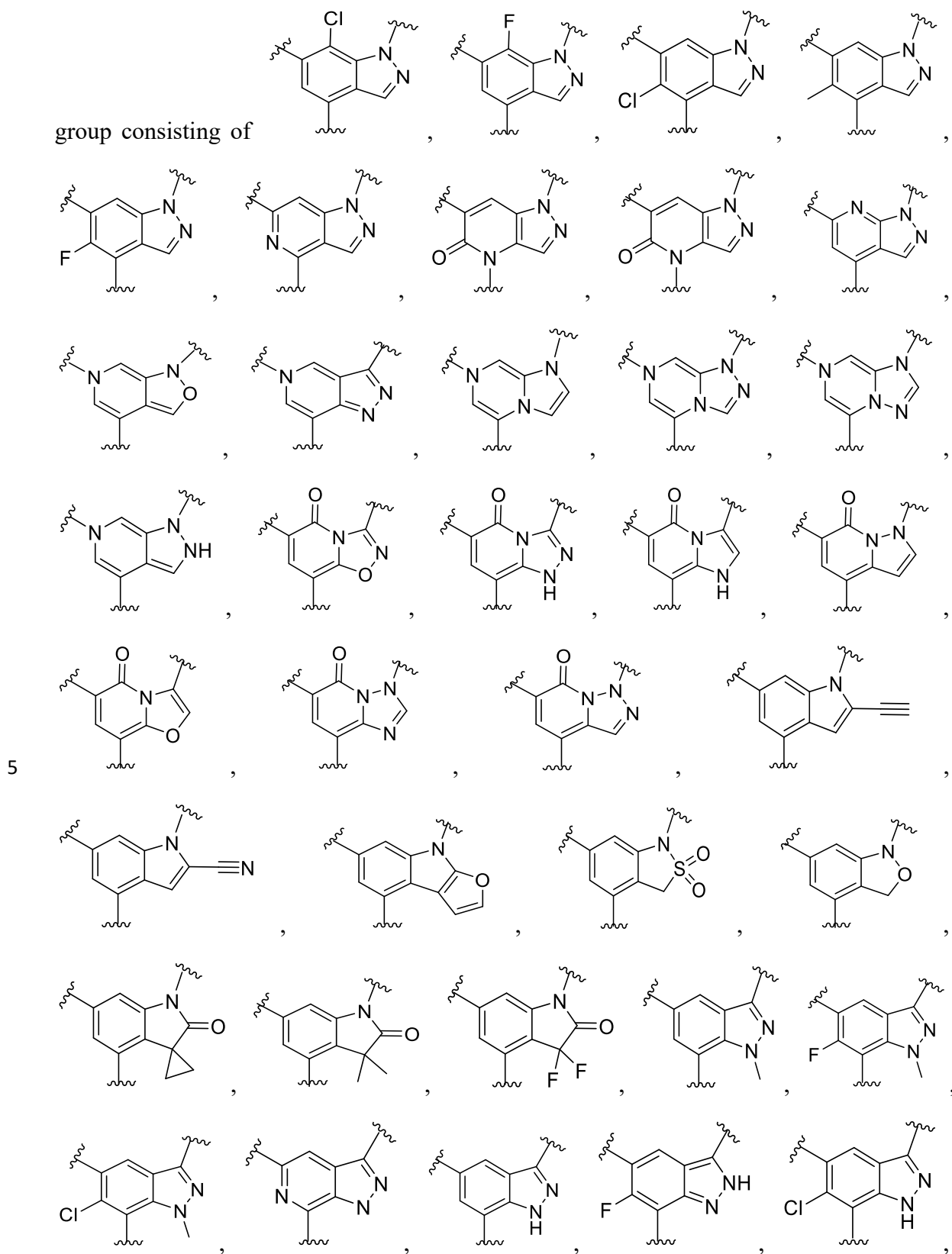


, the structural moiety

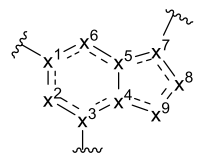
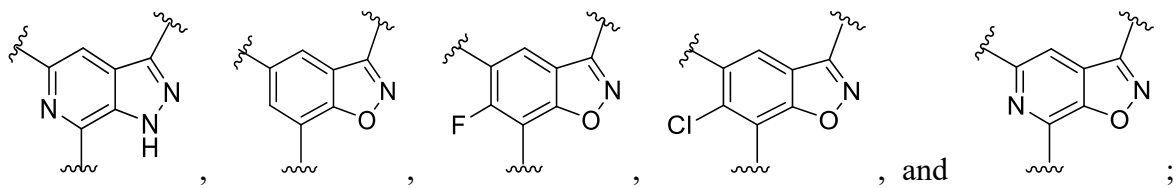


is selected from the

group consisting of

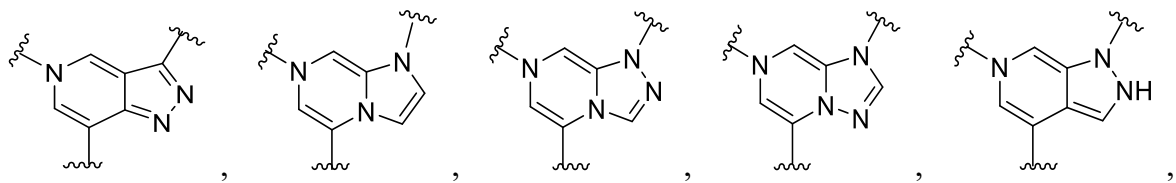
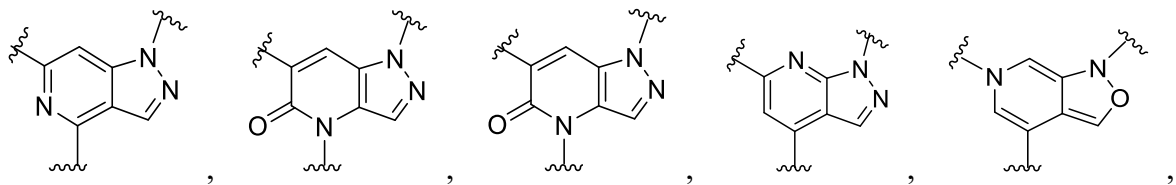
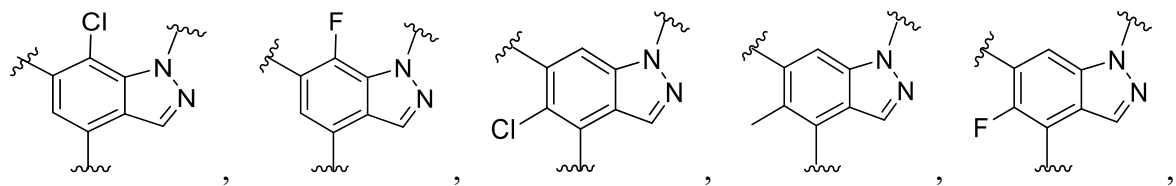


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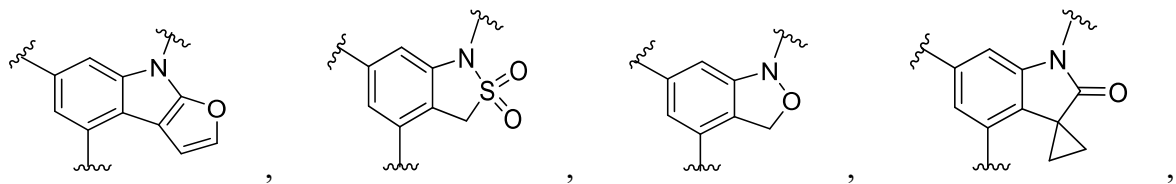
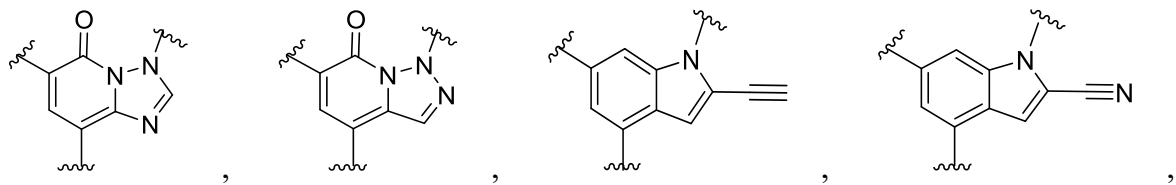
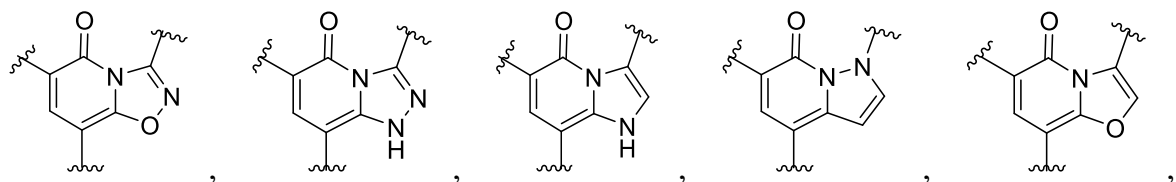


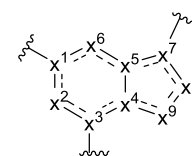
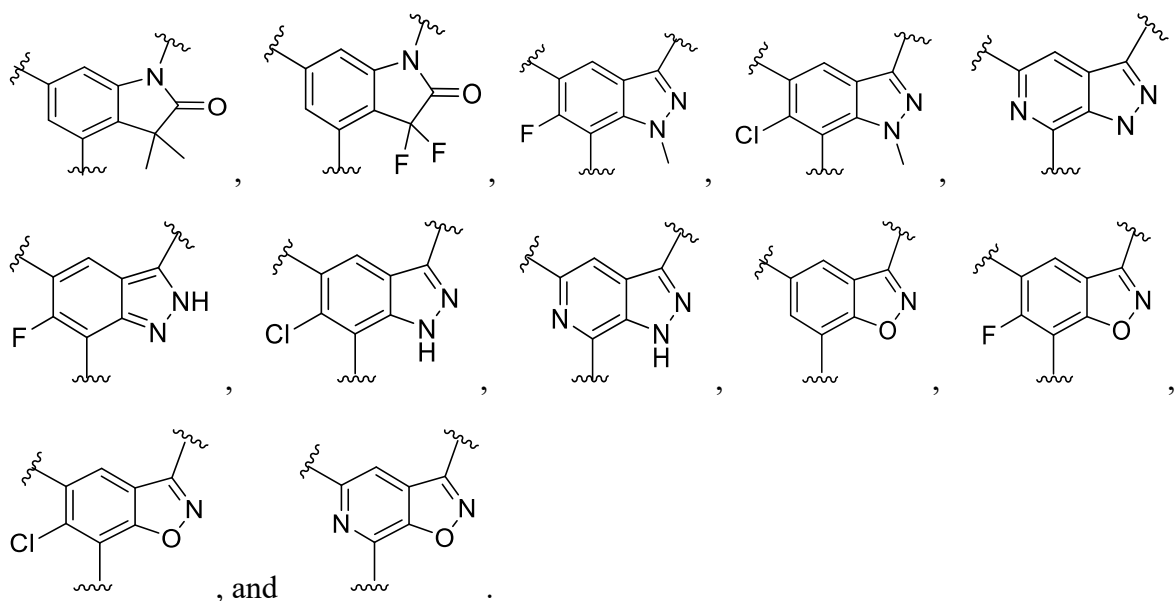
preferably, the structural moiety

is selected from the group consisting of

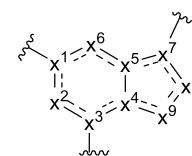
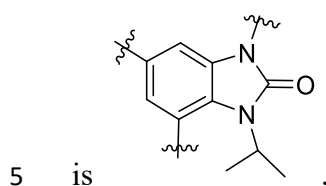


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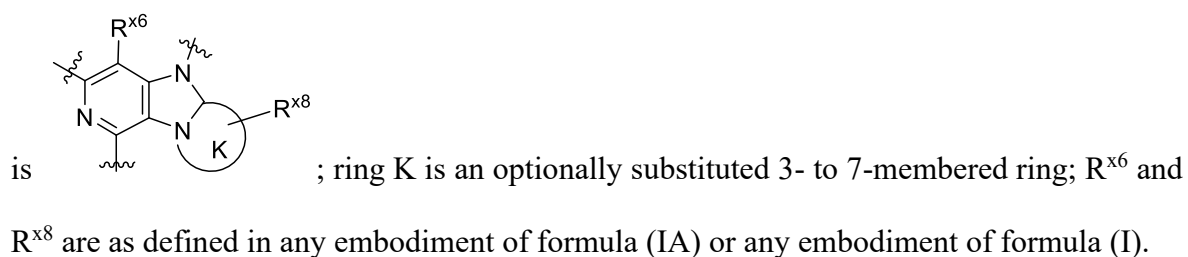




[0409] In some embodiments of the present disclosure, the structural moiety



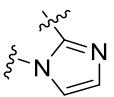
[0410] In some embodiments of the present disclosure, the structural moiety



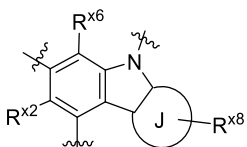
[0411] In some embodiments of the present disclosure, ring K is an optionally substituted 3- to 7-membered ring.

[0412] In some embodiments of the present disclosure, ring K is 5- to 6-membered heterocyclyl or 5- to 6-membered heteroaryl, wherein the 5- to 6-membered heterocyclyl or

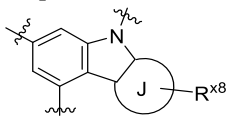
5- to 6-membered heteroaryl is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, and C₁₋₆ hydroxyalkyl; R^{a1}, R^{a2}, R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0413] In some embodiments of the present disclosure, ring K is .

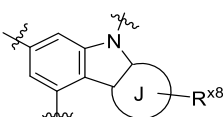
[0414] In some embodiments of the present disclosure, the structural moiety

; ring J is an optionally substituted 3- to 7-membered ring; R^{x2}, R^{x6}, and R^{x8} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

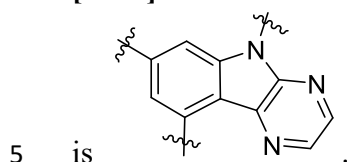
[0415] In some embodiments of the present disclosure, the structural moiety

; ring J is optionally substituted 5- to 6-membered heterocyclyl or 5- to 6-membered heteroaryl; R^{x8} is as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0416] In some embodiments of the present disclosure, the structural moiety

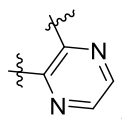
is ; ring J is optionally substituted 6-membered nitrogen-containing heteroaryl; R^{x8} is as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0417] In some embodiments of the present disclosure, the structural moiety

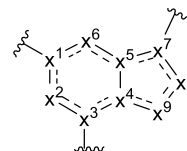


[0418] In some embodiments of the present disclosure, ring J is 5- to 6-membered heterocyclyl or 5- to 6-membered heteroaryl, wherein the 5- to 6-membered heterocyclyl or 5- to 6-membered heteroaryl is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, and C₁₋₆ hydroxyalkyl; R^{a1}, R^{a2}, R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

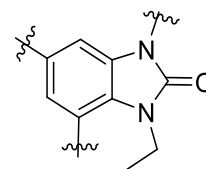
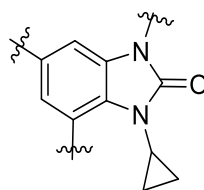
[0419] In some embodiments of the present disclosure, ring J is

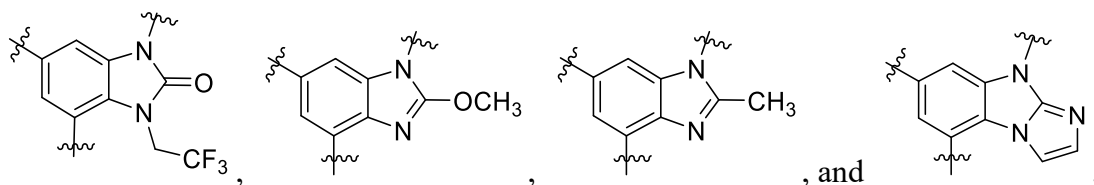


15 [0420] In some embodiments of the present disclosure, the structural moiety

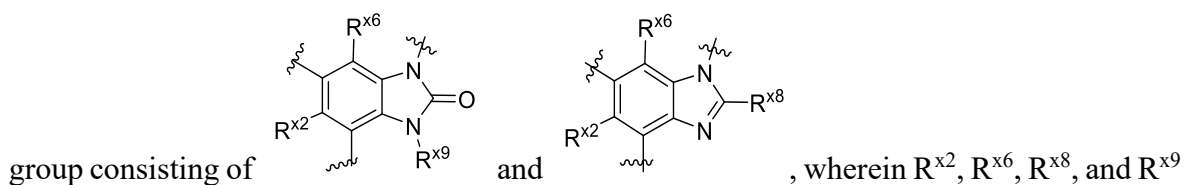
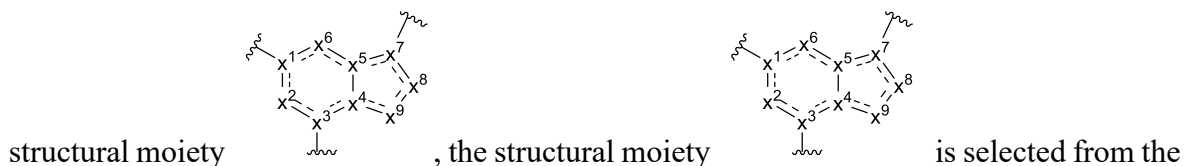


is selected from the group consisting of

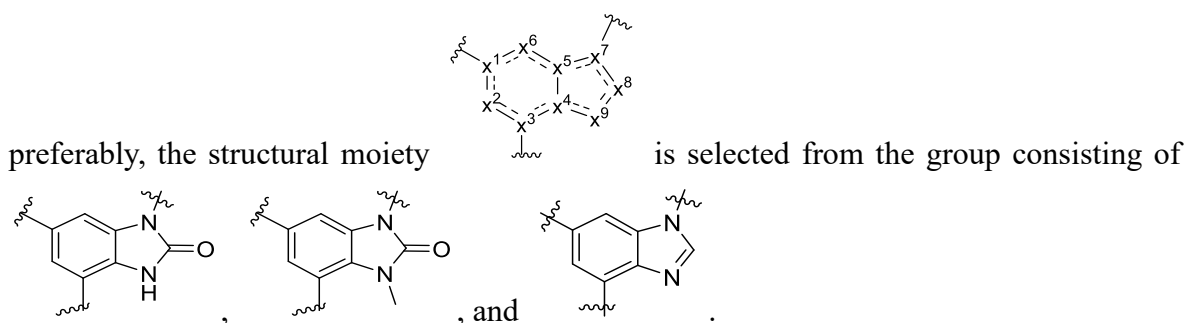




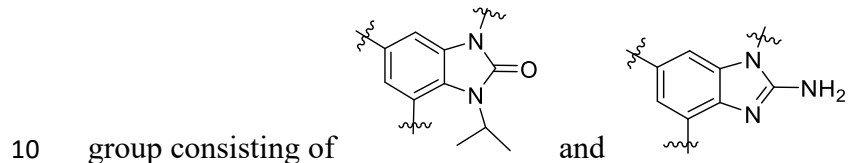
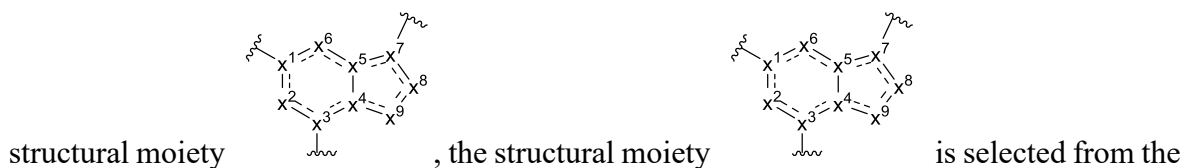
[0421] In some embodiments of the present disclosure, in the above formula containing the



5 are as defined in any embodiment of formula (IA) or any embodiment of formula (I);

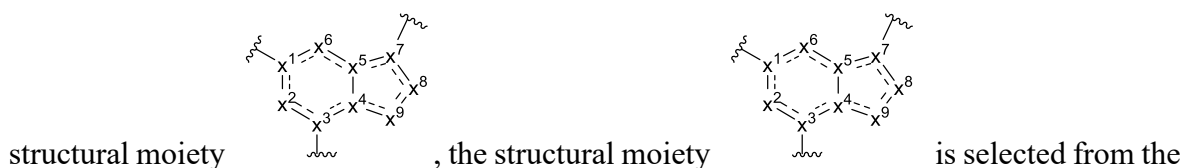


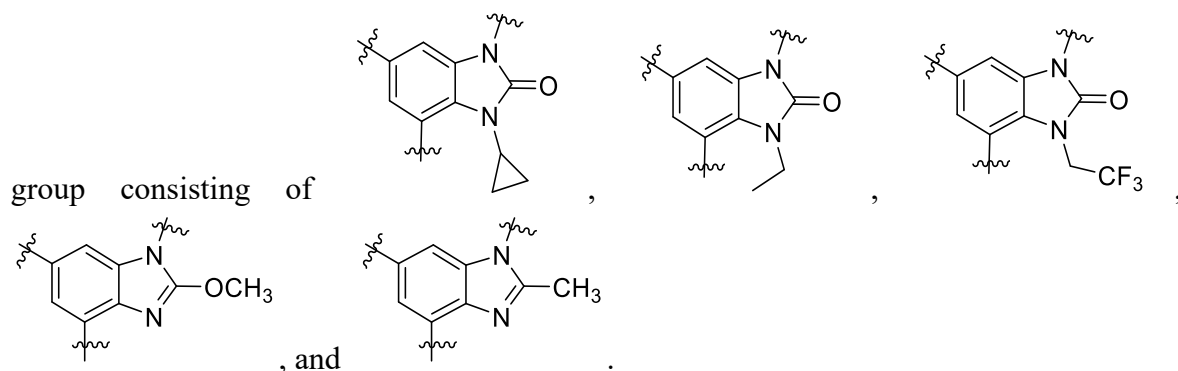
[0422] In some embodiments of the present disclosure, in the above formula containing the



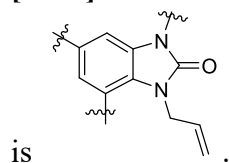
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[0423] In some embodiments of the present disclosure, in the above formula containing the

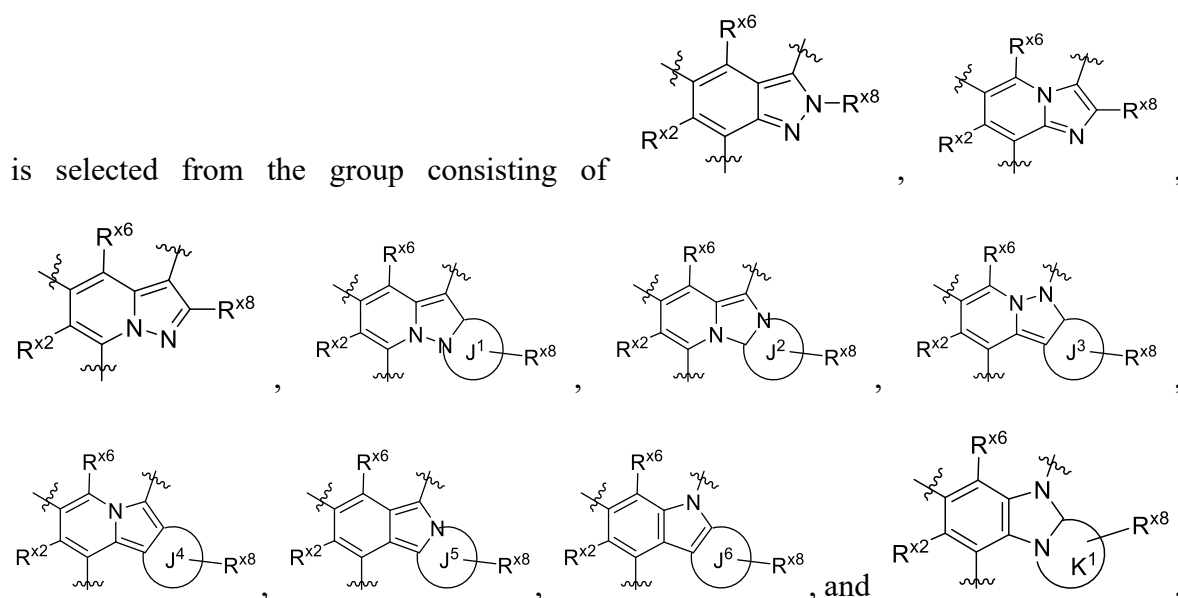




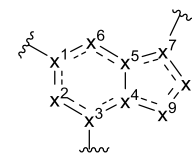
[0424] In some embodiments of the present disclosure, the structural moiety



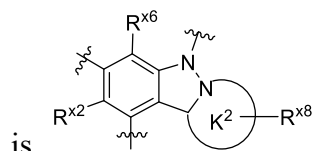
5 [0425] In some embodiments of the present disclosure, the structural moiety



wherein ring J¹, ring J², ring J³, ring J⁴, ring J⁵, ring J⁶, and ring K¹ are identical or different,
 10 and are each independently an optionally substituted 3- to 7-membered ring; R^{x2}, R^{x6}, and
 R^{x8} are as defined in any one of the embodiments of the present disclosure.

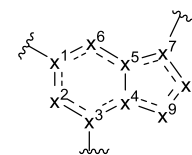


[0426] In some embodiments of the present disclosure, the structural moiety

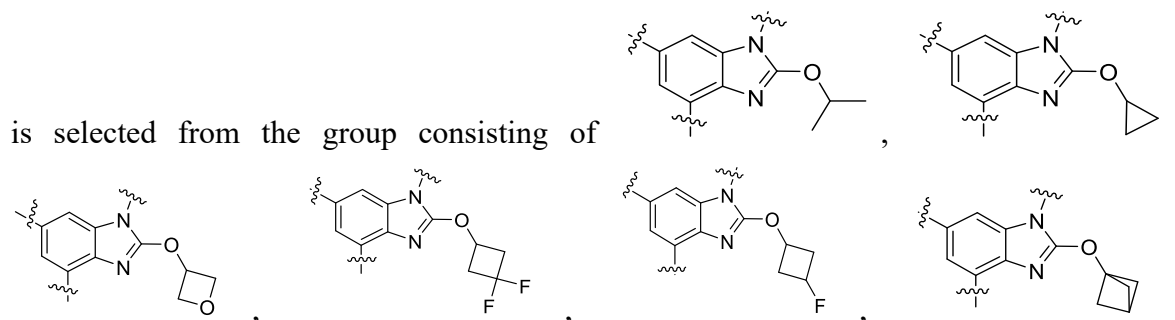


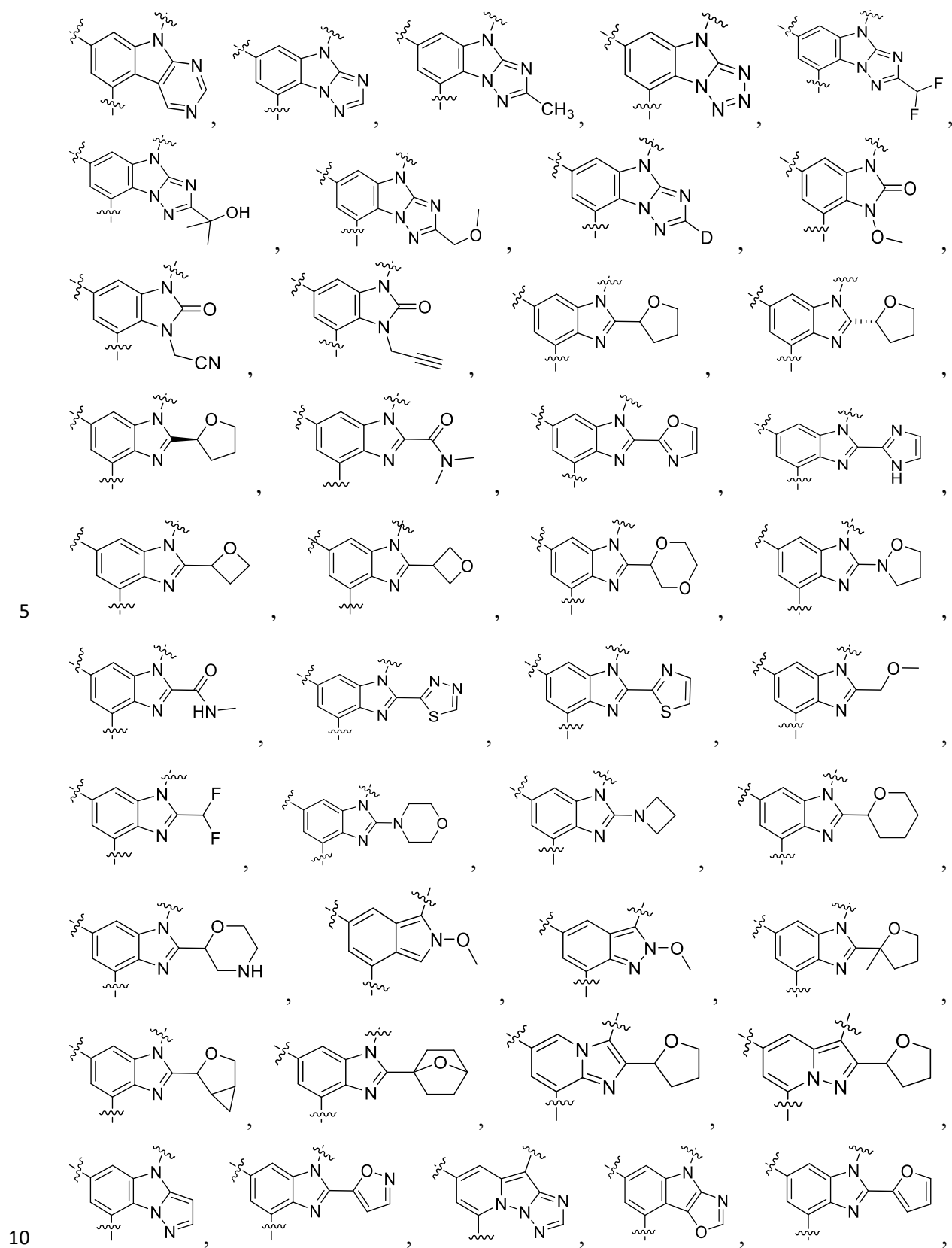
is $\text{R}^{\text{x}2}$, $\text{R}^{\text{x}6}$, and $\text{R}^{\text{x}8}$ are as defined in any one of the embodiments of the present disclosure.

[0427] In some embodiments of the present disclosure, ring J^1 , ring J^2 , ring J^3 , ring J^4 , ring J^5 , ring J^6 , and ring K^1 are identical or different, and are each independently 5- to 6-membered heterocyclyl or 5- to 6-membered heteroaryl, wherein the 5- to 6-membered heterocyclyl or 5- to 6-membered heteroaryl is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-\text{NR}^{\text{a}1}\text{R}^{\text{a}2}$, nitro, hydroxyl, $-\text{C}(\text{O})\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{R}^{\text{ba}}$, $\text{S}(\text{O})_{\text{p}}\text{NR}^{\text{be}}\text{R}^{\text{bf}}$, $-\text{C}(\text{O})\text{OR}^{\text{bb}}$, $-\text{C}(\text{O})\text{NR}^{\text{bc}}\text{R}^{\text{bd}}$, and C_{1-6} hydroxyalkyl; $\text{R}^{\text{a}1}$, $\text{R}^{\text{a}2}$, R^{ba} , R^{bb} , R^{bc} , R^{bd} , R^{be} , and R^{bf} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

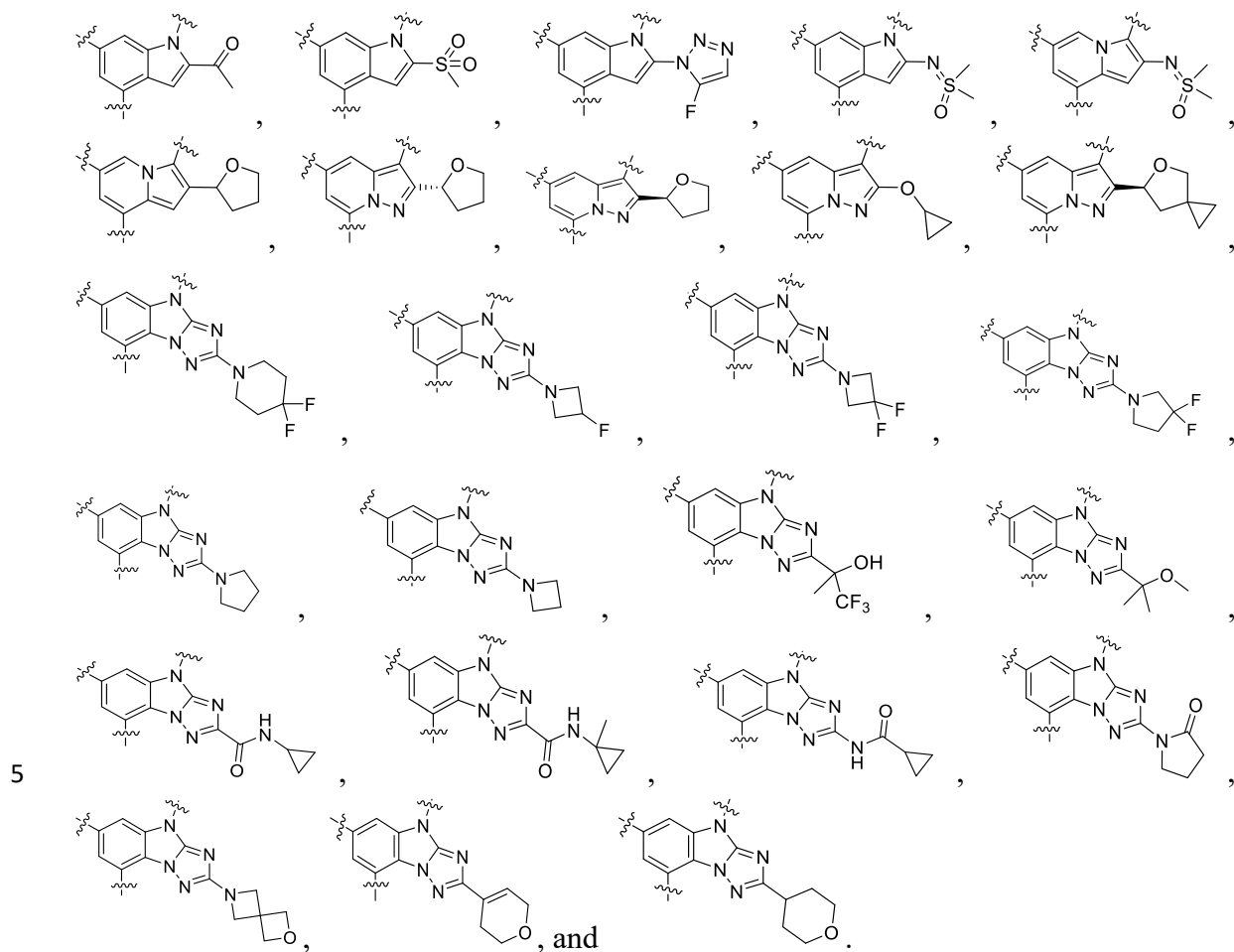


[0428] In some embodiments of the present disclosure, the structural moiety



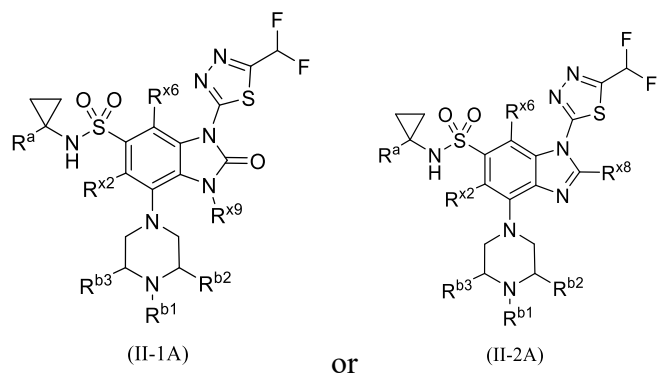


Chemical structures of 15 novel pyrazolo[1,5-a]pyridine derivatives, numbered 1 to 15, showing various substituents and ring systems.



[0430] In some embodiments of the present disclosure, the compound of formula (IA) or formula (I), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof is

10 a compound of formula (II-1A) or formula (II-2A), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:



[0431] wherein

[0432] R^{b1} , R^{b2} , and R^{b3} are identical or different, and are each independently R^b ;

[0433] R^b , R^a , R^{x2} , R^{x6} , R^{x8} , and R^{x9} are as defined in any one of the embodiments of the
 5 present disclosure.

[0434] In some embodiments of the present disclosure, in the compound of formula (II-1A) or formula (II-2A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{b1} , R^{b2} , and R^{b3} are identical or different, and are each independently R^b , wherein
 10 R^b is as defined in any embodiment of formula (IA) or any embodiment of formula (I); preferably, R^{b1} , R^{b2} , and R^{b3} are identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$, wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula
 15 (I); further preferably, R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; R^{b2} and R^{b3} are identical or different, and are each independently C_{1-6} alkyl,

wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I); further preferably, R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; R^{b2} and R^{b3} are identical, and are both C_{1-6} alkyl, wherein

5 R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I); further preferably, R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; R^{b2} and R^{b3} are both methyl, wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I); most preferably, R^{b1}

10 is selected from the group consisting of hydrogen, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; R^{b2} and R^{b3} are both methyl, wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, 3- to 8-membered heterocyclyl, C_{1-6} haloalkyl, and C_{1-6} hydroxyalkyl;

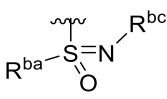
15 **[0435]** R^a , R^{x2} , R^{x6} , R^{x8} , and R^{x9} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0436] In some embodiments of the present disclosure, in the compound of formula (II-1A) or formula (II-2A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative

20 thereof, R^{b1} , R^{b2} , and R^{b3} are identical or different, and are each independently R^b , wherein R^b is as defined in any embodiment of formula (IA) or any embodiment of formula (I);

preferably, R^{b1} , R^{b2} , and R^{b3} are identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$, wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I); further preferably, R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; R^{b2} and R^{b3} are identical or different, and are each independently C_{1-6} alkyl, wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I); further preferably, R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; R^{b2} and R^{b3} are identical, and are both C_{1-6} alkyl, wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I); most preferably, R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; R^{b2} and R^{b3} are both methyl, wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I); R^a , R^{x2} , R^{x6} , R^{x8} , and R^{x9} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

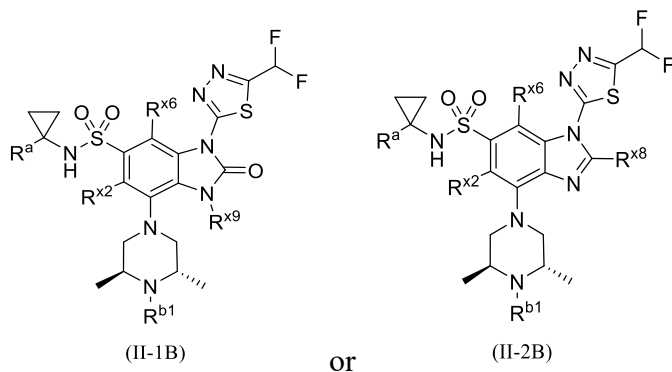
[0437] In some embodiments of the present disclosure, in the compound of formula (II-1A) or formula (II-2A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{b1} , R^{b2} , and R^{b3} are identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 5- to 6-

membered heteroaryl optionally substituted by C₁₋₆ alkyl, , S(O)₂NR^{bc}R^{bf}, and -S(O)R^{ba}; wherein R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0438] In some embodiments of the present disclosure, in the compound of formula (II-1A),
 5 the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{b2} and R^{b3} are identical or different, and are each independently selected from the group consisting of hydrogen and C₁₋₆ alkyl; preferably, R^{b2} and R^{b3} are both hydrogen.

[0439] In some embodiments of the present disclosure, in the compound of formula (II-2A),
 10 the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{b2} and R^{b3} are identical or different, and are each independently selected from the group consisting of hydrogen and C₁₋₆ alkyl; preferably, R^{b2} and R^{b3} are identical or different, and are each independently selected from hydrogen and methyl.

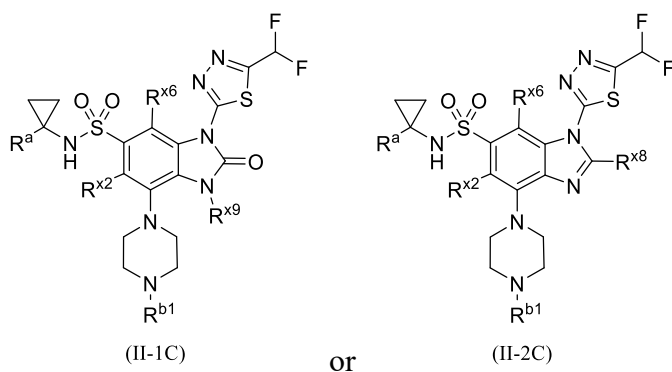
[0440] In some embodiments of the present disclosure, the compound of formula (IA) or
 15 formula (I), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof is a compound of formula (II-1B) or formula (II-2B), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic
 20 derivative thereof:



[0441] wherein

[0442] R^{b1} is R^b; R^b, R^a, R^{x2}, R^{x6}, R^{x8}, and R^{x9} are as defined in any one of the embodiments of the present disclosure.

- 5 [0443] In some embodiments of the present disclosure, the compound of formula (IA) or formula (I), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof is a compound of formula (II-1C) or formula (II-2C), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:
- 10



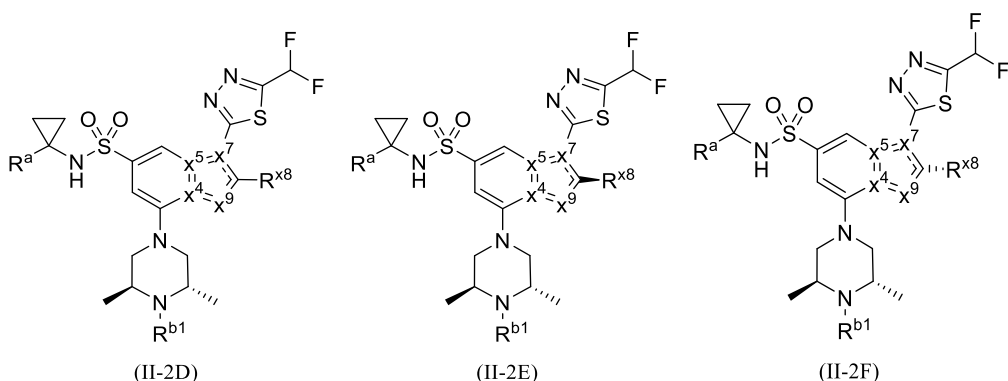
[0444] wherein

[0445] R^{b1} is R^b; R^b, R^a, R^{x2}, R^{x6}, R^{x8}, and R^{x9} are as defined in any one of the embodiments of the present disclosure.

[0446] In some embodiments of the present disclosure, in the compound of formula (II-1B), formula (II-1C), formula (II-2B), or formula (II-2C), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{b1} is R^b , wherein R^b is as defined in any embodiment of formula (IA) or any embodiment of formula (I); preferably, R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$, wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I); more preferably, R^{b1} is selected from the group consisting of hydrogen, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$, wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, 3- to 8-membered heterocyclyl, C_{1-6} haloalkyl, and C_{1-6} hydroxyalkyl;

[0447] R^a , R^{x2} , R^{x6} , R^{x8} , and R^{x9} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0448] In some embodiments of the present disclosure, the compound of formula (IA) or formula (I), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof is a compound of formula (II-2D), formula (II-2E), or formula (II-2F), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:



[0449] wherein

[0450] --- is a single bond or a double bond;

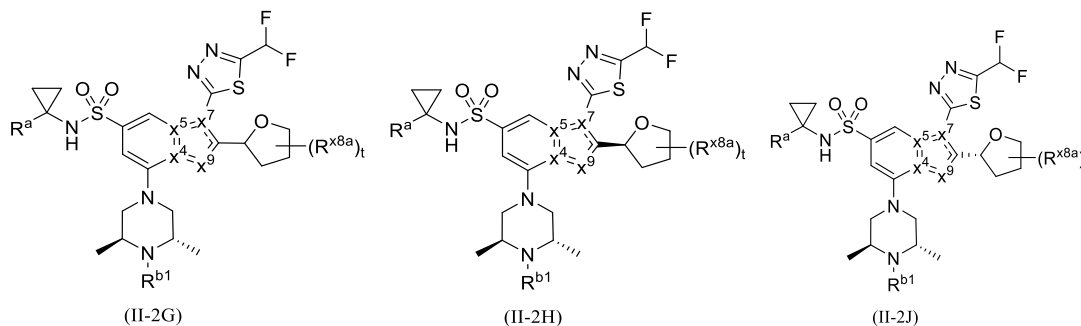
[0451] x^4 , x^5 , x^7 , and x^9 are identical or different, and are each independently selected from
 5 the group consisting of N and C; and the ring containing x^4 , x^5 , x^7 , and x^9 is an aromatic ring;

[0452] R^{x8} is optionally substituted 4- to 7-membered heterocyclyl, preferably optionally substituted 5- to 7-membered heterocyclyl, more preferably optionally substituted 5- to 7-membered oxygen-containing heterocyclyl; wherein the optional substituents are selected from the group consisting of halogen, C_{1-6} alkyl, hydroxyl, -CN, amino, C_{1-6} haloalkyl, and
 10 C_{1-6} hydroxyalkyl;

[0453] R^{b1} is R^b ; R^b and R^a are as defined in any one of the embodiments of the present disclosure.

[0454] In some embodiments of the present disclosure, the compound of formula (IA), formula (I), formula (II-2D), formula (II-2E), or formula (II-2F), the pharmaceutically
 15 acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof is a compound of formula (II-2G), formula (II-2H), or formula (II-2J), a pharmaceutically acceptable salt thereof, a

stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:



[0455] wherein

5 [0456] $\diagup$ is a single bond or a double bond;

[0457] x^4 , x^5 , x^7 , and x^9 are identical or different, and are each independently selected from the group consisting of N and C; and the ring containing x^4 , x^5 , x^7 , and x^9 is an aromatic ring;

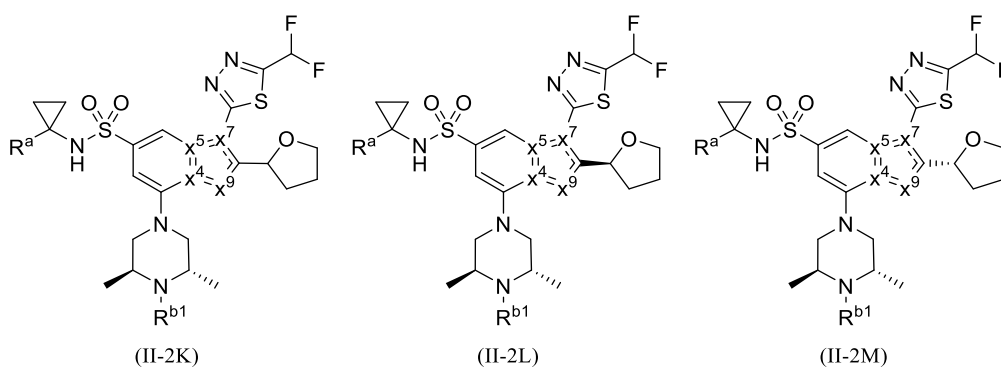
[0458] R^{x8a} is selected from the group consisting of halogen, C_{1-6} alkyl, hydroxyl, -CN, amino, C_{1-6} haloalkyl, and C_{1-6} hydroxyalkyl; alternatively, two R^{x8a} attached to the same
 10 carbon atom, together with the carbon atom to which they are attached, form a 3- to 6-membered cycloalkyl ring; alternatively, two adjacent R^{x8a} , together with the carbon atom to which they are attached, form a 3- to 6-membered cycloalkyl ring;

[0459] t is selected from the group consisting of 0, 1, 2, 3, and 4;

[0460] R^{b1} is R^b ; R^b and R^a are as defined in any one of the embodiments of the present
 15 disclosure.

[0461] In some embodiments of the present disclosure, the compound of formula (IA), formula (I), formula (II-2D), formula (II-2E), formula (II-2F), formula (II-2G), formula (II-2H), or formula (II-2J), the pharmaceutically acceptable salt thereof, the stereoisomer

thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof is a compound of formula (II-2K), formula (II-2L), or formula (II-2M), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:



[0462] wherein

[0463] $\diagup$ is a single bond or a double bond;

[0464] x^4 , x^5 , x^7 , and x^9 are identical or different, and are each independently selected from the group consisting of N and C; and the ring containing x^4 , x^5 , x^7 , and x^9 is an aromatic ring;

10 [0465] R^{b1} is R^b ; R^b and R^a are as defined in any one of the embodiments of the present disclosure.

[0466] In some embodiments of the present disclosure, in the compound of formula (II-2D), formula (II-2G), or formula (II-2K), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, $\diagup$ is a single bond or a double bond; x^4 , x^5 , and x^7 are identical or different, and are each independently selected from the group consisting of N and C; x^9 is selected from the group consisting of N and CH; and the ring containing x^4 , x^5 , x^7 , and x^9 is an aromatic ring;

15

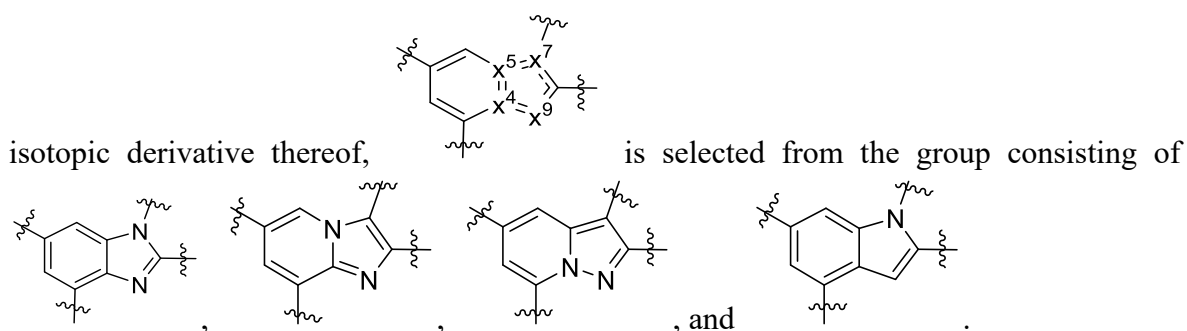
[0467] R^{b1} is R^b ; R^b and R^a are as defined in any one of the embodiments of the present disclosure.

[0468] In some embodiments of the present disclosure, in the compound of formula (II-2D), formula (II-2G), or formula (II-2K), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, x^4 , x^5 , and x^7 are identical or different, and are each independently selected from the group consisting of N and C;

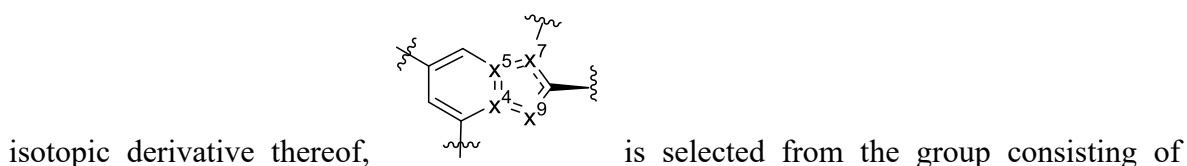
[0469] x^9 is selected from the group consisting of N and CH;

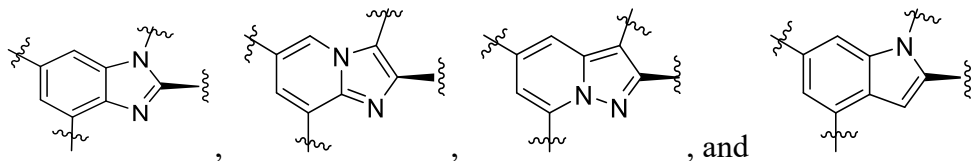
[0470] preferably, the number of N among x^4 , x^5 , x^7 , and x^9 is 1 or 2.

[0471] In some embodiments of the present disclosure, in the compound of formula (II-2D), formula (II-2G), or formula (II-2K), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the

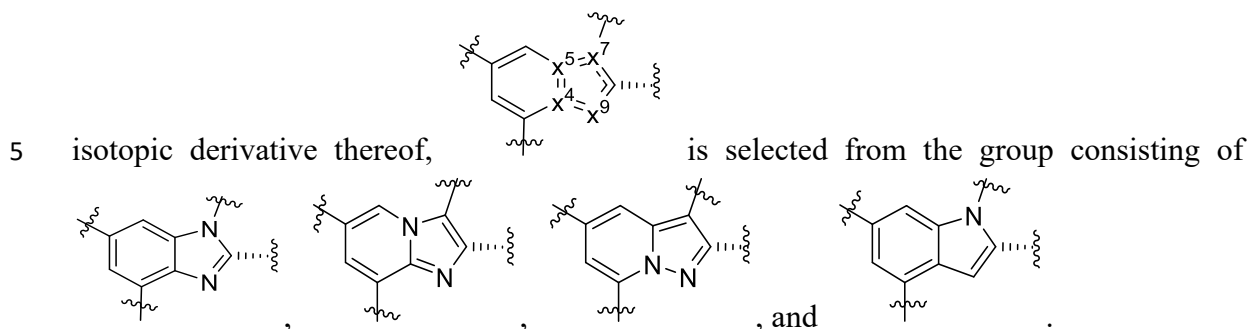


[0472] In some embodiments of the present disclosure, in the compound of formula (II-2E), formula (II-2H), or formula (II-2L), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the





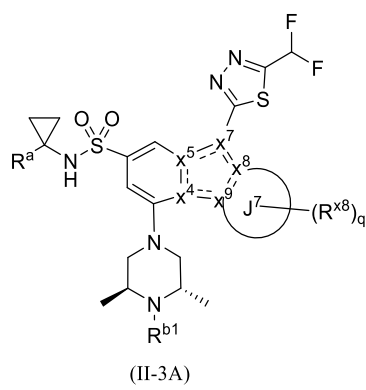
[0473] In some embodiments of the present disclosure, in the compound of formula (II-2F), formula (II-2J), or formula (II-2M), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the



[0474] In some embodiments of the present disclosure, in the compound of formula (II-1B), formula (II-1C), formula (II-2B), or formula (II-2C), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{b1} is R^b , wherein R^b is as defined in any embodiment of formula (IA) or any embodiment of formula (I); preferably, R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$, wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I); R^a , R^{x2} , R^{x6} , R^{x8} , and R^{x9} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0475] In some embodiments of the present disclosure, the compound of formula (IA) or formula (I), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof is

a compound of formula (II-3A), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:



5 [0476] wherein

[0477] $\diagup$ is a single bond or a double bond;

[0478] x^4 , x^5 , x^7 , x^8 , and x^9 are identical or different, and are each independently selected from the group consisting of N and C; and the ring containing x^4 , x^5 , x^7 , x^8 , and x^9 is an aromatic ring;

10 [0479] ring J^7 is selected from the group consisting of 5- to 10-membered heteroaryl and 3- to 8-membered heterocyclyl;

[0480] q is selected from the group consisting of 0, 1, and 2;

[0481] R^{b1} is R^b ; R^b , R^a , and R^{x8} are as defined in any one of the embodiments of the present disclosure.

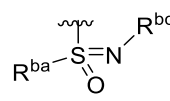
15 [0482] In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, the number of N

among x^4 , x^5 , x^7 , x^8 , and x^9 is 1 or 2.

[0483] In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, ring J^7 is selected
 5 from the group consisting of 5- to 6-membered heteroaryl and 5- to 6-membered heterocyclyl; more preferably, ring J^7 is selected from the group consisting of 5- to 6-membered nitrogen-containing heteroaryl and 5- to 6-membered nitrogen-containing heterocyclyl; further preferably, ring J^7 is 5- to 6-membered nitrogen-containing heteroaryl; most preferably, ring J^7 is 5-membered nitrogen-containing heteroaryl.

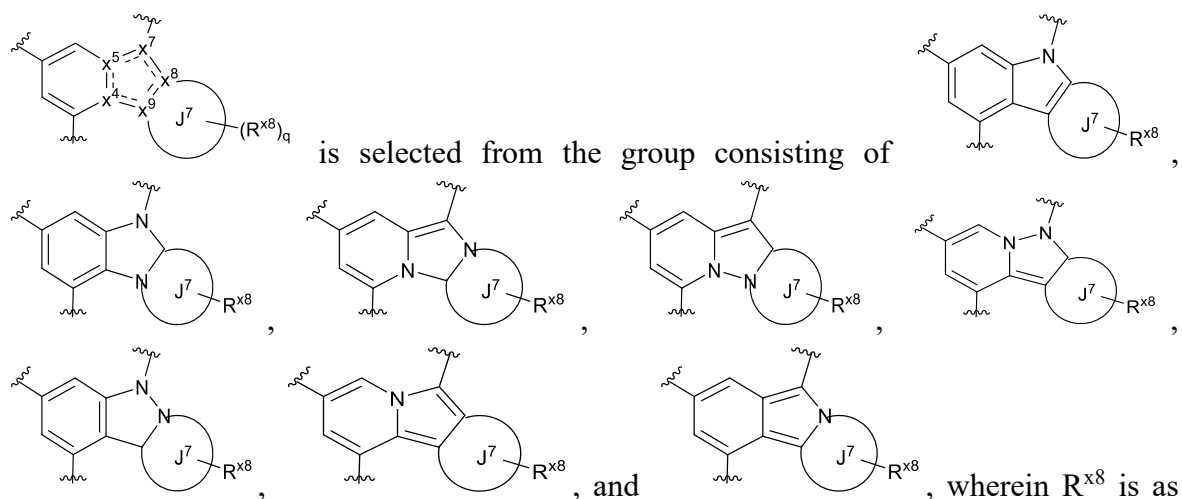
10 **[0484]** In some embodiments of the present disclosure, ring J, ring J^1 , ring J^2 , ring J^3 , ring J^4 , ring J^5 , ring J^6 , ring J^7 , ring K^1 , ring K^2 , and ring K are identical or different, and are each independently a 3- to 7-membered ring, preferably 5- to 10-membered heteroaryl or 3- to 8-membered heterocyclyl, more preferably 5- to 10-membered heteroaryl, further preferably 5- to 6-membered nitrogen-containing heteroaryl, and most preferably 5-membered
 15 nitrogen-containing heteroaryl.

[0485] In some embodiments of the present disclosure, in the compound of formula (II-1A), formula (II-1B), or formula (II-1C), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{b1} is selected from the group consisting of hydrogen, C_{1-6}
 20 hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 5- to 6-membered heteroaryl optionally substituted by C_{1-6} alkyl,


 $\text{S(O)}_2\text{NR}^{\text{bc}}\text{R}^{\text{bf}}$, and $-\text{S(O)}\text{R}^{\text{ba}}$; preferably, R^{bl} is selected from the group consisting of $-\text{S(O)}_2\text{R}^{\text{ba}}$, $-\text{C(O)}\text{R}^{\text{ba}}$, and $-\text{C(O)}\text{NR}^{\text{bc}}\text{R}^{\text{bd}}$, wherein R^{ba} , R^{bb} , R^{bc} , R^{bd} , R^{be} , and R^{bf} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

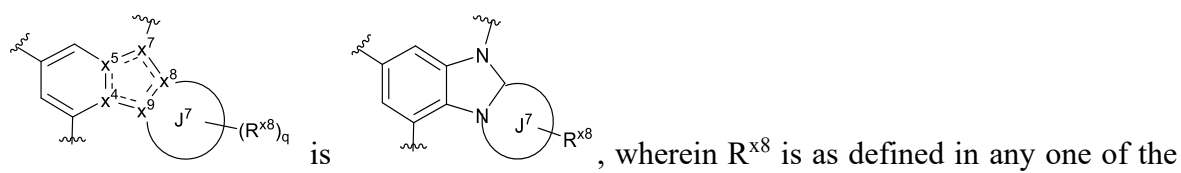
[0486] In some embodiments of the present disclosure, in the compound of formula (II-2A),
 5 formula (II-2B), formula (II-2C), formula (II-2D), formula (II-2E), formula (II-2F), formula (II-2G), formula (II-2H), formula (II-2J), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{bl} is hydrogen.

[0487] In some embodiments of the present disclosure, in the compound of formula (II-3A),
 10 the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,

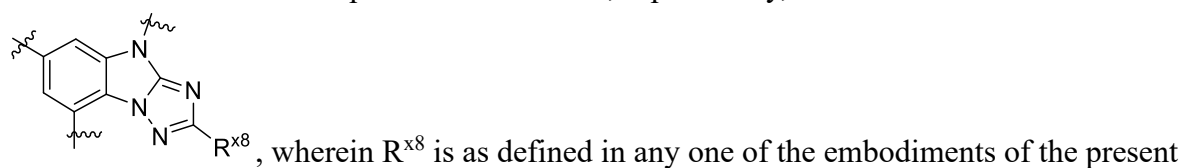


15 defined in any one of the embodiments of the present disclosure.

[0488] In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,



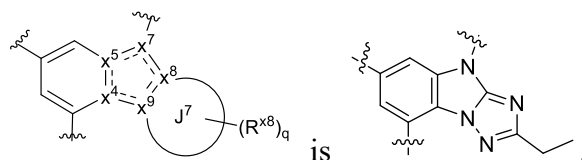
embodiments of the present disclosure; preferably,



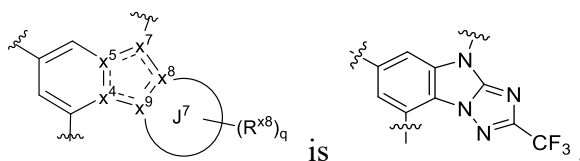
disclosure; more preferably,

5 selected from the group consisting of hydrogen, deuterium, halogen, hydroxyl, amino; C_{1-6} alkyl optionally substituted by one or more substituents selected from the group consisting of halogen and hydroxyl; C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy- C_{1-6} alkyl; and 3- to 8-membered heterocyclyl optionally substituted by one or more substituents selected from the group consisting of halogen and C_{1-6} alkyl.

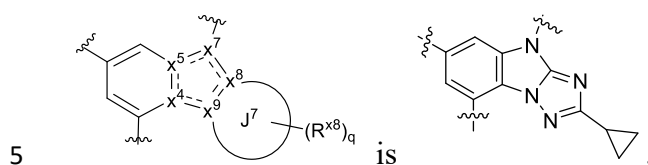
10 **[0489]** In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,



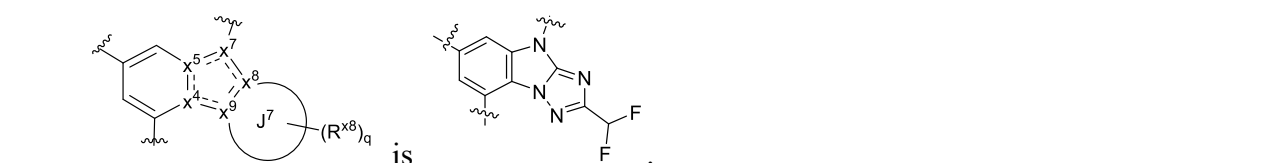
[0490] In some embodiments of the present disclosure, in the compound of formula (II-3A),
 15 the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,



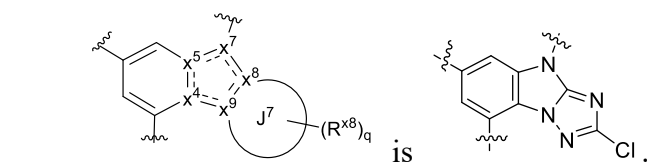
[0491] In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,



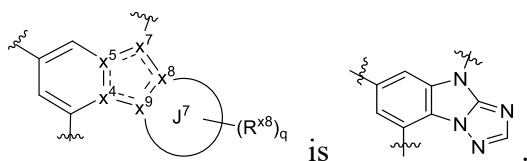
[0492] In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,



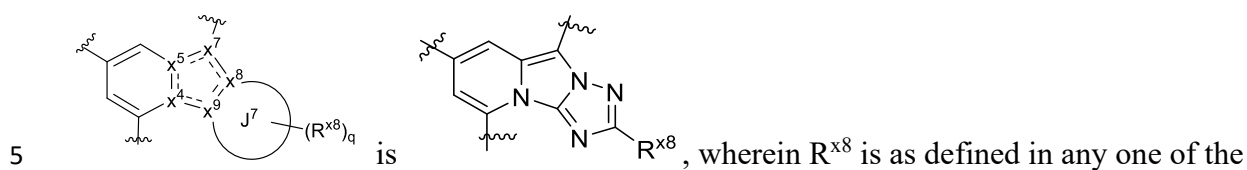
[0493] In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,



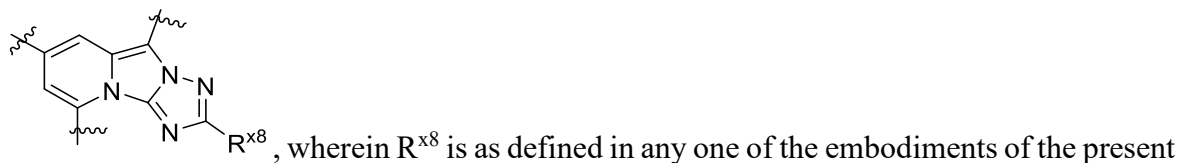
[0494] In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,



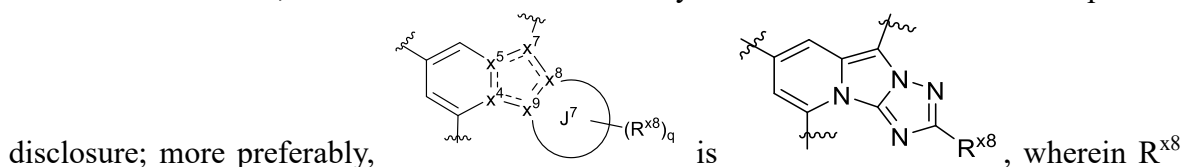
[0495] In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,



embodiments of the present disclosure; preferably,



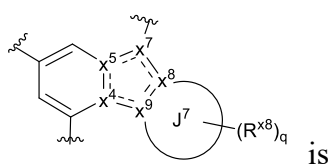
disclosure; more preferably,



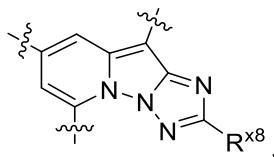
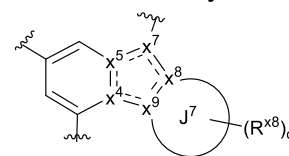
is selected from the group consisting of hydrogen, deuterium, halogen, hydroxyl, amino; C_{1-6} alkyl optionally substituted by one or more substituents selected from the group consisting of halogen and hydroxyl; C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy- C_{1-6} alkyl; and 3- to 8-membered heterocyclyl optionally substituted by one or more substituents selected from the group consisting of halogen and C_{1-6} alkyl.

[0496] In some embodiments of the present disclosure, in the compound of formula (II-3A),

15 the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,

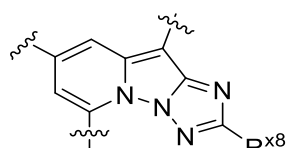
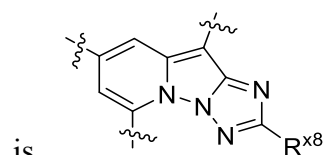
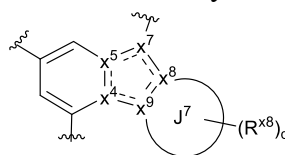


is

, wherein R^{x8} is as defined in any one of the

is

embodiments of the present disclosure; preferably,

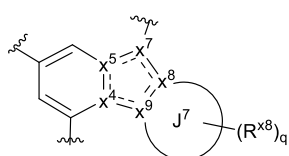
, wherein R^{x8} is as defined in any one of the embodiments of the

present disclosure; more preferably,

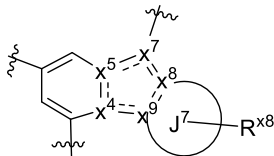
is

- 5 wherein R^{x8} is selected from the group consisting of hydrogen, deuterium, halogen, hydroxyl, amino; C_{1-6} alkyl optionally substituted by one or more substituents selected from the group consisting of halogen and hydroxyl; C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy- C_{1-6} alkyl; and 3- to 8-membered heterocyclyl optionally substituted by one or more substituents selected from the group consisting of halogen and C_{1-6} alkyl.

- 10 **[0497]** In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,



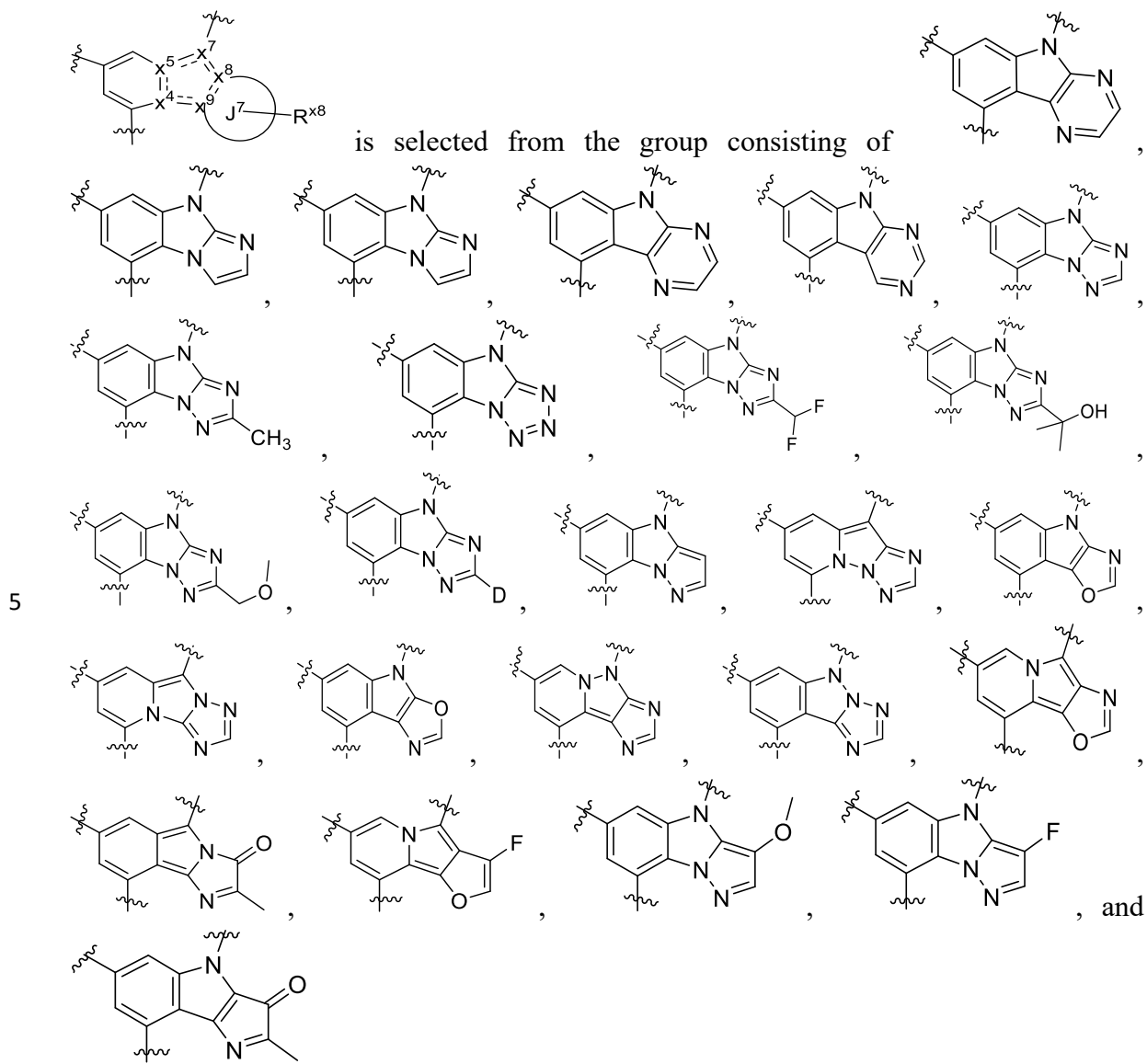
is

, wherein R^{x8} is as defined in any one of the

embodiments of the present disclosure.

- 15 **[0498]** In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof,

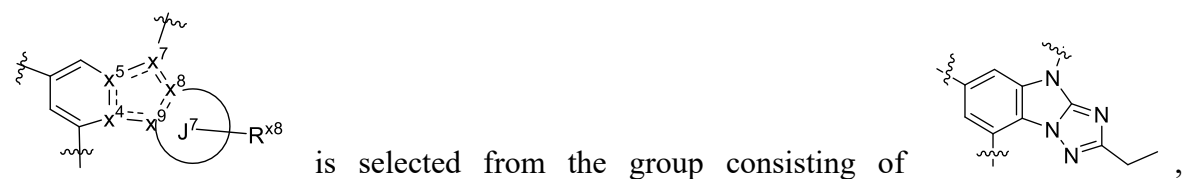
the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,

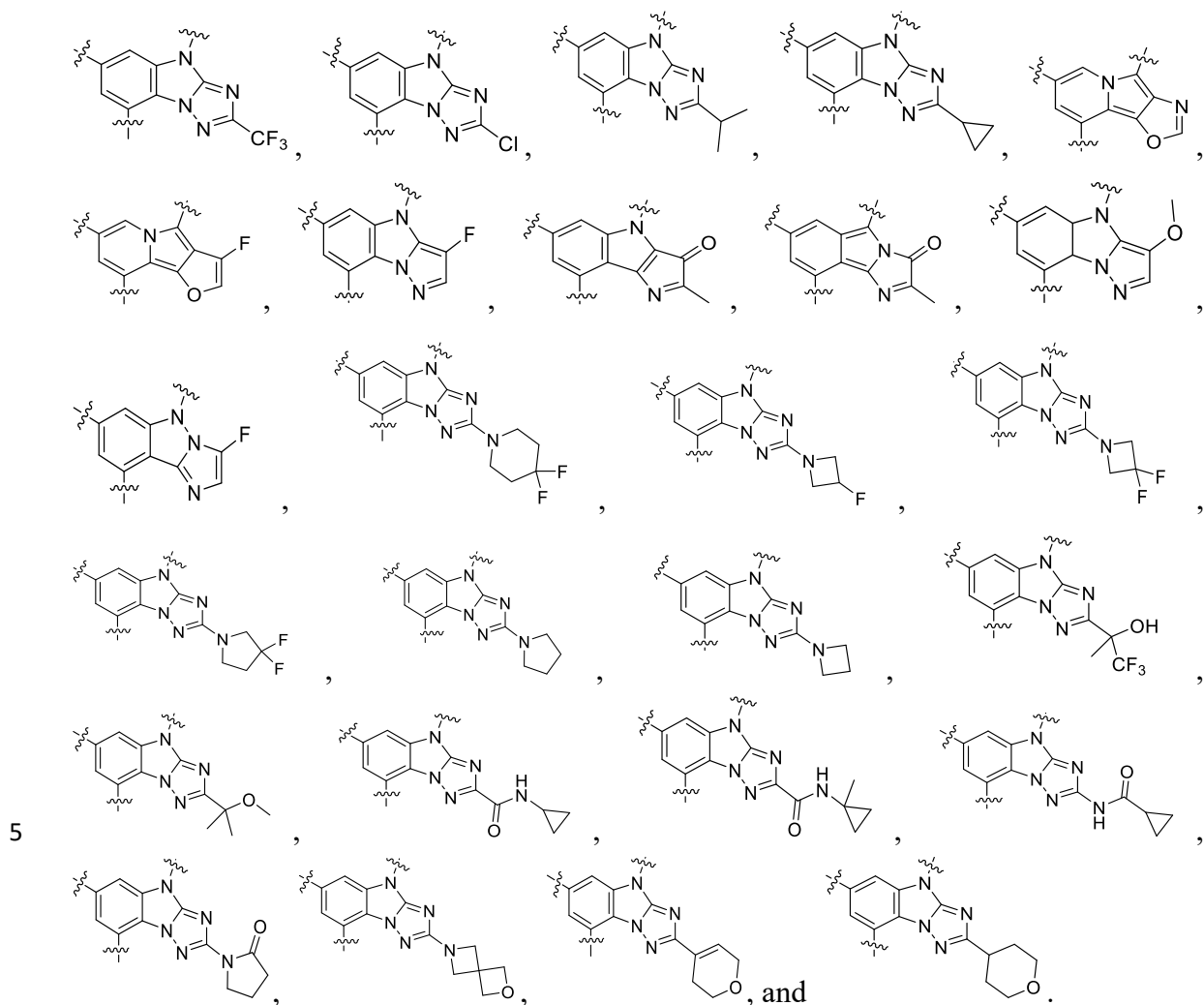


[0499] In some embodiments of the present disclosure, in the compound of formula (II-3A),

the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof,

the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof,





[0500] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (II-1A), formula (II-1B), formula (II-2A), formula (II-2B), formula (II-1C), formula (II-2C), formula (II-3A), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), or formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is -CD₃.

15 [0501] In some embodiments of the present disclosure, in the compound of formula (IA),

formula (I), formula (II), formula (II-1A), formula (II-1B), formula (II-2A), formula (II-2B), formula (II-1C), formula (II-2C), formula (II-3A), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), or formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of hydrogen, cyano, formyl, -CONH₂, -CH₂OH, -CH₂OC₁₋₄ alkyl, C₁₋₄ alkyl, C₁₋₄ haloalkyl, and C₂₋₆ haloalkenyl; preferably, R^a is selected from the group consisting of -CH₃, -CH₂F, -CN, and -CH₂=CHF.

[0502] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (II-1A), formula (II-1B), formula (II-2A), formula (II-2B), formula (II-1C), formula (II-2C), formula (II-3A), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), or formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of -CH₃, -CH₂F, and -CN.

[0503] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (II-1A), formula (II-1B), formula (II-2A), formula (II-2B), formula (II-1C), formula (II-2C), formula (II-3A), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-

4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), or formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of -CHF₂ and -CHF₃.

5 **[0504]** In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula
10 (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, each R^b is identical or different, and is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, -C(O)R^{ba}, -C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd}; wherein R^{ba}, R^{bb}, R^{bc}, and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment
15 of formula (I); preferably, each R^b is identical or different, and is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, -C(O)R^{ba}, and -C(O)NR^{bc}R^{bd}; wherein R^{ba}, R^{bc}, and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

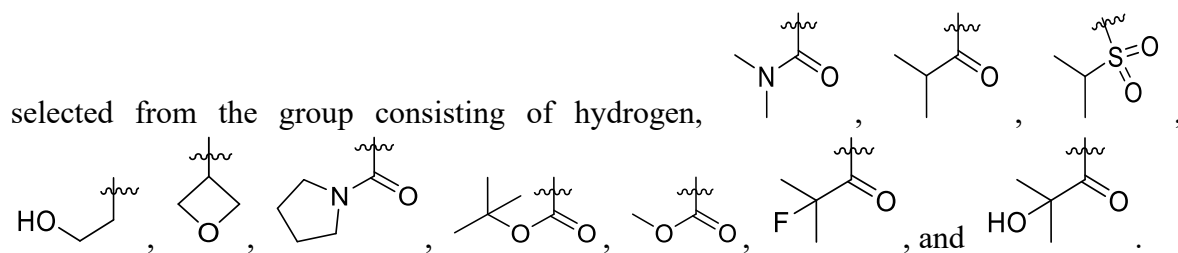
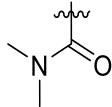
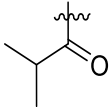
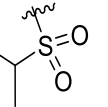
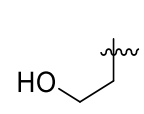
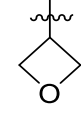
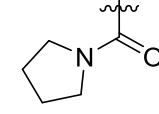
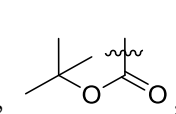
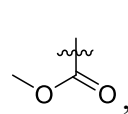
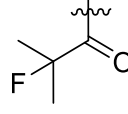
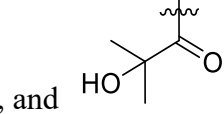
[0505] In some embodiments of the present disclosure, in the compound of formula (IA),
20 formula (I), formula (II), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A),

formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^b and R^{b1} are each identical or different, and are each independently selected from the group consisting of C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, and $-S(O)_2R^{ba}$; wherein R^{ba} is as defined in any embodiment of formula (IA) or any embodiment of formula (I); preferably, R^b and R^{b1} are each identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, and $-S(O)_2R^{ba}$; wherein R^{ba} is selected from the group consisting of hydrogen, C_{1-6} alkyl, 3- to 8-membered heterocyclyl, C_{1-6} haloalkyl, and C_{1-6} hydroxyalkyl.

[0506] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^b and R^{b1} are each identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)OR^{bb}$, $-C(O)R^{ba}$, $-C(O)NR^{bc}R^{bd}$, and 5- to 6-

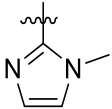
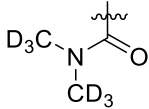
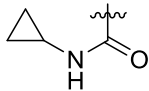
membered heteroaryl optionally substituted by C₁₋₆ alkyl; wherein R^{ba}, R^{bb}, R^{bc}, and R^{bd} are identical or different, and are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, 3- to 8-membered heterocyclyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ deuterioalkyl, and 3- to 8-membered cycloalkyl.

5 **[0507]** In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula
10 (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^b and R^{bl} are each identical or different, and are each independently

selected from the group consisting of hydrogen, , , , , , , , , , , and .

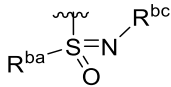
15 **[0508]** In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula
20 (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer

thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^b and R^{b1} are each identical or different, and are each independently

selected from the group consisting of , , and .

[0509] In some embodiments of the present disclosure, in the compound of formula (IA),

5 formula (I), formula (II), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer
10 thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^b and R^{b1} are each identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 5- to 6-membered

heteroaryl optionally substituted by C_{1-6} alkyl, , $S(O)_2NR^{be}R^{bf}$, and $-S(O)R^{ba}$;

15 wherein R^{ba} , R^{bb} , R^{bc} , R^{bd} , R^{be} , and R^{bf} are as defined in any one of the embodiments of the present disclosure.

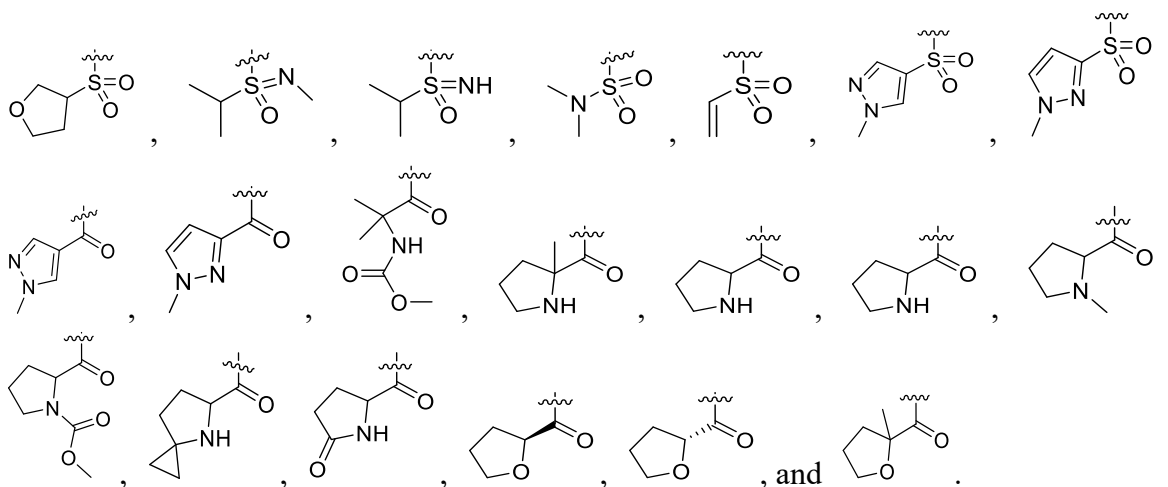
[0510] In some embodiments of the present disclosure, in the compound of formula (IA),

formula (I), formula (II), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A),
20 formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A),

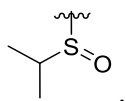
formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{b2} and R^{b3} are identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl; preferably, R^{b2} and R^{b3} are identical or different, and are each independently selected from the group consisting of hydrogen, methyl, vinyl, and ethynyl.

[0511] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^b and R^{b1} are each identical or different, and are each independently

[illegible]



[0512] In some embodiments of the present disclosure, in the compound of formula (IA),
 5 formula (I), formula (II), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A),
 formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A),
 formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A),
 formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula
 (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer
 10 thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic
 derivative thereof, R^b and R^{b1} are each identical or different, and are each independently



[0513] In some embodiments of the present disclosure, in the compound of formula (IA),
 formula (I), formula (II), formula (II-1A), formula (II-1B), formula (II-2A), formula (II-2B),
 15 formula (II-1C), formula (II-2C), formula (II-3A), formula (I-1), formula (I-1A), formula (I-
 2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-
 4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-
 6), or formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof,

the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, each R^b is identical or different, and is independently selected from the group consisting of hydrogen, C_{1-6} alkyl, $-C(O)R^{ba}$, and $-C(O)NR^{bc}R^{bd}$; wherein R^{ba} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

5 **[0514]** In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-5), formula (I-5A), formula (I-6), or formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the
10 isotopic derivative thereof, x^2 is selected from the group consisting of N and CR^{x2} ; wherein R^{x2} is selected from the group consisting of H, halogen, and C_{1-6} alkyl, preferably H, Cl, F, and CH_3 .

[0515] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula
15 (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), or formula (II-2B), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x2} is selected from the group consisting of H,
20 halogen, and C_{1-6} alkyl, preferably H, Cl, F, and CH_3 .

[0516] In some embodiments of the present disclosure, in the compound of formula (IA),

formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-5), formula (I-5A), formula (I-6), or formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x2} is selected from the group consisting of H, Cl, F, and CH_3 .

[0517] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), or formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, x^6 is selected from the group consisting of N and CR^{x6} ; wherein R^{x6} is selected from the group consisting of H, halogen, and C_{1-6} alkyl, preferably H, Cl, F, and CH_3 .

[0518] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), or formula (II-2B), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x6} is selected from the group consisting of H, halogen, and C_{1-6} alkyl, preferably H, Cl, F, or CH_3 .

[0519] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-4), formula (I-4A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-2A), or formula (II-2B), the
 5 pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x6} is selected from the group consisting of H, Cl, F, and CH_3 .

[0520] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), or formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, x^9 is selected from the group consisting of N, NR^{x9} , CR^{x9} , and $CR^{x9}R^{x9}$; wherein R^{x9} , at each
 10 occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, and C_{1-6} alkyl, preferably H, Cl, F, and CH_3 ; alternatively, two R^{x9} attached to the same carbon atom, together with the atom to which they are attached, form a C_{3-6} cycloalkyl ring, wherein the C_{3-6} cycloalkyl is preferably cyclopropyl.

[0521] In some embodiments of the present disclosure, in the compound of formula (IA),
 20 formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula

(I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), or formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, x^9 is O.

5 **[0522]** In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (I-a), formula (II-1A), formula (II-1C), or formula (II-1B), the
10 pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x9} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, and C_{1-6} alkyl, preferably H, Cl, F, CH_3 , and $CH(CH_3)_2$.

[0523] In some embodiments of the present disclosure, in the compound of formula (IA),
15 formula (I), formula (II), formula (I-1), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (I-a), formula (II-1A), formula (II-1C), or formula (II-1B), the
pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the
20 N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x9} , at each occurrence, is identical or different, and is independently selected from the group consisting

of ethyl, cyclopropyl, and $-\text{CH}_2\text{CF}_3$.

[0524] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (I-a), formula (II-1A), formula (II-1C), or formula (II-1B), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, $\text{R}^{\text{x}9}$, at each occurrence, is identical or different, and is independently .

[0525] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1C), or formula (II-1B), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, $\text{R}^{\text{x}9}$, at each occurrence, is identical or different, and is independently selected from the group consisting of H, Cl, F, and CH_3 .

[0526] In some embodiments of the present disclosure, in the above formula containing two $\text{R}^{\text{x}9}$, two $\text{R}^{\text{x}9}$ attached to the same carbon atom, together with the atom to which they are attached, form a 3- to 6-membered cycloalkyl ring, wherein the 3- to 6-membered cycloalkyl is preferably cyclopropyl.

[0527] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), or
 5 formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, x^8 is selected from the group consisting of N, NR^{x8} , CR^{x8} , and $CR^{x8}R^{x8}$; wherein R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, amino, $C\equiv CH$, CN, and C_{1-6} alkyl.

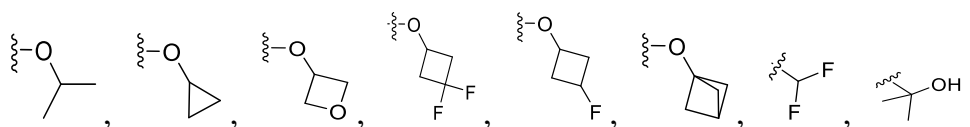
[0528] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), or formula (I-5A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof,
 10 the solvate thereof, or the isotopic derivative thereof, x^8 is C(=O).

[0529] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula
 20 (I-6A), formula (II-2A), formula (II-2C), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the

N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, amino, $C\equiv CH$, CN, and C_{1-6} alkyl.

[0530] In some embodiments of the present disclosure, in the compound of formula (IA),
 5 formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-2A), formula (II-2C), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the
 10 N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of methyl, amino, and methoxy.

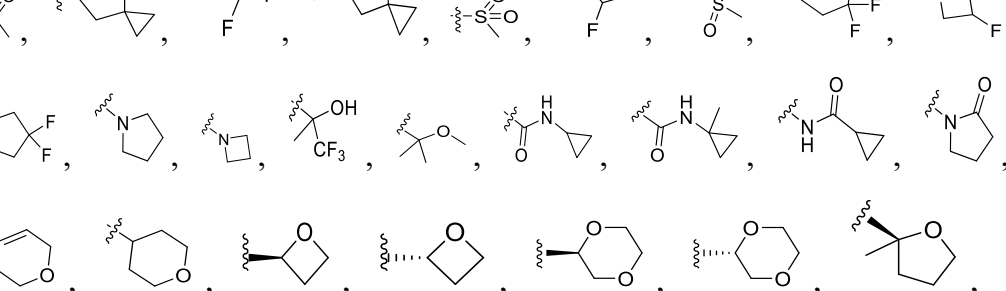
[0531] In some embodiments of the present disclosure, in the compound of formula (IA),
 formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula
 15 (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-2A), formula (II-2C), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the
 N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x8} , at each
 20 occurrence, is identical or different, and is independently selected from the group consisting

of deuterium, 

formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-2A), formula (II-2C), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the

of oxo, Cl, F, ethyl, trifluoromethyl, isopropyl, cyclopropyl,

15



[0533] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-2A), formula (II-2C), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of hydrogen, deuterium, oxo, halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy- C_{1-6} alkyl, $-NHC(O)R^{ba}$, $-OR^f$, $-C(O)R^{ba}$, $-S(O)_2R^{ba}$, $-N=S(O)R^{ba}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered heterocyclyl, and 5- to 10-membered heteroaryl; wherein the C_{1-6} alkyl, 3- to 8-membered heterocyclyl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, hydroxyl, and C_{1-6} alkyl; R^f , R^{ba} , R^{bc} , and R^{bd} are as defined in any one of the embodiments of the present disclosure.

[0534] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-2A), formula (II-2C), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the

N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x8} , at each occurrence, is identical or different, and is independently 3- to 8-membered heterocyclyl optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, hydroxyl, C_{1-6} hydroxyalkyl, and C_{1-6} haloalkyl, preferably 5- to 6-membered heterocyclyl optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, hydroxyl, C_{1-6} hydroxyalkyl, and C_{1-6} haloalkyl, more preferably 5- to 6-membered oxygen-containing heterocyclyl optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, hydroxyl, C_{1-6} hydroxyalkyl, and C_{1-6} haloalkyl, further preferably 5-membered oxygen-containing heterocyclyl optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, hydroxyl, C_{1-6} hydroxyalkyl, and C_{1-6} haloalkyl, further preferably tetrahydrofuranyl optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, hydroxyl, C_{1-6} hydroxyalkyl, and C_{1-6} haloalkyl, and most preferably tetrahydrofuranyl. In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-2A), formula (II-2C), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x8} , at each occurrence, is identical or different, and is independently

selected from the group consisting of hydrogen, deuterium, oxo, halogen, hydroxyl, amino; C₁₋₆ alkyl optionally substituted by one or more substituents selected from the group consisting of halogen and hydroxyl; C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkoxy-C₁₋₆ alkyl; and 3- to 8-membered heterocyclyl optionally substituted by one or more substituents
5 selected from the group consisting of halogen and C₁₋₆ alkyl.

[0535] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula
10 (I-6A), formula (II-2A), formula (II-2C), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^f, at each occurrence, is identical or different, and is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl; 3- to 6-membered cycloalkyl optionally
15 substituted by one or more substituents selected from the group consisting of halogen and C₁₋₆ alkyl; and 3- to 6-membered heterocyclyl optionally substituted by one or more substituents selected from the group consisting of halogen and C₁₋₆ alkyl.

[0536] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-a), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula
20 (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), or

formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x8} and R^{x9} , together with the atom to which they are attached, form a 3- to 7-membered ring, wherein the 3- to 7-membered ring is selected from the group consisting of 3- to 7-membered heterocyclyl, C_{3-7} cycloalkyl, C_{3-7} carbocyclyl, and 5- to 6-membered heteroaryl; wherein preferably, the 5- to 6-membered heteroaryl is furyl.

[0537] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-a), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), or formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x8} and R^{x9} , together with the atom to which they are attached, form a pyrazinyl ring.

[0538] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-a), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), or formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{x8} and R^{x9} , together with the atom to which they are attached, form a 5-membered nitrogen-containing heteroaryl ring.

[0539] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-a), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), or
 5 formula (I-6A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, Rx8 and Rx9, together with the atom to which they are attached, form a 6-membered nitrogen-containing heteroaryl ring.

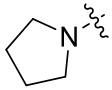
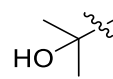
[0540] In some embodiments of the present disclosure, in the compound of formula (IA),
 10 formula (I), formula (II), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer
 15 thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{ba} is selected from the group consisting of hydrogen, C₁₋₆ alkyl, 3- to 8-membered heterocyclyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ deuterioalkyl, 3- to 8-membered cycloalkyl, C₂₋₆ alkenyl, and 5- to 6-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered heterocyclyl, 3- to 8-membered cycloalkyl, and 5- to 6-membered
 20 heteroaryl are optionally substituted by one or more substituents selected from the group consisting of C₁₋₆ alkyl, halogen, C₁₋₆ deuterioalkyl, C₁₋₆ haloalkyl, hydroxyl, C₁₋₆ alkoxy, C₁₋

deuteroalkoxy, $-C(O)OR^{bb1}$, and $-NR^{a1}R^{a2}$; R^{bb1} , R^{a1} , and R^{a2} are as defined in any one of the embodiments of the present disclosure.

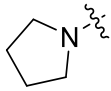
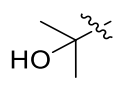
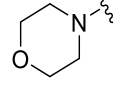
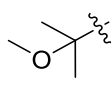
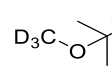
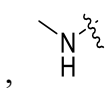
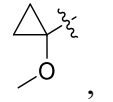
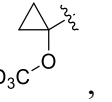
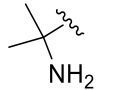
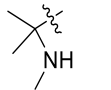
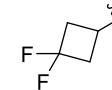
[0541] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{bc} and R^{bd} are identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} deuteroalkyl, and 3- to 8-membered cycloalkyl.

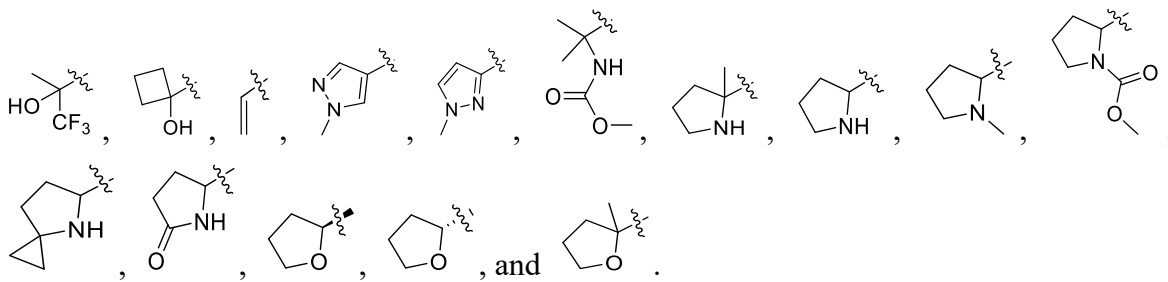
[0542] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-4), formula (I-4A), formula (I-4'), formula (I-4'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{a1} , R^{a2} , R^{bb} , and R^{bb1} are identical or different, and are each independently selected from the group consisting of hydrogen and C_{1-6} alkyl.

[0543] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C),
 5 formula (II-2C), formula (II-2A), or formula (II-2B), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{ba} , R^{bb} , R^{bc} , and R^{bd} are identical or different, and are each independently selected from the group consisting of hydrogen, methyl, $-CD_3$,

isopropyl, *tert*-butyl, , , , and .

10 **[0544]** In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula (II-2B), or formula (II-3A), the pharmaceutically
 15 acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{ba} is selected from the group

consisting of hydrogen, isopropyl, *tert*-butyl, methoxy, *tert*-butoxy, , ,
, , , , , , , , ,
, , , , , , , , , ,



[0545] In some embodiments of the present disclosure, in the compound of formula (IA),
formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula
5 (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-5), formula
(I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C),
formula (II-2C), formula (II-2A), formula (II-2B), or formula (II-3A), the pharmaceutically
acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof,
the solvate thereof, or the isotopic derivative thereof, R^{bc} and R^{bd} are identical or different,
10 and are each independently selected from the group consisting of hydrogen, methyl, -CD₃,
isopropyl, *tert*-butyl, and .

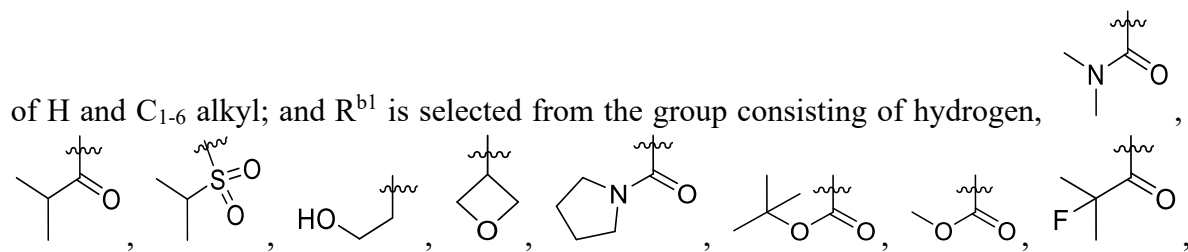
[0546] In some embodiments of the present disclosure, in the compound of formula (IA), formula (I), formula (II), formula (I-a), formula (I-1), formula (I-1A), formula (I-2), formula (I-2A), formula (I-3), formula (I-3A), formula (I-3'), formula (I-3'A), formula (I-5), formula (I-5A), formula (I-6), formula (I-6A), formula (II-1A), formula (II-1B), formula (II-1C), formula (II-2C), formula (II-2A), formula (II-2B), or formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^{be} and R^{bf} are identical or different, and are each independently selected from the group consisting of hydrogen, methyl, and isopropyl.

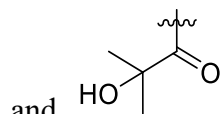
[0547] In some embodiments of the present disclosure, in the compound of formula (II-1A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of -CH₃, -CH₂F, -CN, -CH₂=CHF, -CHF₂, and -CHF₃; R^{x2} is H; R^{x6} is H; R^{x9}, at each occurrence, is identical or different, and is independently selected from the group consisting of methyl, ethyl, isopropyl, cyclopropyl, and -CH₂CF₃; and R^{b1} is selected from the group consisting of hydrogen, C₁₋₆ hydroxyalkyl, 3- to 8-membered heterocyclyl, -S(O)₂R^{ba}, -C(O)R^{ba}, -C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd}; wherein R^{ba}, R^{bb}, R^{bc}, and R^{bd} are identical or different, and are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ deuterioalkyl, 3- to 8-membered heterocyclyl, 3- to 8-membered cycloalkyl, C₁₋₆ haloalkyl, and C₁₋₆ hydroxyalkyl; R^{b2} and R^{b3} are both H.

[0548] In some embodiments of the present disclosure, in the compound of formula (II-1A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of -CH₃, -CH₂F, -CN, and -CH₂=CHF; R^{x2} is selected from the group consisting of H, halogen, and C₁₋₆ alkyl; R^{x6} is selected from the group consisting of H, halogen, and C₁₋₆ alkyl; R^{x9}, at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, and C₁₋₆ alkyl; and R^{b1} is selected from the group consisting of hydrogen, C₁₋₆ alkyl, -C(O)R^{ba}, -C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd}; R^{b2} and R^{b3} are identical, and are both C₁₋₆ alkyl; wherein R^{ba}, R^{bb}, R^{bc}, and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0549] In some embodiments of the present disclosure, in the compound of formula (II-1A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of $-CH_3$, $-CH_2F$, $-CN$, and $-CH_2=CHF$; R^{x2} is H; R^{x6} is H; R^{x9} , at each
 5 occurrence, is identical or different, and is independently selected from the group consisting of H and C_{1-6} alkyl; and R^{b1} is selected from the group consisting of hydrogen, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, 3- to 8-membered
 10 heterocyclyl, C_{1-6} haloalkyl, and C_{1-6} hydroxyalkyl; R^{b2} and R^{b3} are identical or different, and are each independently selected from the group consisting of H and C_{1-6} alkyl.

[0550] In some embodiments of the present disclosure, in the compound of formula (II-1A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from
 15 the group consisting of $-CH_3$, $-CH_2F$, $-CN$, and $-CH_2=CHF$; R^{x2} is H; R^{x6} is H; R^{x9} , at each occurrence, is identical or different, and is independently selected from the group consisting



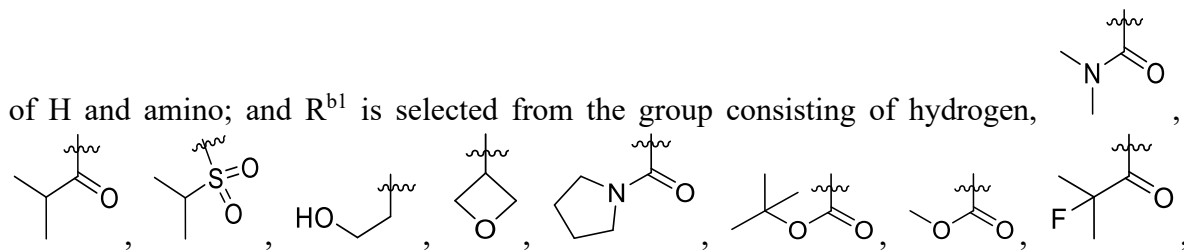
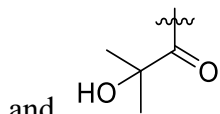
and  ; R^{b2} and R^{b3} are identical, and are both selected from the group consisting
 20 of H and methyl.

[0551] In some embodiments of the present disclosure, in the compound of formula (II-2A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of $-CH_3$, $-CH_2F$, $-CN$, and $-CH_2=CHF$; R^{x2} is selected from the group consisting of H, halogen, and C_{1-6} alkyl; R^{x6} is selected from the group consisting of H, halogen, and C_{1-6} alkyl; R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, amino, $C\equiv CH$, CN , and C_{1-6} alkyl; and R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; R^{b2} and R^{b3} are identical, and are both C_{1-6} alkyl; wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0552] In some embodiments of the present disclosure, in the compound of formula (II-2A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of $-CH_3$, $-CH_2F$, $-CN$, and $-CH_2=CHF$; R^{x2} is H; R^{x6} is H; R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, amino, $C\equiv CH$, CN , and C_{1-6} alkyl; and R^{b1} is selected from the group consisting of hydrogen, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, 3- to 8-membered heterocyclyl, C_{1-6} haloalkyl, and C_{1-6} hydroxyalkyl; R^{b2} and R^{b3} are identical or different, and are each independently selected from the group consisting of H

and C₁₋₆ alkyl.

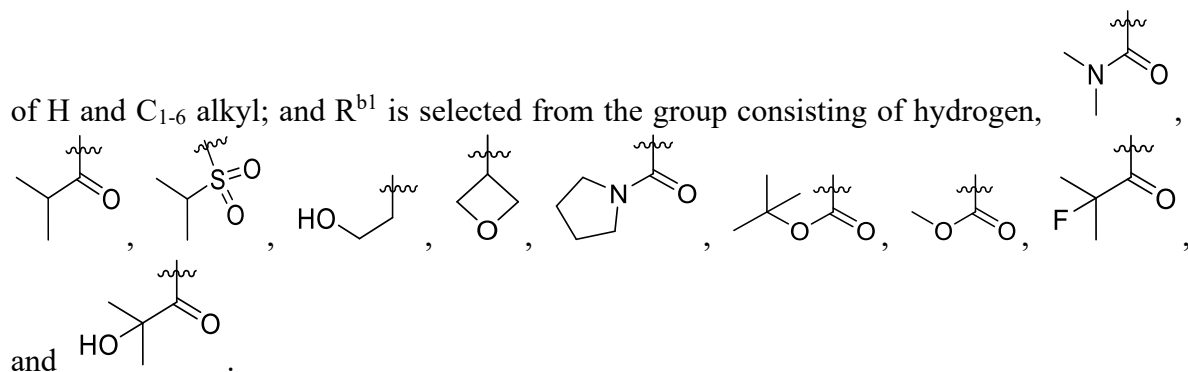
[0553] In some embodiments of the present disclosure, in the compound of formula (II-2A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of -CH₃, -CH₂F, -CN, and -CH₂=CHF; R^{x2} is H; R^{x6} is H; R^{x8}, at each occurrence, is identical or different, and is independently selected from the group consisting

of H and amino; and R^{b1} is selected from the group consisting of hydrogen, , and ; R^{b2} and R^{b3} are identical, and are both selected from the group consisting of H and methyl.

[0554] In some embodiments of the present disclosure, in the compound of formula (II-1B), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of -CH₃, -CH₂F, -CN, and -CH₂=CHF; R^{x2} is selected from the group consisting of H, halogen, and C₁₋₆ alkyl; R^{x6} is selected from the group consisting of H, halogen, and C₁₋₆ alkyl; R^{x9}, at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, and C₁₋₆ alkyl; and R^{b1} is selected from the group consisting of hydrogen, C₁₋₆ alkyl, -C(O)R^{ba}, -C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd}; wherein R^{ba}, R^{bb}, R^{bc}, and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

[0555] In some embodiments of the present disclosure, in the compound of formula (II-1B), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of $-CH_3$, $-CH_2F$, $-CN$, and $-CH_2=CHF$; R^{x2} is H; R^{x6} is H; R^{x9} , at each
 5 occurrence, is identical or different, and is independently selected from the group consisting of H and C_{1-6} alkyl; and R^{b1} is selected from the group consisting of hydrogen, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, 3- to 8-membered
 10 heterocyclyl, C_{1-6} haloalkyl, and C_{1-6} hydroxyalkyl.

[0556] In some embodiments of the present disclosure, in the compound of formula (II-1B), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of $-CH_3$, $-CH_2F$, $-CN$, and $-CH_2=CHF$; R^{x2} is H; R^{x6} is H; R^{x9} , at each
 15 occurrence, is identical or different, and is independently selected from the group consisting



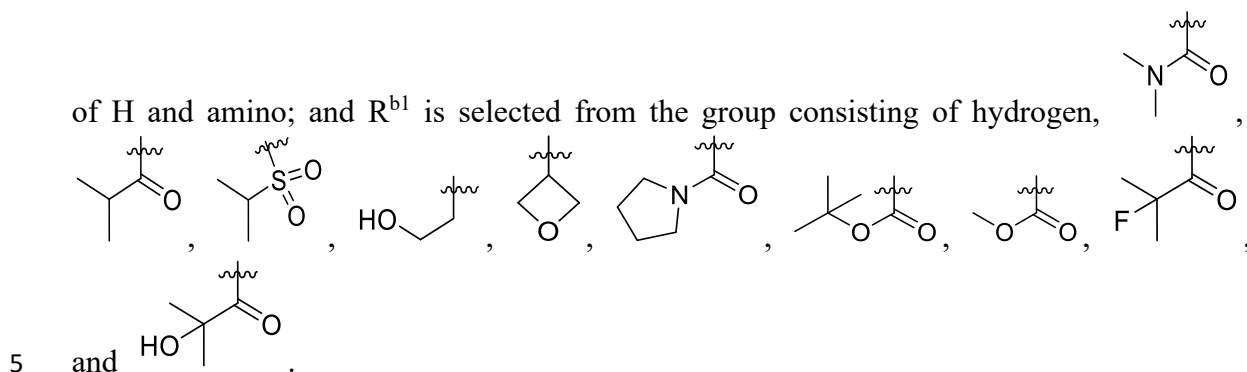
[0557] In some embodiments of the present disclosure, in the compound of formula (II-2B),
 20 the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof,

the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of $-CH_3$, $-CH_2F$, $-CN$, and $-CH_2=CHF$; R^{x2} is selected from the group consisting of H, halogen, and C_{1-6} alkyl; R^{x6} is selected from the group consisting of H, halogen, and C_{1-6} alkyl; R^{x8} , at each occurrence, is identical or different, and is independently
 5 selected from the group consisting of H, halogen, amino, $C\equiv CH$, CN , and C_{1-6} alkyl; and R^{b1} is selected from the group consisting of hydrogen, C_{1-6} alkyl, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are as defined in any embodiment of formula (IA) or any embodiment of formula (I).

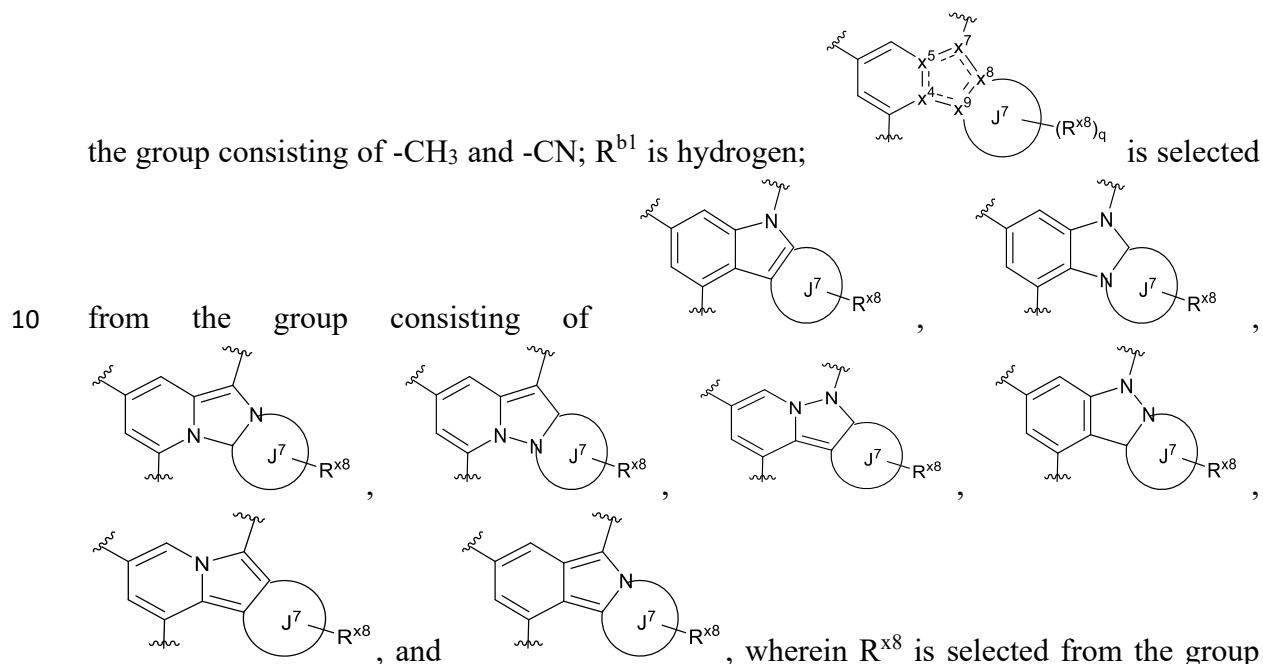
[0558] In some embodiments of the present disclosure, in the compound of formula (II-2B),
 10 the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from the group consisting of $-CH_3$, $-CH_2F$, $-CN$, and $-CH_2=CHF$; R^{x2} is H; R^{x6} is H; R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, halogen, amino, $C\equiv CH$, CN , and C_{1-6} alkyl; and R^{b1} is selected from the group
 15 consisting of hydrogen, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; wherein R^{ba} , R^{bb} , R^{bc} , and R^{bd} are identical or different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, 3- to 8-membered heterocyclyl, C_{1-6} haloalkyl, and C_{1-6} hydroxyalkyl.

[0559] In some embodiments of the present disclosure, in the compound of formula (II-2B),
 20 the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from

the group consisting of -CH₃, -CH₂F, -CN, and -CH₂=CHF; R^{x2} is H; R^{x6} is H; R^{x8}, at each occurrence, is identical or different, and is independently selected from the group consisting



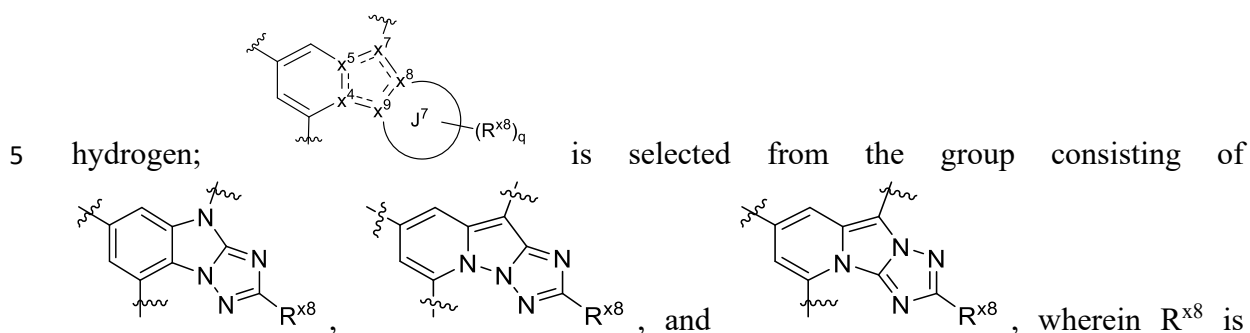
[0560] In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is selected from



consisting of hydrogen, deuterium, halogen, hydroxyl, amino; C₁₋₆ alkyl optionally substituted by one or more substituents selected from the group consisting of halogen and hydroxyl; C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkoxy-C₁₋₆ alkyl; and 3- to 8-membered heterocyclyl optionally substituted by one or more substituents selected from the group

consisting of halogen and C₁₋₆ alkyl.

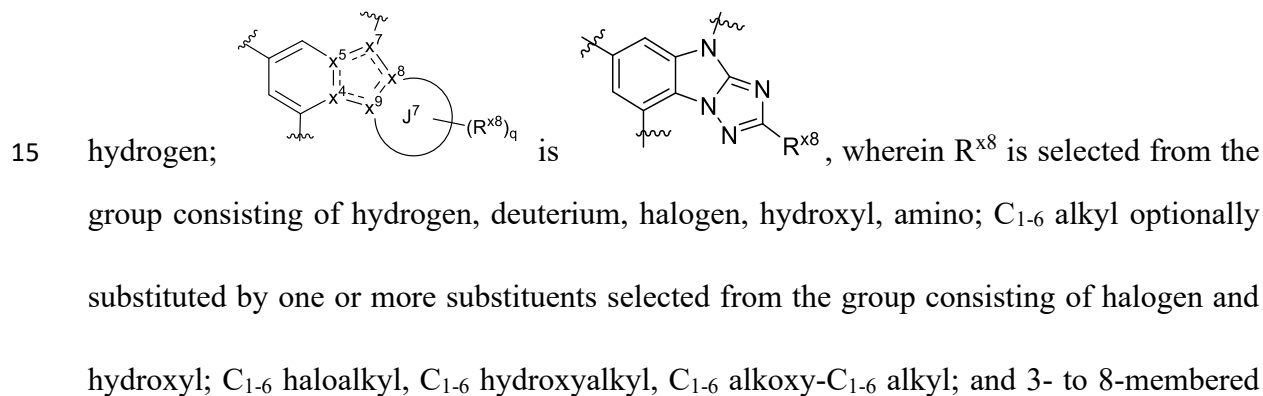
[0561] In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is -CH₃; R^{b1} is



selected from the group consisting of hydrogen, deuterium, halogen, hydroxyl, amino; C₁₋₆ alkyl optionally substituted by one or more substituents selected from the group consisting of halogen and hydroxyl; C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkoxy-C₁₋₆ alkyl; and 3- to

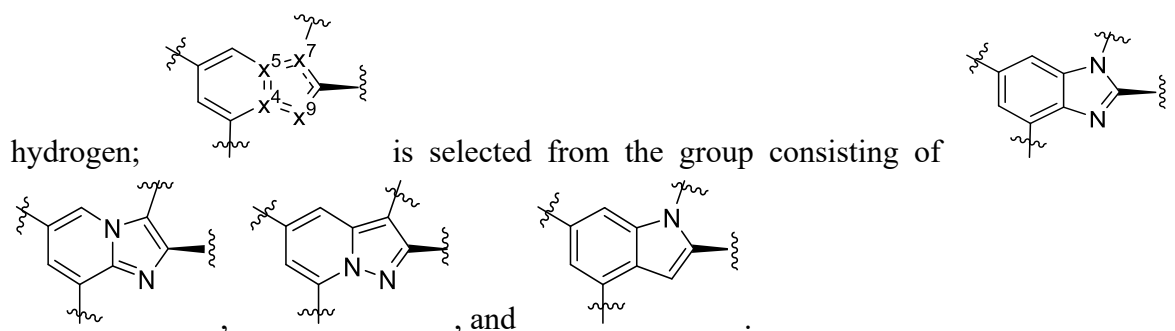
10 8-membered heterocyclyl optionally substituted by one or more substituents selected from the group consisting of halogen and C₁₋₆ alkyl.

[0562] In some embodiments of the present disclosure, in the compound of formula (II-3A), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is -CH₃; R^{b1} is

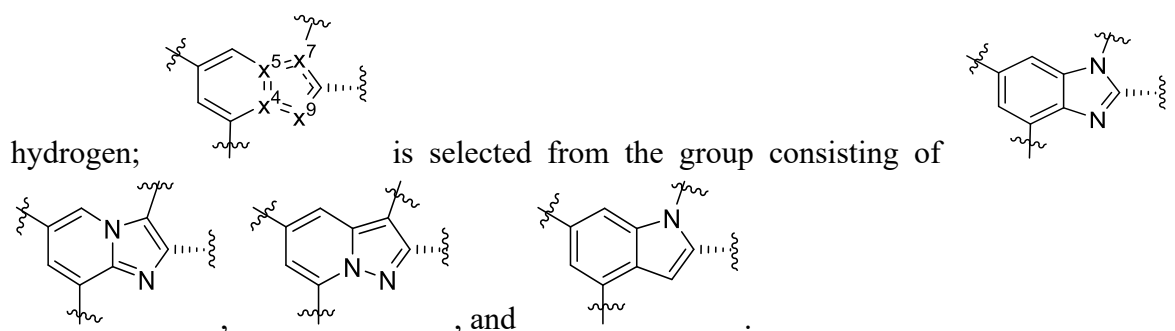


heterocyclyl optionally substituted by one or more substituents selected from the group consisting of halogen and C₁₋₆ alkyl.

[0563] In some embodiments of the present disclosure, in the compound of formula (II-2L), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is -CH₃; R^{b1} is



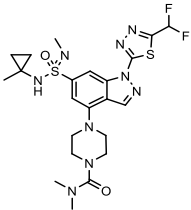
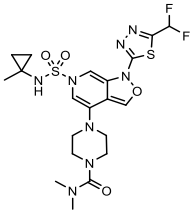
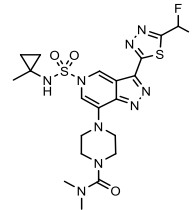
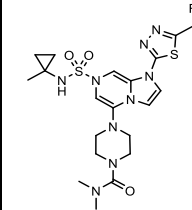
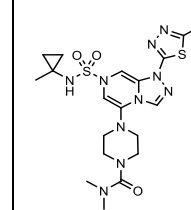
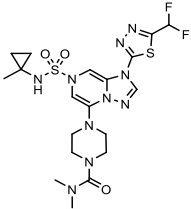
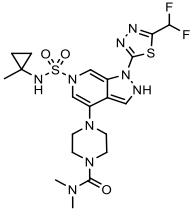
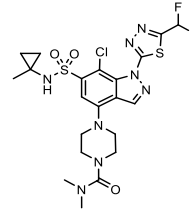
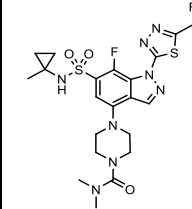
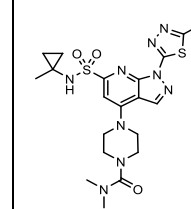
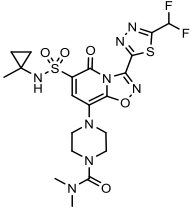
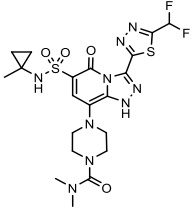
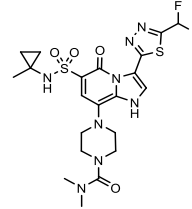
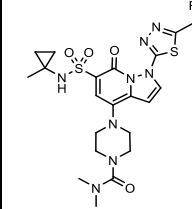
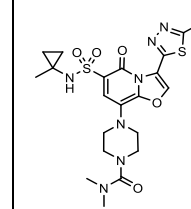
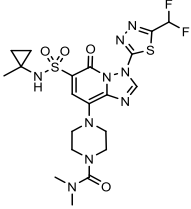
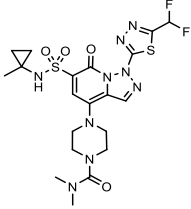
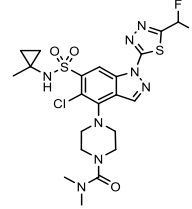
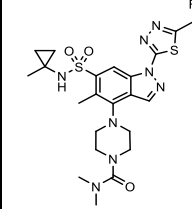
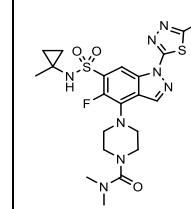
[0564] In some embodiments of the present disclosure, in the compound of formula (II-2M), the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof, R^a is -CH₃; R^{b1} is

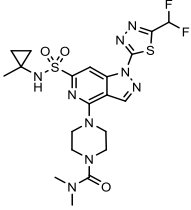
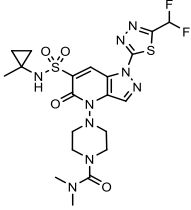
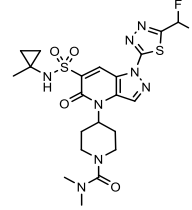
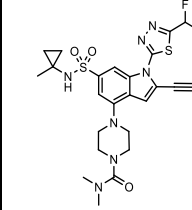
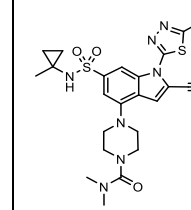
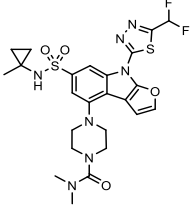
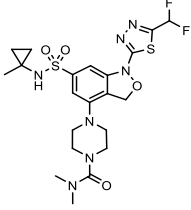
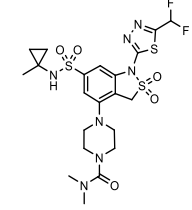
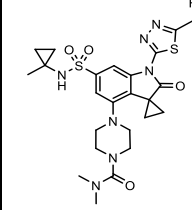
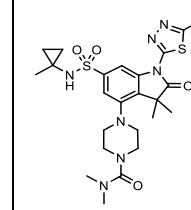
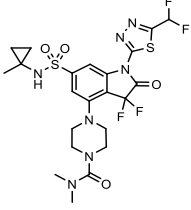
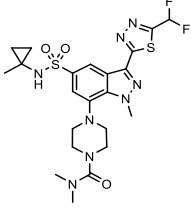
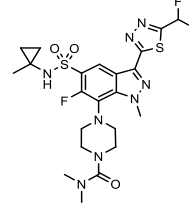
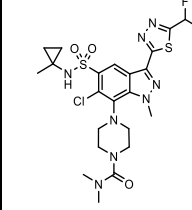
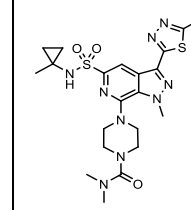
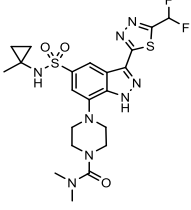
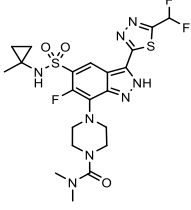
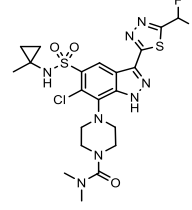
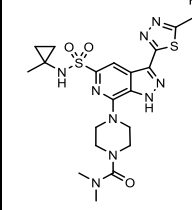
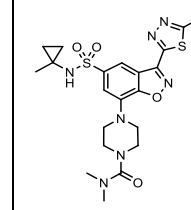
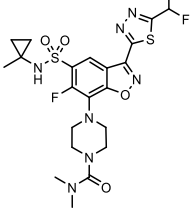
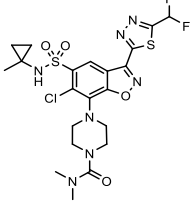
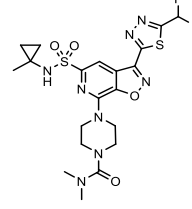
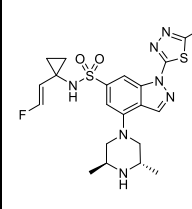
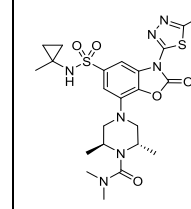


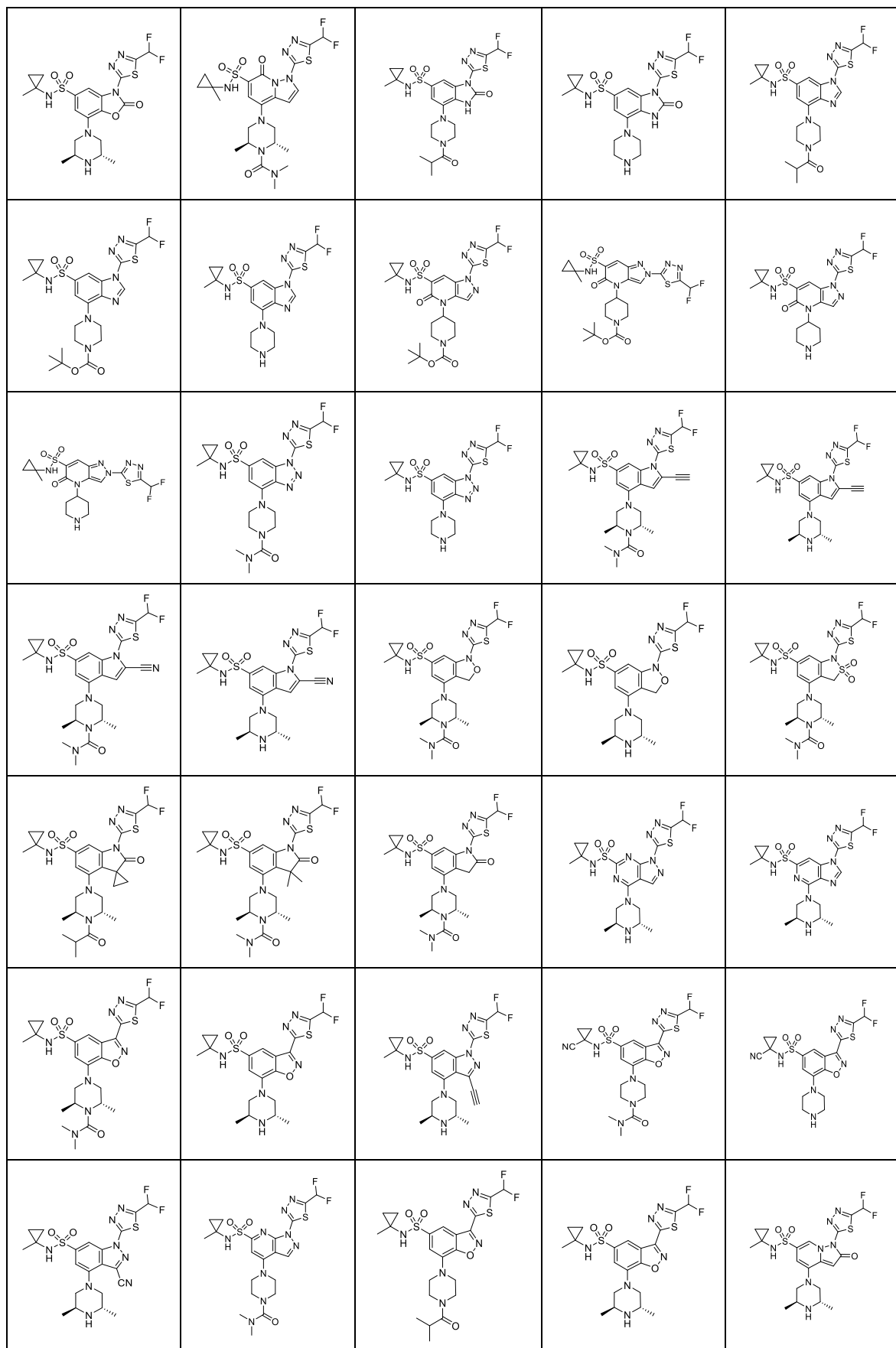
[0565] The present disclosure further provides the following compounds, and pharmaceutically acceptable salts thereof, or stereoisomers thereof, prodrugs thereof, N-oxides thereof, solvates thereof, or isotopic derivatives thereof, wherein the compound may be selected from the group consisting of any one of the structures listed in Table 1 below, and pharmaceutically acceptable salts thereof, or stereoisomers thereof, prodrugs thereof, N-

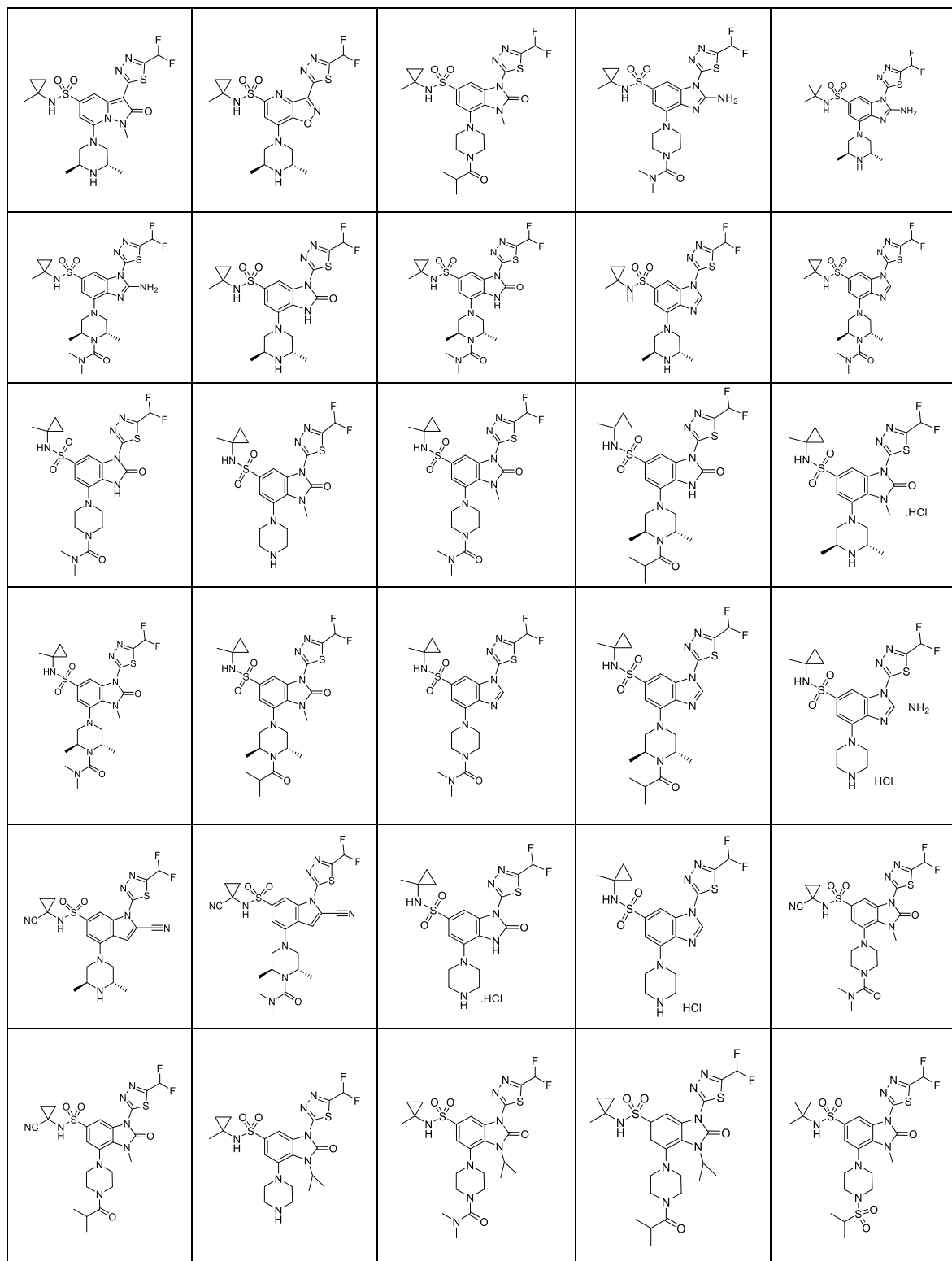
oxides thereof, solvates thereof, or isotopic derivatives thereof,

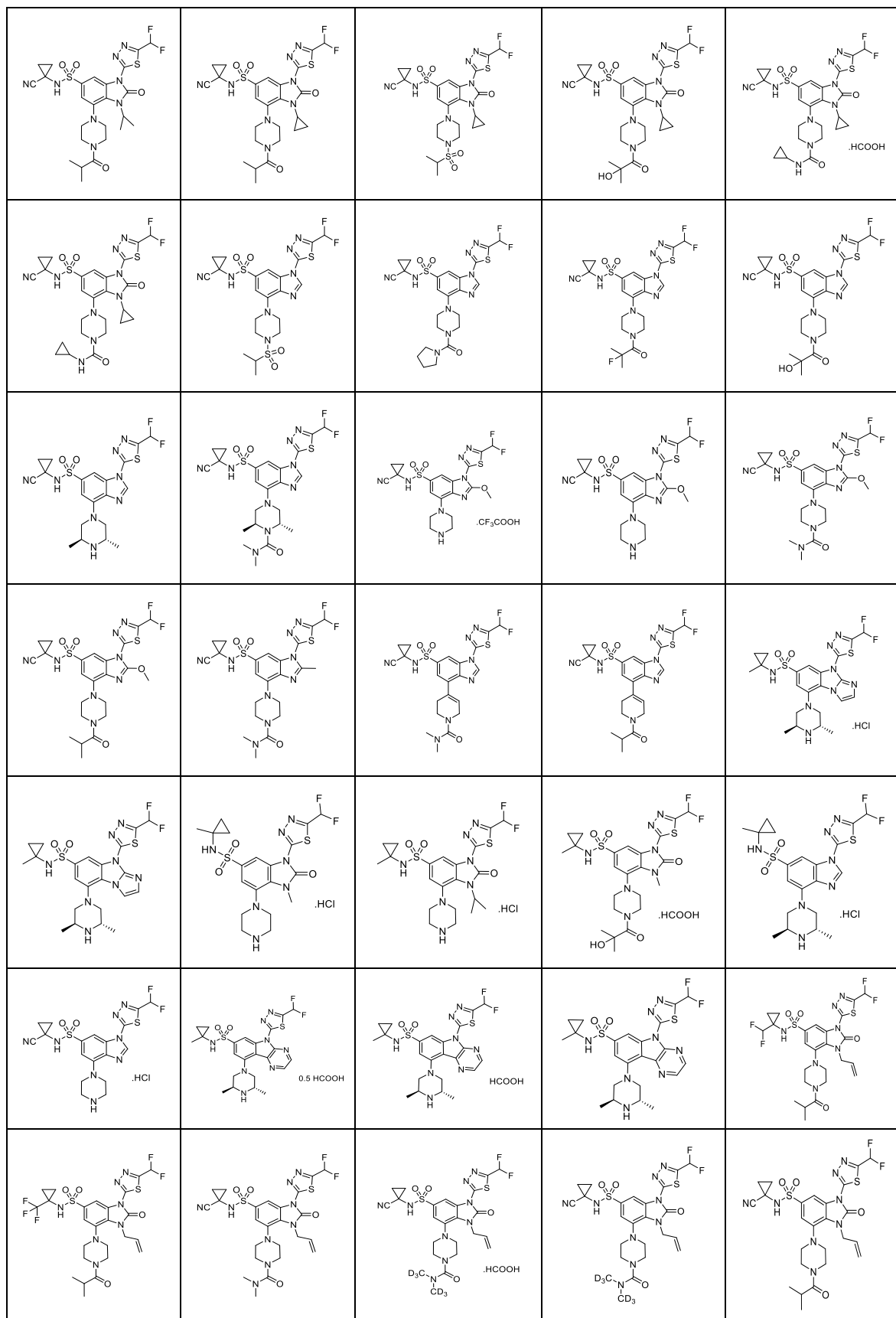
[0566] Table 1

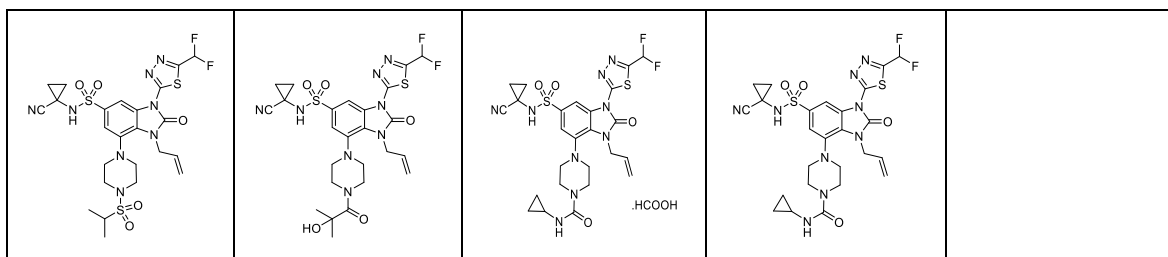
Example 1	Example 2	Example 3	Example 4	Example 5
				
Example 6	Example 7	Example 8	Example 9	Example 10
				
Example 11	Example 12	Example 13	Example 14	Example 15
				
Example 16	Example 17	Example 18	Example 19	Example 20
				
Example 21	Example 22	Example 23	Example 24	Example 25
				

				
Example 26	Example 27	Example 28	Example 29	Example 30
				
Example 31	Example 32	Example 33	Example 34	Example 35
				
Example 36	Example 37	Example 38	Example 39	Example 40
				
Example 41	Example 42	Example 43		
				



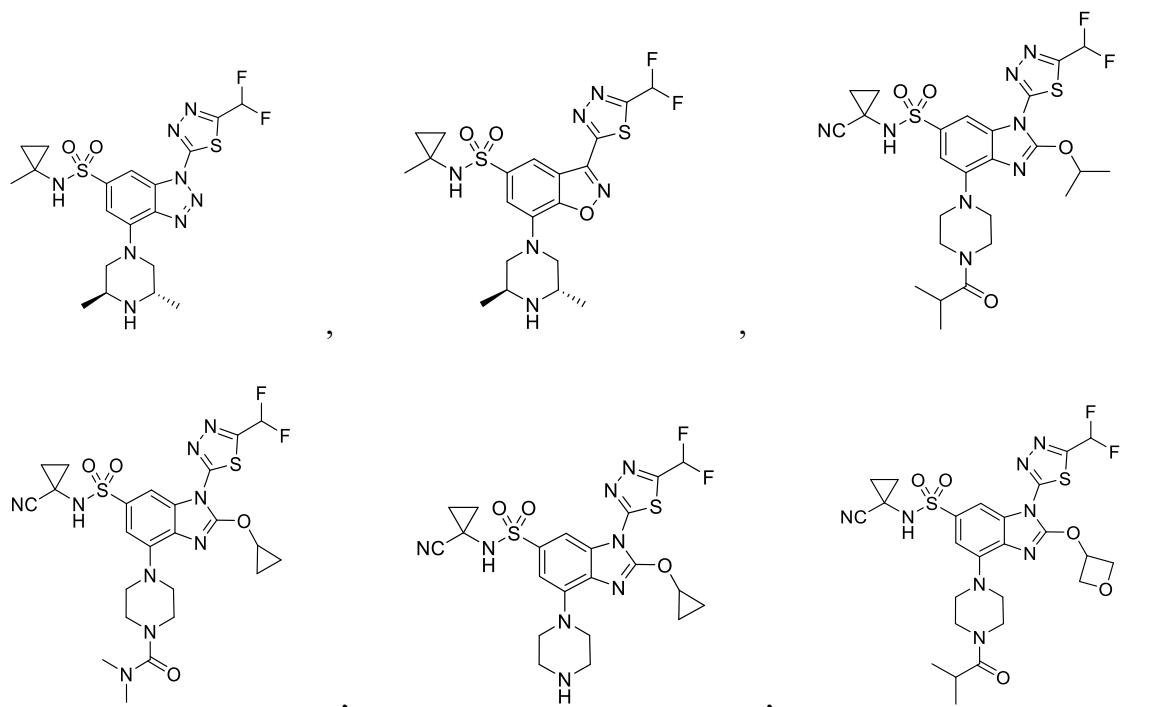


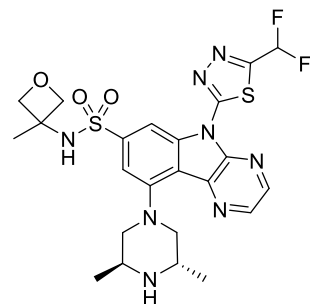
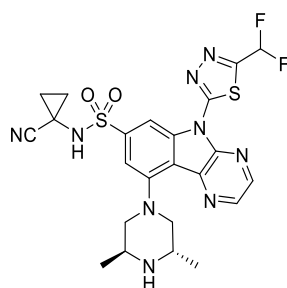
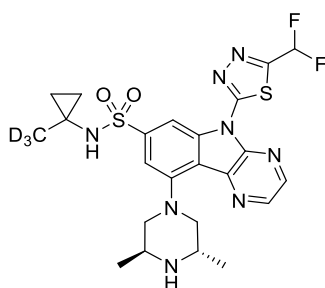
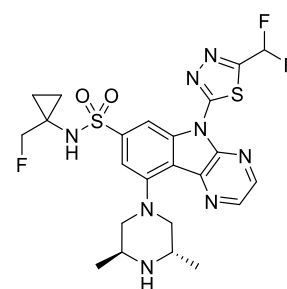
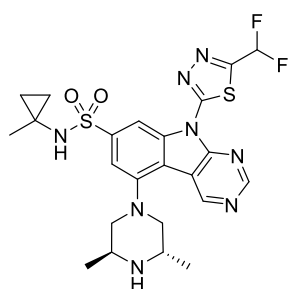
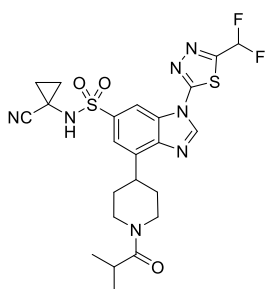
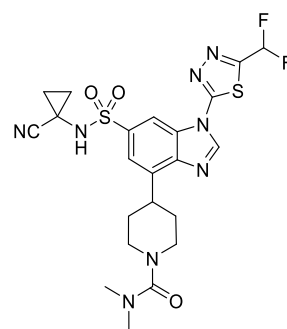
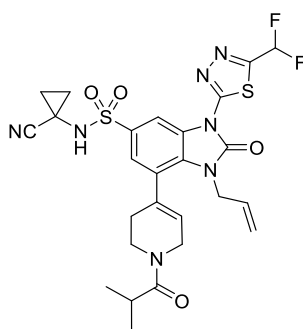
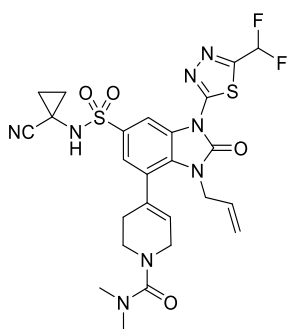
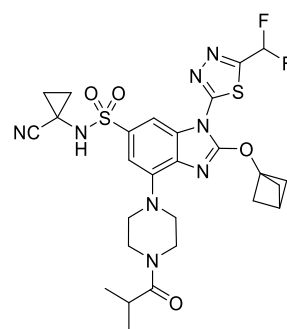
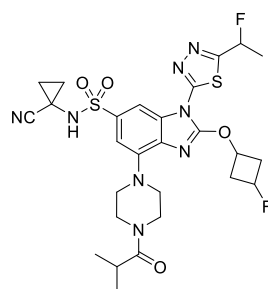
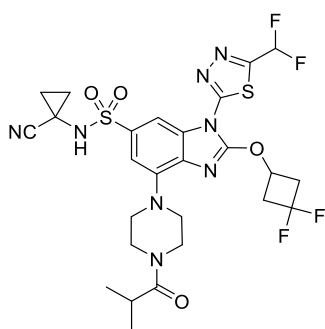
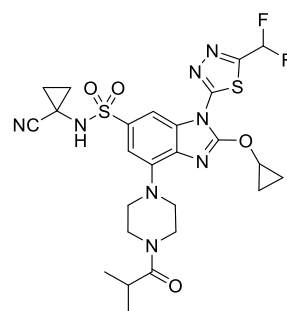
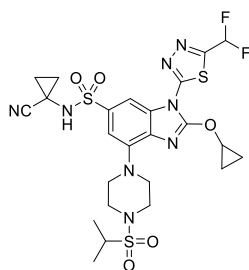
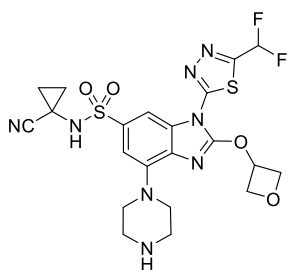


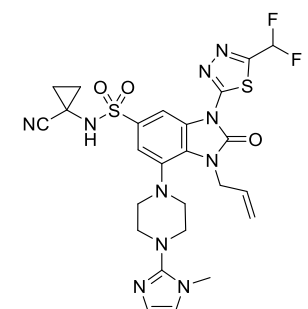
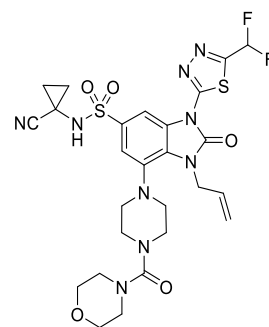
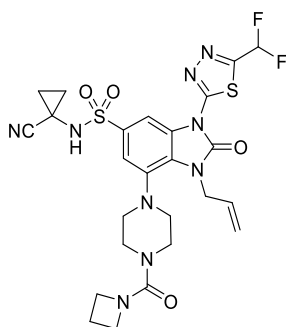
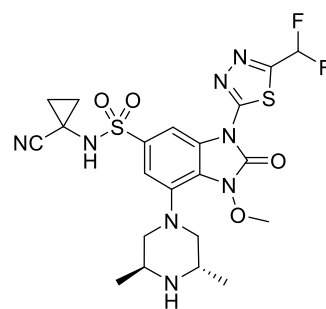
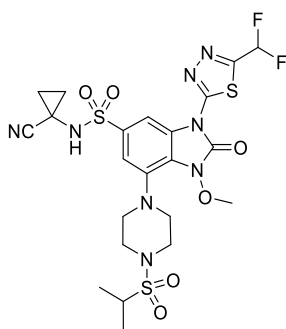
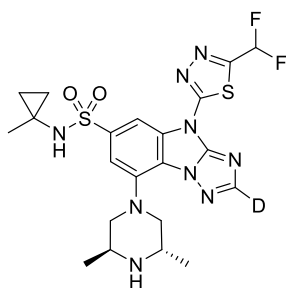
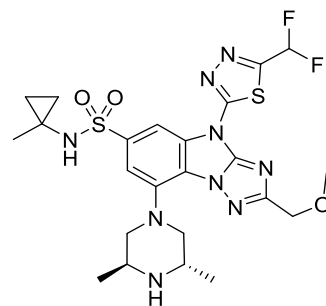
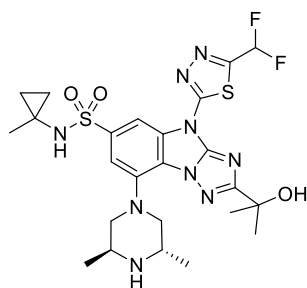
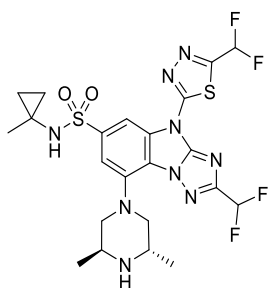
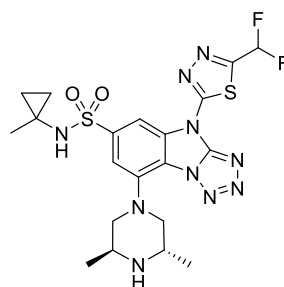
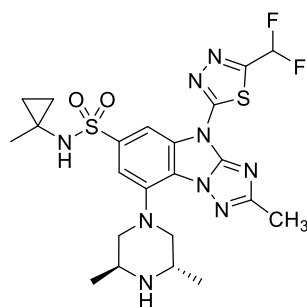
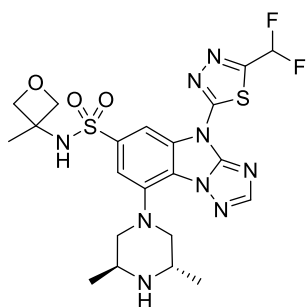
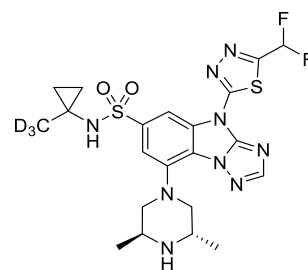
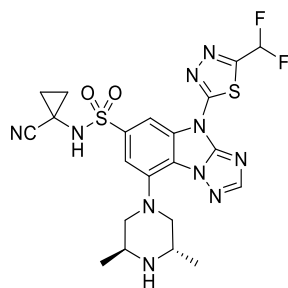
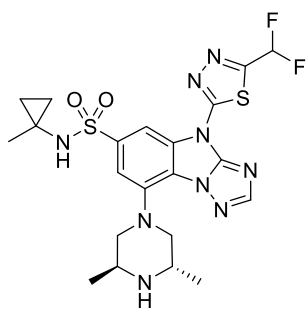


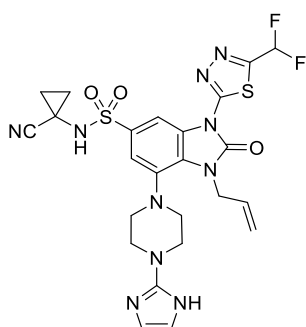
[0567] The present disclosure further provides the following compounds, and pharmaceutically acceptable salts thereof, or stereoisomers thereof, prodrugs thereof, N-oxides thereof, solvates thereof, or isotopic derivatives thereof, wherein the compound may

5 be selected from the group consisting of any one of the following structures, and pharmaceutically acceptable salts thereof, or stereoisomers thereof, prodrugs thereof, N-oxides thereof, solvates thereof, or isotopic derivatives thereof,

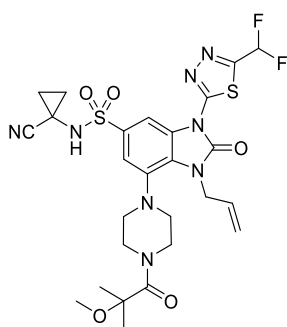




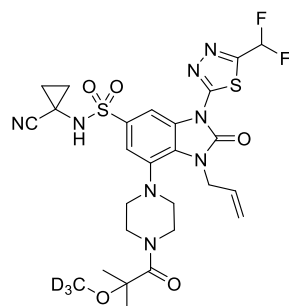




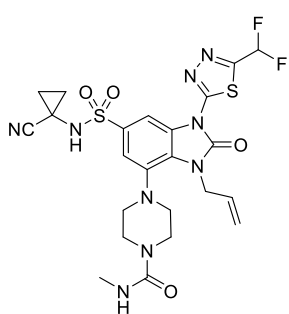
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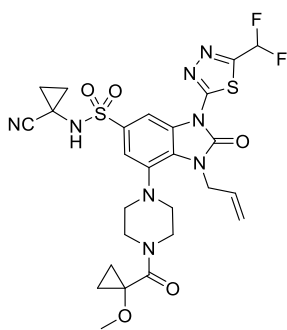
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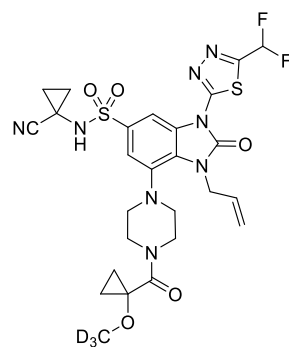
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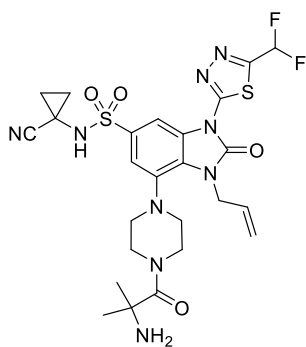
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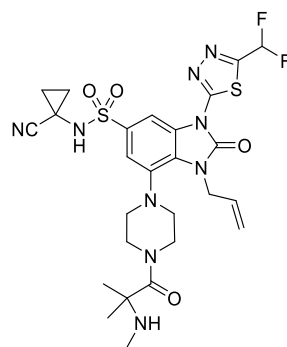
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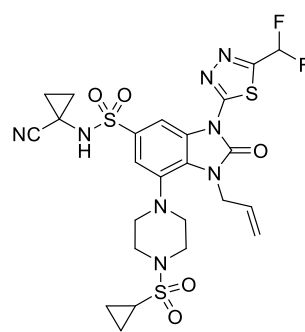
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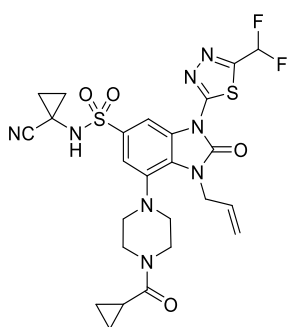
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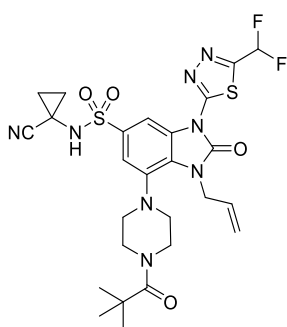
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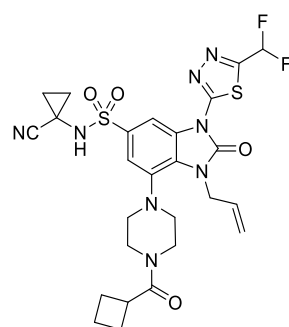
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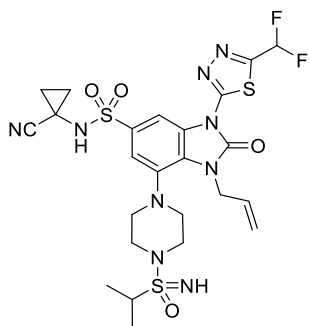
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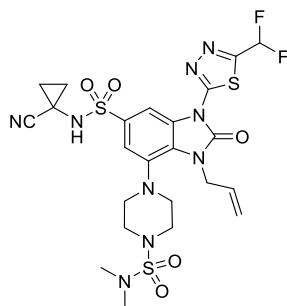
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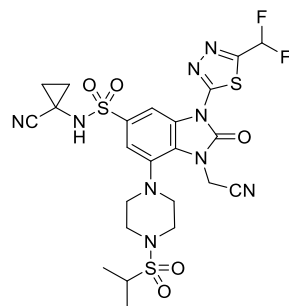




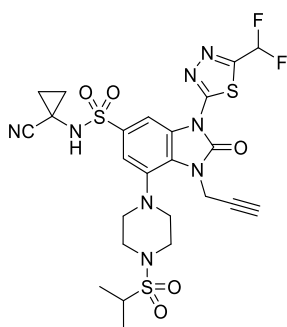
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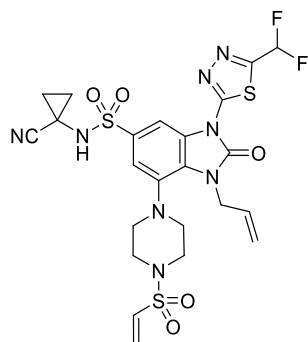
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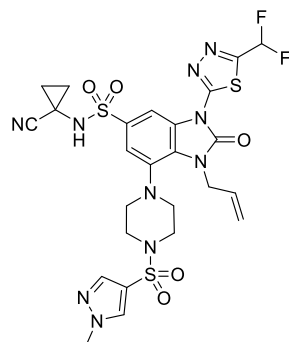
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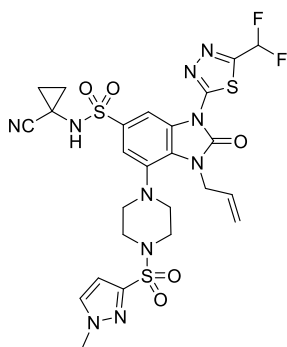
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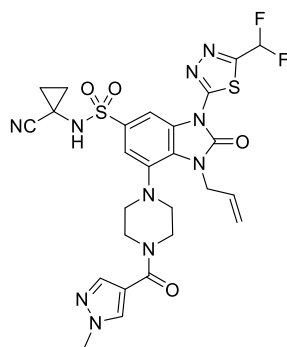
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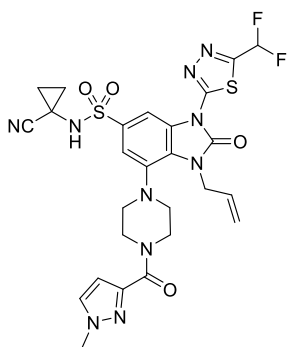
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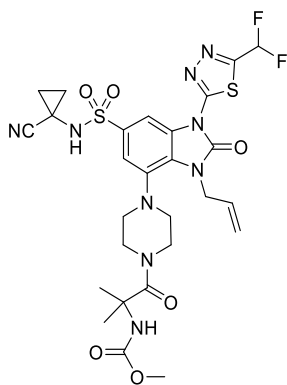
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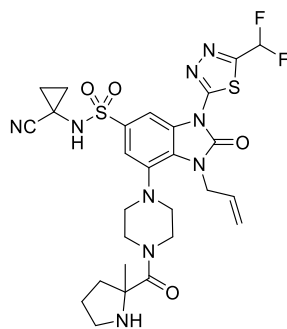
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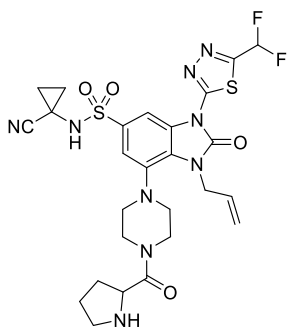
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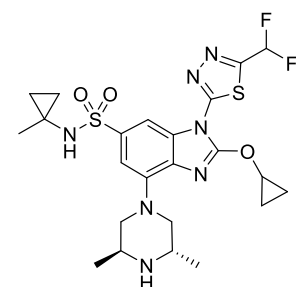
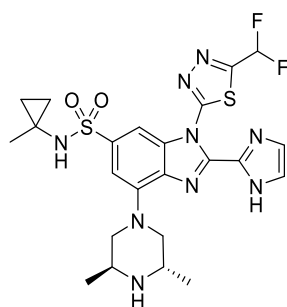
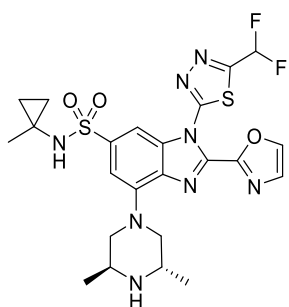
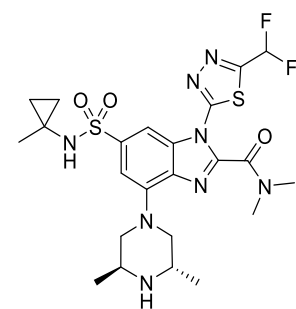
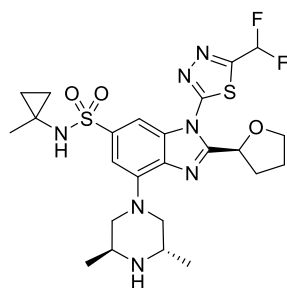
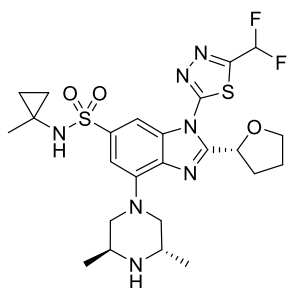
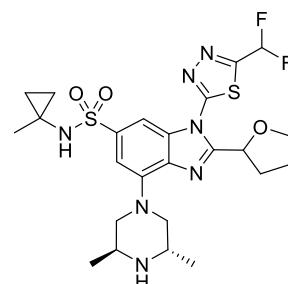
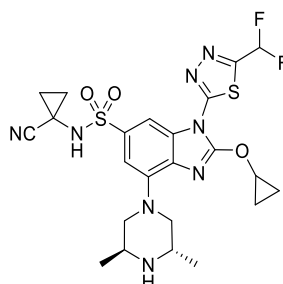
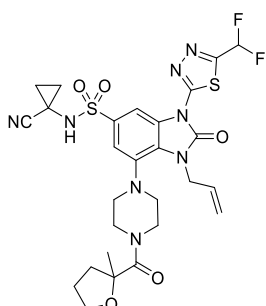
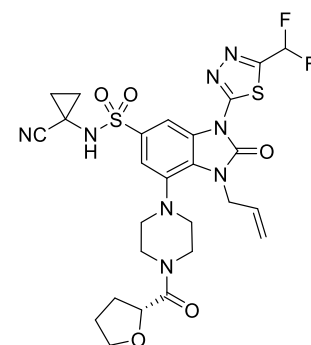
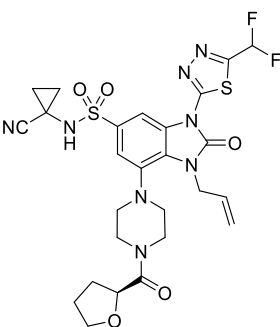
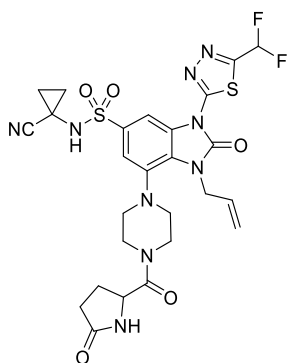
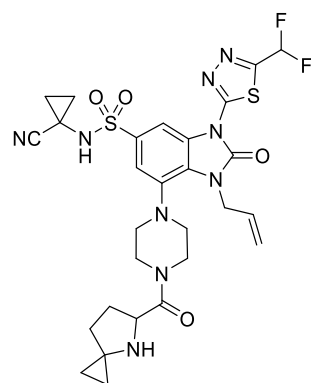
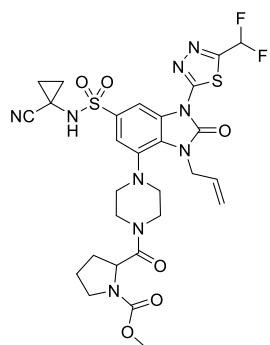
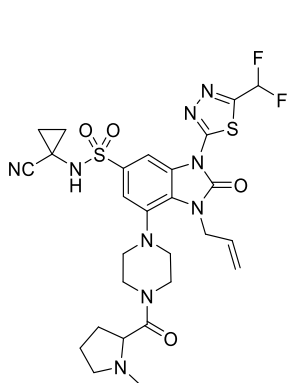
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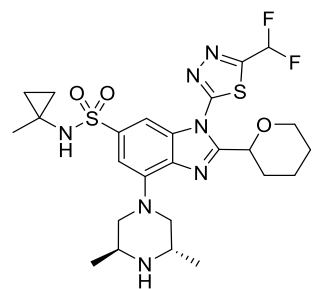
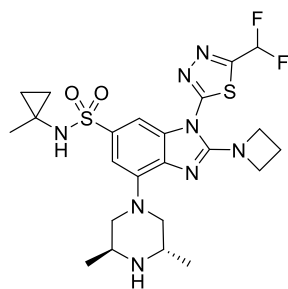
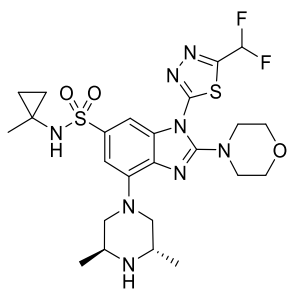
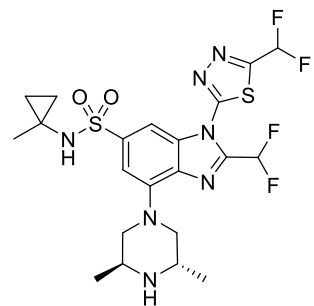
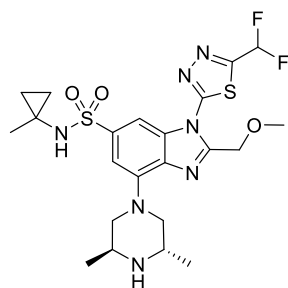
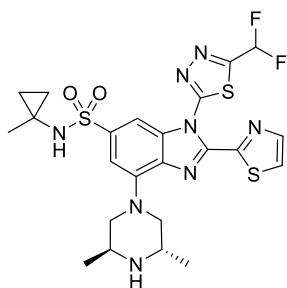
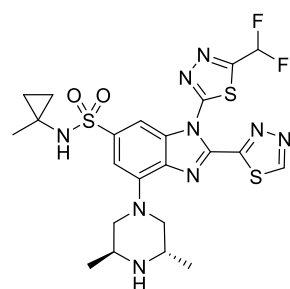
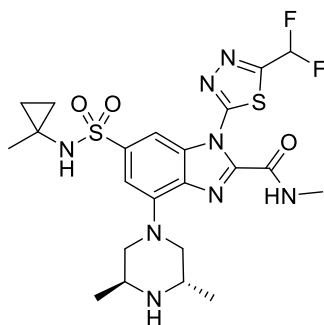
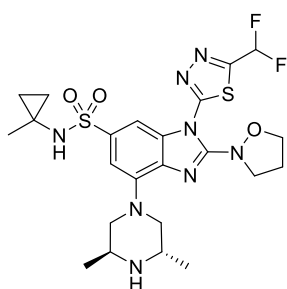
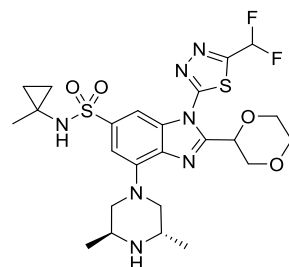
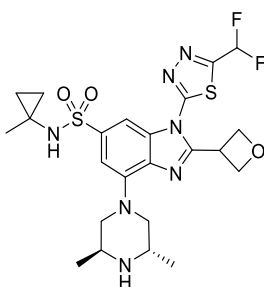
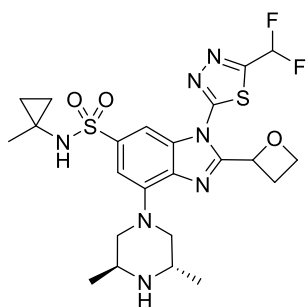
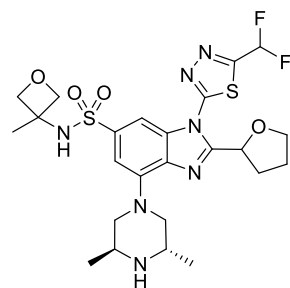
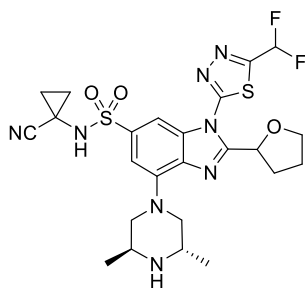
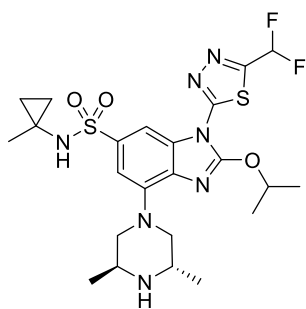


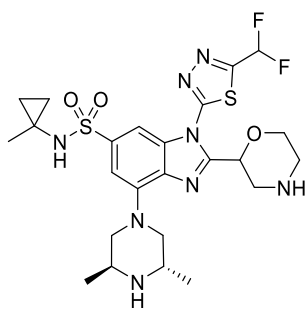
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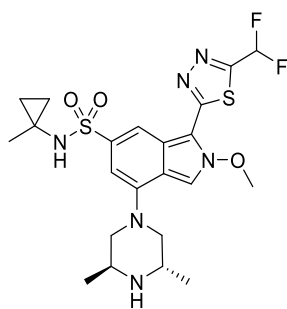
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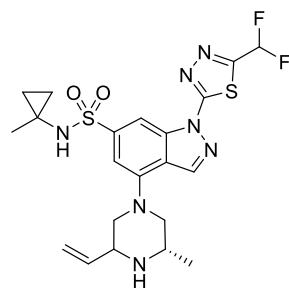




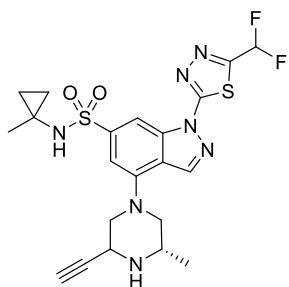
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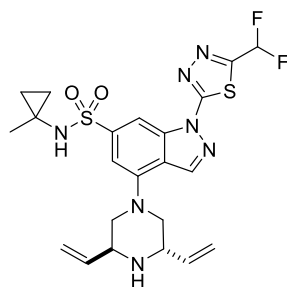
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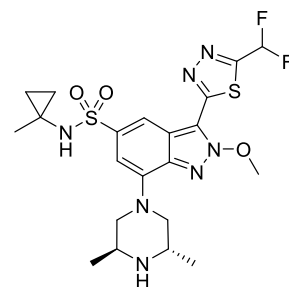
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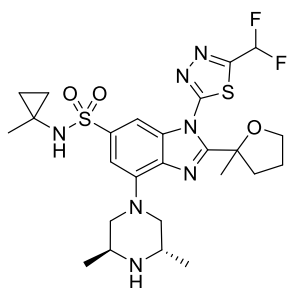
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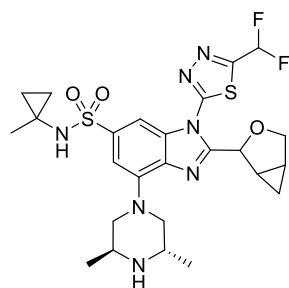
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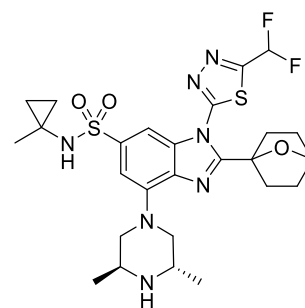
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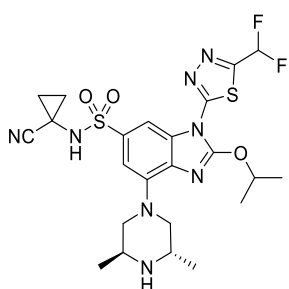
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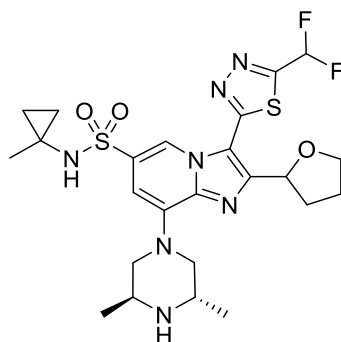
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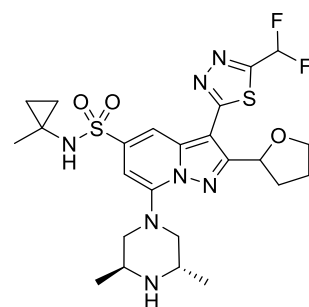
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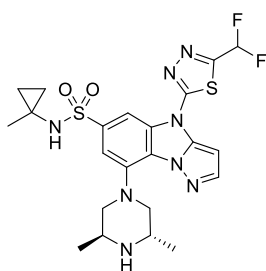
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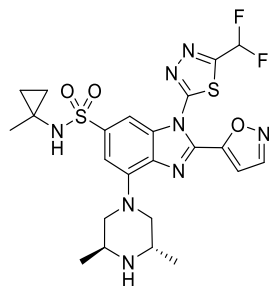
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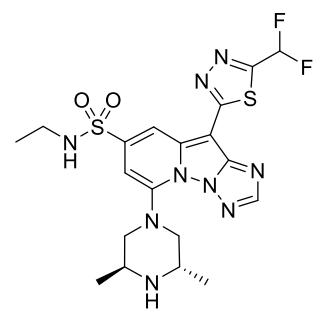
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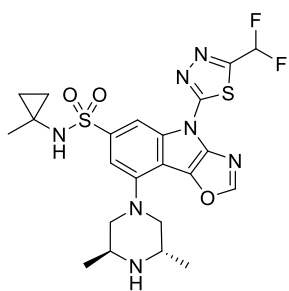
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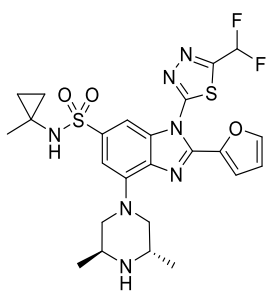
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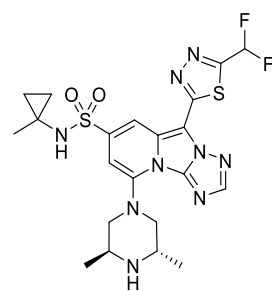
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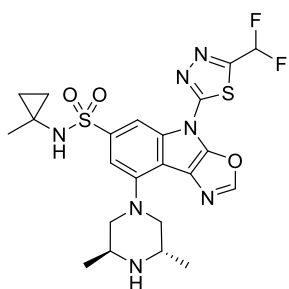
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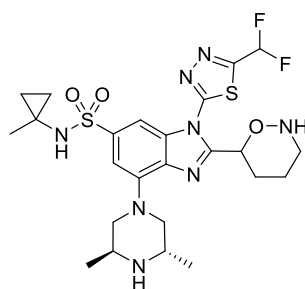
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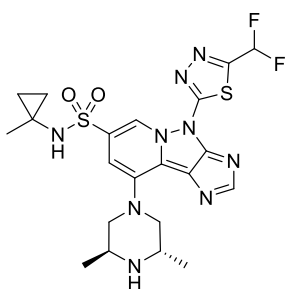
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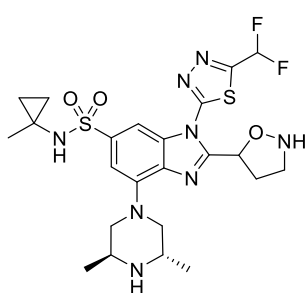
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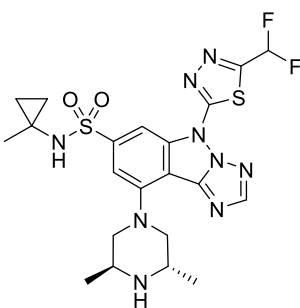
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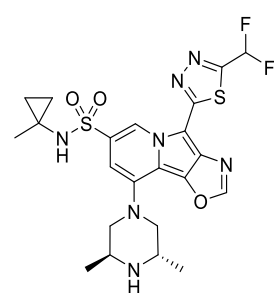
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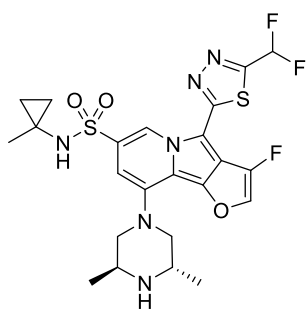
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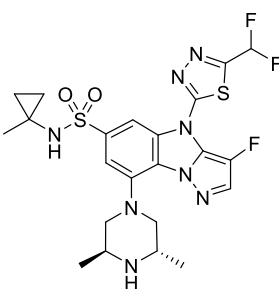
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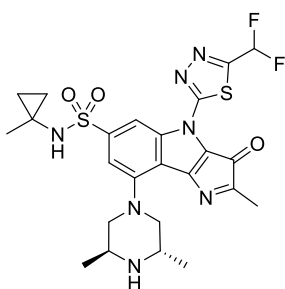
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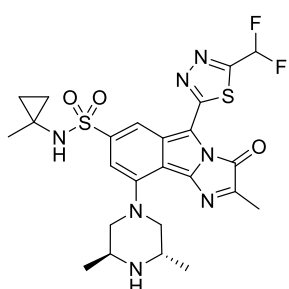
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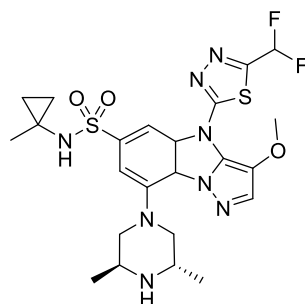
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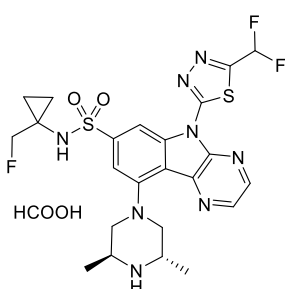
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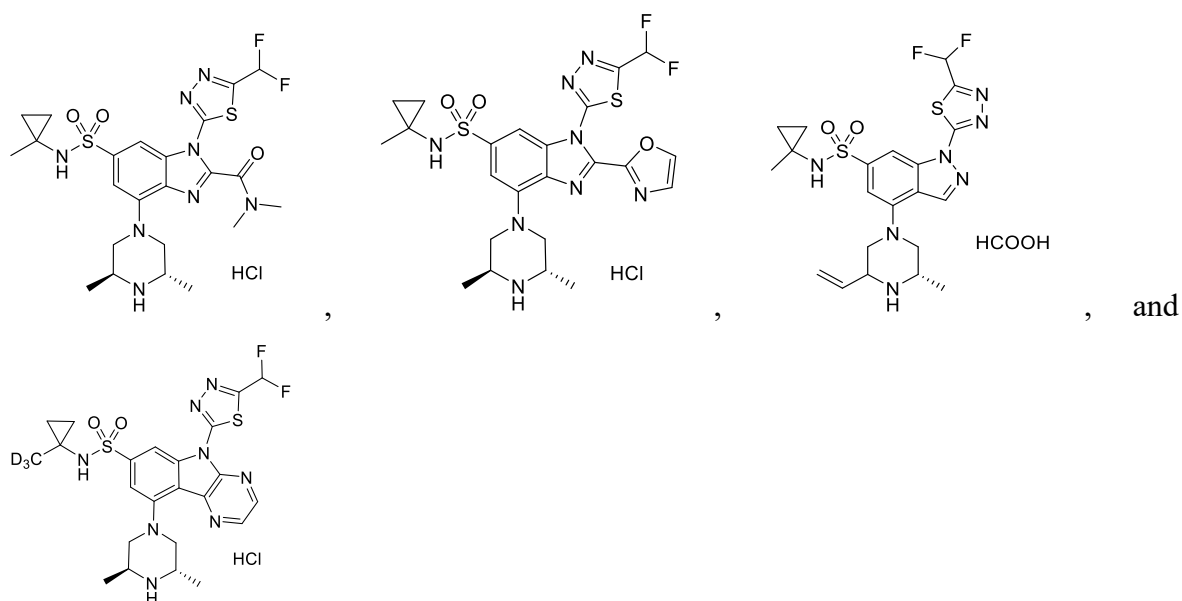


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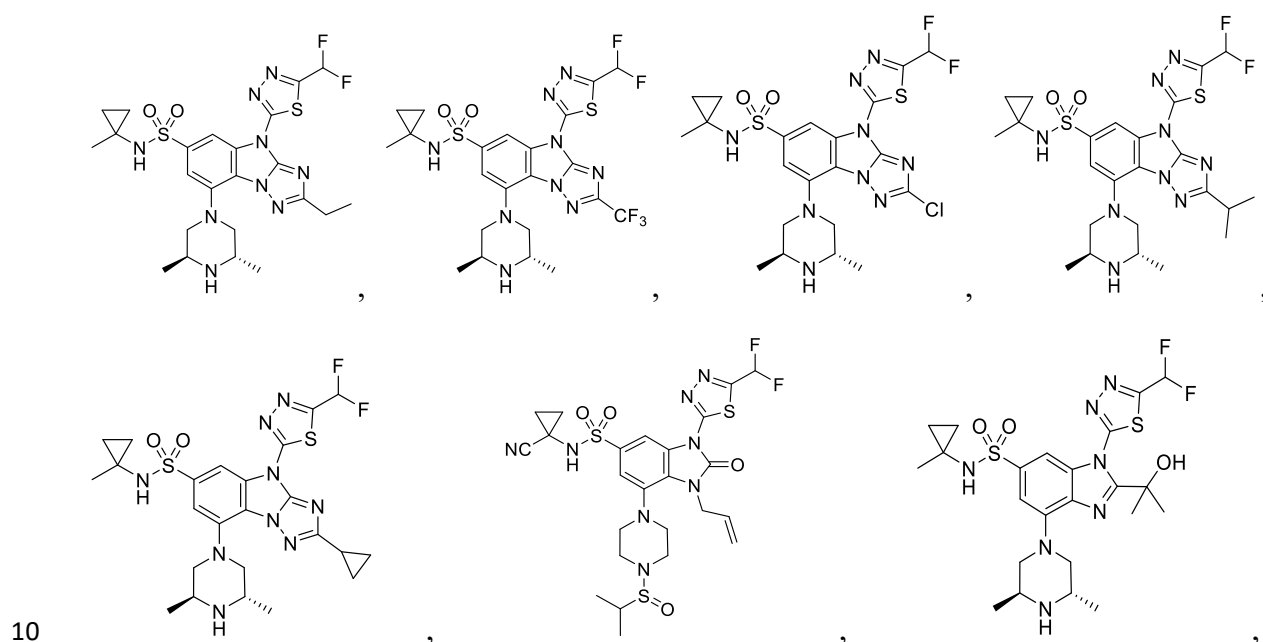


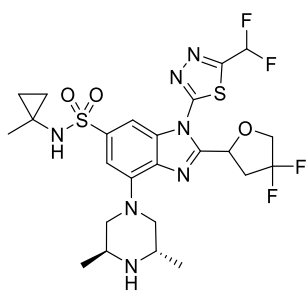
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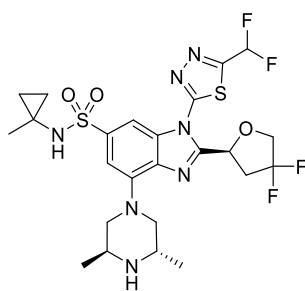


[0568] The present disclosure further provides the following compounds, and pharmaceutically acceptable salts thereof, or stereoisomers thereof, prodrugs thereof, N-oxides thereof, solvates thereof, or isotopic derivatives thereof, wherein the compound may be selected from the group consisting of any one of the following structures, and pharmaceutically acceptable salts thereof, or stereoisomers thereof, prodrugs thereof, N-oxides thereof, solvates thereof, or isotopic derivatives thereof,

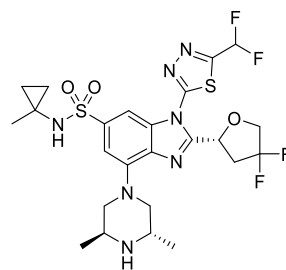




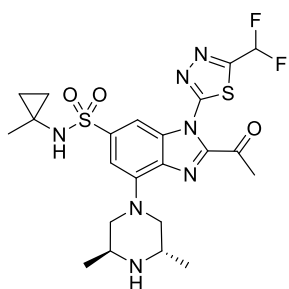
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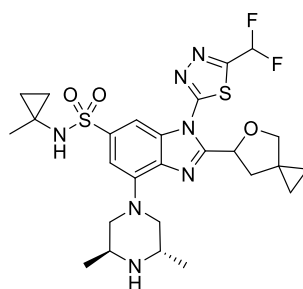
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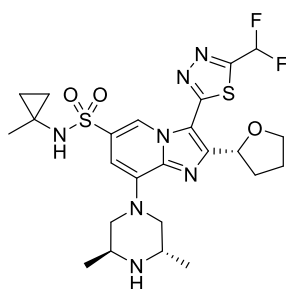
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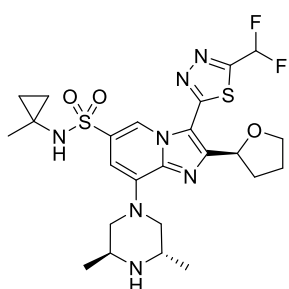
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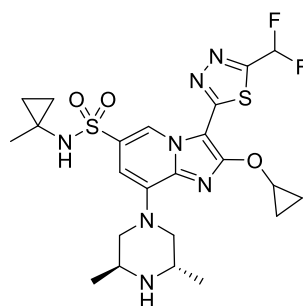
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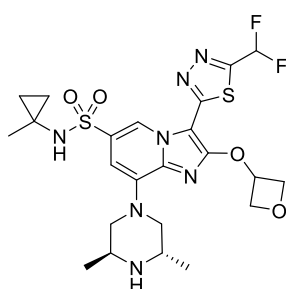
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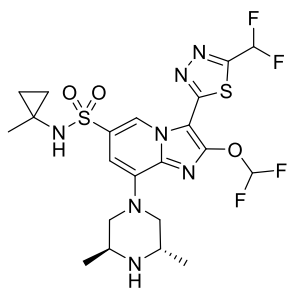
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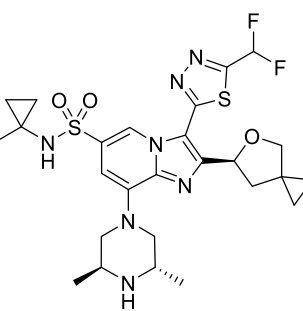
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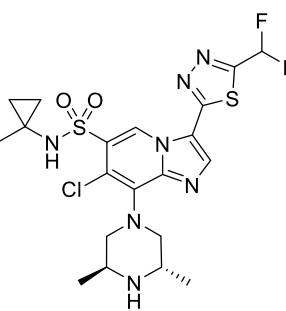
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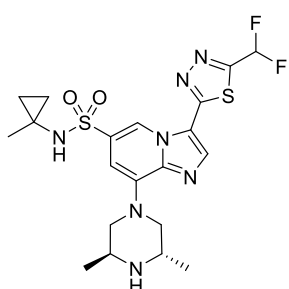
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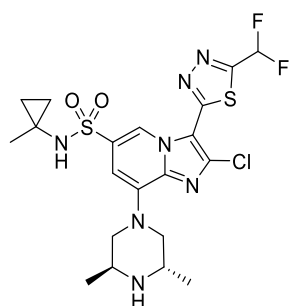
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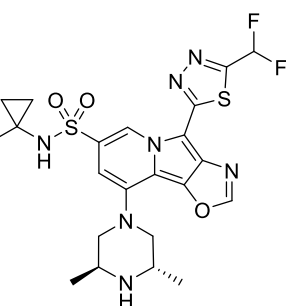
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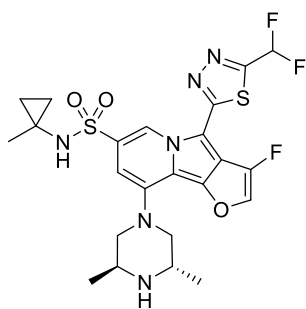
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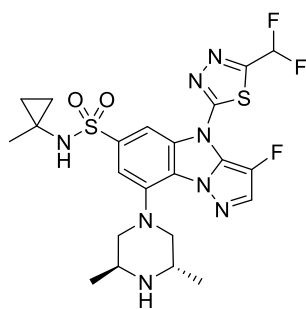
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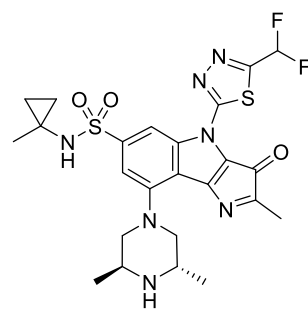
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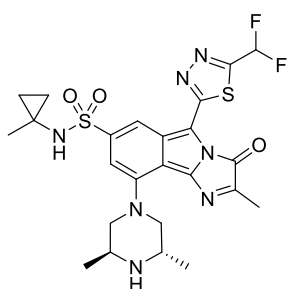
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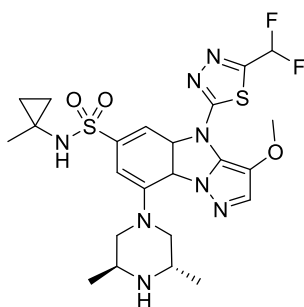
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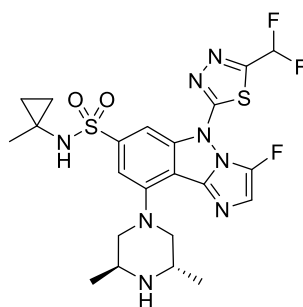
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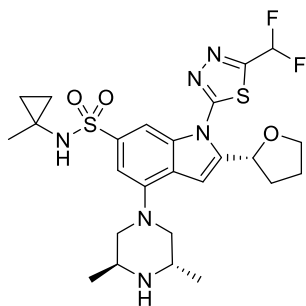
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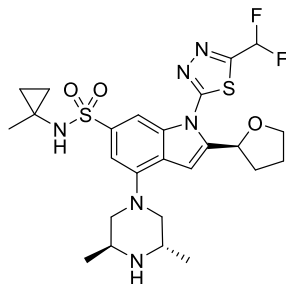
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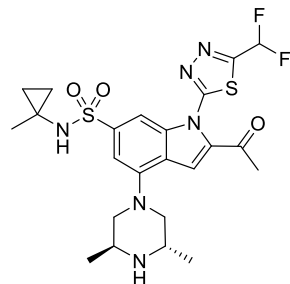
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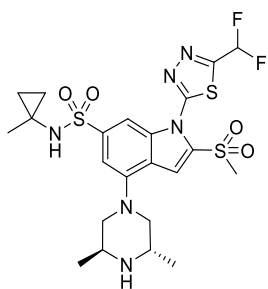
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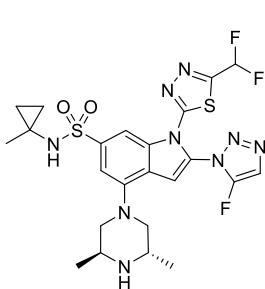
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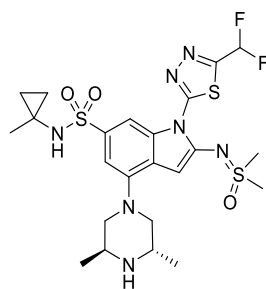
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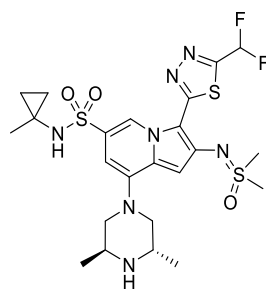
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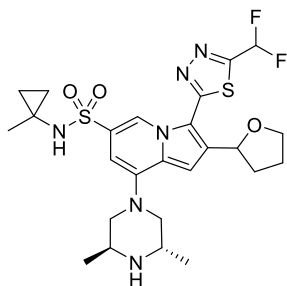
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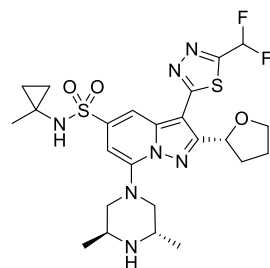
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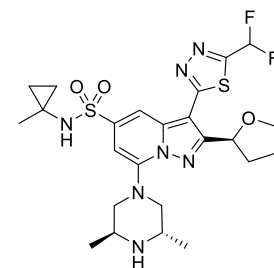
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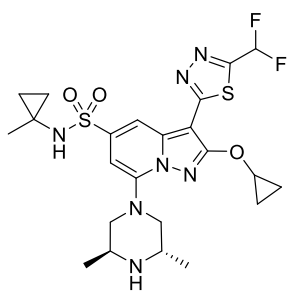
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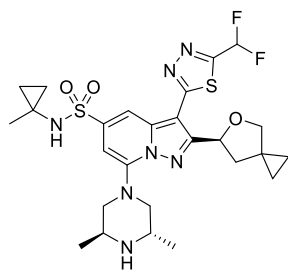
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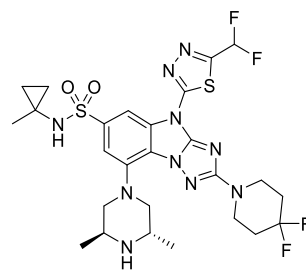
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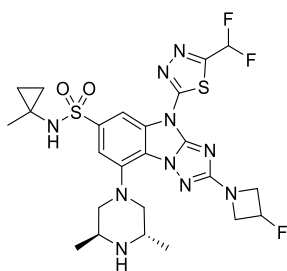
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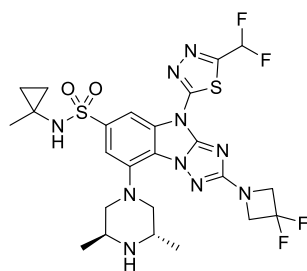
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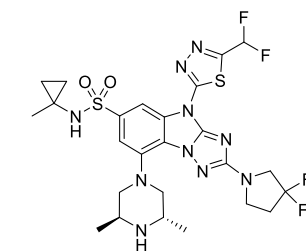
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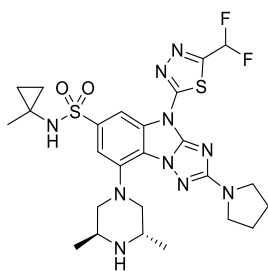
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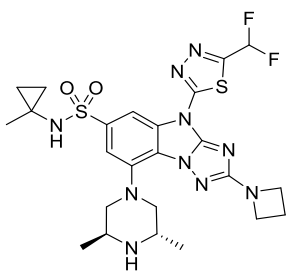
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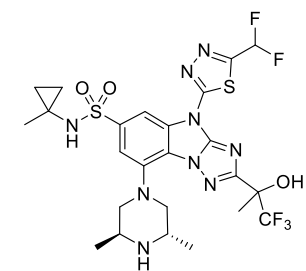
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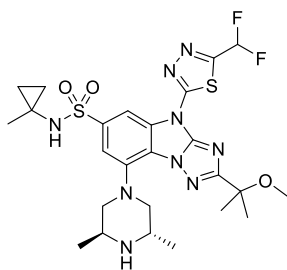
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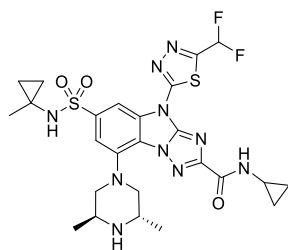
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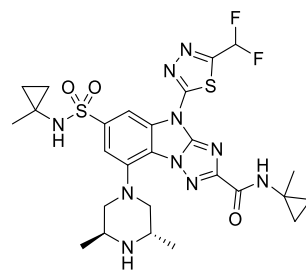
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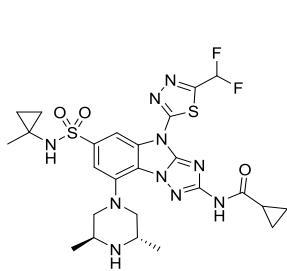
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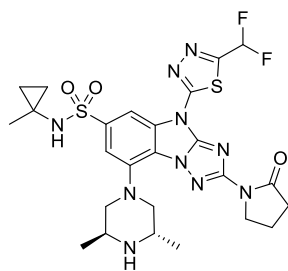
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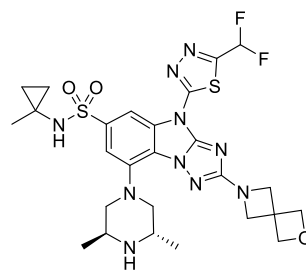
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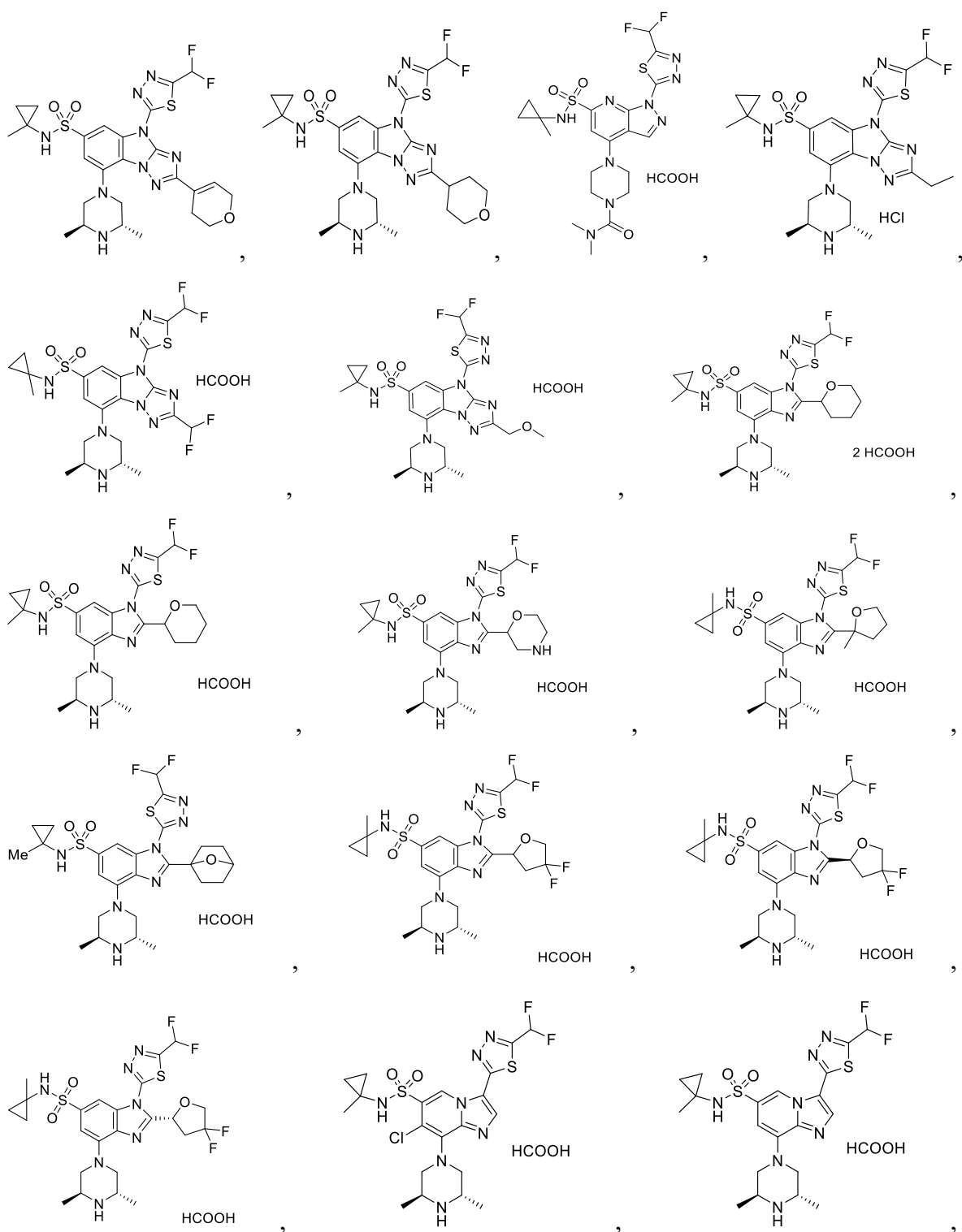
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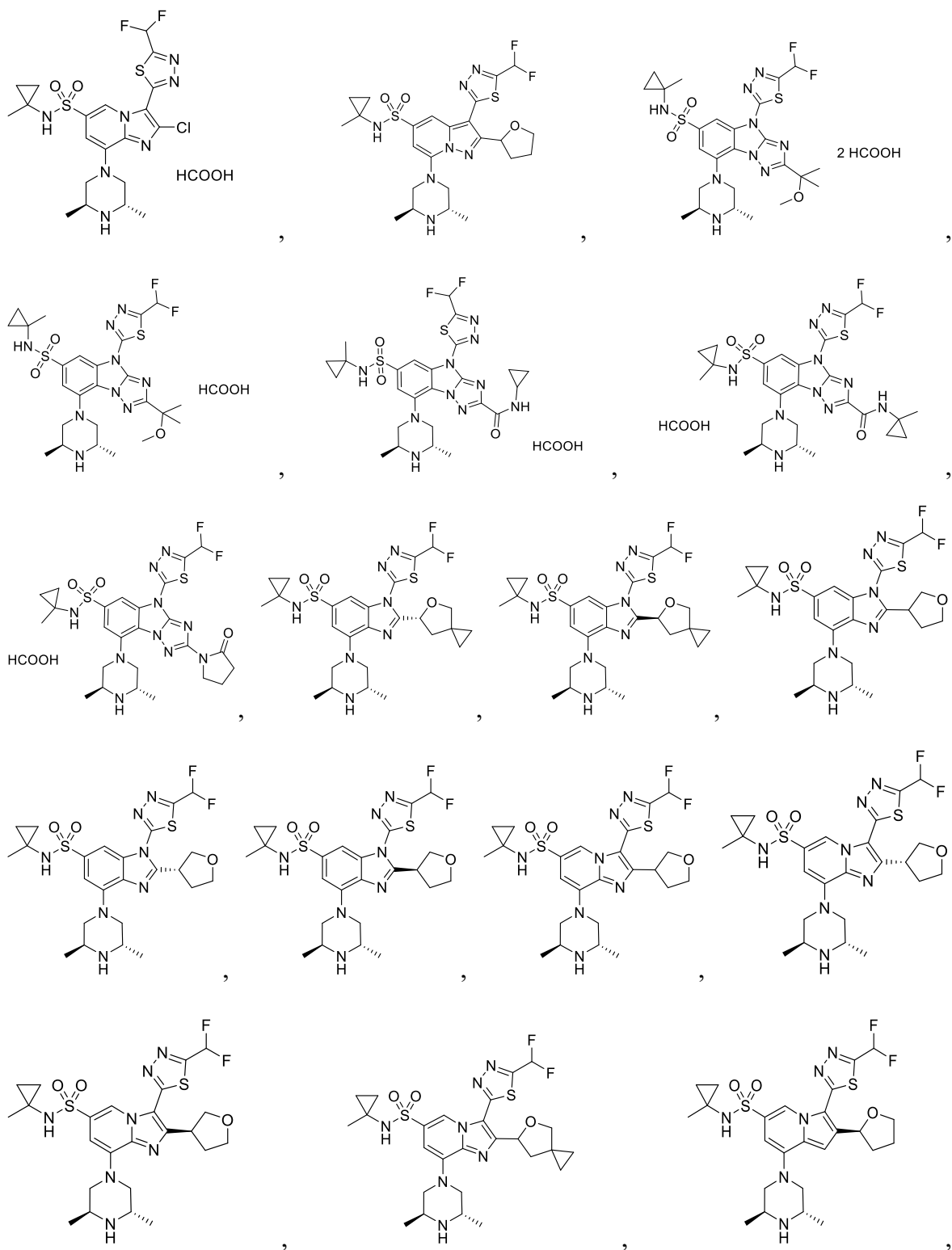


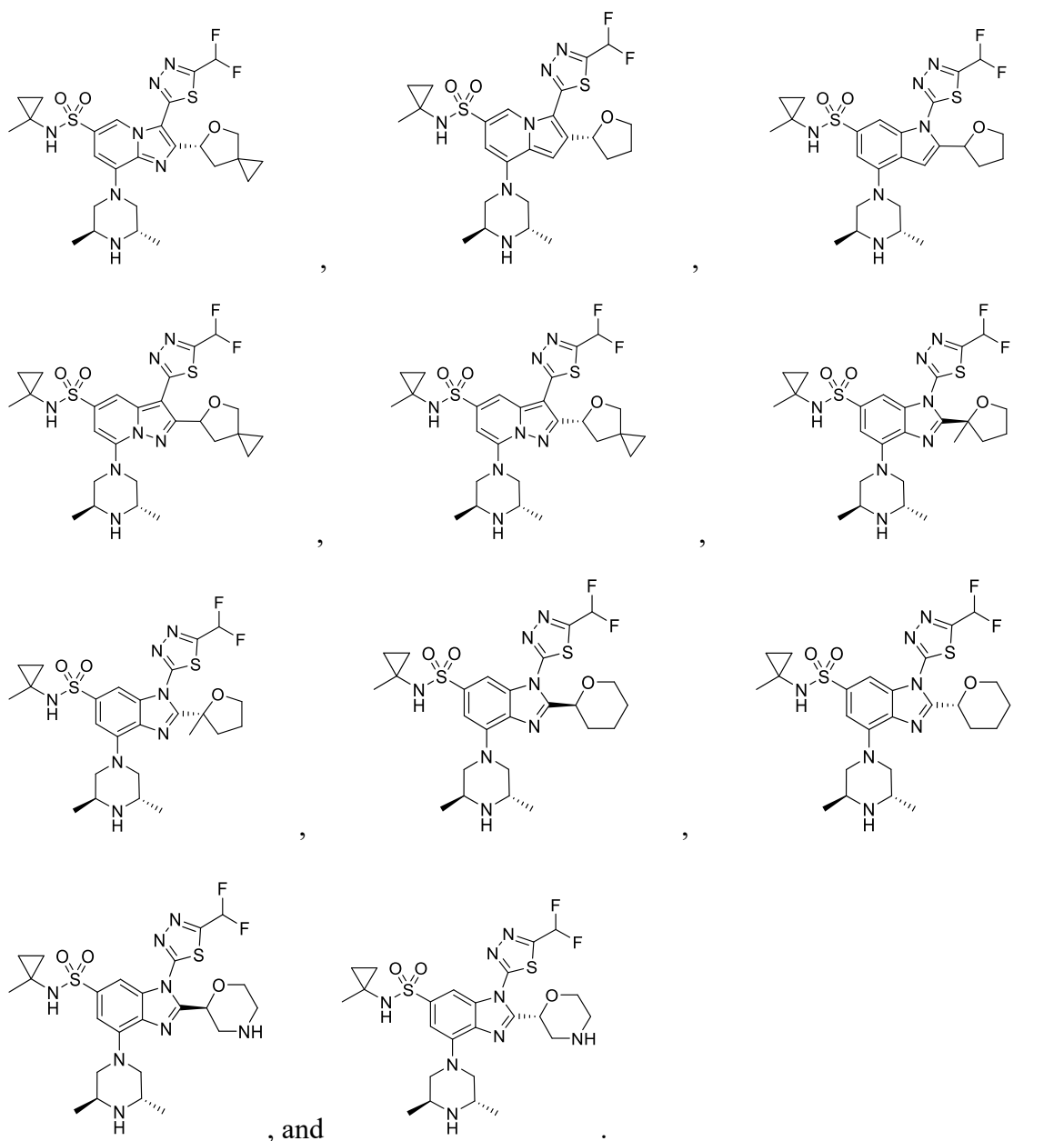
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5 **[0569]** The present disclosure further provides a pharmaceutical composition comprising (preferably a therapeutically effective amount of) the compound described above, or a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof, and a pharmaceutically acceptable carrier.

10 **[0570]** The present disclosure further provides the use of the compound described above, or

a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof, or the pharmaceutical composition described above, in the manufacture of a medicament for the treatment of PARG-mediated cancer.

5 **[0571]** The present disclosure further provides the compound described above, or a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof, or the pharmaceutical composition described above, for use in the treatment of PARG-mediated cancer.

10 **[0572]** The present disclosure further provides a method of treating PARG-mediated cancer, comprising administering to a patient a therapeutically effective amount of the compound described above, or a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof, or the pharmaceutical composition described above.

15 **[0573]** Preferably, the cancer according to the present disclosure is selected from the group consisting of ovarian cancer, pancreatic cancer, breast cancer, and prostate cancer.

[0574] Technical effect

20 **[0575]** 1. The binding conformation (active conformation) of the compounds of the present disclosure within the PARG protein structure highly overlaps with their lowest energy conformation (low-energy conformation), and the energy difference between the two conformations is minimal. Therefore, in actual binding to the PARG enzyme, the

compounds of the present disclosure are expected to exhibit binding activity similar to or superior to that of the compound in Reference Example 1.

[0576] 2. The compounds of the present disclosure exhibit strong inhibitory activity against the PARG enzyme.

5 **[0577] Description and definition**

[0578] Unless otherwise specified, the following terms and phrases used herein have the following meanings. A specific term or phrase should not be considered indefinite or unclear in the absence of a particular definition, but should be understood in the ordinary sense.

10 **[0579]** The term “pharmaceutically acceptable” refers to those compounds, materials, compositions and/or dosage forms, which are suitable for use in contact with human and animal tissues within the scope of reasonable medical judgment, without excessive toxicity, irritation, allergic reaction, or other problems or complications, and is commensurate with a reasonable benefit/risk ratio.

15 **[0580]** The term “pharmaceutically acceptable salt” refers to a derivative prepared by the compound of the present disclosure with a relatively nontoxic acid or base. These salts may be prepared during the synthesis, separation, and purification of the compound, or the free form of the purified compound may be used alone to react with a suitable acid or base. When the compound contains a relatively acidic functional group, the compound reacts with
20 alkali metal, alkaline earth metal hydroxide, or organic amine to obtain an alkali addition salt, including cations based on alkali metals and alkaline earth metals, as well as non-toxic

ammonium, quaternary ammonium, and amine cations. Salts of amino acids are also encompassed. When the compound contains a relatively basic functional group, the compound reacts with an organic acid or an inorganic acid to obtain an acid addition salt, such as a hydrochloride salt and a formate salt.

5 **[0581]** The term “pharmaceutically acceptable carrier” refers to a medium generally acceptable in the art for delivering a biologically active agent to animals, particularly mammals, including, for example, an adjuvant, an excipient, or a vehicle, such as a diluent, a preservative, a filler, a flow regulator, a disintegrant, a wetting agent, an emulsifier, a suspending agent, a sweetener, a flavor, a fragrance, an antibacterial agent, an antifungal
10 agent, a lubricant, and a dispersant, depending on the route of administration and the nature of dosage forms. The pharmaceutically acceptable carrier is formulated according to a number of factors that are within the purview of those skill in the art. The factors include, but are not limited to, the type and nature of the active agent formulated, the subjects to which the composition containing the agent is to be administered, the expected route of
15 administration of the composition, and the target therapeutic indication. The pharmaceutically acceptable carriers include both aqueous and non-aqueous media and various solid and semisolid dosage forms. In addition to the active agent, such carriers include many different ingredients and additives, and such additional ingredients included in prescriptions for a variety of reasons (*e.g.*, stabilizing the active agent and binders) are
20 well known to those of ordinary skill in the art.

[0582] The term “prodrug” refers to certain derivatives of the compound of the present

disclosure that themselves possess little or no pharmacological activity, which contain a cleavable group and are converted into the compound of the present disclosure through solvolysis or decomposition under physiological conditions. Types of prodrugs include, but are not limited to, amides, esters, anhydrides, and salts. The term “ester” refers to a derivative formed with a suitable alcohol when the compound of the present disclosure contains an acidic group (*e.g.*, carboxylic acid); or a derivative formed with a suitable acid (including an organic acid or an inorganic acid) when the compound of the present disclosure contains a hydroxyl group. Preparation methods of prodrugs are well known to those skilled in the art.

10 **[0583]** The term “solvate” refers to an association or complex of one or more solvent molecules with the compound of the present disclosure. The term “hydrate” may be used when the solvent is water. The solvent molecules may be stoichiometric or non-stoichiometric.

[0584] The term “nitrogen oxide” or “N-oxide” refers to a derivative formed by further oxidation of the nitrogen atom in a nitrogen-containing group. Common N-oxides include N-oxides of tertiary amines or N-oxides of nitrogen atoms in nitrogen-containing heterocycles. Synthetic methods of N-oxides are well known to those skilled in the art, including oxidation of heterocycles and tertiary amines using peroxyacids such as peracetic acid and *m*-chloroperoxybenzoic acid, hydrogen peroxide, alkyl hydroperoxides such as *tert*-butyl hydroperoxide, sodium perborate, and dioxiranes such as dimethyldioxirane.

15

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[0585] The term “prophylactically or therapeutically effective amount” refers to an amount of the compound of the present disclosure, or a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof, that is sufficient to provide a reasonable benefit/risk ratio for the treatment and/or prevention of a disorder in any medical therapy. However, it should be recognized that the total daily dosage of the compound of formula (I) of the present disclosure, or a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof, and a composition thereof, should be determined by the attending physician within the scope of sound medical judgment.

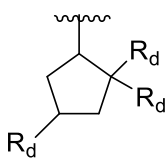
10 For any particular patient, the specific therapeutically effective dosage level depends on a variety of factors, including a disorder being treated and the severity of the disorder; activity of a specific compound used; a specific composition used; age, weight, general health status, sex, and diet of the patient; time of administration, route of administration, and excretion rate of the specific compound used; duration of treatment; drugs used in combination with or concurrently with the specific compound used; and similar factors known in the medical field.

[0586] The term “optionally” means that an atom may be substituted by a substituent or not. Unless otherwise specified, the type and number of substituents may be arbitrary on the basis of chemical feasibility. For example, the term “optionally substituted by one or more R_d” means that an atom may be substituted by one or more R_d or may not be substituted by R_d.

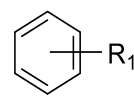
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[0587] When any variable (*e.g.*, R_d) occurs more than once in the composition or structure

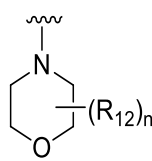
of a compound, the definition of the variable at each occurrence is independent. For

example,  indicates that the cyclopentyl group is substituted by 3 R_d, and each R_d has an independent option.

[0588] When the bond of a substituent may be cross-connected to two atoms on a ring, the
5 substituent may be bonded to any atom on the ring. For example, the structure moiety

 indicates that the substituent R₁ may be substituted at any position on a benzene ring.

[0589] When a substituent listed herein does not indicate through which atom it is connected to a compound included but not specifically mentioned in the general formula, such
10 substituent may be bonded through any of its atoms. For example, when pyrazole is used as a substituent, it means that any carbon atom or nitrogen atom on the pyrazole ring is connected to the substituted group. When  appears in a structure, it indicates that

the atom is a bonding atom. For example,  indicates that the nitrogen atom on the morpholine ring is a bonding atom.

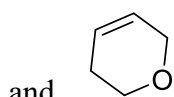
[0590] Unless otherwise specified, the term “ring” refers to saturated, partially saturated, or
15 unsaturated monocyclic and polycyclic systems, and the term “polycyclic” includes spiro rings, fused rings, or bridged rings. A group derived from a ring by removal of hydrogen atoms is referred to as a “cyclic group”, which includes monovalent rings, divalent rings (commonly referred to as ylene rings), trivalent rings, tetravalent rings, *etc.*, depending on

the number of substituents attached to the ring. In the present disclosure, the term “cyclic group” does not further distinguish the valency of the ring. Representative “rings” include substituted or unsubstituted heterocyclyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, cycloalkynyl, heterocycloalkynyl, aryl, or heteroaryl groups. The term “hetero” refers to substituted or unsubstituted heteroatoms and their oxidized forms, also referred to as heteroatom groups. The heteroatoms are generally selected from the group consisting of N, O, S, and P. The oxidized forms generally include NO, P(O), SO, and S(O)₂. The nitrogen atom may be substituted, *i.e.*, NR (where R is H or another substituent defined herein). The number of atoms on the ring is typically defined as the number of ring members. For example, “3- to 6-membered heterocycloalkyl” refers to a ring formed by 3 to 6 atoms arranged around, each ring optionally containing 1 to 3 heteroatoms and/or heteroatom groups, *i.e.*, N, O, S, NO, SO, S(O)₂, P(O), or NR, and each ring is optionally substituted by an R group as defined herein.

[0591] Unless otherwise specified, the term “cycloalkyl” refers to a saturated or unsaturated monocyclic or polycyclic hydrocarbon group. The cycloalkyl group is preferably C₃₋₈ monocyclic cycloalkyl (also referred to as 3- to 8-membered cycloalkyl), more preferably C₃₋₇ monocyclic cycloalkyl (also referred to as 3- to 7-membered cycloalkyl), and even more preferably C₃₋₆ monocyclic cycloalkyl (also referred to as 3- to 6-membered cycloalkyl). Examples of these monocyclic cycloalkyl groups include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. Unless otherwise specified, the cycloalkyl groups described in the present disclosure include monocyclic

cycloalkyl, spiro cycloalkyl, fused cycloalkyl, and bridged cycloalkyl.

[0592] Unless otherwise specified, the term “heterocyclyl” refers to a non-aromatic monocyclic or polycyclic ring containing a certain number of heteroatoms and/or heteroatom groups, which may be saturated or partially saturated (*e.g.*, containing one, two, or more double bonds). The heteroatoms and/or heteroatom groups are generally selected from the group consisting of N, O, S, P, NO, SO, S(O)₂, P(O), and NR, wherein the carbon atoms in the heterocycle are optionally oxo-substituted, *i.e.*, forming -C(O)-. The “heterocyclyl” group is preferably 3- to 8-membered heterocyclyl or 3- to 8-membered monocyclic heterocyclyl, more preferably 3- to 7-membered heterocyclyl or 3- to 7-membered monocyclic heterocyclyl, and even more preferably 5- to 6-membered heterocyclyl or 5- to 6-membered monocyclic heterocyclyl. Examples of these monocyclic heterocyclyl groups include, but are not limited to, piperidinyl, piperazinyl, morpholinyl, tetrahydropyranyl, 1,4-dioxanyl, pyrrolidinyl, tetrahydrofuranyl, [1,2]oxazolinyl, isoxazolinyl, oxetanyl, azetidiny,

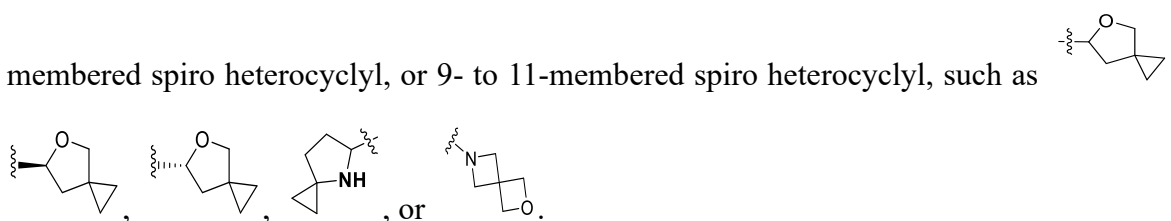


Polycyclic heterocyclyl groups include spiro heterocyclyl, fused heterocyclyl, and bridged heterocyclyl. Unless otherwise specified, the heterocyclyl groups described in the present disclosure include monocyclic heterocyclyl, spiro heterocyclyl, fused heterocyclyl, and bridged heterocyclyl. For example, the 3- to 8-membered heterocyclyl includes 3- to 8-membered spiro heterocyclyl, 3- to 8-membered fused heterocyclyl, and 3- to 8-membered bridged heterocyclyl.

[0593] Unless otherwise specified, the term “spiro heterocyclyl” refers to a 5- to 20-membered polycyclic heterocyclic group in which rings share one atom (referred to as a

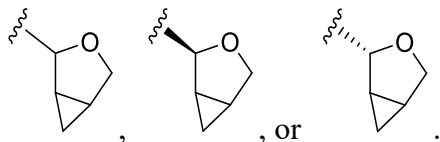
spiro atom), wherein the ring system optionally contains one or more double bonds, and wherein the heteroatoms are selected from the group consisting of N, O, S, P, P(O), NO, SO, and S(O)₂. The spiro heterocyclyl is preferably 5- to 13-membered spiro heterocyclyl, 6- to 12-membered spiro heterocyclyl, 5- to 11-membered spiro heterocycloalkyl, 7- to 11-

5 membered spiro heterocyclyl, or 9- to 11-membered spiro heterocyclyl, such as

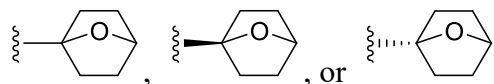


[0594] Unless otherwise specified, the term “fused heterocyclyl” refers to a 5- to 20-membered polycyclic heterocyclic group in which rings share a pair of adjacent atoms, wherein one or more rings may contain one or more double bonds, and wherein the heteroatoms are selected from the group consisting of N, O, S, P, P(O), NO, SO, and S(O)₂. The fused heterocyclyl is preferably 6- to 14-membered, more preferably 7- to 10-membered (*e.g.*, 7-membered, 8-membered, 9-membered, or 10-membered), and even more preferably 7- to 10-membered fused heterocyclyl. According to the number of rings involved, it may be classified into bicyclic, tricyclic, tetracyclic, and other polycyclic fused heterocyclyl, which is preferably bicyclic or tricyclic fused heterocyclyl, and more preferably 3-membered/4-membered, 3-membered/5-membered, 3-membered/6-membered, 4-membered/4-membered, 4-membered/5-membered, 4-membered/6-membered, 5-membered/3-membered, 5-membered/4-membered, 5-membered/5-membered, 5-membered/6-membered, 6-membered/3-membered, 6-membered/4-membered, 6-membered/5-membered, 6-membered/6-membered, 6-membered/7-membered, 7-

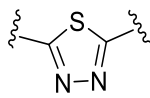
membered/5-membered, or 7-membered/6-membered bicyclic fused heterocyclyl, such as



[0595] Unless otherwise specified, the term “bridged heterocyclyl” refers to a 5- to 14-membered polycyclic heterocyclic group in which any two rings share two atoms that are not directly connected, wherein the ring system may contain one or more double bonds, and wherein the heteroatom groups are selected from the group consisting of N, O, S, P, P(O), NO, SO, and S(O)₂. The bridged heterocyclyl is preferably 6- to 14-membered, and more preferably 7- to 10-membered (*e.g.*, 7-membered, 8-membered, 9-membered, or 10-membered) bridged heterocyclyl. According to the number of rings involved, it may be classified into bicyclic, tricyclic, tetracyclic, and other polycyclic bridged heterocyclyl, which is preferably bicyclic, tricyclic, or tetracyclic bridged heterocyclyl, and more preferably bicyclic bridged heterocyclyl, such as



[0596] Unless otherwise specified, the term “heteroaryl” refers to a stable monocyclic aromatic hydrocarbon (monocyclic heteroaryl) or polycyclic aromatic hydrocarbon (polycyclic heteroaryl) containing at least one heteroatom or heteroatom group (selected from the group consisting of N, O, S, P, P(O), NO, SO, S(O)₂, and NR). The heteroaryl group is preferably 5- to 10-membered heteroaryl; more preferably 5-membered or 6-membered monocyclic heteroaryl; even more preferably 5-membered or 6-membered monocyclic heteroaryl containing nitrogen or sulfur atoms (also referred to as 5- to 6-membered heteroaryl). Examples of heteroaryl groups include, but are not limited to,



, imidazolyl, pyrazolyl, oxazolyl, thiazolyl, isoxazolyl, furyl, and triazolyl.

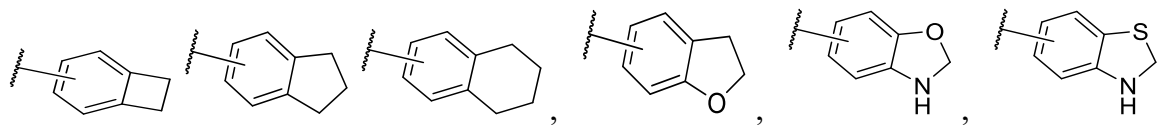
The polycyclic heteroaryl also includes a monocyclic heteroaryl group fused with one or more aryl groups, wherein the point of attachment is on the aromatic ring, and in such cases, the number of ring atoms continues to represent the number of ring atoms in the polycyclic

5 heteroaromatic ring system. The polycyclic heteroaryl also includes a monocyclic heteroaryl group fused with one or more cycloalkyl or heterocyclyl groups, wherein the point of attachment is on the monocyclic heteroaromatic ring, and in such cases, the number of ring atoms continues to represent the number of ring atoms in the polycyclic heteroaromatic ring system.

10 **[0597]** The term “aryl” refers to a monocyclic all-carbon aromatic ring (*i.e.*, monocyclic aryl) or a polycyclic aromatic ring system (*i.e.*, polycyclic aryl) having a conjugated π -electron system, which contains 6 to 14 (*e.g.*, 6, 7, 8, 9, 10, 11, 12, 13, or 14) ring atoms (*i.e.*, 6- to 14-membered aryl). The aryl group is preferably an aryl group having 6 to 10 ring atoms (*i.e.*, 6- to 10-membered aryl). The monocyclic aryl is, for example, phenyl. Non-

15 limiting examples of the polycyclic aryl include naphthyl, anthryl, phenanthryl, *etc.* The polycyclic aryl also includes a phenyl group fused with one or more heterocyclyl or cycloalkyl groups, or a naphthyl group fused with one or more heterocyclyl or cycloalkyl groups, wherein the point of attachment is on the phenyl or naphthyl ring, and in such cases, the number of ring atoms continues to represent the number of ring atoms in the polycyclic aromatic ring system. Non-limiting examples include:

20



etc.

[0598] Unless otherwise specified, when a group is not indicated as being substituted by any substituent, it is considered to be unsubstituted.

- 5 **[0599]** Unless otherwise specified, the term “alkyl” refers to a linear or branched saturated hydrocarbon group. The alkyl group is preferably C₁₋₆ alkyl, and more preferably C₁₋₄ alkyl. Examples of alkyl groups include, but are not limited to, methyl, ethyl, *n*-propyl, isopropyl, butyl, isobutyl, pentyl, isopentyl, neopentyl, and *n*-hexyl.

- [0600]** Unless otherwise specified, the term “hydroxyalkyl” refers to an alkyl group substituted by one or more hydroxyl groups, preferably an alkyl group substituted by one hydroxyl group (*i.e.*, -alkyl-OH). The “hydroxyalkyl” group is preferably C₁₋₆ hydroxyalkyl, and more preferably -C₁₋₆ alkyl-OH.
- 10

- [0601]** Unless otherwise specified, the term “alkoxy” refers to an alkyl group connected through an oxygen bridge, *i.e.*, a group obtained by replacing the hydrogen atom in a hydroxyl group with an alkyl group. The alkoxy group is preferably C₁₋₆ alkoxy, and more preferably C₁₋₄ alkoxy. Examples of alkoxy groups include, but are not limited to, methoxy, ethoxy, *n*-propoxy, isopropoxy, *n*-butoxy, *sec*-butoxy, *tert*-butoxy, *n*-pentoxy, neopentoxy, and *n*-hexyloxy.
- 15

- [0602]** Unless otherwise specified, the term “halogen” refers to a fluorine, chlorine, bromine, or iodine atom.
- 20

[0603] Unless otherwise specified, the term “haloalkyl” refers to an alkyl group in which

one or more hydrogen atoms are substituted by halogen atoms. The haloalkyl is preferably C₁₋₆ haloalkyl, and more preferably C₁₋₄ haloalkyl. Examples of haloalkyl groups include, but are not limited to, monofluoromethyl, difluoromethyl, trifluoromethyl, trichloromethyl, tribromomethyl, 2,2,2-trifluoroethyl, and 2,2,2-trichloroethyl.

5 **[0604]** Unless otherwise specified, the term “haloalkoxy” refers to an alkoxy group in which one or more hydrogen atoms are substituted by halogen atoms.

[0605] Specifically, all combinations of substituents and/or variants thereof described herein are permissible only when such combinations result in stable compounds.

[0606] Unless otherwise specified, the term “alkenyl” refers to a linear or branched alkenyl
10 group (or an alkyl group containing at least one carbon-carbon double bond, wherein the alkyl group is as defined above) derived by removal of one hydrogen atom, including “C₂₋₆ alkenyl”, “C₂₋₅ alkenyl”, “C₂₋₄ alkenyl”, and “C₂₋₃ alkenyl”. Specific examples include, but are not limited to, -CH=CH₂, -CH=CHCH₃, -C(CH₂)=CH₂, -CH=CHCH₂CH₃, and -CH₂CH=CHCH₃.

15 **[0607]** Unless otherwise specified, the term “alkynyl” refers to a linear or branched alkynyl group (or an alkyl group containing at least one carbon-carbon triple bond, wherein the alkyl group is as defined above) derived by removal of one hydrogen atom, including “C₂₋₅ alkynyl”, “C₂₋₄ alkynyl”, and “C₂₋₃ alkynyl”. Specific examples include, but are not limited to, -C≡CH, -C≡CHCH₃, CH=CHCH₂-, and CH≡C-C≡C-.

20 **[0608]** The term “hydroxy” refers to -OH.

[0609] The term “amino” refers to -NH₂.

[0610] The term “cyano” refers to -CN.

[0611] The term “oxo” or “oxo group” refers to “=O”.

[0612] The compounds of the present disclosure may exist in specific stereoisomeric forms.

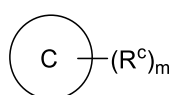
The term “stereoisomer” refers to isomers that have the same structure but differ in the spatial arrangement of their atoms. These include *cis* and *trans* (or *Z* and *E*) isomers, (-)- and (+)-isomers, (*R*)- and (*S*)-enantiomers, diastereomers, (*D*)- and (*L*)-isomers, tautomers, atropisomers, conformational isomers, and mixtures thereof (*e.g.*, racemates and mixtures of diastereomers). Substituents in the compounds of the present disclosure may contain additional asymmetric atoms. All such stereoisomers and mixtures thereof are encompassed within the scope of the present disclosure. Optically active (-)- and (+)-isomers, (*R*)- and (*S*)-enantiomers, and (*D*)- and (*L*)-isomers may be prepared by chiral synthesis, chiral reagents, or other conventional techniques. One isomer of a compound of the present disclosure may be prepared by asymmetric synthesis or using chiral auxiliaries. Alternatively, when the molecule contains a basic functional group (*e.g.*, an amino group) or an acidic functional group (*e.g.*, a carboxyl group), the compound reacts with an appropriate optically active acid or base to form diastereomeric salt, followed by diastereomeric resolution using conventional methods known in the art to obtain pure isomers. Furthermore, the separation of enantiomers and diastereomers is typically accomplished by chromatography.

[0613] In the chemical structures of the compounds of the present disclosure, the bond “—” indicates an unspecified configuration. That is, if chiral isomers are present in the chemical

structure, the bond “ $\diagup$ ” may be “ $\cdots$ ” or “ $\diagup$ ”, or may include both “ $\cdots$ ” and “ $\diagup$ ” configurations. For all carbon-carbon double bonds, even if only one configuration is named, both *Z* and *E* configurations are included.

[0614] The compounds of the present disclosure include all suitable isotopic derivatives thereof. The term “isotopic derivative” refers to a compound in which at least one atom is replaced by another atom having the same atomic number but a different atomic mass. Examples of isotopes that may be incorporated into the compounds of the present disclosure include stable and radioactive isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, sulfur, fluorine, chlorine, bromine, and iodine, such as ^2H (deuterium, D), ^3H (tritium, T), ^{11}C , ^{13}C , ^{14}C , ^{15}N , ^{17}O , ^{18}O , ^{32}P , ^{33}P , ^{33}S , ^{34}S , ^{35}S , ^{36}S , ^{18}F , ^{36}Cl , ^{82}Br , ^{123}I , ^{124}I , ^{125}I , ^{129}I , and ^{131}I , preferably deuterium. Compared to non-deuterated drugs, deuterated drugs offer advantages such as reduced toxic side effects, increased drug stability, enhanced therapeutic efficacy, and prolonged biological half-life. All isotopic variations of the compounds of the present disclosure, whether radioactive or non-radioactive, are encompassed within the scope of the present disclosure. Each available hydrogen atom attached to a carbon atom may be independently replaced by a deuterium atom, and such substitution may be partial or complete. Partial deuterium substitution means that at least one hydrogen atom is replaced by at least one deuterium atom.

[0615] When the bond of a substituent may be cross-connected to a ring, it indicates that the substituent may be bonded to any atom on the ring. For example, the structural moiety



indicates that the substituent R^c may be substituted at any position on ring C,

and the number of R^c is m.

[0616] In substituent structures, the dash “-” indicates the point of attachment for the substituent. For example, -CH₃ indicates that the substituent is attached via the carbon atom.

5 **[0617]** In the examples of the present disclosure, the naming of the title compound is converted from the compound structure by means of ChemDraw. If there is any inconsistency between the compound name and the compound structure, it may be determined by synthesizing relevant information and reaction routes; if it cannot be confirmed by other methods, the given structural formula of the compound shall prevail.

10 **[0618]** The preparation methods of some compounds in the present disclosure refer to the preparation methods of the aforementioned similar compounds. Those skilled in the art should know that when using or referring to the preparation methods cited therein, the feed ratio of reactants, reaction solvent, reaction temperature, and the like may be appropriately adjusted based on the specific reactants employed.

15 **[0619]** The compounds of the present disclosure may be prepared by a variety of synthetic methods well known to those skilled in the art, including the specific embodiments listed below, the embodiments formed by their combination with other chemical synthesis methods, and equivalent alternatives well known to those skilled in the art. Preferred embodiments include, but are not limited to, the examples of the present disclosure.

20

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0620] The following examples provide a detailed description of the present disclosure, but do not imply any adverse limitation on the present disclosure. The present disclosure has been described in detail herein, and its specific embodiments have also been disclosed. It will be apparent to those skilled in the art that various modifications and improvements may be made to the specific embodiments of the present disclosure without departing from the spirit and scope of the present disclosure.

[0621] In the examples of the present disclosure, the naming of the title compound is converted from the compound structure by means of ChemDraw. If there is any inconsistency between the compound name and the compound structure, it may be determined by synthesizing relevant information and reaction routes; if it cannot be confirmed by other methods, the given structural formula of the compound shall prevail. The preparation methods of some compounds in the present disclosure refer to the preparation methods of the aforementioned similar compounds. Those skilled in the art should know that when using or referring to the preparation methods cited therein, the feed ratio of reactants, reaction solvent, reaction temperature, and the like may be appropriately adjusted based on the specific reactants employed. The compounds of the present disclosure may be prepared by a variety of synthetic methods well known to those skilled in the art, including the specific embodiments listed below, the embodiments formed by their combination with other chemical synthesis methods, and equivalent alternatives well known to those skilled in the art. Preferred embodiments include, but are not limited to, the examples of the present disclosure.

[0622] 1. Summary of Experimental Instruments

[0623] The structures of the compounds of the present disclosure were determined by nuclear magnetic resonance (NMR) or/and liquid chromatography-mass spectrometry (LC-MS), or ultra-performance liquid chromatography-mass spectrometry (UPLC-MS).

5 **[0624]** NMR measurements were performed using a Bruker Neo 400M or Bruker Ascend 400 NMR spectrometer with deuterated dimethyl sulfoxide (DMSO-*d*₆), deuterated methanol (CD₃OD), deuterated chloroform (CDCl₃) and deuterium oxide (D₂O) as the solvents and tetramethylsilane (TMS) as the internal standard. NMR chemical shifts (δ) are expressed in parts per million (ppm).

10 **[0625]** LC-MS analyses were performed using an Agilent 1200 & 6120B single quadrupole mass spectrometer or a Shimadzu LC-20AD XR & MS 2020 single quadrupole mass spectrometer, with electrospray ionization (ESI) as the ion source.

[0626] HPLC analyses were performed using a Shimadzu 20AD XR high-performance liquid chromatograph.

15 **[0627]** Preparative HPLC analyses were performed using Gilson GX281 333/334 Pump or Gilson TRILUTION LC.

[0628] Chiral HPLC analyses were performed using Waters Arc with 2998 with QDA.

[0629] Supercritical fluid chromatography (SFC) analyses were performed using Waters ACQUITY UPCC with QDA.

20 **[0630]** The starting materials and intermediates directly used in the present disclosure may be synthesized according to methods known in the art or purchased commercially.

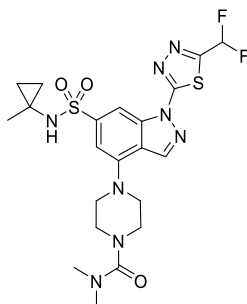
Experimental methods for which specific conditions are not indicated in the examples are typically performed under conventional conditions or according to the conditions recommended by the manufacturer of the starting materials or commercial products.

Reagents for which specific sources are not indicated are commercially available standard reagents.

[0631] The progress of reactions in the examples may be monitored by conventional methods such as thin-layer chromatography (TLC) and LC-MS. The eluent system for column chromatography used in purification and the developing solvent system for TLC may consist of one or more of the following solvents: dichloromethane, methanol, *n*-hexane, ethyl acetate, petroleum ether, ethyl acetate, acetone, dichloromethane, and the like. The volume ratio of the solvents may be adjusted according to the polarity of the compounds or by adding a small amount of basic or acidic reagents such as triethylamine, acetic acid, or trifluoroacetic acid.

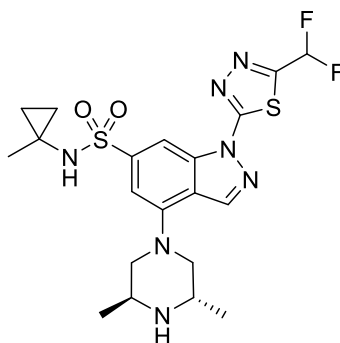
[0632] 2. Synthetic Examples

[0633] Reference Example 1:



[0634] The preparation method refers to patent WO2021055744.

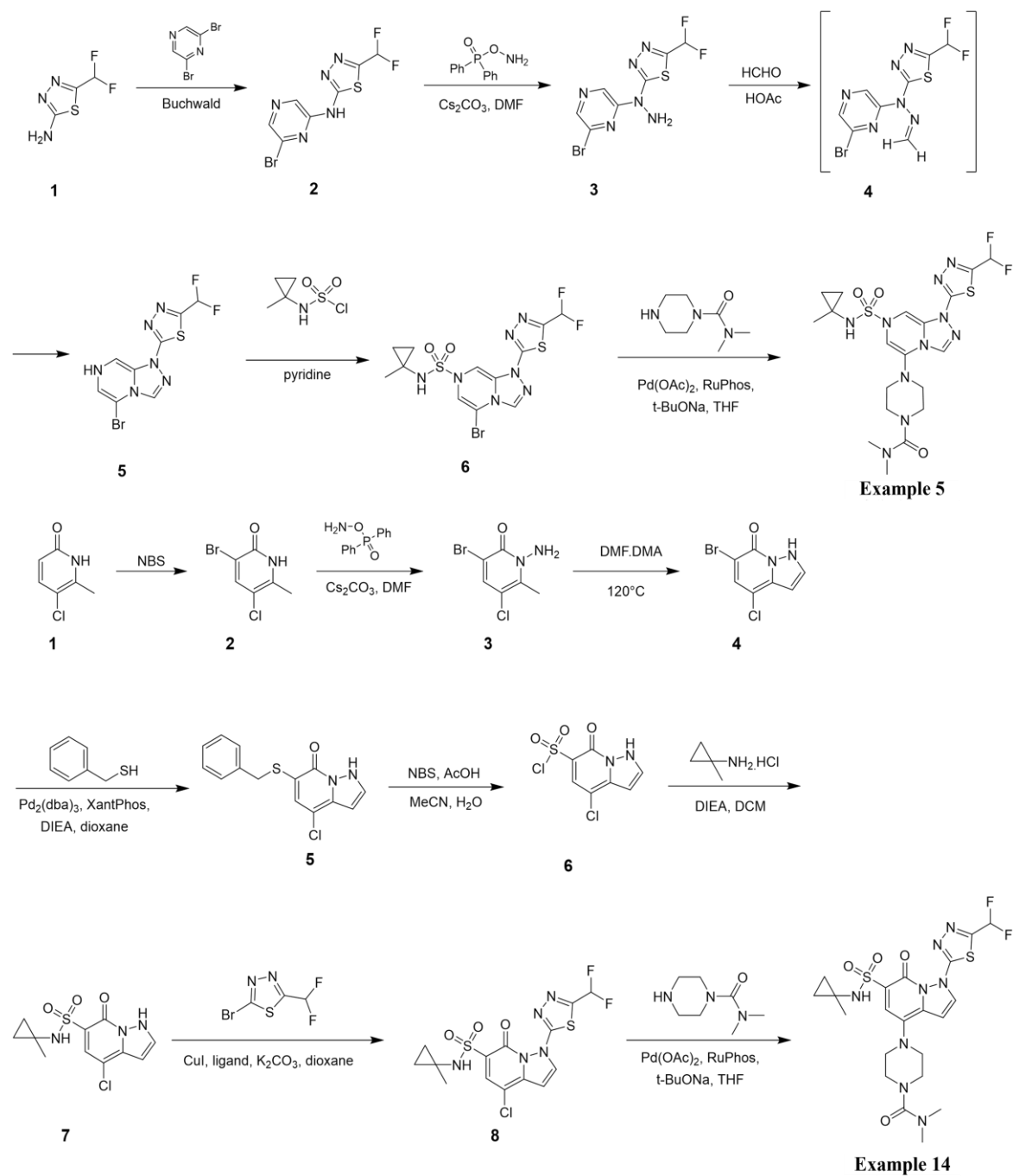
[0635] Comparative compound:

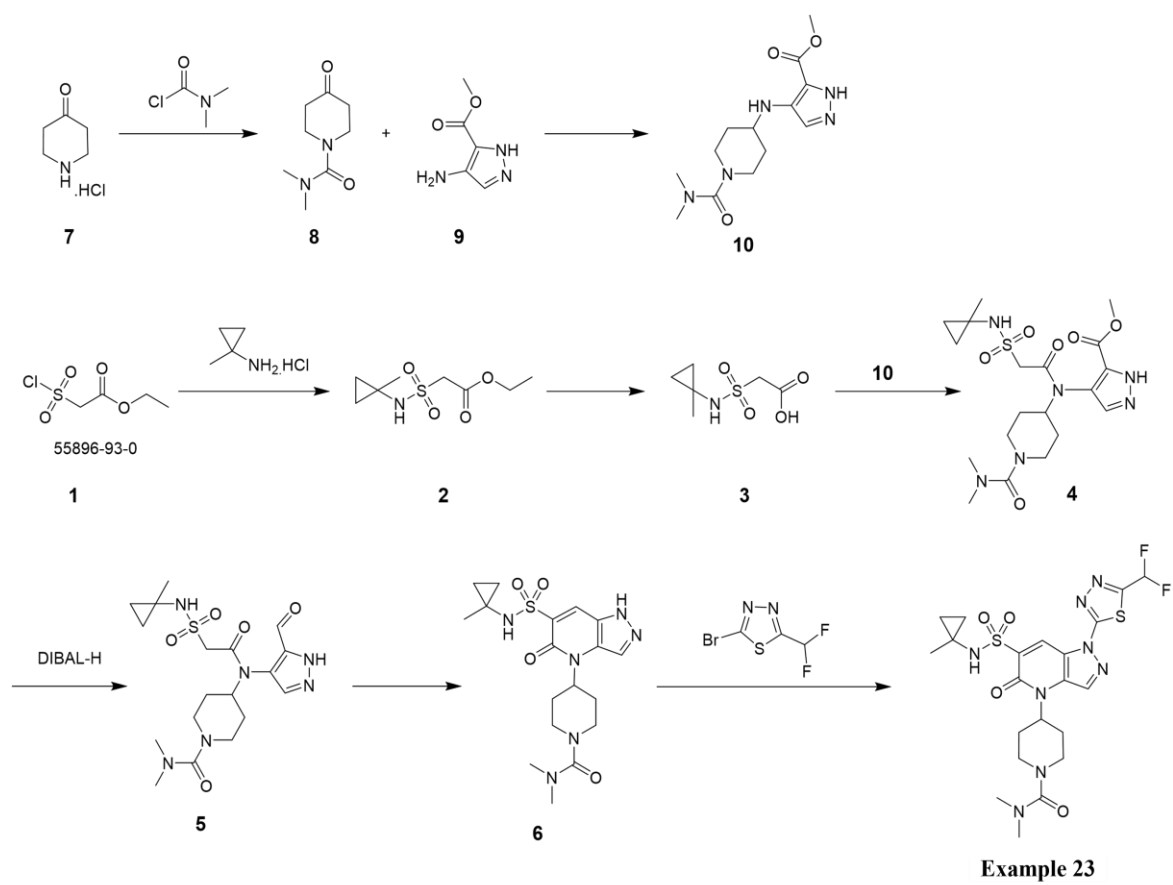


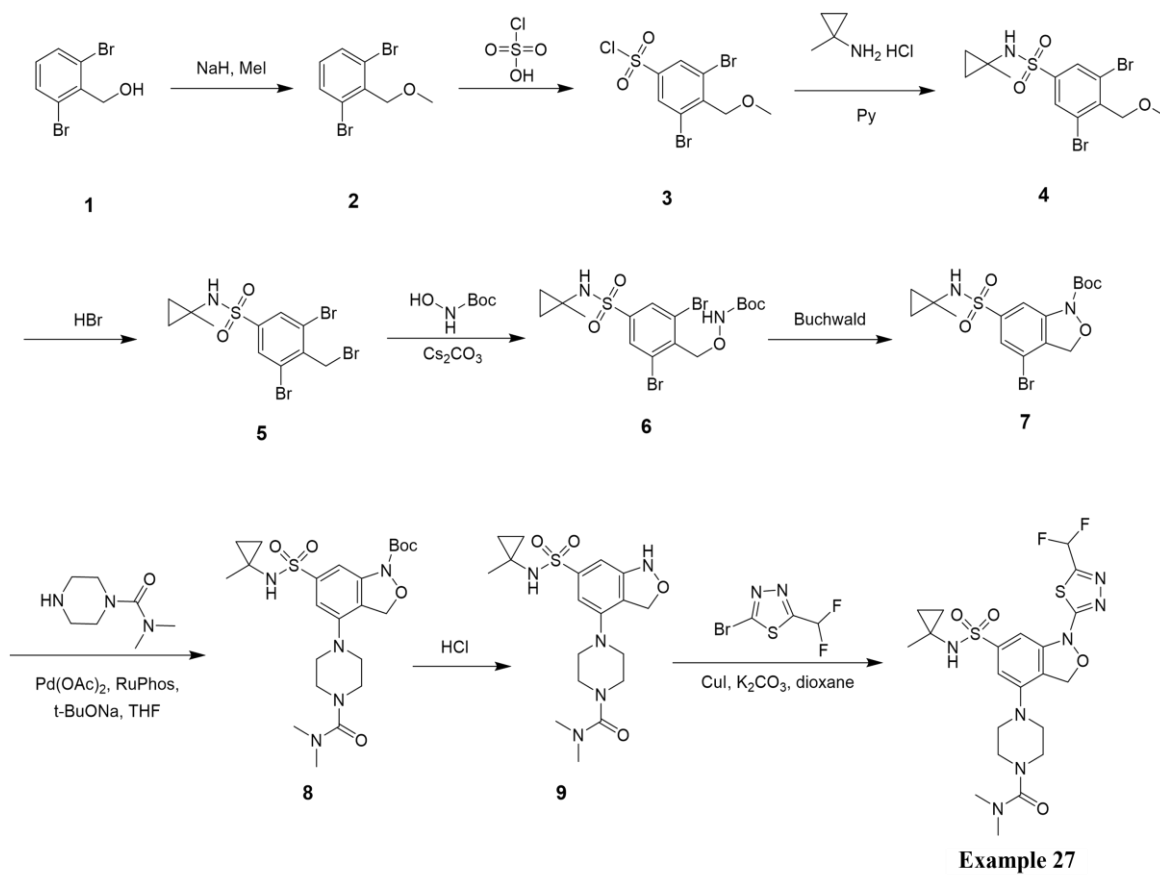
[0636] The preparation method refers to the synthesis of compound of formula A in patent WO2023183850A1.

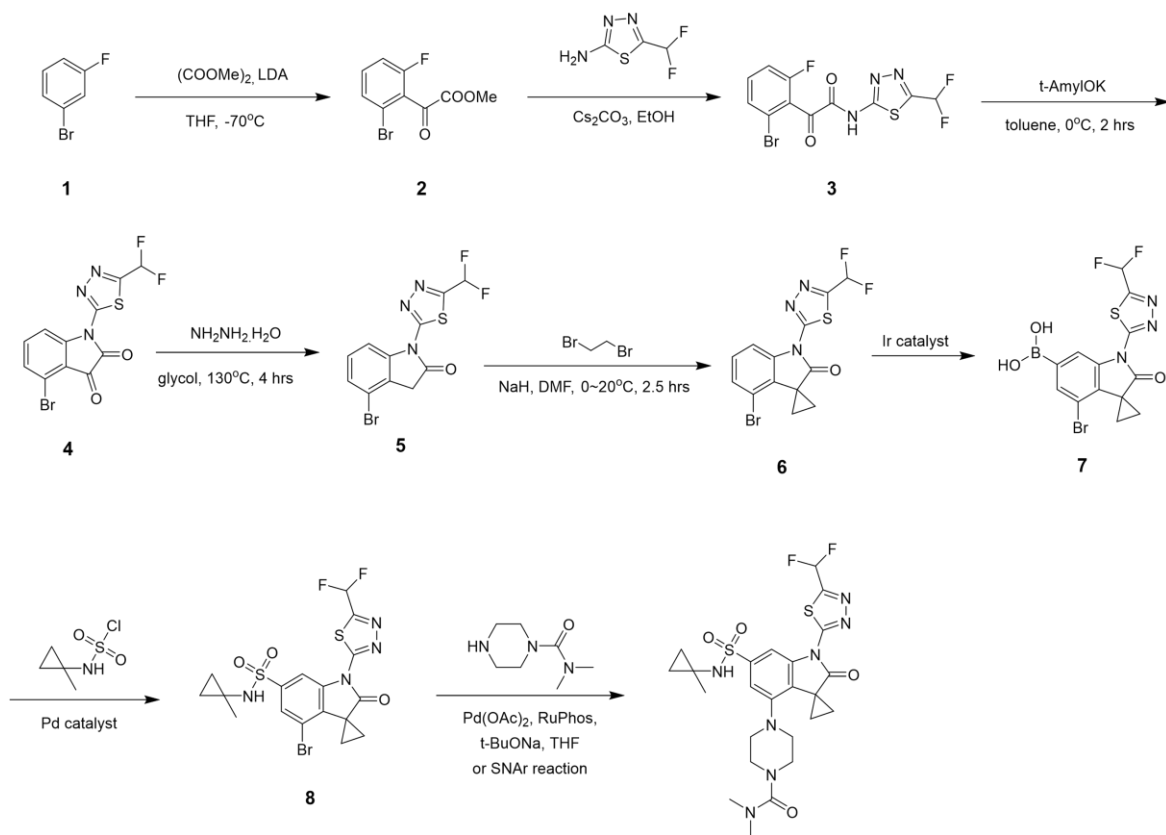
[0637] The lowest energy conformation (low-energy conformation) of Reference Example 1 was calculated using Spartan software at the ω B97X-D/6-31G* level of theory. In the low-energy conformation of Reference Example 1, the difluoromethyl-substituted thiazole moiety is coplanar with the benzopyrazole core, and the S atom of the thiazole moiety tends to orient away from the sulfonamide moiety (corresponding to a dihedral angle of 0 degrees in the energy barrier diagram). In the binding conformation of Reference Example 1 with the PARG protein, the dihedral angle between the difluoromethyl-substituted thiazole moiety and the benzopyrazole core is only 1.5 degrees, which is highly consistent with the low-energy conformation of Reference Example 1, fully explaining the high binding activity of Reference Example 1 with the PARG protein as reported in patent WO2021055744. Generally, when the structural difference between the lowest energy conformation (low-energy conformation) of a small molecule and its binding conformation (active conformation) in a protein is minimal, the energy loss during the conversion from the low-energy conformation to the active conformation is also minimal. Consequently, the compound binds more readily to the protein and exhibits higher binding activity.

[0638] The synthetic routes for some examples of the present disclosure are as follows:

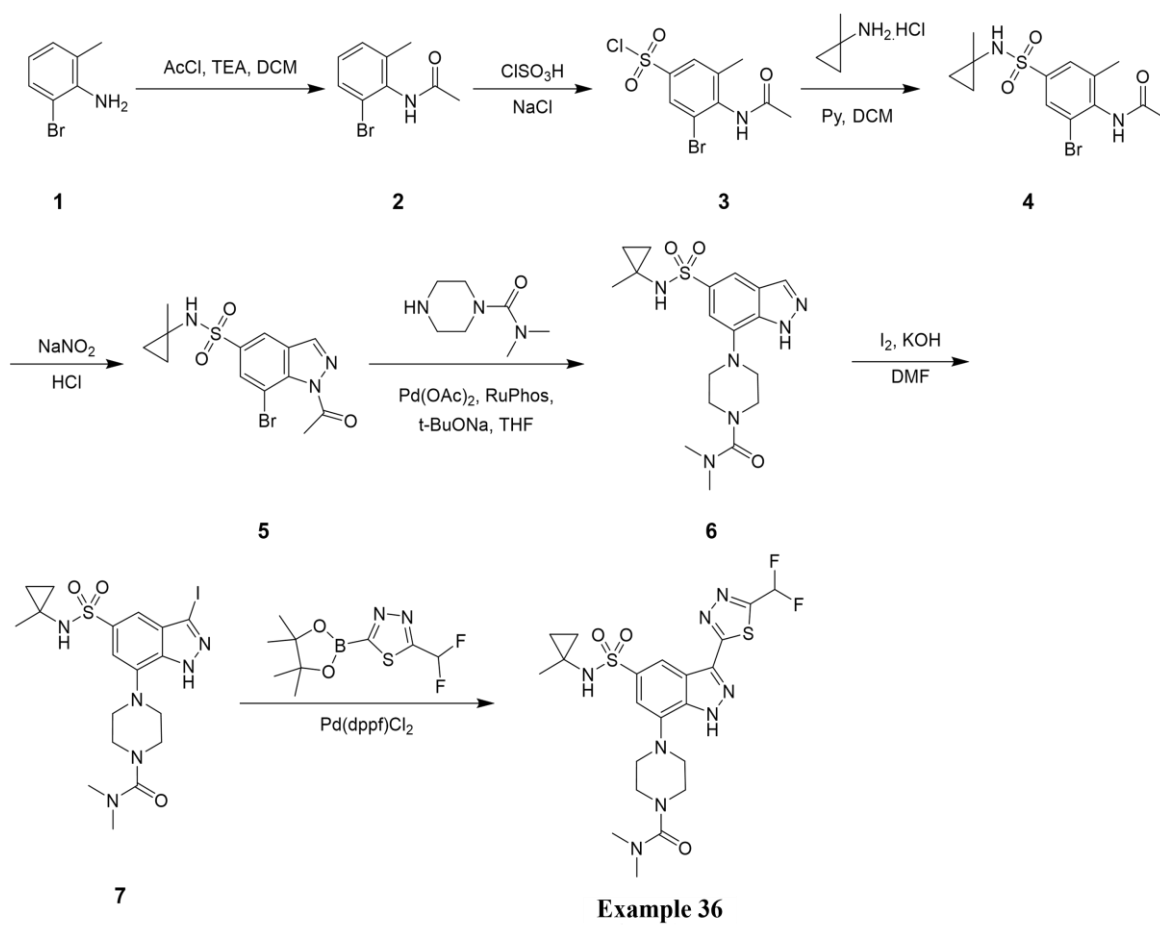


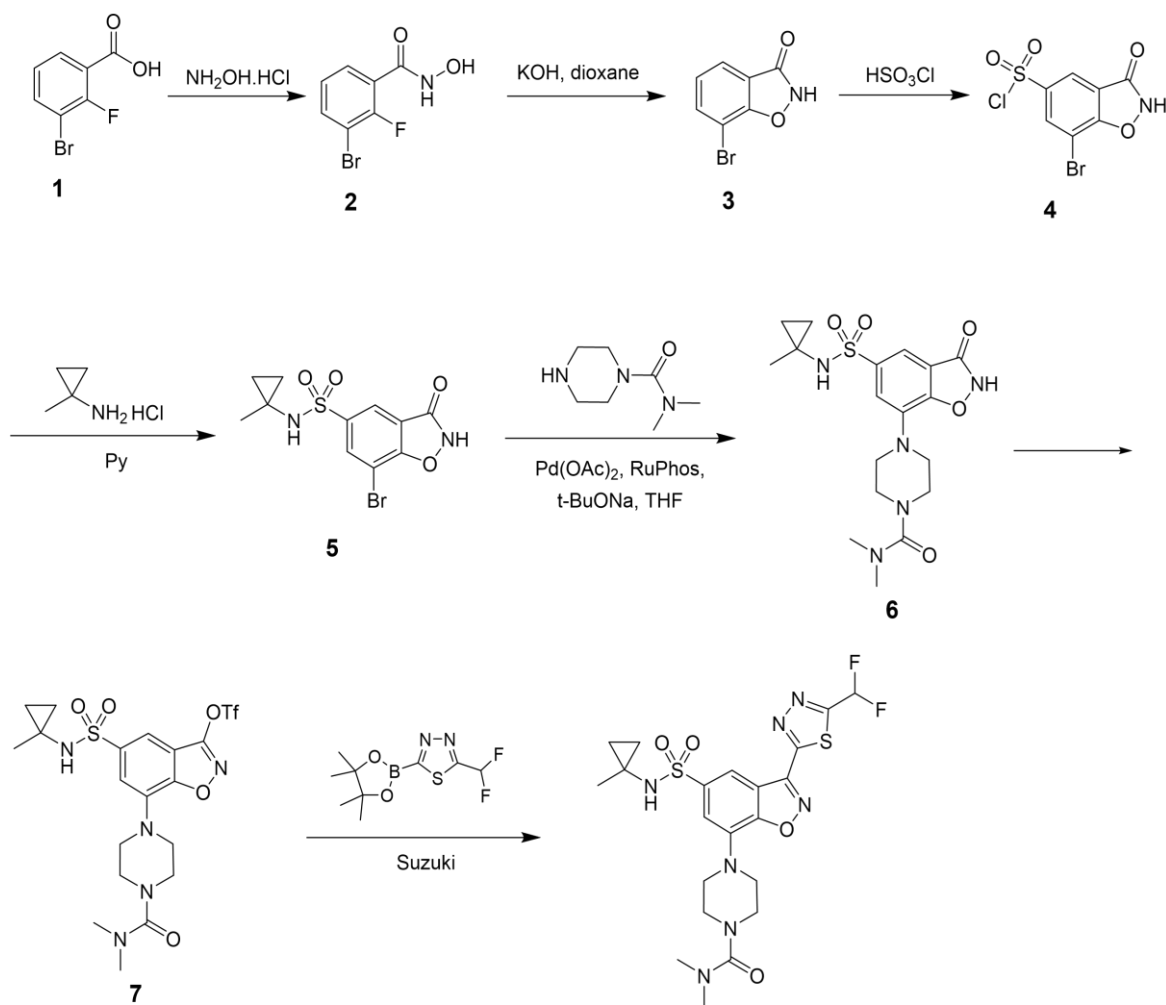






Example 29

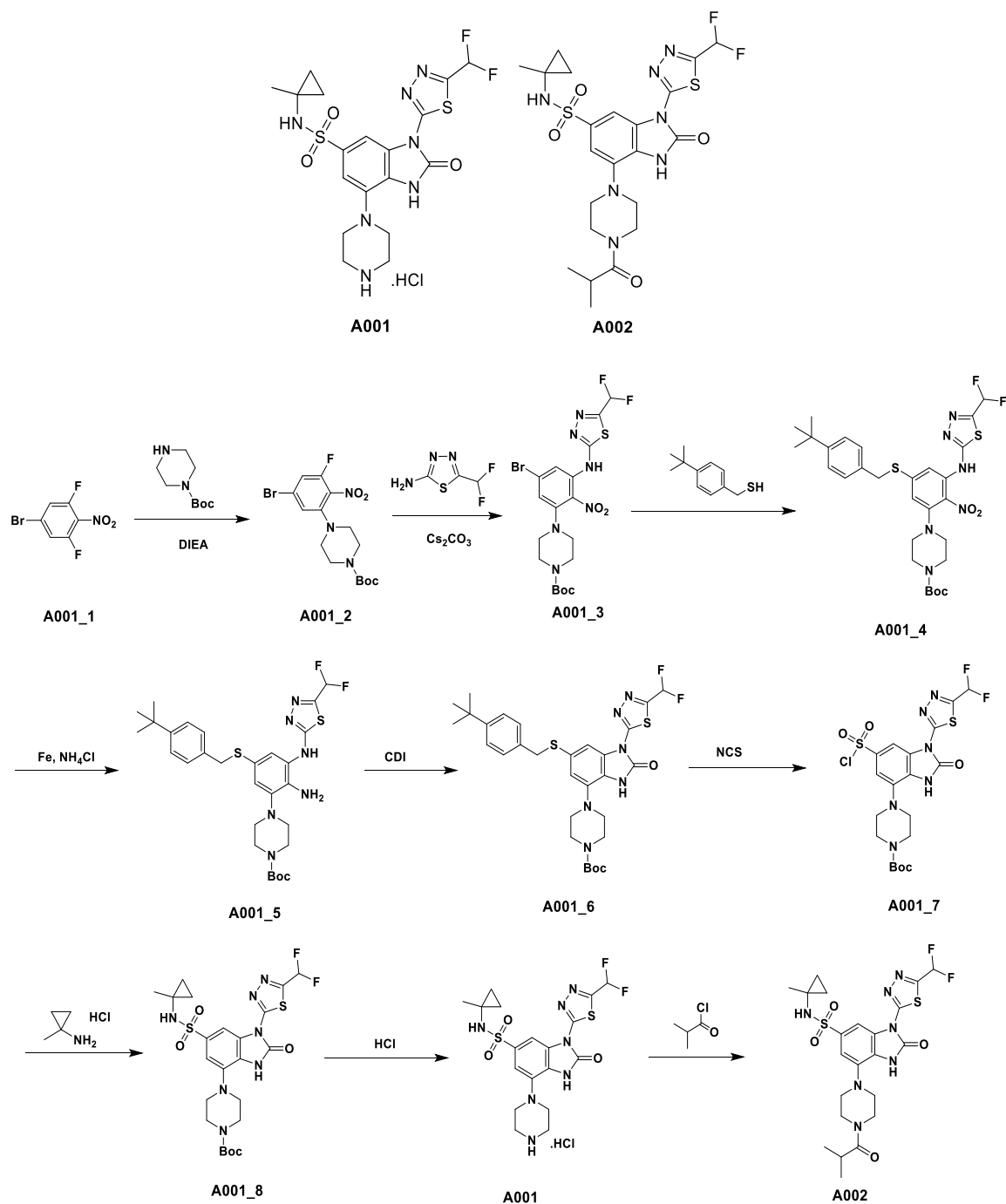


**Example 40**

[0639] The compounds in other examples listed in Table 1 of the present disclosure, such as Example 1, Example 2, Example 3, Example 4, Example 6, Example 7, Example 8, Example 9, Example 10, Example 11, Example 12, Example 13, Example 15, Example 16, Example 17, Example 18, Example 19, Example 20, Example 21, Example 22, Example 24, Example 25, Example 26, Example 28, Example 30, Example 31, Example 32, Example 33, Example 34, Example 35, Example 37, Example 38, Example 39, Example 41, Example 42, Example 43, and other described compounds, were prepared with reference to any one of the above synthetic procedures.

[0640] Specific Synthetic Examples:

[0641] Example A001 and Example A002



5 **[0642]** Step 1: Synthesis of compound A001_2

[0643] 005_1 (10.0 g, 42.0 mmol, 1.00 eq) and N-Boc piperazine (7.83 g, 42.0 mmol) were

dissolved in N,N-dimethylacetamide (100 mL), followed by addition of N,N-diisopropylethylamine (27.1 g, 210 mmol). The reaction mixture was heated to 110°C and stirred for 16 hours. After completion of the reaction, the reaction mixture was cooled to room temperature, quenched with water (600 mL), and extracted with ethyl acetate (100 mL
5 × 3). The organic phases were combined, washed with brine (100 mL × 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain A001_2 (16.4 g).

[0644] MS (ESI) M/Z: 348.1, 350.2 [M-55]⁺.

[0645] ¹H NMR (400 MHz, CDCl₃-d): δ 7.10 - 7.07 (m, 1H), 7.04 - 7.03 (m, 1H), 3.53 (t,
10 J = 4.8 Hz, 4H), 3.01 (t, J = 4.8 Hz, 4H), 1.48 (s, 9H).

[0646] Step 2: Synthesis of compound A001_3

[0647] Cesium carbonate (19.3 g, 59.3 mmol) and 5-(difluoromethyl)-1,3,4-thiadiazol-2-amine (4.49 g, 29.6 mmol) were added to a solution of A001_2 (8.00 g, 19.8 mmol) in N,N-dimethylacetamide (80 mL). The reaction mixture was heated to 110°C under nitrogen
15 atmosphere and stirred for 16 hours. After completion of the reaction, the reaction mixture was cooled to room temperature, quenched with water (500 mL), and extracted with ethyl acetate (100 mL × 3). The organic phases were combined, washed with brine (100 mL × 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain A001_3 (6.7
20 g).

[0648] MS (ESI) M/Z: 533.1, 535.1 [M-H]⁻.

[0649] Step 3: Synthesis of compound A001_4

[0650] A001_3 (5.70 g, 10.6 mmol), 4-*tert*-butylbenzyl mercaptan (2.11 g, 11.7 mmol), and N,N-diisopropylethylamine (3.44 g, 26.6 mmol) were dissolved in 1,4-dioxane (60 mL). The system was purged with nitrogen three times, followed by addition of Pd₂(dba)₃ (974 mg, 1.06 mmol) and Xantphos (1.23 g, 2.13 mmol, 0.20 eq), and purged with nitrogen three additional times. The reaction mixture was heated to 70°C and stirred for 1 hour. After completion of the reaction, the reaction mixture was cooled to room temperature, quenched with water (200 mL), and extracted with ethyl acetate (50 mL × 3). The organic phases were combined, washed with brine (100 mL × 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain A001_4 (4.75 g).

[0651] MS (ESI) M/Z: 633.2 [M-H]⁻.

[0652] ¹H NMR (400 MHz, CDCl₃-*d*): δ 7.75 (s, 1H), 7.37 - 7.27 (m, 4H), 6.91 (t, *J* = 53.6 Hz, 1H), 6.61 (s, 1H), 4.22 (s, 2H), 3.53 (t, *J* = 4.8 Hz, 4H), 2.94 (t, *J* = 4.8 Hz, 4H), 1.48 (s, 9H), 1.31 (s, 9H).

[0653] Step 4: Synthesis of compound A001_5

[0654] A001_4 (4.20 g, 6.62 mmol) was dissolved in ethanol (30 mL) and water (10 mL), followed by addition of iron powder (1.85 g, 33.0 mmol) and ammonium chloride (1.77 g, 33.0 mmol). The reaction mixture was heated to 80°C and stirred for 1.5 hours. After completion of the reaction, the reaction mixture was cooled to room temperature and filtered through diatomite. The filtrate was diluted with water (100 mL) and extracted with ethyl

acetate (50 mL $\times$ 3). The organic phases were combined, washed with brine (50 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain A001_5 (2.4 g).

5 [0655] MS (ESI) M/Z: 603.3 [M-H]⁻.

[0656] ¹H NMR (400 MHz, DMSO-*d*₆): δ 9.81 (s, 1H), 7.49 - 7.18 (m, 4H), 7.11 - 7.09 (m, 2H), 6.55 (d, *J* = 2.0 Hz, 1H), 4.91 (s, 2H), 3.93 (s, 2H), 3.52 - 3.38 (m, 4H), 2.68 - 2.55 (m, 4H), 1.41 (s, 9H), 1.23 (s, 9H).

[0657] Step 5: Synthesis of compound A001_6

10 [0658] A001_5 (430 mg, 711 μ mol) was dissolved in tetrahydrofuran (10 mL), followed by addition of carbonyldiimidazole (173 mg, 1.07 mmol, 1.50 eq). The reaction mixture was heated to 70°C and stirred for 1 hour. After completion of the reaction, the reaction mixture was cooled to room temperature and directly concentrated under reduced pressure to obtain a crude product. The crude product was triturated with methyl *tert*-butyl ether (5
15 mL) at room temperature, filtered, and the filter cake was collected to obtain A001_6 (360 mg).

[0659] MS (ESI) M/Z: 629.2 [M-H]⁻.

[0660] ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.11 (s, 1H), 8.10 (s, 1H), 7.61 (t, *J* = 53.2 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.03 (s, 1H), 6.66 (s, 1H), 4.13 (s, 2H), 3.50 - 3.48 (m, 4H), 2.79 - 2.77 (m, 4H), 1.43 (s, 9H), 1.23 (s, 9H).
20

[0661] Step 6: Synthesis of compound A001_7

[0662] A001_6 (250 mg, 396 μ mol) was dissolved in acetic acid (2.5 mL), water (1.25 mL), and dichloromethane (2.5 mL). The mixture was cooled to 0°C in an ice-salt bath, and N-chlorosuccinimide (159 mg, 1.19 mmol, 3.00 eq) was added in portions. After the addition was completed, the reaction mixture was slowly warmed to 20°C and stirred for 4 hours.

5 After completion of the reaction, the reaction mixture was cooled to 0°C, then slowly added with saturated sodium bicarbonate aqueous solution to adjust the pH to approximately 5, and extracted with dichloromethane (5 mL $\times$ 3). The organic phases were combined, washed with brine (10 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation to obtain A001_7 (220 mg) as a crude product, which
10 was directly used in the next step.

[0663] MS (ESI) M/Z: 549.2, 551.4 [M-H]⁻.

[0664] Step 7: Synthesis of compound A001_8

[0665] 1-Methylcyclopropanamine hydrochloride (141 mg, 1.31 mmol) and N,N-diisopropylethylamine (253 mg, 1.96 mmol) were dissolved in dichloromethane (0.9 mL),
15 followed by addition of a solution of A001_7 (180 mg, 327 μ mol) in dichloromethane (0.9 mL). The reaction mixture was stirred at 20°C for 1 hour. After completion of the reaction, the reaction mixture was quenched with water (5 mL) and extracted with ethyl acetate (5 mL $\times$ 3). The organic phases were combined, washed with brine (5 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary
20 evaporation. The residue was purified by column chromatography to obtain A001_8 (110 mg).

[0666] MS (ESI) M/Z: 584.2 [M-H]⁻.

[0667] ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.44 (s, 1H), 8.52 (d, *J* = 1.2 Hz, 1H), 8.08 (s, 1H), 7.63 (t, *J* = 53.2 Hz, 1H), 7.37 (d, *J* = 1.2 Hz, 1H), 3.58 - 3.56 (m, 4H), 2.98 - 2.96 (m, 4H), 1.44 (s, 9H), 1.07 (s, 3H), 0.64 - 0.62 (m, 2H), 0.39 - 0.36 (m, 2H).

5 [0668] Step 8: Synthesis of compound A001

[0669] A001_8 (60 mg, 102 μmol) was dissolved in ethyl acetate (1 mL), followed by addition of 4 M HCl in methanol (2 mL). The reaction mixture was stirred at 20°C for 1 hour. After completion of the reaction, the reaction mixture was directly concentrated under reduced pressure to obtain a crude product (50 mg, hydrochloride salt). 20 mg of the
10 crude product was purified by preparative HPLC (acidic conditions, chromatographic column: Phenomenex Luna C18) to obtain A001 (11.81 mg, hydrochloride salt).

[0670] MS (ESI) M/Z: 486.0 [M+H]⁺.

[0671] ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.51 (s, 1H), 9.20 - 8.96 (m, 2H), 8.55 (d, *J* = 1.2 Hz, 1H), 8.17 (s, 1H), 7.64 (t, *J* = 53.2 Hz, 1H), 7.39 (s, 1H), 3.48 - 3.42 (m, 4H), 3.42 -
15 3.38 (m, 4H), 1.07 (s, 3H), 0.64 - 0.62 (m, 2H), 0.39 - 0.37 (m, 2H).

[0672] Step 9: Synthesis of compound A002

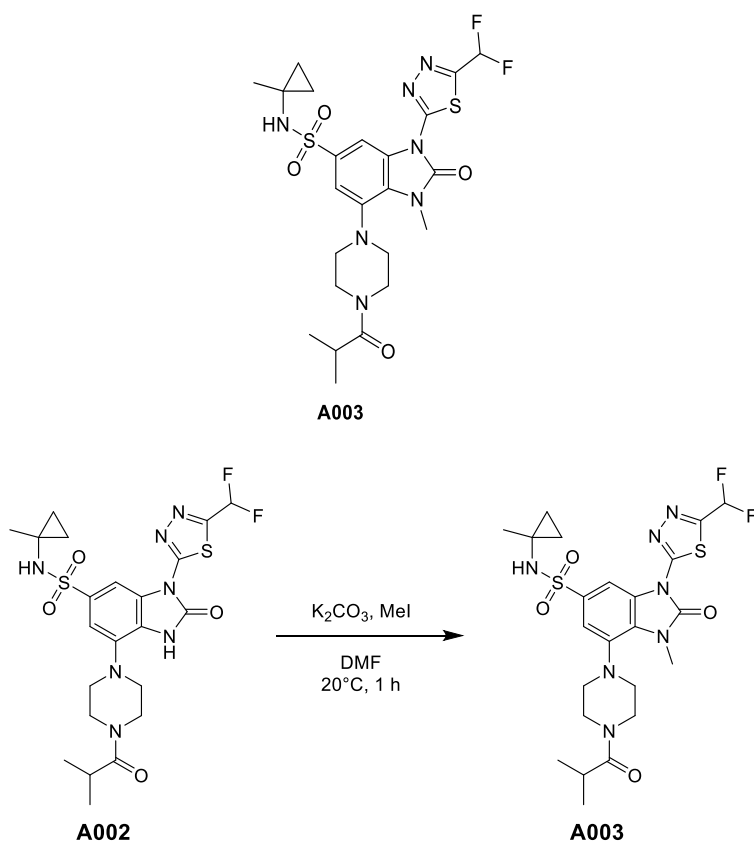
[0673] A001 (50 mg, 95.8 μmol, hydrochloride salt) and triethylamine (48.5 mg, 479 μmol) were dissolved in N,N-dimethylformamide (0.5 mL), followed by addition of 2-methylpropanoyl chloride (12.3 mg, 115 μmol). The reaction mixture was stirred at 20°C
20 for 1 hour. After completion of the reaction, the reaction mixture was quenched with water (0.1 mL) and purified by preparative HPLC (neutral conditions, chromatographic column:

Waters Xbridge Prep OBD C18) to obtain A002 (27.2 mg).

[0674] MS (ESI) M/Z: 556.2 [M+H]⁺.

[0675] ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.48 (s, 1H), 8.52 (d, *J* = 1.2 Hz, 1H), 8.07 (s, 1H), 7.62 (t, *J* = 53.2 Hz, 1H), 7.35 (d, *J* = 1.2 Hz, 1H), 3.74 - 3.70 (m, 4H), 3.02 - 2.91 (m, 5H), 1.05 - 1.03 (m, 9H), 0.64 - 0.61 (m, 2H), 0.38 - 0.35 (m, 2H).

[0676] Example A003



[0677] Step 1: Synthesis of A003

[0678] A002 (15 mg, 27.0 μmol) and potassium carbonate (7.46 mg, 54.0 μmol) were dissolved in N,N-dimethylformamide (0.2 mL). Iodomethane (5.75 mg, 40.5 μmol) was added in one portion at 20°C. The reaction mixture was stirred at 20°C for 1 hour. After completion of the reaction, the reaction mixture was quenched with water (2 mL) and

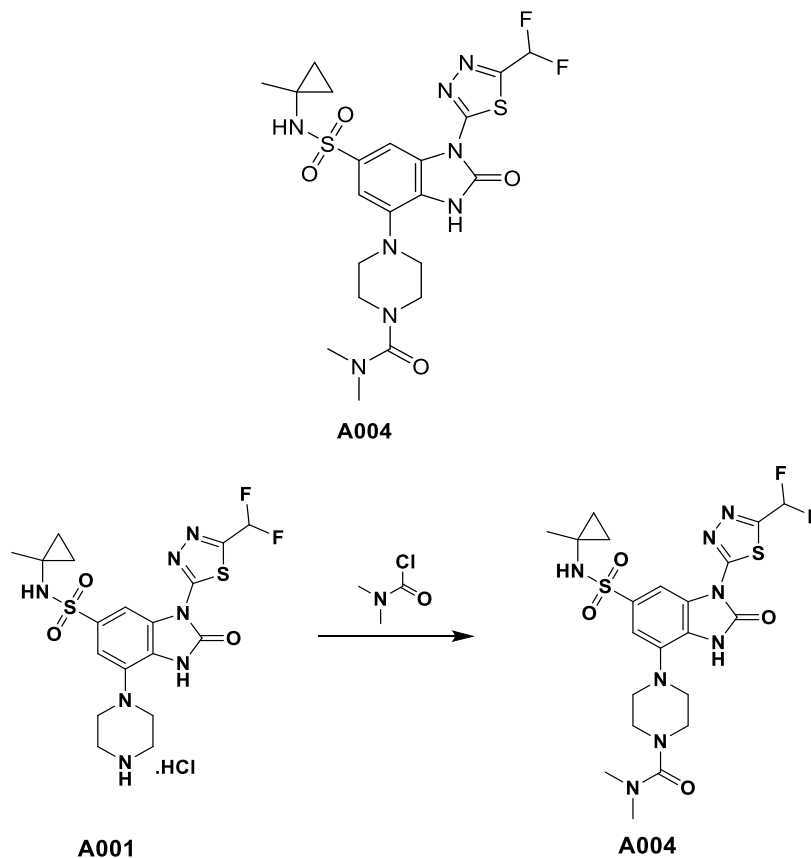
extracted with ethyl acetate (2 mL $\times$ 3). The organic phases were combined, washed with brine (2 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The crude product was purified by preparative HPLC (neutral conditions, column: Waters Xbridge Prep OBD C18) to obtain A003 (1.2 mg).

5 **[0679]** MS (ESI) M/Z : 570.2 $[M+H]^+$.

[0680] ^1H NMR (400 MHz, DMSO- d_6): δ 8.66 (d, J = 1.6 Hz, 1H), 8.13 (s, 1H), 7.77 - 7.50 (m, 2H), 4.52 - 4.50 (m, 1H), 4.07 - 4.06 (m, 1H), 3.80 (s, 3H), 3.45 - 3.42 (m, 1H), 3.18 - 3.16 (m, 2H), 2.98 - 2.80 (m, 3H), 2.71 - 2.68 (m, 1H), 1.08 - 1.05 (m, 9H), 0.64 - 0.62 (m, 2H), 0.40 - 0.37 (m, 2H).

10

[0681] Example A004



[0682] Step 1: Synthesis of compound A004

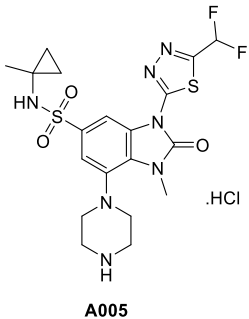
[0683] A001 (7 mg, 14.4 μmol) and triethylamine (14.6 mg, 144 μmol , 10.00 eq) were dissolved in DCM (2.0 mL), followed by addition of dimethylcarbamoyl chloride (15.5 mg, 144 μmol). The reaction mixture was stirred at 23°C for 20 hours. The reaction mixture was quenched with water (5 mL) and extracted three times with ethyl acetate. The organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, concentrated, and purified by preparative chromatography (acidic conditions, 0.1% FA, chromatographic column: YMC-Actus Triart C18 ExRS) to obtain A004 (4.0 mg).

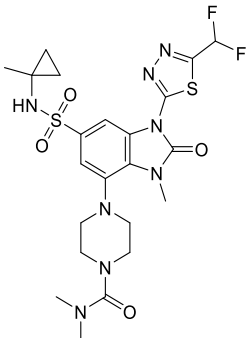
[0684] MS (ESI) M/Z : 557.1 $[M+H]^+$.

[0685] ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.41 (s, 1H), 7.89 (s, 1H), 7.58 (t, $J = 53.4$ Hz, 1H), 7.23 (s, 1H), 3.36 - 3.32 (m, 4H), 3.17 - 3.09 (m, 4H), 2.79 (s, 6H), 1.04 (s, 3H), 0.66 - 0.58 (m, 2H), 0.37 - 0.31 (m, 2H).

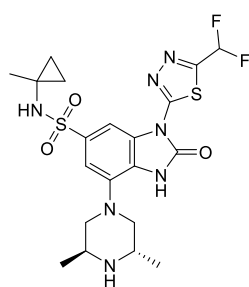
[0686] Example A005 and Example A006

[0687] Table 2

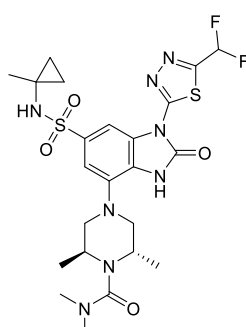
Example	Structural formula	Structural characterization
A005	 A005	^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 8.94 (s, 2H), 8.69 (d, $J = 1.6$ Hz, 1H), 8.26 (s, 1H), 7.80 - 7.49 (m, 2H), 3.78 (s, 3H), 3.45 - 3.38 (m, 2H), 3.30 - 3.20 (m, 4H), 3.17 - 3.03 (m, 2H), 1.08 (s, 3H), 0.66 - 0.59 (m, 2H), 0.42 - 0.36 (m, 2H). MS (ESI) M/Z: 500.0 $[M+H]^+$.

A006	 A006	¹H NMR (400 MHz, DMSO-<i>d</i>₆): δ 8.65 (d, <i>J</i> = 1.6 Hz, 1H), 8.14 (s, 1H), 7.77 - 7.50 (m, 2H), 3.79 (s, 3H), 3.61 - 3.58 (m, 2H), 3.12 - 3.08 (m, 4H), 2.86 - 2.83 (m, 2H), 2.80 (s, 6H), 1.07 (s, 3H), 0.64 - 0.61 (m, 2H), 0.40 - 0.36 (m, 2H). MS (ESI) M/Z: 571.1 [M+H]⁺.
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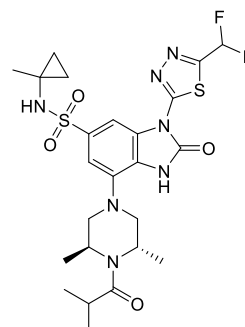
[0688] Example A007, Example A008, and Example A009



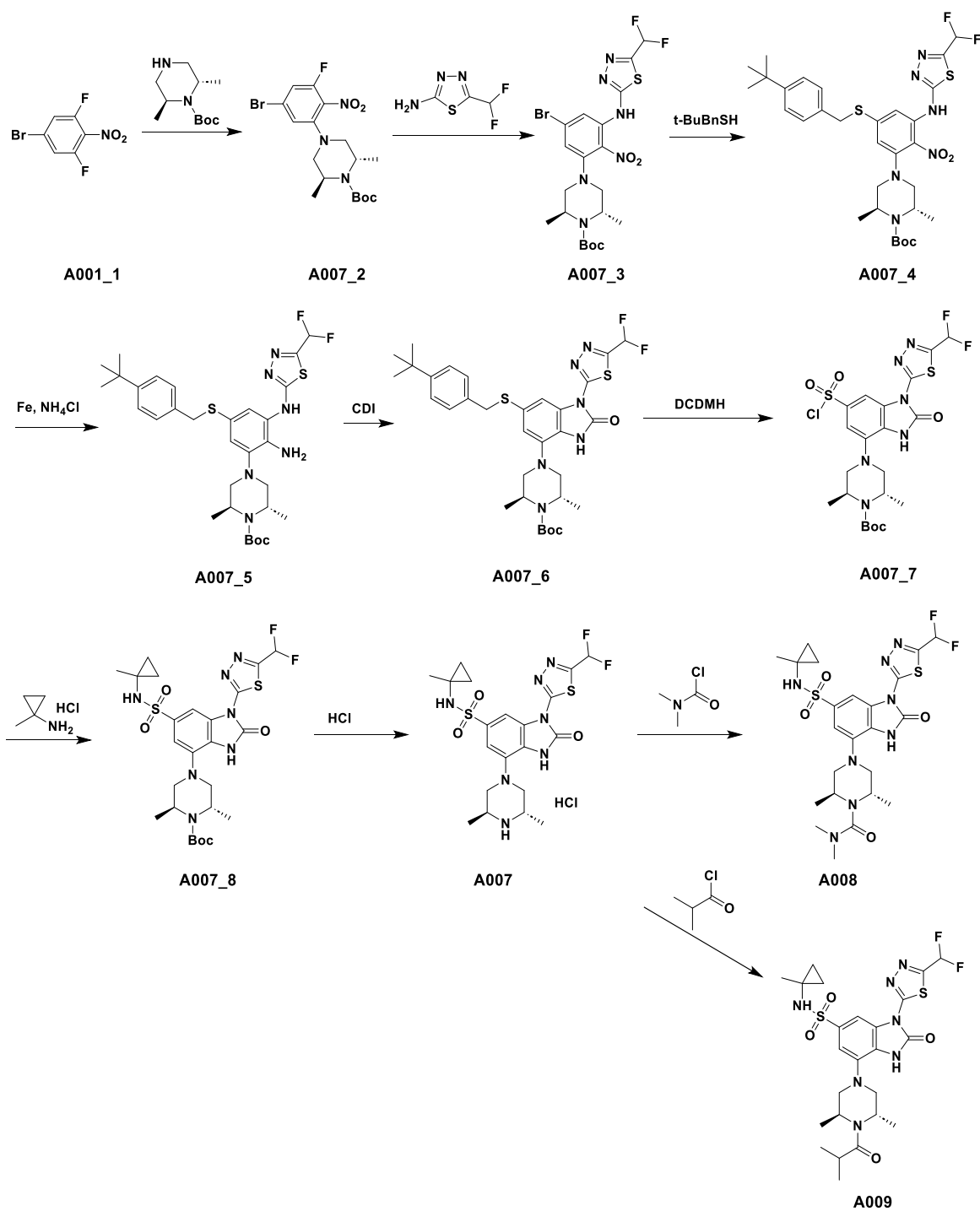
A007



A008



A009



[0689] Step 1: Synthesis of compound A007_2

[0690] A001_1 (3.00 g, 12.6 mmol) and N,N-diisopropylethylamine (8.15 g, 63.0 mmol) were dissolved in N,N-dimethylacetamide (30 mL), followed by addition of *tert*-butyl

5 (2S,6S)-2,6-dimethylpiperazine-1-carboxylate (2.70 g, 12.6 mmol). The reaction mixture

was heated to 110°C and stirred for 3 hours. The reaction mixture was cooled to room temperature, then quenched with water (100 mL), and extracted with ethyl acetate (30 mL × 3). The organic phase was washed with brine (50 mL × 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was
5 purified by column chromatography to obtain A007_2 (5.06 g).

[0691] MS (ESI) M/Z: 332.2, 334.2 [M-Boc]⁺.

[0692] ¹H NMR (400 MHz, DMSO-*d*₆): δ 7.21 - 7.18 (m, 1H), 7.14 (s, 1H), 4.06 - 4.03 (m, 2H), 3.79 - 3.75 (m, 2H), 2.99 - 2.96 (m, 2H), 1.42 (s, 9H), 1.15 (d, *J* = 6.4 Hz, 6H).

[0693] Step 2: Synthesis of compound A007_3

10 **[0694]** Cesium carbonate (11.4 g, 35.1 mmol) and 5-(difluoromethyl)-1,3,4-thiadiazol-2-amine (2.65 g, 17.6 mmol) were added to a solution of A007_2 (5.06 g, 11.7 mmol) in N,N-dimethylacetamide (50 mL). The reaction mixture was heated to 110°C and stirred for 16 hours. The reaction mixture was cooled to room temperature, then quenched with water (100 mL), and extracted with ethyl acetate (30 mL × 3). The organic phase was washed
15 with brine (50 mL × 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain A007_3 (3.65 g).

[0695] MS (ESI) M/Z: 561.1, 563.1 [M-H]⁻.

[0696] Step 3: Synthesis of compound A007_4

20 **[0697]** A007_3 (3.10 g, 5.50 mmol), 4-*tert*-butylbenzyl mercaptan (1.09 g, 6.05 mmol), and N,N-diisopropylethylamine (1.78 g, 13.8 mmol) were dissolved in 1,4-dioxane (31 mL).

The system was purged with nitrogen three times, followed by addition of $\text{Pd}_2(\text{dba})_3$ (504 mg, 550 μmol) and Xantphos (637 mg, 1.10 mmol), and purged with nitrogen three additional times. The reaction mixture was heated to 70°C and stirred for 1 hour. The reaction mixture was cooled to room temperature, then quenched with water (50 mL), and
5 extracted with ethyl acetate (30 mL $\times$ 3). The organic phase was washed with brine (50 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain A007_4 (3.65 g).

[0698] MS (ESI) M/Z : 663.2 $[\text{M}+\text{H}]^+$.

10 **[0699]** Step 4: Synthesis of compound A007_5

[0700] A007_4 (3.65 g, 5.51 mmol) was dissolved in ethanol (30 mL) and water (10 mL), followed by addition of iron powder (1.54 g, 27.5 mmol) and ammonium chloride (1.47 g, 27.5 mmol). The reaction mixture was heated to 80°C and stirred for 1.5 hours. The reaction mixture was cooled to room temperature and filtered through diatomite. The
15 filtrate was diluted with water (50 mL) and extracted with ethyl acetate (50 mL $\times$ 3). The organic phase was washed with brine (50 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain A007_5 (2.08 g).

[0701] MS (ESI) M/Z : 633.2 $[\text{M}+\text{H}]^+$.

20 **[0702]** ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 9.81 (s, 1H), 7.46 - 7.19 (m, 4H), 7.14 - 7.12 (m, 2H), 6.59 (d, $J = 2.0$ Hz, 1H), 4.82 (s, 2H), 3.96 - 3.92 (m, 4H), 2.99 - 2.96 (m, 2H), 2.48 -

2.44 (m, 2H), 1.42 (s, 9H), 1.37 (d, $J = 6.4$ Hz, 6H), 1.24 (s, 9H).

[0703] Step 5: Synthesis of compound A007_6

[0704] A007_5 (600 mg, 948 μ mol) was dissolved in tetrahydrofuran (12 mL), followed by addition of carbonyldiimidazole (231 mg, 1.42 mmol). The reaction mixture was heated to 70°C and stirred for 2 hours. The reaction mixture was cooled to room temperature, then quenched with water (10 mL), and extracted with ethyl acetate (10 mL $\times$ 3). The organic phase was washed with brine (20 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain A007_6 (720 mg).

[0705] MS (ESI) M/Z : 657.3 $[M-H]^-$.

[0706] ^1H NMR (400 MHz, DMSO- d_6): δ 11.74 (s, 1H), 7.97 (s, 1H), 7.61 (t, $J = 53.2$ Hz, 1H), 7.31 - 7.24 (m, 4H), 6.58 (s, 1H), 4.16 - 4.14 (m, 2H), 4.07 - 4.02 (m, 2H), 3.76 - 3.73 (m, 2H), 2.88 - 2.86 (m, 2H), 1.43 (s, 9H), 1.23 (s, 9H), 1.19 - 1.17 (m, 6H).

[0707] Step 6: Synthesis of compound A007_7

[0708] A007_6 (570 mg, 865 μ mol) was dissolved in acetic acid (0.9 mL), water (1.8 mL), and acetonitrile (6.3 mL). The mixture was cooled to 0°C in an ice-salt bath, and 1,3-dichloro-5,5-dimethylhydantoin (341 mg, 1.73 mmol) was added in portions. After the addition was completed, the reaction mixture was slowly warmed to 20°C and stirred for 2 hours. The reaction mixture was cooled again to 0°C, then quenched with water (10 mL), and extracted with dichloromethane (5 mL $\times$ 3). The organic phase was washed with brine (10 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated

by rotary evaporation to obtain A007_7 (500 mg) as a crude product, which was directly used in the next step.

[0709] MS (ESI) M/Z: 577.2 [M-H]⁻.

[0710] Step 7: Synthesis of compound A007_8

5 **[0711]** 1-Methylcyclopropanamine hydrochloride (372 mg, 3.45 mmol) and N,N-diisopropylethylamine (670 mg, 5.18 mmol) were dissolved in dichloromethane (5 mL), followed by addition of a solution of A007_7 (500 mg, 864 μ mol) in dichloromethane (3 mL). The reaction mixture was stirred at 20°C for 2 hours. The reaction mixture was quenched with water (10 mL) and extracted with ethyl acetate (10 mL $\times$ 3). The organic
10 phase was washed with brine (10 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain A007_8 (260 mg).

[0712] MS (ESI) M/Z: 612.3 [M-H]⁻.

[0713] ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.11 (s, 1H), 8.41 (s, 1H), 8.11 (s, 1H), 7.64 (t,
15 J = 53.2 Hz, 1H), 7.27 (s, 1H), 4.14 - 4.11 (m, 2H), 3.96 - 3.93 (m, 2H), 3.07 - 3.04 (m, 2H), 1.45 (s, 9H), 1.26 - 1.23 (m, 6H), 1.08 (s, 3H), 0.66 - 0.63 (m, 2H), 0.38 - 0.35 (m, 2H).

[0714] Step 8: Synthesis of compound A007

[0715] A007_8 (30 mg, 48.9 μ mol) was dissolved in ethyl acetate (0.3 mL), followed by addition of 4 M HCl in ethyl acetate (1 mL). The reaction mixture was stirred at 20°C for
20 1 hour. The reaction mixture was directly concentrated under reduced pressure to obtain a crude product (25 mg, salt), which was directly used in the next step. 20 mg of the crude

product was purified by preparative chromatography (salt, chromatographic column: Phenomenex Luna C18) to obtain A007 (9.91 mg, hydrochloride salt).

[0716] MS (ESI) M/Z: 514.3 [M+H]⁺.

[0717] ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.47 (s, 1H), 9.11 (s, 2H), 8.55 (s, 1H), 8.18 (s, 1H), 7.64 (t, *J* = 53.2 Hz, 1H), 7.38 (s, 1H), 3.93 - 3.91 (m, 2H), 3.41 - 3.38 (m, 2H), 2.82 - 2.78 (m, 2H), 1.35 (d, *J* = 6.4 Hz, 6H), 1.08 (s, 3H), 0.64 - 0.62 (m, 2H), 0.40 - 0.37 (m, 2H).

[0718] Step 9: Synthesis of compound A008

[0719] A007 (17 mg, 30.9 μmol) and N,N-diisopropylethylamine (24.0 mg, 185 μmol) were dissolved in N-methylpyrrolidone (0.2 mL), followed by addition of dimethylcarbamoyl chloride (4.99 mg, 46.4 μmol, 1.50 eq). The reaction mixture was heated to 35°C and stirred for 16 hours. The reaction mixture was quenched with water (0.1 mL). The residue was purified by preparative chromatography (neutral conditions, chromatographic column: Waters Xbridge Prep OBD C18) to obtain A008 (9.64 mg).

[0720] MS (ESI) M/Z: 585.2 [M+H]⁺.

[0721] ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.42 (s, 1H), 8.51 (s, 1H), 8.09 (s, 1H), 7.63 (t, *J* = 53.2 Hz, 1H), 7.35 (s, 1H), 3.74 - 3.70 (m, 2H), 3.28 - 3.25 (m, 2H), 2.91 (s, 6H), 2.62 - 2.60 (m, 2H), 1.09 - 1.07 (m, 9H) 0.64 - 0.61 (m, 2H), 0.39 - 0.36 (m, 2H).

[0722] Step 10: Synthesis of compound A009

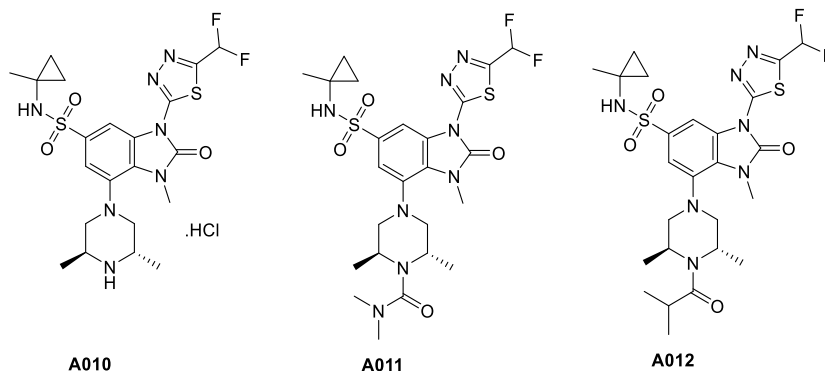
[0723] A007 (20 mg, 36.4 μmol) and triethylamine (22.1 mg, 218 μmol) were dissolved in N,N-dimethylacetamide (0.1 mL), followed by addition of 2-methylpropanoyl chloride (4.26 mg, 40.0 μmol). The reaction mixture was stirred at 20°C for 1 hour. The reaction

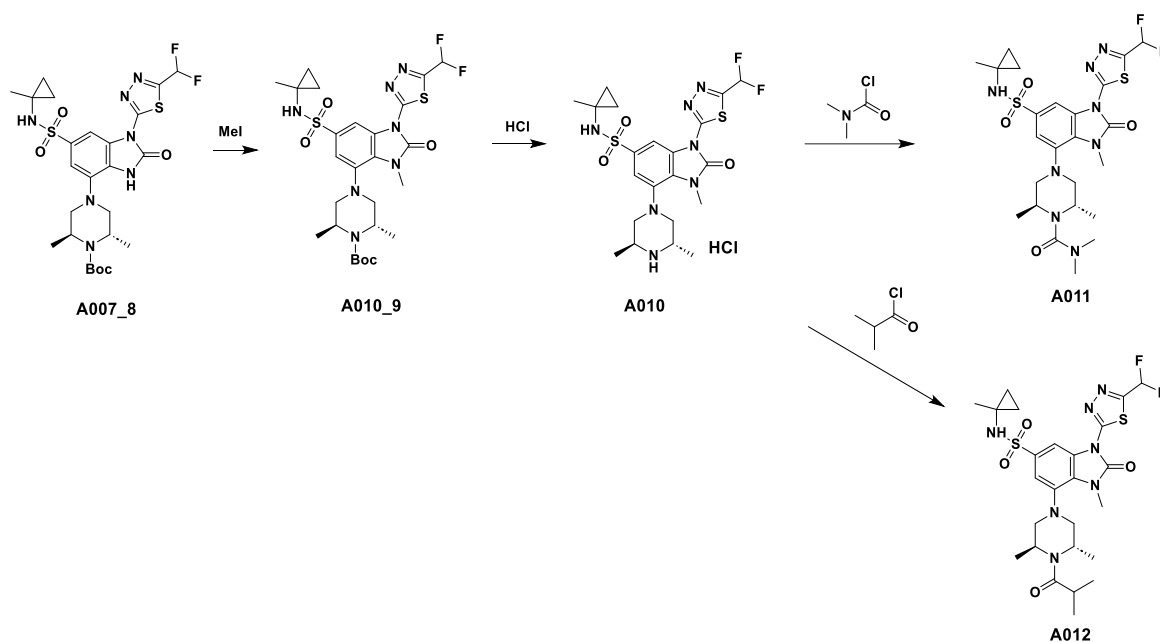
mixture was quenched with water (0.1 mL). The residue was purified by preparative chromatography (neutral conditions, chromatographic column: Waters Xbridge Prep OBD C18) to obtain A009 (9.05 mg).

[0724] MS (ESI) M/Z : 584.2 $[M+H]^+$.

5 **[0725]** ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 12.01 (s, 1H), 8.38 (s, 1H), 8.06 (s, 1H), 7.63 (t, $J = 53.2$ Hz, 1H), 7.25 (s, 1H), 4.32 - 4.30 (m, 2H), 4.13 - 4.10 (m, 2H), 3.22 - 3.19 (m, 2H), 2.82 - 2.79 (m, 1H), 1.26 - 1.25 (m, 6H), 1.07 - 1.05 (m, 9H), 0.68 - 0.63 (m, 2H), 0.37 - 0.35 (m, 2H).

[0726] Example A010, Example A011, and Example A012





[0727] Step 1: Synthesis of compound A010_9

[0728] A007_8 (140 mg, 228 μ mol) and potassium carbonate (63.1 mg, 456 μ mol) were dissolved in N,N-dimethylformamide (2 mL), followed by addition of iodomethane (48.6 mg, 342 μ mol). The reaction mixture was stirred at 20°C for 1 hour. The reaction mixture was quenched with water (2 mL) and extracted with ethyl acetate (2 mL $\times$ 3). The organic phase was washed with brine (2 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by preparative chromatography on a silica gel plate to obtain A010_9 (50 mg).

[0729] MS (ESI) M/Z: 626.3 [M-H]⁻.

[0730] Step 2: Synthesis of compound A010

[0731] A010_9 (50 mg, 79.7 μ mol) was dissolved in ethyl acetate (1 mL), followed by addition of 4 M HCl in ethyl acetate (2 mL). The reaction mixture was stirred at 20°C for 1 hour. The reaction mixture was directly concentrated under reduced pressure to obtain

A010 (55 mg, hydrochloride salt) as a crude product, which was directly used in the next step. 15 mg of the crude product was purified by preparative chromatography (acidic conditions, chromatographic column: Phenomenex Luna C18) to obtain A010 (7.31 mg, hydrochloride salt).

5 **[0732]** MS (ESI) M/Z : 528.1 $[M+H]^+$.

[0733] ^1H NMR (400 MHz, DMSO- d_6): δ 9.25 (s, 2H), 8.71 (s, 1H), 8.28 (s, 1H), 7.78 - 7.51 (m, 2H), 3.88 - 3.72 (m, 2H), 3.78 (s, 3H), 3.38 - 3.35 (m, 2H), 3.10 - 3.06 (m, 1H), 2.65 - 2.58 (m, 1H), 1.51 (d, J = 5.6 Hz, 3H), 1.25 (d, J = 4.4 Hz, 3H), 1.09 (s, 3H), 0.64 - 0.62 (m, 2H), 0.41 - 0.38 (m, 2H).

10 **[0734]** Step 3: Synthesis of compound A011

[0735] A010 (15 mg, 26.6 μ mol) and N,N-diisopropylethylamine (20.6 mg, 160 μ mol, 6.00 eq) were dissolved in N-methylpyrrolidone (0.2 mL), followed by addition of dimethylcarbamoyl chloride (4.29 mg, 38.9 μ mol, 1.50 eq). The reaction mixture was heated to 35°C and stirred for 16 hours. The reaction mixture was quenched with water
15 (0.1 mL). The residue was purified by preparative chromatography (neutral conditions, chromatographic column: Waters Xbridge Prep OBD C18) to obtain A011 (6.65 mg).

[0736] MS (ESI) M/Z : 599.2 $[M+H]^+$.

[0737] ^1H NMR (400 MHz, DMSO- d_6): δ 8.66 (s, 1H), 8.17 (s, 1H), 7.77 - 7.51 (m, 2H), 3.82 (s, 3H), 3.68 - 3.60 (m, 2H), 3.27 - 3.19 (m, 2H), 2.99 - 2.96 (m, 1H), 2.92 (s, 6H), 2.33
20 - 2.30 (m, 1H), 1.23 - 1.19 (m, 3H), 1.08 (s, 3H), 1.00 - 0.97 (m, 3H), 0.64 - 0.62 (m, 2H), 0.40 - 0.38 (m, 2H).

[0738] Step 4: Synthesis of compound A012

[0739] A010 (15 mg, 26.6 μmol) and triethylamine (16.2 mg, 160 μmol , 6.00 eq) were dissolved in N,N-dimethylacetamide (0.1 mL), followed by addition of 2-methylpropanoyl chloride (4.25 mg, 39.9 μmol , 1.50 eq). The reaction mixture was stirred at 20°C for 1 hour.

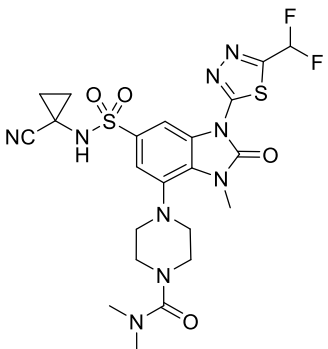
5 The reaction mixture was quenched with water (0.1 mL). The residue was purified by preparative chromatography (neutral conditions, chromatographic column: Waters Xbridge Prep OBD C18) to obtain A012 (4.96 mg).

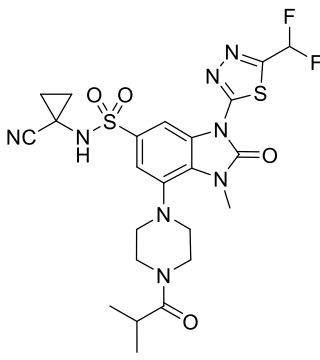
[0740] MS (ESI) M/Z: 598.2 $[\text{M}+\text{H}]^+$.

[0741] ^1H NMR (400 MHz, DMSO- d_6): δ 8.60 (s, 1H), 8.15 (s, 1H), 7.77 - 7.51 (m, 2H),
10 4.27 - 4.23 (m, 2H), 3.79 - 3.75 (m, 5H), 3.04 - 3.02 (m, 2H), 2.89 - 2.82 (m, 1H), 1.32 (d, J
= 7.0 Hz, 6H), 1.08 - 1.04 (m, 9H), 0.66 - 0.60 (m, 2H), 0.41 - 0.35 (m, 2H).

[0742] Example A013 and Example A014

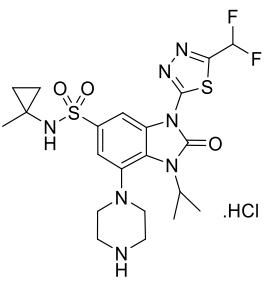
[0743] Table 3

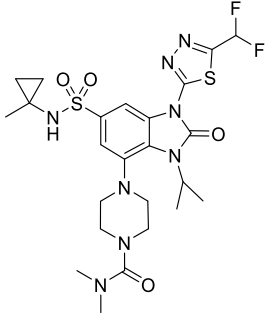
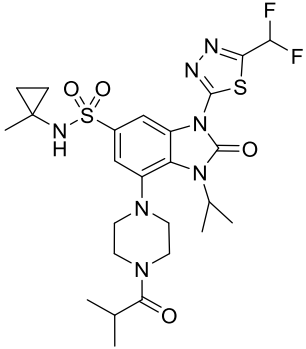
Example	Structural formula	Structural characterization
A013	 A013	^1H NMR (400 MHz, CDCl_3-d): δ 8.84 (s, 1H), 7.81 (s, 1H), 7.05 (t, J = 53.6 Hz, 1H), 6.28 (s, 1H), 3.91 (s, 3H), 3.75 - 3.71 (m, 2H), 3.24 - 3.14 (m, 2H), 3.13 - 3.03 (m, 4H), 2.92 (s, 6H), 1.68 - 1.62 (m, 2H), 1.47 - 1.41 (m, 2H). MS (ESI) M/Z: 582.1 $[\text{M}+\text{H}]^+$.

Example	Structural formula	Structural characterization
A014	 A014	¹H NMR (400 MHz, CDCl₃-d): δ 8.85 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 (d, <i>J</i> = 1.2 Hz, 1H), 7.06 (t, <i>J</i> = 53.6 Hz, 1H), 6.24 (s, 1H), 4.84 - 4.71 (m, 1H), 4.11 - 4.00 (m, 1H), 3.92 (s, 3H), 3.52 - 3.39 (m, 1H), 3.19 - 3.16 (m, 2H), 3.06 - 2.91 (m, 3H), 2.89 - 2.81 (m, 1H), 1.67 - 1.65 (m, 2H), 1.46 - 1.42 (m, 2H), 1.23 - 1.18 (m, 6H). MS (ESI) M/Z: 581.2 [M+H]⁺.

[0744] Example A017, Example A018, and Example A019

[0745] Table 4

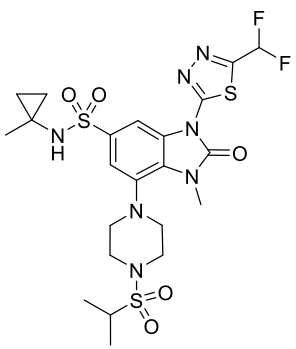
Example	Structural formula	Structural characterization
A017	 A017	¹H NMR (400 MHz, DMSO-<i>d</i>₆): δ 9.11 (s, 2H), 8.73 (d, <i>J</i> = 1.6 Hz, 1H), 8.27 (s, 1H), 7.77 - 7.51 (m, 2H), 5.76 - 5.67 (m, 1H), 3.45 - 3.41 (m, 2H), 3.27 - 3.23 (m, 4H), 3.13 - 3.07 (m, 2H), 1.57 (d, <i>J</i> = 6.8 Hz, 6H), 1.10 (s, 3H), 0.65 - 0.62 (m, 2H), 0.42 - 0.39 (m, 2H). MS (ESI) M/Z: 528.2 [M+H]⁺.

A018	 A018	¹H NMR (400 MHz, DMSO-<i>d</i>₆): δ 8.70 (s, 1H), 8.16 (s, 1H), 7.77 - 7.50 (m, 2H), 5.91 - 5.84 (m, 1H), 3.64 - 3.61 (m, 2H), 3.09 - 3.01 (m, 4H), 2.89 - 2.84 (m, 2H), 2.81 (s, 6H), 1.57 (d, <i>J</i> = 6.8 Hz, 6H), 1.08 (s, 3H), 0.65 - 0.62 (m, 2H), 0.41 - 0.38 (m, 2H). MS (ESI) M/Z: 599.2 [M+H]⁺.
A019	 A019	¹H NMR (400 MHz, DMSO-<i>d</i>₆): δ 8.70 (s, 1H), 8.14 (s, 1H), 7.77 - 7.51 (m, 2H), 5.94 - 5.83 (m, 1H), 4.54 - 4.51 (m, 1H), 4.13 - 4.09 (m, 1H), 3.38 - 3.36 (m, 1H), 3.16 - 3.13 (m, 2H), 2.97 - 2.92 (m, 1H), 2.87 - 2.83 (m, 2H), 2.69 - 2.67 (m, 1H), 1.57 (d, <i>J</i> = 6.4 Hz, 6H), 1.08 - 1.02 (m, 9H), 0.65 - 0.62 (m, 2H), 0.41 - 0.38 (m, 2H). MS (ESI) M/Z: 598.2 [M+H]⁺.

[0746] Example A023

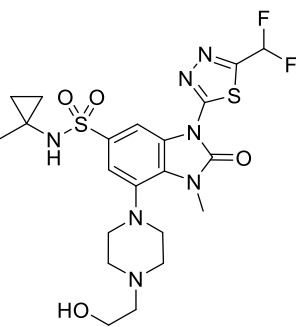
[0747] Table 5

Example	Structural formula	Structural characterization
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A023	 A023	¹H NMR (400 MHz, DMSO-<i>d</i>₆): δ 8.67 (d, <i>J</i> = 1.6 Hz, 1H), 8.14 (s, 1H), 7.77 - 7.50 (m, 2H), 3.78 (s, 3H), 3.72 - 3.68 (m, 2H), 3.44 - 3.41 (m, 1H), 3.29 - 3.19 (m, 4H), 2.88 - 2.85 (m, 2H), 1.28 (d, <i>J</i> = 6.8 Hz, 6H), 1.07 (s, 3H), 0.65 - 0.62 (m, 2H), 0.40 - 0.37 (m, 2H). MS (ESI) M/Z: 606.1 [M+H]⁺.
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[0748] Example A024

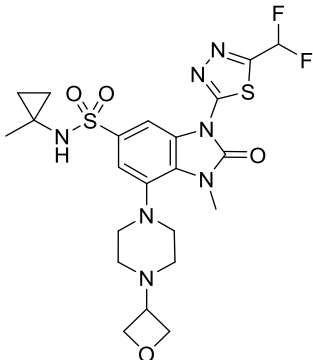
[0749] Table 6

Example	Structural formula	Structural characterization
A024	 A024	¹H NMR (400 MHz, CDCl₃-<i>d</i>) δ 8.89 (d, <i>J</i> = 1.2 Hz, 1H), 7.77 (d, <i>J</i> = 1.2 Hz, 1H), 7.06 (t, <i>J</i> = 53.6 Hz, 1H), 5.00 (s, 1H), 3.92 (s, 3H), 3.72 - 3.70 (m, 2H), 3.12 - 3.09 (m, 4H), 3.04 - 3.01 (m, 2H), 2.68 (t, <i>J</i> = 5.2 Hz, 2H), 2.60 - 2.58 (m, 1H), 2.53 - 2.51 (m, 2H), 1.26 (s, 3H), 0.85 - 0.83 (m, 2H), 0.54 - 0.51 (m, 2H). MS (ESI) M/Z: 544.1 [M+H]⁺.

[0750] Example A026

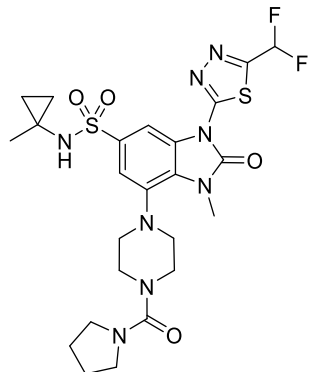
[0751] Table 7

Example	Structural formula	Structural characterization
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A026	 A026	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.65 (d, <i>J</i> = 1.6 Hz, 1H), 8.15 (s, 1H), 7.77 - 7.50 (m, 2H), 4.60 - 4.57 (m, 2H), 4.51 - 4.48 (m, 2H), 3.76 (s, 3H), 3.56 - 3.52 (m, 1H), 3.12 - 3.10 (m, 2H), 2.93 - 2.81 (m, 4H), 2.21 - 2.17 (m, 2H), 1.08 (s, 3H), 0.65 - 0.62 (m, 2H), 0.40 - 0.37 (m, 2H). MS (ESI) M/Z: 556.2 [M+H]⁺.
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[0752] Example A027

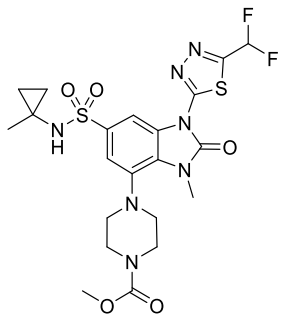
[0753] Table 8

Example	Structural formula	Structural characterization
A027	 A027	¹H NMR (400 MHz, CDCl₃-<i>d</i>): δ 8.89 (d, <i>J</i> = 1.2 Hz, 1H), 7.76 (d, <i>J</i> = 1.6 Hz, 1H), 7.06 (t, <i>J</i> = 53.6 Hz, 1H), 5.09 (s, 1H), 3.92 (s, 3H), 3.84 - 3.79 (m, 2H), 3.44 (t, <i>J</i> = 6.8 Hz, 4H), 3.21 - 3.12 (m, 2H), 3.11 - 3.02 (m, 4H), 1.92 - 1.86 (m, 4H), 1.25 (s, 3H), 0.86 - 0.80 (m, 2H), 0.54 - 0.49 (m, 2H). MS (ESI) M/Z: 597.2 [M+H]⁺.

[0754] Example A028

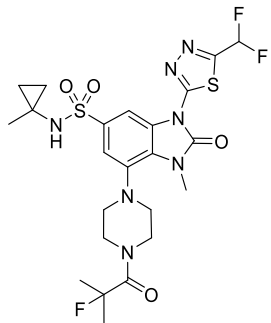
[0755] Table 9

Example	Structural formula	Structural characterization
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A028	 A028	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.66 (s, 1H), 8.13 (s, 1H), 7.77 - 7.50 (m, 2H), 4.06 - 3.99 (m, 2H), 3.79 (s, 3H), 3.65 (s, 3H), 3.25 - 3.10 (m, 4H), 2.81 - 2.71 (m, 2H), 1.07 (s, 3H), 0.64 - 0.61 (m, 2H), 0.40 - 0.37 (m, 2H). MS (ESI) M/Z: 558.2 [M+H]⁺.
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[0756] Example A029

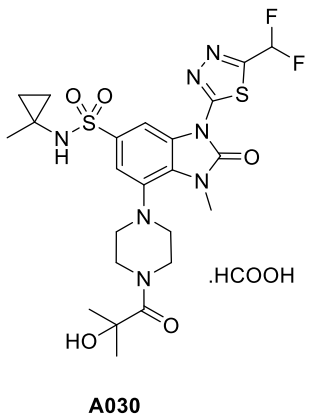
[0757] Table 10

Example	Structural formula	Structural characterization
A029	 A029	¹H NMR (400 MHz, DMSO-<i>d</i>₆): δ 8.67 (d, <i>J</i> = 1.2 Hz, 1H), 8.13 (s, 1H), 7.77 - 7.51 (m, 2H), 4.49 - 4.40 (m, 2H), 3.81 (s, 3H), 3.48 - 3.38 (m, 1H), 3.28 - 3.12 (m, 2H), 3.11 - 2.96 (m, 1H), 2.78 - 2.68 (m, 2H), 1.63 (s, 3H), 1.57 (s, 3H), 1.06 (s, 3H), 0.64 - 0.61 (m, 2H), 0.40 - 0.37 (m, 2H). MS (ESI) M/Z: 588.2 [M+H]⁺.

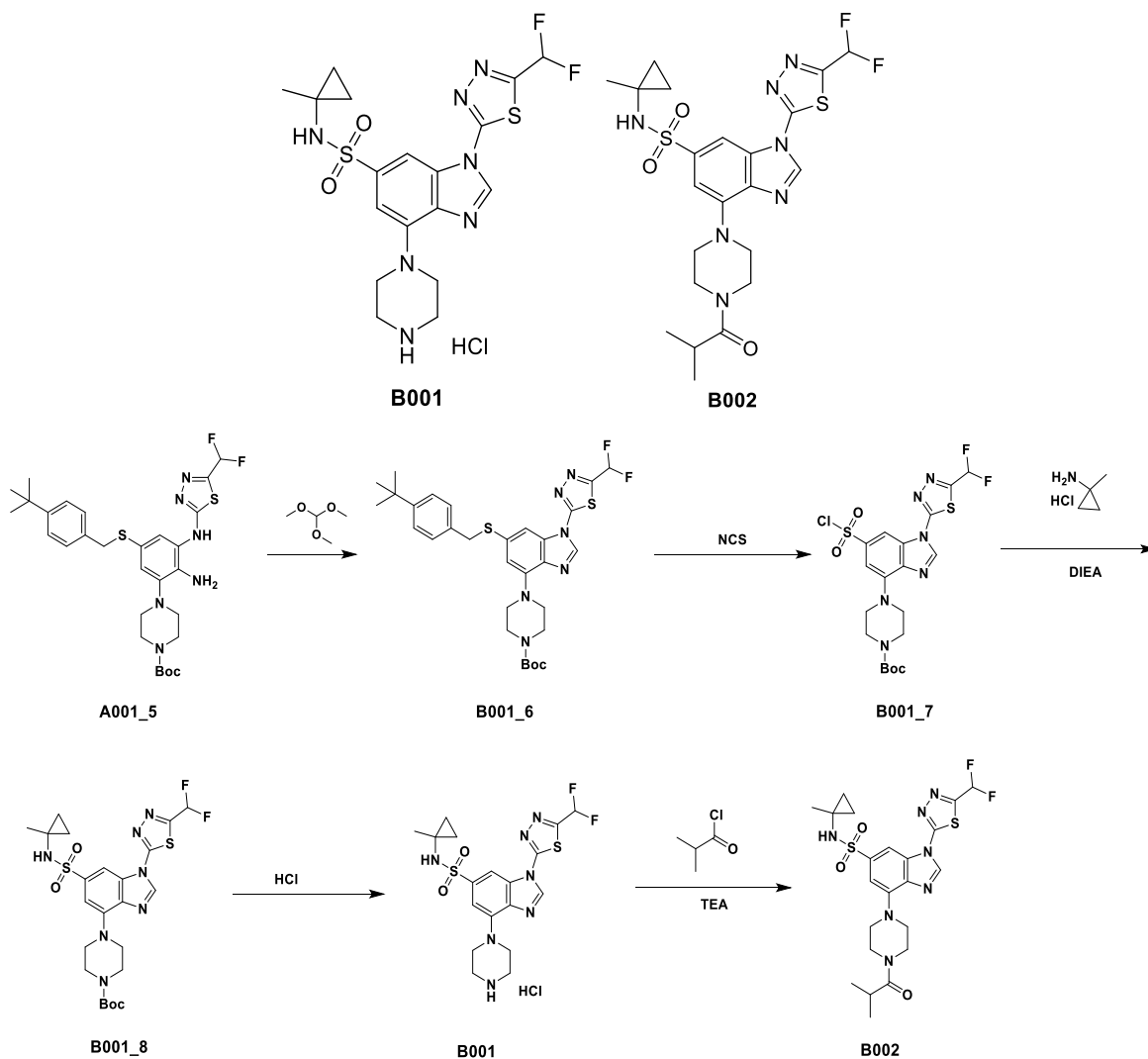
[0758] Example A030

[0759] Table 11

Example	Structural formula	Structural characterization
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A030	 A030	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.66 (s, 1H), 8.15 (s, 1H), 7.77 - 7.50 (m, 2H), 5.50 (s, 1H), 5.02 - 4.52 (m, 2H), 3.81 (s, 3H), 3.17 - 2.77 (m, 6H), 1.36 (s, 6H), 1.07 (s, 3H), 0.64 - 0.61 (m, 2H), 0.40 - 0.37 (m, 2H). MS (ESI) M/Z: 586.1 [M+H]⁺.
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[0760] Example B001 and Example B002



[0761] Step 1: Synthesis of compound B001_6

[0762] A001_5 (800 mg, 1.32 mmol) was dissolved in trimethyl orthoformate (8.00 mL), followed by addition of *p*-toluenesulfonic acid (22.7 mg, 132 μ mol, 0.10 eq). The reaction mixture was heated to 100°C and stirred for 1 hour. After completion of the reaction, the reaction mixture was cooled to room temperature, quenched with water (20 mL), and
5 extracted with ethyl acetate (20 mL $\times$ 3). The organic phases were combined, washed with brine (30 mL $\times$ 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation to obtain B001_6 (700 mg) as a crude product, which was directly used in the next step.

[0763] MS (ESI) *M/Z*: 615.2 [M+H]⁺.

10 [0764] ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.80 (s, 1H), 7.80 - 7.53 (m, 2H), 7.33 - 7.27 (m, 4H), 6.60 (s, 1H), 4.23 (s, 2H), 3.51 - 3.48 (m, 4H), 3.37 - 3.35 (m, 4H), 1.43 (s, 9H), 1.24 (s, 9H).

[0765] Step 2: Synthesis of compound B001_7

[0766] B001_6 (315 mg, 512 μ mol) was dissolved in dichloromethane (4.00 mL), acetic
15 acid (4.00 mL), and water (2.00 mL). The mixture was cooled to 0°C in an ice-salt bath, and N-chlorosuccinimide (205 mg, 1.54 mmol) was added in portions. After the addition was completed, the reaction mixture was slowly warmed to 20°C and stirred for 4 hours. Two parallel reactions were carried out simultaneously and combined for work-up after completion. The reaction mixture was cooled again to 0°C, then slowly added with
20 saturated sodium bicarbonate aqueous solution to adjust the pH to approximately 5, and extracted with dichloromethane (20 mL $\times$ 2). The organic phases were combined, washed

with brine (30 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation to obtain B001_7 (548 mg) as a crude product, which was directly used in the next step.

[0767] MS (ESI) M/Z: 479.2, 481.1 [M-55]⁺.

5 **[0768]** Step 3: Synthesis of compound B001_8

[0769] 1-Methylcyclopropanamine hydrochloride (440 mg, 4.10 mmol) and N,N-diisopropylethylamine (529 mg, 4.10 mmol) were dissolved in dichloromethane (5.00 mL). The mixture was cooled to 0°C, and a solution of B001_7 (548 mg, 1.02 mmol) in dichloromethane (5 mL) was slowly added dropwise thereto. After the addition was
10 completed, the reaction mixture was slowly warmed to 20°C and stirred for 1 hour. After completion of the reaction, the reaction mixture was quenched with water (20 mL) and extracted with dichloromethane (20 mL $\times$ 2). The organic phases were combined, washed with brine (30 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography
15 (SiO₂, petroleum ether/ethyl acetate = 1/0 to 1/1) to obtain B001_8 (100 mg).

[0770] MS (ESI) M/Z: 514.1 [M-55]⁺.

[0771] ¹H NMR (400 MHz, DMSO-*d*₆): δ 9.04 (s, 1H), 8.24 (s, 1H), 8.13 (s, 1H), 7.67 (t, *J* = 53.2 Hz, 1H), 7.20 (s, 1H), 3.57 (s, 8H), 1.43 (s, 9H), 1.04 (s, 3H), 0.63 (t, *J* = 5.6 Hz, 2H), 0.37 (t, *J* = 5.6 Hz, 2H).

20 **[0772]** Step 4: Synthesis of compound B001

[0773] B001_8 (60.0 mg, 105 μ mol, 1.00 eq) was dissolved in methanol (0.5 mL), followed

by dropwise addition of 4 M HCl in methanol (2 mL). The reaction mixture was stirred at 20°C for 2 hours. After completion of the reaction, the reaction mixture was directly concentrated under reduced pressure to obtain B001 (54.43 mg, hydrochloride salt).

[0774] MS (ESI) M/Z: 470.0 [M+H]⁺.

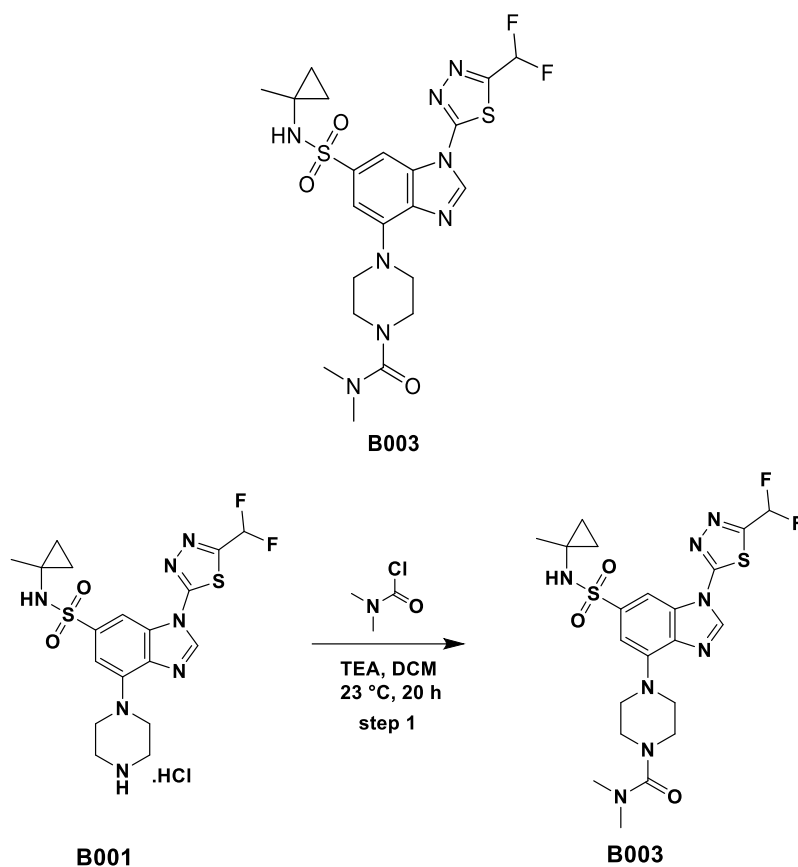
5 **[0775]** ¹H NMR (400 MHz, DMSO-*d*₆): δ 9.24 (s, 1H), 9.09 (s, 1H), 8.30 (s, 1H), 8.20 (s, 1H), 7.68 (t, *J* = 53.0 Hz, 1H), 7.26 (s, 1H), 3.83 (t, *J* = 4.8 Hz, 4H), 3.35 (s, 4H), 1.05 (s, 3H), 0.63 (t, *J* = 5.6 Hz, 2H), 0.39 - 0.36 (m, 2H).

[0776] Step 5: Synthesis of compound B002

[0777] B001 (37.0 mg, 73.1 μmol, hydrochloride salt) and triethylamine (29.6 mg, 292 μmol) were dissolved in dichloromethane (1.00 mL). The mixture was cooled to 0°C, followed by addition of 2-methylpropanoyl chloride (15.6 mg, 146 μmol). After the addition was completed, the reaction mixture was slowly warmed to 20°C and stirred for 1 hour. After completion of the reaction, the reaction mixture was quenched with water (5 mL) and extracted with dichloromethane (5 mL × 2). The organic phases were combined, washed with brine (5 mL × 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The crude product was purified by preparative chromatography on a silica gel plate to obtain B002 (23.38 mg).

[0778] MS (ESI) M/Z: 540.1 [M+H]⁺.

20 **[0779]** ¹H NMR (400 MHz, DMSO-*d*₆): δ 9.05 (s, 1H), 8.25 (s, 1H), 8.14 (s, 1H), 7.67 (t, *J* = 53.2 Hz, 1H), 7.20 (s, 1H), 3.76 - 3.71 (m, 4H), 3.62 - 3.57 (m, 4H), 2.99 - 2.92 (m, 1H), 1.05 - 1.03 (m, 9H), 0.64 (t, *J* = 5.6 Hz, 2H), 0.37 (t, *J* = 5.6 Hz, 2H).

[0780] Example B003**[0781]** Step 1: Synthesis of compound B003

[0782] B001 (8 mg, 15.8 μmol) and triethylamine (16.0 mg, 158 μmol) were dissolved in DCM (2.0 mL), followed by addition of dimethylcarbamoyl chloride (17.0 mg, 158 μmol , 10 eq). The reaction mixture was stirred at 23°C for 20 hours. The reaction mixture was quenched with water (5 mL) and extracted three times with ethyl acetate. The organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, concentrated, and purified by preparative chromatography (acidic conditions, 0.1% FA, chromatographic column: YMC-Actus Triart C18 ExRS) to obtain B003 (2.1 mg).

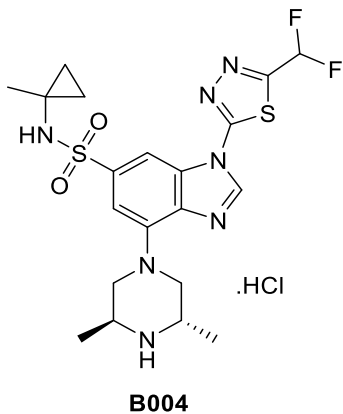
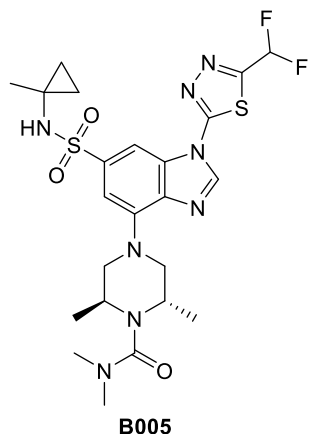
[0783] MS (ESI) M/Z: 541.1 $[\text{M}+\text{H}]^+$.

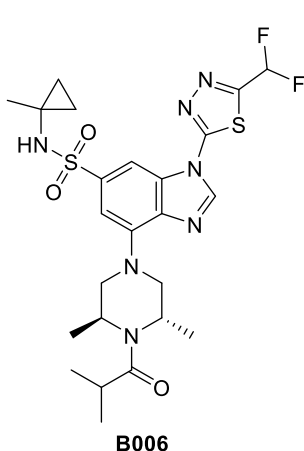
[0784] ^1H NMR (400 MHz, DMSO- d_6) 9.04 (s, 1H), 8.25 (d, $J = 1.4$ Hz, 1H), 8.16 (s, 1H),

7.68 (t, $J = 53.0$ Hz, 1H), 7.22 (d, $J = 1.6$ Hz, 1H), 3.66 - 3.56 (m, 4H), 3.40 - 3.30 (m, 4H), 2.81 (s, 6H), 1.05 (s, 3H), 0.67 - 0.61 (m, 2H), 0.40 - 0.35 (m, 2H).

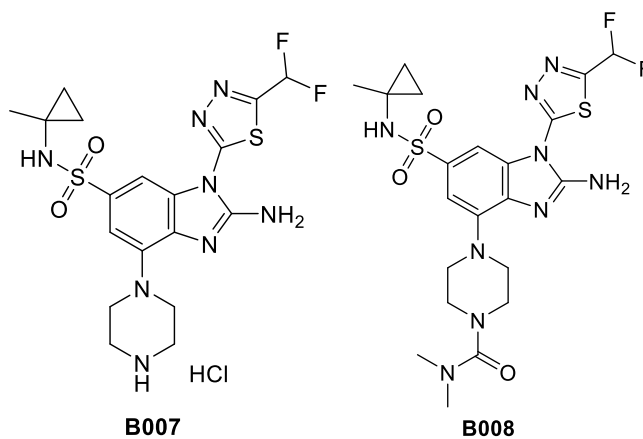
[0785] Example B004, Example B005, and Example B006

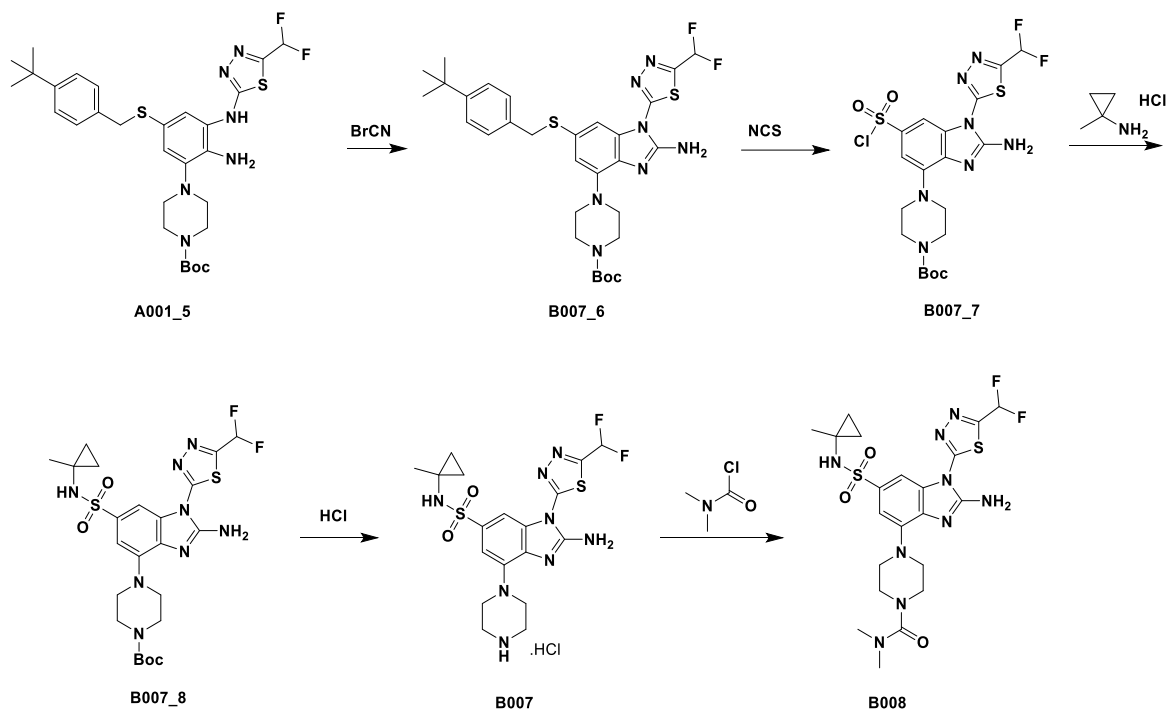
[0786] Table 12

Example	Structural formula	Structural characterization
B004	 B004	¹H NMR (400 MHz, DMSO-<i>d</i>₆): δ 9.22 - 9.09 (m, 2H), 9.08 (s, 1H), 8.29 (s, 1H), 8.20 (s, 1H), 7.69 (t, $J = 53.2$ Hz, 1H), 7.25 (s, 1H), 3.84 - 3.81 (m, 2H), 3.78 - 3.68 (m, 4H), 1.43 (d, $J = 6.4$ Hz, 6H), 1.06 (s, 3H), 0.71 - 0.59 (m, 2H), 0.45 - 0.33 (m, 2H). MS (ESI) M/Z: 498.1 [M+H]⁺.
B005	 B005	¹H NMR (400 MHz, DMSO-<i>d</i>₆): δ 9.03 (s, 1H), 8.20 (d, $J = 1.2$ Hz, 1H), 8.16 (s, 1H), 7.68 (t, $J = 52.8$ Hz, 1H), 7.20 (d, $J = 1.2$ Hz, 1H), 3.66 - 3.51 (m, 6H), 2.90 (s, 6H), 1.13 (d, $J = 5.6$ Hz, 6H), 1.05 (s, 3H), 0.69 - 0.59 (m, 2H), 0.40 - 0.34 (m, 2H). MS (ESI) M/Z: 569.3 [M+H]⁺.

B006	 B006	¹H NMR (400 MHz, DMSO-<i>d</i>₆): δ 8.97 (s, 1H), 8.11 (s, 1H), 8.06 (s, 1H), 7.68 (t, <i>J</i> = 53.2 Hz, 1H), 7.01 (s, 1H), 4.46 - 4.33 (m, 2H), 4.14 - 3.98 (m, 4H), 2.86 - 2.78 (m, 1H), 1.32 - 1.17 (m, 6H), 1.08 - 1.04 (m, 9H), 0.68 - 0.62 (m, 2H), 0.40 - 0.34 (m, 2H). MS (ESI) M/Z: 568.2 [M+H]⁺.
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[0787] Example B007 and Example B008





[0788] Step 1: Synthesis of compound B007_6

[0789] A001_5 (100 mg, 165 mmol) was dissolved in a mixture of dichloromethane (2 mL) and *tert*-butanol (0.4 mL), followed by addition of cyanogen bromide (101 mg, 960 mmol, 5.81 eq). The reaction mixture was stirred at 20°C for 12 hours. The reaction mixture was cooled to 0°C, then slowly added with saturated sodium bicarbonate aqueous solution to adjust the pH to approximately 7, and extracted with dichloromethane (10 mL × 3). The organic phase was washed with saturated brine (10 mL × 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation to obtain B007_6 (138 mg) as a crude product, which was directly used in the next step.

[0790] MS (ESI) *M/Z*: 630.2 [*M*+*H*]⁺.

[0791] ¹H NMR (400 MHz, DMSO-*d*₆): δ 7.65 (t, *J* = 52.8 Hz, 1H), 7.29 - 7.26 (m, 3H), 7.25 - 7.22 (m, 2H), 7.18 - 7.16 (m, 2H), 6.46 (s, 1H), 4.08 (s, 2H), 3.47 - 3.45 (m, 4H), 3.19

- 3.16 (m, 4H), 1.43 (s, 9H), 1.23 (s, 9H).

[0792] Step 2: Synthesis of compound B007_7

[0793] B007_6 (100 mg, 158.7 mmol) was dissolved in a mixture of dichloromethane (1.5 mL), acetic acid (1.5 mL), and water (0.75 mL). The reaction mixture was cooled to 0°C, and N-chlorosuccinimide (83 mg, 624 mmol) was added in portions. After the addition was completed, the reaction mixture was slowly warmed to 20°C and stirred for 2 hours. The reaction mixture was cooled to 0°C, then slowly added with saturated sodium bicarbonate aqueous solution to adjust the pH to approximately 6, and extracted with dichloromethane (20 mL × 3). The organic phase was washed with brine (20 mL × 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation to obtain B007_7 (87 mg) as a crude product, which was directly used in the next step.

[0794] MS (ESI) M/Z: 548.2, 550.1 [M-H]⁻.

[0795] Step 3: Synthesis of compound B007_8

[0796] 1-Methylcyclopropanamine hydrochloride (68 mg, 632.7 μmol) and N,N-diisopropylethylamine (82 mg, 632.7 μmol) were dissolved in dichloromethane (2 mL). The mixture was cooled to 0°C, and a solution of B007_7 (87 mg, 158 mmol) in dichloromethane (1 mL) was slowly added dropwise thereto. After the addition was completed, the reaction mixture was slowly warmed to 20°C and stirred for 1 hour. The reaction mixture was quenched with water (20 mL) and extracted with dichloromethane (20 mL × 2). The organic phase was washed with brine (30 mL × 1), dried over anhydrous

sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by preparative chromatography on a silica gel plate to obtain B007_8 (7 mg) as a crude product, which was directly used in the next step.

[0797] MS (ESI) M/Z: 583.3 [M-H]⁻.

5 **[0798]** Step 4: Synthesis of compound B007

[0799] B007_8 (5 mg, 8.55 μmol) was dissolved in methanol (0.5 mL), followed by dropwise addition of 4 M HCl in methanol (2 mL). The reaction mixture was stirred at 20°C for 2 hours. The reaction was monitored by LCMS until completion. The reaction mixture was evaporated to dryness under a stream of nitrogen and purified by preparative chromatography (acidic conditions, chromatographic column: Phenomenex Luna C18) to
10 obtain B007 (1.36 mg, hydrochloride salt).

[0800] MS (ESI) M/Z: 485.1 [M+H]⁺.

[0801] ¹H NMR (400 MHz, DMSO-*d*₆): δ 9.02 (s, 2H), 7.93 (s, 1H), 7.69 - 7.54 (m, 4H), 7.14 (s, 1H), 3.65 - 3.62 (m, 4H), 3.35 - 3.31 (m, 4H), 1.03 (s, 3H), 0.63 - 0.61 (m, 2H), 0.37
15 - 0.34 (m, 2H).

[0802] Step 5: Synthesis of compound B008

[0803] B007 (9 mg, 17.2 μmol) and triethylamine (20.9 mg, 207 μmol) were dissolved in N,N-dimethylformamide (0.75 mL). The mixture was cooled to 0°C, followed by addition of dimethylcarbamoyl chloride (2.2 mg, 20.7 μmol). After the addition was completed, the
20 reaction mixture was slowly warmed to 20°C and stirred for 1 hour. The reaction was monitored by LCMS until completion. The reaction mixture was quenched with water (5

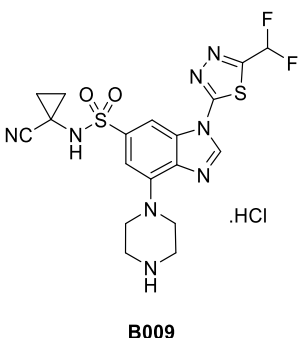
mL) and extracted with dichloromethane (5 mL $\times$ 2). The organic phase was washed with brine (5 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by preparative chromatography (neutral conditions, chromatographic column: Waters Xbridge Prep OBD C18) to obtain B008 (6.53 mg).

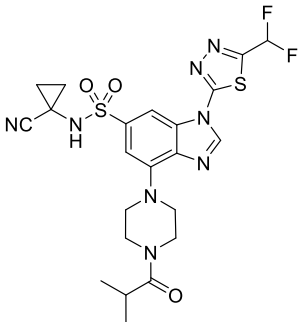
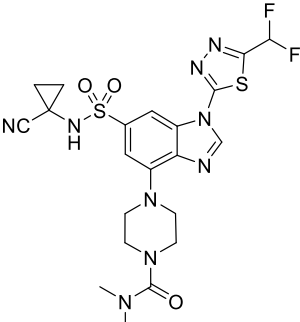
[0804] MS (ESI) M/Z: 556.2 [M+H]⁺.

[0805] ¹H NMR (400 MHz, DMSO-*d*₆): δ 7.89 (s, 1H), 7.82 - 7.53 (m, 2H), 7.49 (s, 2H), 7.12 (s, 1H), 3.43 - 3.41 (m, 4H), 3.33 - 3.30 (m, 4H), 2.79 (s, 6H), 1.01 (s, 3H), 0.62 - 0.59 (m, 2H), 0.35 - 0.32 (m, 2H).

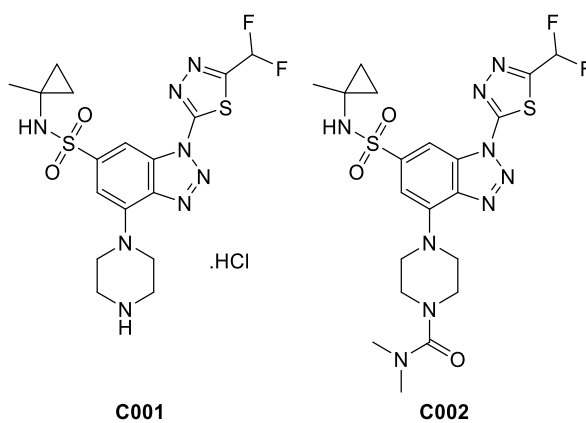
[0806] Example B009, Example B010, and Example B011

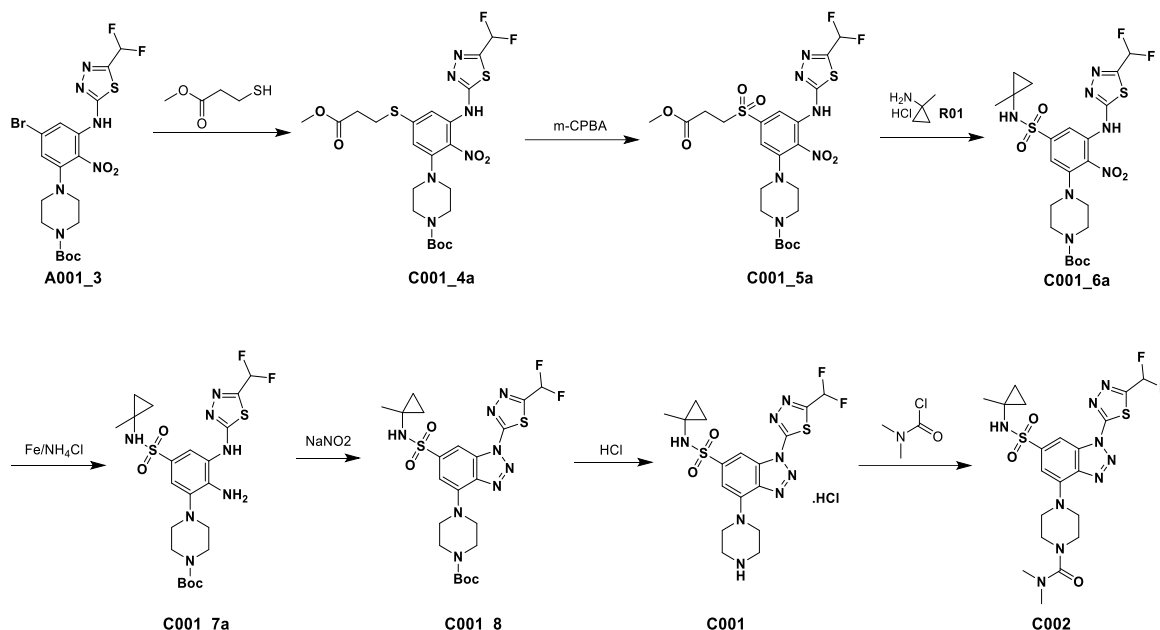
[0807] Table 13

Example	Structural formula	Structural characterization
B009	 B009	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.29 (s, 1H), 9.24 (s, 2H), 9.13 (s, 1H), 8.36 (s, 1H), 7.69 (t, <i>J</i> = 53.2 Hz, 1H), 7.30 (s, 1H), 3.89 - 3.86 (m, 4H), 3.28 - 3.25 (m, 4H), 1.44 - 1.40 (m, 2H), 1.33 - 1.29 (m, 2H). MS (ESI) M/Z: 481.1 [M+H]⁺.

Example	Structural formula	Structural characterization
B010	 B010	¹H NMR (400 MHz, DMSO-<i>d</i>₆): δ 9.17 (s, 1H), 9.09 (s, 1H), 8.30 (d, <i>J</i> = 1.6 Hz, 1H), 7.68 (t, <i>J</i> = 53.2 Hz, 1H), 7.22 (d, <i>J</i> = 1.2 Hz, 1H), 3.81 - 3.69 (m, 4H), 3.67 - 3.54 (m, 4H), 3.01 - 2.89 (m, 1H), 1.44 - 1.37 (m, 2H), 1.31 - 1.24 (m, 2H), 1.04 (d, <i>J</i> = 6.4 Hz, 6H). MS (ESI) M/Z: 551.1 [M+H]⁺.
B011	 B011	¹H NMR (400 MHz, DMSO-<i>d</i>₆): δ 9.20 (s, 1H), 9.07 (s, 1H), 8.29 (d, <i>J</i> = 1.2 Hz, 1H), 7.68 (t, <i>J</i> = 52.8 Hz, 1H), 7.23 (s, 1H), 3.65 - 3.61 (m, 4H), 3.39 - 3.34 (m, 4H), 2.80 (s, 6H), 1.44 - 1.36 (m, 2H), 1.30 - 1.22 (m, 2H). MS (ESI) M/Z: 552.0 [M+H]⁺.

[0808] Example C001 and Example C002





[0809] Step 1: Synthesis of compound C001_4a

[0810] A001_3 (2.00 g, 3.74 mmol), methyl 3-mercaptopropionate (493 mg, 4.11 mmol), and N,N-diisopropylethylamine (1.55 g, 11.9 mmol) were dissolved in 1,4-dioxane (20 mL).

- 5 The system was purged with nitrogen three times, followed by addition of $\text{Pd}_2(\text{dba})_3$ (342 mg, 374 μmol , 0.10 eq) and Xantphos (432 mg, 747 μmol , 0.20 eq), and purged with nitrogen three additional times. The reaction mixture was heated to 85°C and stirred for 2 hours. Three identical parallel reactions were carried out and finally combined for work-up. The reaction mixture was cooled to room temperature, then quenched with water (200 mL), and
- 10 extracted with ethyl acetate (100 mL $\times$ 3). The organic phase was washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain C001_4a (2.87 g).

[0811] MS (ESI) M/Z : 575.1 $[\text{M}+\text{H}]^+$.

[0812] Step 2: Synthesis of compound C001_5a

[0813] C001_4a (2.87 g, 4.99 mmol) was dissolved in dichloromethane (30 mL). The reaction mixture was cooled to 0°C, and *m*-chloroperoxybenzoic acid (3.04 g, 14.9 mmol, 85% purity) was added in portions. The reaction mixture was stirred at 0°C for 1 hour.

5 The reaction was monitored by LCMS until completion. The reaction mixture was allowed to warm to room temperature, then quenched with saturated sodium sulfite aqueous solution (30 mL), and extracted with ethyl acetate (30 mL × 3). The organic phase was washed with brine (30 mL × 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography
10 to obtain C001_5a (1.6 g).

[0814] MS (ESI) M/Z: 606.9 [M+H]⁺.

[0815] Step 3: Synthesis of compound C001_6a

[0816] C001_5a (1.00 g, 1.65 mmol) was dissolved in methanol (30 mL). The system was purged with nitrogen three times, then cooled to 0°C, followed by addition of sodium
15 methoxide (445 mg, 8.24 mmol). The reaction mixture was stirred at 0°C for 30 minutes, followed by addition of dichloromethane (20 mL), and stirred at room temperature for another 30 minutes. TLC indicated completion of the reaction. 1-Amino-1-cyclopropanecarbonitrile hydrochloride (709 mg, 6.59 mmol) was added at 0°C, and the mixture was stirred until the solid dissolved. The solvent was removed by rotary
20 evaporation at room temperature, and the residue was dried under oil pump vacuum for 15 minutes. 3Å molecular sieves and N,N-dimethylformamide (30 mL) were added.

Triethylamine (166 mg, 1.65 mmol) and N-chlorosuccinimide (660 mg, 4.95 mmol) were added in an ice bath. The reaction mixture was stirred at 0°C for 2 hours. The reaction mixture was extracted with ethyl acetate (30 mL × 3), washed once with dilute sodium bisulfite solution and once with water. The organic phase was washed with brine (20 mL × 2), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain C001_6a (550 mg).

[0817] MS (ESI) M/Z: 590.2 [M+H]⁺.

[0818] Step 4: Synthesis of compound C001_7a

[0819] C001_6a (40.0 mg, 67.8 μmol) was dissolved in ethanol (0.3 mL) and water (0.1 mL), followed by addition of iron powder (18.9 mg, 339 μmol) and ammonium chloride (18.1 mg, 339 μmol). The reaction mixture was heated to 80°C and stirred for 1.5 hours. The reaction mixture was cooled to room temperature and filtered through diatomite. The filtrate was diluted with water (5 mL) and extracted with ethyl acetate (5 mL × 3). The organic phase was washed with brine (5 mL × 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain C001_7a (14 mg).

[0820] MS (ESI) M/Z: 558.2 [M-H]⁻.

[0821] Step 5: Synthesis of compound C001_8

[0822] C001_7a (14.0 mg, 25.0 μmol) was dissolved in acetic acid (0.2 mL), followed by addition of sodium nitrite (2.42 mg, 35.0 μmol). The reaction mixture was stirred at 25°C

for 1 hour. The reaction mixture was quenched with water (10 mL) and extracted with ethyl acetate (5 mL $\times$ 3). The organic phase was washed with brine (5 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation to obtain C001_8 (10 mg) as a crude product, which was directly used in the next step.

5 [0823] MS (ESI) M/Z: 569.2 [M-H]⁻.

[0824] Step 6: Synthesis of compound C001

[0825] C001_8 (10.0 mg, 17.5 μ mol) was dissolved in ethyl acetate (0.5 mL), followed by addition of 4 M HCl in ethyl acetate (1 mL). The reaction mixture was stirred at 25°C for 1 hour. The reaction was monitored by TLC until completion. The reaction mixture was
10 directly concentrated under reduced pressure to obtain C001 (9 mg, hydrochloride salt).

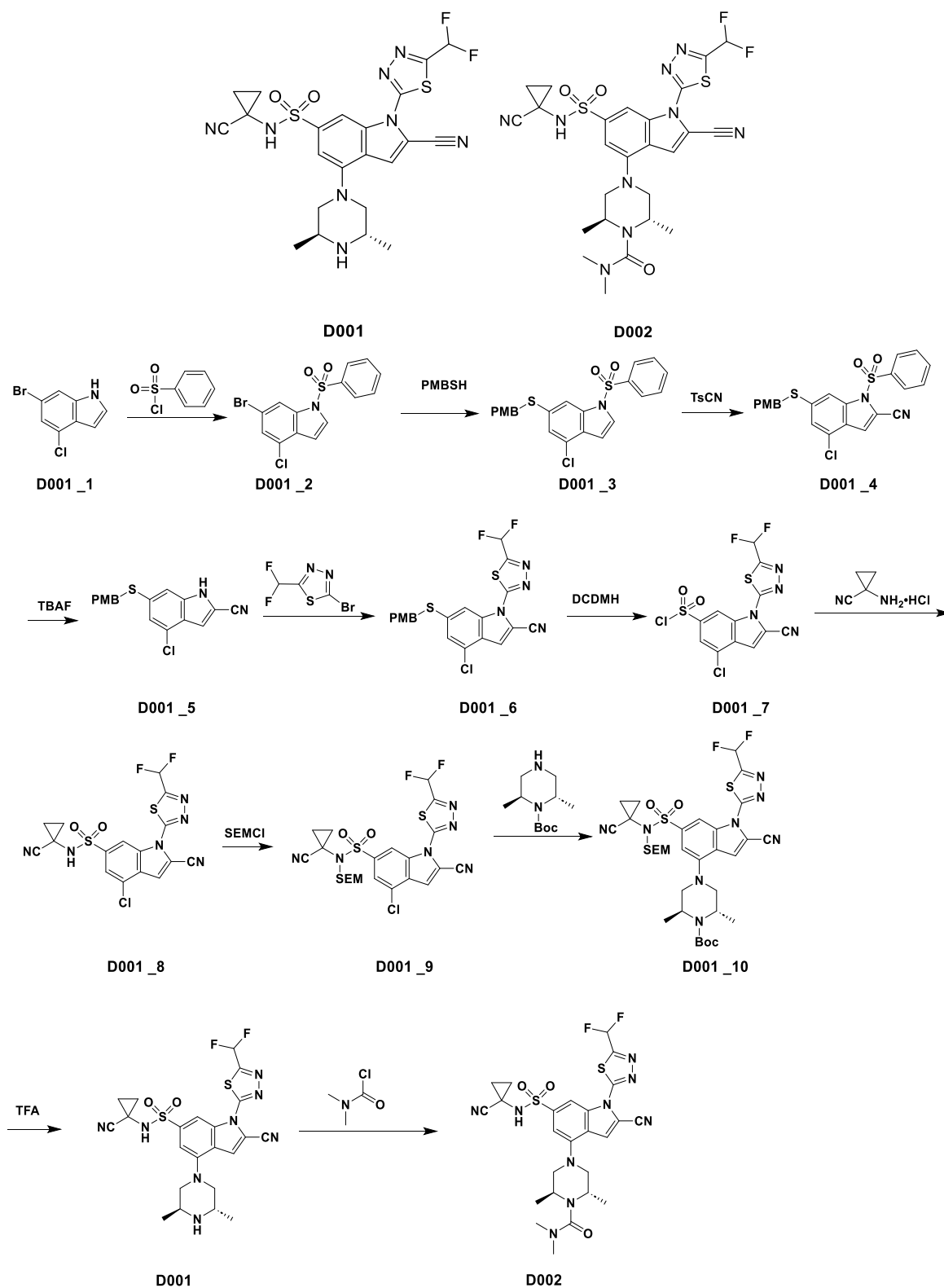
[0826] Step 7: Synthesis of compound C002

[0827] C001 (9.00 mg, 17.7 μ mol) and triethylamine (2.69 mg, 26.6 μ mol) were dissolved in N,N-dimethylformamide (0.2 mL), followed by addition of dimethylcarbonyl chloride (2.86 mg, 26.6 μ mol). The reaction mixture was stirred at 25°C for 1 hour. The reaction
15 was monitored by LCMS until completion. The reaction mixture was quenched with water (0.1 mL). The residue was purified by preparative chromatography (neutral conditions, chromatographic column: Waters Xbridge Prep OBD C18) to obtain C002 (2.08 mg).

[0828] MS (ESI) M/Z: 542.2 [M+H]⁺.

[0829] ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.39 (s, 1H), 8.19 (s, 1H), 7.68 (t, *J* = 52.8 Hz, 1H), 7.21 (s, 1H), 3.89 - 3.86 (m, 4H), 3.42 - 3.39 (m, 4H), 2.82 (s, 6H), 1.09 (s, 3H), 0.70 -
20 0.64 (m, 2H), 0.44 - 0.38 (m, 2H).

[0830] Example D001 and Example D002



[0831] Step 1: Synthesis of compound D001_2

[0832] D001_1 (4.30 g, 18.7 mmol), tetrabutylammonium bromide (601 mg, 1.87 mmol), and sodium hydroxide (1.34 g, 33.6 mmol) were dissolved in dichloromethane (50.0 mL) and H₂O (10 mL). The mixture was cooled to 0°C in an ice-water bath, followed by dropwise addition of benzenesulfonyl chloride (3.95 g, 22.4 mmol), and stirred at 0°C for 5 0.5 hours. The reaction mixture was quenched with water (50 mL) and extracted with dichloromethane (100 mL × 2). The organic phase was washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The crude product was triturated in acetonitrile (10 mL), filtered, and concentrated to dryness to obtain D001_2 (6.5 g).

10 [0833] MS (ESI) M/Z: 367.9, 369.9 [M-H]⁻.

[0834] ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.07 - 8.05 (m, 3H), 8.01 (d, *J* = 4.0 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.66 - 7.61 (m, 3H), 6.88 (d, *J* = 3.6 Hz, 1H).

[0835] Step 2: Synthesis of compound D001_3

[0836] D001_2 (5.00 g, 13.5 mmol), 4-methoxybenzyl mercaptan (2.08 g, 13.5 mmol), and 15 N,N-diisopropylethylamine (3.57 g, 27.6 mmol) were dissolved in 1,4-dioxane (80 mL). The system was purged with nitrogen three times, followed by addition of Pd₂(dba)₃ (371 mg, 405 μmol) and Xantphos (468 mg, 809 μmol), and purged with nitrogen three additional times. The reaction mixture was heated to 110°C and stirred for 1 hour. The reaction mixture was cooled to room temperature, filtered, and the filtrate was concentrated by rotary 20 evaporation. The residue was purified by column chromatography to obtain D001_3 (5.70 g).

[0837] MS (ESI) M/Z: 442.1, 444.1 [M-H]⁻.

[0838] ¹H NMR (400 MHz, CDCl₃-d): δ 7.88 (s, 1H), 7.75 (d, *J* = 7.2 Hz, 2H), 7.56 - 7.53 (m, 2H), 7.44 (t, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.8 Hz, 2H), 7.20 (s, 1H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.72 (s, 1H), 4.15 (s, 2H), 3.80 (s, 3H).

5 [0839] Step 3: Synthesis of compound D001_4

[0840] Lithium diisopropylamide (2 M in tetrahydrofuran, 9.29 mL) was added dropwise to a solution of D001_3 (5.50 g, 12.4 mmol) in tetrahydrofuran (60 mL) at -60°C. After the addition was completed, the reaction mixture was stirred at -60°C for 0.5 hours. A solution of 4-toluenesulfonyl cyanide (2.92 g, 16.1 mmol) in tetrahydrofuran (10 mL) was then added dropwise thereto. After the addition was completed, the reaction mixture was warmed to -40°C and stirred for another 1 hour. The reaction mixture was quenched at room temperature with saturated ammonium chloride aqueous solution (100 mL) and extracted with ethyl acetate (100 mL × 2). The organic phase was washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain D001_4 (2.10 g).

[0841] MS (ESI) M/Z: 466.9, 468.7 [M-H]⁻.

[0842] ¹H NMR (400 MHz, CDCl₃-d): δ 7.99 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.61 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 8.4 Hz, 2H), 7.39 (s, 1H), 7.37 (d, *J* = 6.4 Hz, 2H), 7.26 (s, 1H), 6.89 (d, *J* = 8.8 Hz, 2H), 4.25 (s, 2H), 3.80 (s, 3H).

[0843] Step 4: Synthesis of compound D001_5

[0844] D001_4 (1.00 g, 2.13 mmol) was dissolved in tetrahydrofuran (10 mL), followed by addition of tetrabutylammonium fluoride (1 M in tetrahydrofuran, 10.7 mL). The reaction mixture was heated to 50°C and stirred for 0.5 hours. The reaction mixture was cooled to room temperature, quenched with dilute hydrochloric acid aqueous solution (0.3 N, 30 mL), and extracted with ethyl acetate (20 mL × 2). The organic phase was washed with water (50 mL), dried over anhydrous sodium sulfate, filtered, and concentrated to obtain D001_5 (700 mg).

[0845] MS (ESI) M/Z: 326.9, 328.8 [M-H]⁻.

[0846] ¹H NMR (400 MHz, CDCl₃-d): δ 11.26 (s, 1H), 7.43 (s, 1H), 7.18 (d, *J* = 8.8 Hz, 2H), 7.13 (s, 1H), 7.10 (s, 1H), 6.79 (d, *J* = 8.8 Hz, 2H), 4.04 (s, 2H), 3.77 (s, 3H).

[0847] Step 5: Synthesis of compound D001_6

[0848] D001_5 (1.40 g, 4.26 mmol), 2-bromo-5-(difluoromethyl)-1,3,4-thiadiazole (1.10 g, 5.11 mmol), and cesium carbonate (1.39 g, 4.26 mmol) were dissolved in N,N-dimethylformamide (15 mL). The reaction mixture was heated to 80°C and stirred for 1 hour. The reaction mixture was cooled to room temperature, quenched with ice water (50 mL), and extracted with ethyl acetate (50 mL × 2). The organic phase was washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain D001_6 (1.60 g).

[0849] MS (ESI) M/Z: 462.9, 464.8 [M+H]⁺.

[0850] ¹H NMR (400 MHz, CDCl₃-d): δ 8.13 (s, 1H), 7.58 (s, 1H), 7.33 (s, 1H), 7.30 (d, *J*

= 8.8 Hz, 2H), 7.08 (t, J = 53.6 Hz, 1H), 6.84 (d, J = 8.8 Hz, 2H), 4.21 (s, 2H), 3.78 (s, 3H).

[0851] Step 6: Synthesis of compound D001_7

[0852] D001_6 (1.00 g, 2.16 mmol), acetic acid (1 mL), and water (0.5 mL) were dissolved in acetonitrile (30 mL). The mixture was cooled to -15°C, and 1,3-dichloro-5,5-dimethylhydantoin (638 mg, 3.24 mmol) was added in portions. The resulting mixture was then stirred at the same temperature for 1 hour. The reaction was monitored by LCMS until completion. The reaction mixture was quenched with water (50 mL) and extracted with dichloromethane (50 mL $\times$ 2). The organic phase was washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation to obtain D001_7 (883 mg).

[0853] MS (ESI) M/Z : 389.0, 390.9. (The sulfonyl chloride of D001_7 appears as the corresponding sulfonic acid in LCMS).

[0854] Step 7: Synthesis of compound D001_8

[0855] 1-Aminocyclopropanecarbonitrile hydrochloride (512 mg, 4.32 mmol) and pyridine (683 mg, 8.63 mmol) were dissolved in *N,N*-dimethylformamide (10 mL). The reaction mixture was cooled to 0°C in an ice-water bath. A solution of D001_7 (883 mg, 2.16 mmol) in dichloromethane (10 mL) was added dropwise thereto at 0°C. The resulting mixture was then stirred at 0°C for 20 minutes. The reaction mixture was quenched with water (50 mL) and extracted with dichloromethane (50 mL $\times$ 2). The organic phase was washed with water (100 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography

to obtain D001_8 (530 mg).

[0856] MS (ESI) M/Z: 455.0, 457.0 [M+H]⁺.

[0857] ¹H NMR (400 MHz, CDCl₃-d): δ 8.94 (s, 1H), 8.00 (s, 1H), 7.75 (s, 1H), 7.09 (t, *J* = 53.2 Hz, 1H), 5.74 (s, 1H), 1.68 - 1.64 (m, 2H), 1.52 - 1.48 (m, 2H).

5 **[0858]** Step 8: Synthesis of compound D001_9

[0859] D001_8 (200 mg, 440 μmol) and cesium carbonate (683 mg, 8.63 mmol) were dissolved in N,N-dimethylformamide (5 mL). 2-(Trimethylsilyl)ethoxymethyl chloride (88.0 mg, 528 μmol) was added dropwise thereto at 25°C. The reaction mixture was stirred for 1 hour. The reaction mixture was quenched with ice water (10 mL) and extracted with
10 ethyl acetate (10 mL × 2). The organic phase was washed with brine (10 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain D001_9 (250 mg).

[0860] MS (ESI) M/Z: 583.1, 585.1 [M-H]⁻.

[0861] ¹H NMR (400 MHz, CDCl₃-d): δ 8.95 (s, 1H), 8.02 (s, 1H), 7.73 (s, 1H), 7.09 (t, *J* = 53.6 Hz, 1H), 4.91 (s, 2H), 3.61 - 3.56 (m, 2H), 1.78 - 1.74 (m, 2H), 1.60 - 1.56 (m, 2H),
15 0.94 - 0.89 (m, 2H), 0.00 (s, 9H).

[0862] Step 9: Synthesis of compound D001_10

[0863] D001_9 (50.0 mg, 85.5 μmol), *tert*-butyl (2S,6S)-2,6-dimethylpiperazine-1-carboxylate (91.6 mg, 427 μmol), and potassium carbonate (35.4 mg, 256 μmol) were
20 dissolved in 1,4-dioxane (4 mL). The system was purged with nitrogen three times, followed by addition of RuPhos Pd G3 (35.7 mg, 42.7 μmol) and RuPhos (19.9 mg, 42.7

μmol), and purged with nitrogen three additional times. The reaction mixture was heated to 90°C and stirred for 16 hours. Six parallel reactions were carried out and finally combined for purification. After cooling to room temperature, the six parallel reactions were combined. The reaction mixture was directly filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain D001_10 (100 mg) as a crude product.

[0864] MS (ESI) M/Z: 761.1 [M-H]⁻.

[0865] Step 10: Synthesis of compound D001

[0866] D001_10 (10.0 mg, 13.1 μmol) was dissolved in dichloromethane (1.5 mL). Trifluoroacetic acid (0.5 mL) was added thereto at 25°C. The reaction mixture was stirred at 25°C for 2 hours. The reaction was monitored by LCMS until completion. The reaction mixture was concentrated under reduced pressure at 25°C. The crude product was purified by preparative chromatography (neutral conditions, column: Waters Xbridge Prep OBD C18) to obtain D001 (3.11 mg).

[0867] MS (ESI) M/Z: 533.1 [M+H]⁺.

[0868] ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.16 - 8.12 (m, 2H), 7.69 (t, *J* = 53.2 Hz, 1H), 7.20 (s, 1H), 3.65 - 3.50 (m, 2H), 3.38 - 3.35 (m, 2H), 3.05 - 3.01 (m, 2H), 1.44 - 1.40 (m, 2H), 1.29 - 1.27 (m, 6H), 1.24 - 1.23 (m, 2H).

[0869] Step 11: Synthesis of compound D002

[0870] D001 (12.0 mg, 22.5 μmol) and triethylamine (3.42 mg, 33.8 μmol, 1.50 eq) were dissolved in N,N-dimethylformamide (2 mL). Dimethylcarbamoyl chloride (5.75 mg, 40.5

μmol , 1.50 eq) was added in one portion at 20°C. After the addition was completed, the reaction mixture was heated to 40°C and stirred for 36 hours. After completion of the reaction monitored by LCMS, the reaction mixture was quenched with water (0.1 mL). The crude product was purified by preparative chromatography (neutral conditions, column:

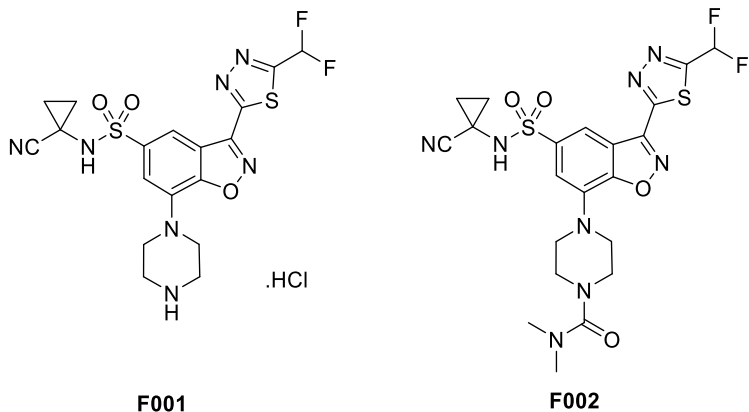
5 Waters Xbridge Prep OBD C18) to obtain D002 (4.82 mg).

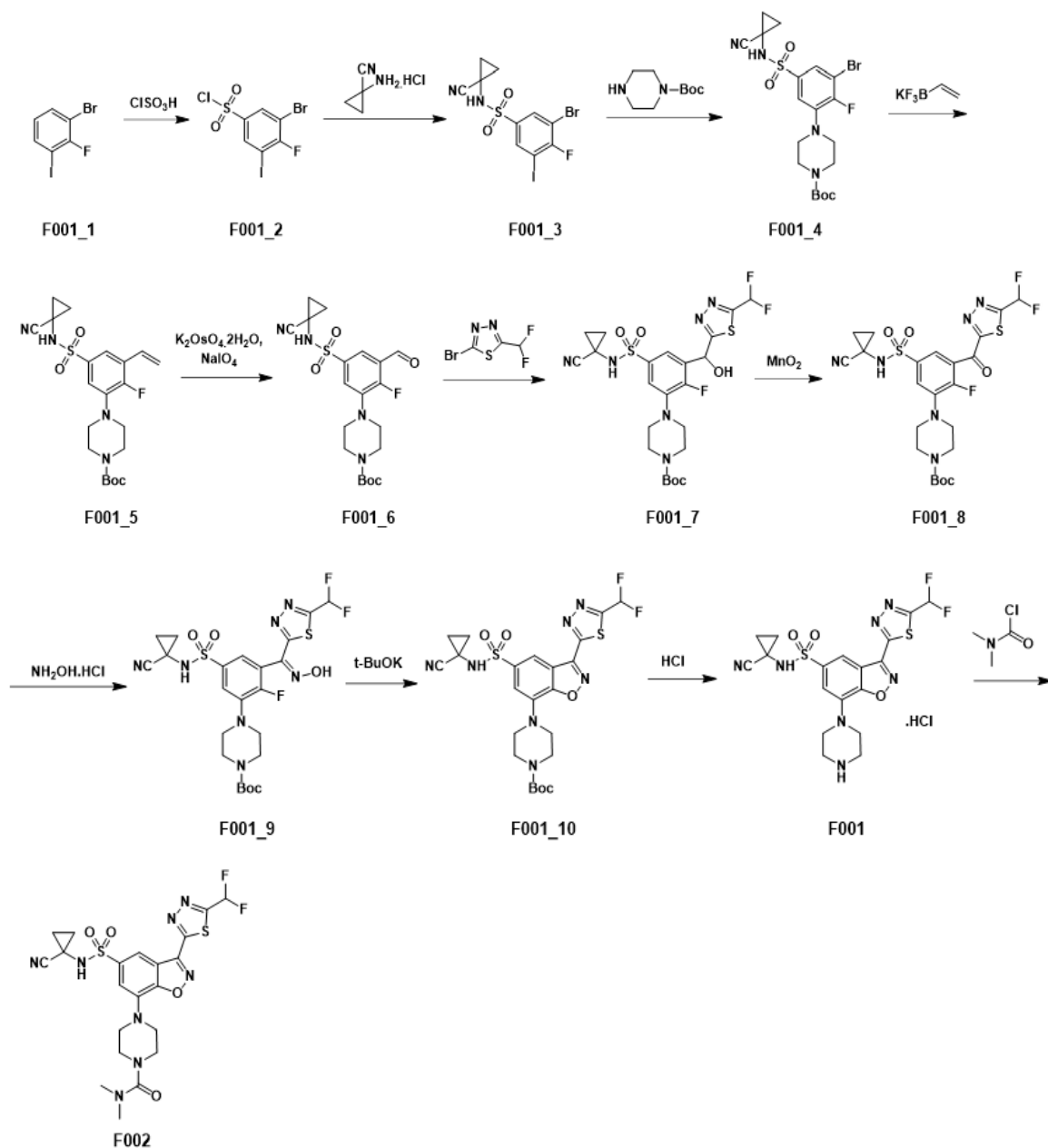
[0871] MS (ESI) M/Z : 604.0 $[M+H]^+$.

[0872] ^1H NMR (400 MHz, $\text{DMSO-}d_6$): δ 9.21 (s, 1H), 8.16 (s, 2H), 7.69 (t, $J = 53.2$ Hz, 1H), 7.21 (s, 1H), 3.66 - 3.64 (m, 2H), 3.41 - 3.37 (m, 2H), 3.09 - 3.04 (m, 2H), 2.91 (s, 6H), 1.44 - 1.41 (m, 2H), 1.30 - 1.28 (m, 2H), 1.19 - 1.15 (m, 6H).

10

[0873] Example F001 and Example F002





[0874] Step 1: Synthesis of compound F001_2

[0875] Chlorosulfonic acid (58.1 g, 499 mmol) was added to a three-necked flask, cooled to 0°C in an ice-salt bath, and F001_1 (30.0 g, 99.7 mmol) was added in portions. The reaction mixture was stirred at 0°C for 0.5 hours. Sodium chloride (5.83 g, 99.7 mmol) was then added in portions. The reaction mixture was slowly warmed to 20°C and stirred for 0.5 hours, then slowly heated to 90°C and stirred for 2 hours. The reaction mixture was

cooled to room temperature, then slowly poured into ice water (300 mL) to quench, and extracted with ethyl acetate (200 mL $\times$ 3). The organic phase was washed with water (200 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain F001_2 (14.9 g).

[0876] MS (ESI) M/Z: 379.0, 381.1 [M-H]⁻. (The sulfonyl chloride of F001_2 appears as the corresponding sulfonic acid in LCMS).

[0877] ¹H NMR (400 MHz, DMSO-*d*₆): δ 7.93 - 7.91 (m, 1H), 7.77 - 7.75 (m, 1H).

[0878] Step 2: Synthesis of compound F001_3

[0879] 1-Aminocyclopropanecarbonitrile hydrochloride (6.63 g, 56.0 mmol) was dissolved in dichloromethane (30 mL) and pyridine (41 mL), followed by portionwise addition of 031_2 (14.9 g, 37.3 mmol). The reaction mixture was stirred at 20°C for 1 hour. The reaction mixture was slowly poured into ice water (100 mL) to quench, and extracted with ethyl acetate (100 mL $\times$ 3). The organic phase was sequentially washed with 1 N hydrochloric acid aqueous solution (100 mL), brine (100 mL), saturated sodium bicarbonate aqueous solution (100 mL), and brine (100 mL $\times$ 2), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was triturated with petroleum ether (100 mL) at room temperature, filtered, and the filter cake was collected to obtain F001_3 (15.4 g).

[0880] MS (ESI) M/Z: 443.0, 445.0 [M-H]⁻.

[0881] ¹H NMR (400 MHz, DMSO-*d*₆): δ 9.33 (s, 1H), 8.22 - 8.20 (m, 1H), 8.11 - 8.09 (m,

1H), 1.50 - 1.47 (m, 2H), 1.34 - 1.32 (m, 2H).

[0882] Step 3: Synthesis of compound F001_4

[0883] F001_3 (4.00 g, 8.99 mmol), N-Boc piperazine (3.35 g, 18.0 mmol), and cesium carbonate (7.32 g, 22.5 mmol) were dissolved in 1,4-dioxane (20 mL). The system was
5 purged with nitrogen three times, followed by addition of XPhos Pd G2 (1.41 g, 1.80 mmol), and purged with nitrogen three additional times. The reaction mixture was heated to 110°C and stirred for 5 hours. Five parallel reactions were carried out and finally combined for purification. After cooling to room temperature, the five parallel reactions were combined. The reaction mixture was quenched with water (200 mL) and extracted with ethyl acetate
10 (100 mL × 3). The organic phase was washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain F001_4 (2.6 g).

[0884] MS (ESI) M/Z: 501.0, 503.2 [M-H]⁻.

[0885] Step 4: Synthesis of compound F001_5

[0886] F001_4 (2.5 g, 4.97 mmol), potassium vinyltrifluoroborate (4.17 g, 31.1 mmol), and triethylamine (1.51 g, 14.9 mmol) were dissolved in isopropanol (30 mL). The system was
15 purged with nitrogen three times, followed by addition of Pd(dppf)Cl₂·CH₂Cl₂ (811 mg, 993 μmol), and purged with nitrogen three additional times. The reaction mixture was heated to 100°C and stirred for 2 hours. The reaction mixture was cooled to room temperature,
20 then quenched with water (200 mL), and extracted with ethyl acetate (50 mL × 3). The organic phase was washed with brine (100 mL), dried over anhydrous sodium sulfate,

filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain F001_5 (1.4 g).

[0887] MS (ESI) M/Z: 449.4 [M-H]⁻.

[0888] Step 5: Synthesis of compound F001_6

5 **[0889]** Sodium periodate (2.53 g, 11.8 mmol) and potassium osmate dihydrate (229 mg, 622 μmol) were added to a solution of F001_5 (8.00 g, 19.8 mmol) in tetrahydrofuran (50 mL) and water (25 mL). The reaction mixture was stirred at 20°C for 2 hours. The reaction mixture was quenched with water (100 mL) and extracted with ethyl acetate (50 mL × 3). The organic phase was washed with brine (50 mL × 3), dried over anhydrous sodium
10 sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain F001_6 (1.6 g).

[0890] MS (ESI) M/Z: 451.3 [M-H]⁻.

[0891] ¹H NMR (400 MHz, DMSO-*d*₆): δ 10.27 (s, 1H), 9.24 (s, 1H), 7.84 - 7.82 (m, 1H), 7.70 - 7.68 (m, 1H), 3.53 - 3.50 (m, 4H), 3.12 - 3.09 (m, 4H), 1.47 - 1.45 (m, 2H), 1.43 (s,
15 9H), 1.33 - 1.29 (m, 2H).

[0892] Step 6: Synthesis of compound F001_7

[0893] 2-Bromo-5-(difluoromethyl)-1,3,4-thiadiazole (7.13 g, 33.2 mmol) was dissolved in tetrahydrofuran (10 mL). The system was purged with nitrogen three times, then cooled to -60°C, and isopropylmagnesium chloride-lithium chloride complex (1.3 M in
20 tetrahydrofuran, 25.5 mL) was slowly added dropwise thereto. After the addition was completed, the reaction mixture was stirred at -60°C for 2 hours. A solution of F001_6 (1.5

g, 3.31 mmol) in tetrahydrofuran (10 mL) was then added dropwise thereto. After the addition was completed, the reaction mixture was naturally warmed to 20°C and stirred for another 16 hours. The reaction mixture was quenched in an ice bath with saturated ammonium chloride aqueous solution (100 mL) and extracted with ethyl acetate (100 mL × 2). The organic phase was washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain F001_7 (870 mg).

[0894] MS (ESI) M/Z: 587.2 [M-H]⁻.

[0895] Step 7: Synthesis of compound F001_8

[0896] F001_7 (870 mg, 1.48 mmol) was dissolved in dichloromethane (30 mL), followed by addition of manganese dioxide (2.57 g, 29.6 mmol). The reaction mixture was stirred at 20°C for 1 hour. The reaction mixture was filtered through diatomite. The filtrate was diluted with water (100 mL) and extracted with ethyl acetate (50 mL × 3). The organic phase was washed with brine (50 mL × 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain F001_8 (540 mg).

[0897] MS (ESI) M/Z: 585.2 [M-H]⁻.

[0898] Step 8: Synthesis of compound F001_9

[0899] F001_8 (150 mg, 256 μmol) was dissolved in ethanol (2 mL), followed by addition of hydroxylamine hydrochloride (88.9 mg, 1.28 mmol). The reaction mixture was heated to 80°C and stirred for 1 hour. The reaction mixture was cooled to room temperature and

directly concentrated under reduced pressure to obtain a crude product. The residue was purified by column chromatography to obtain F001_9 (70 mg).

[0900] MS (ESI) M/Z: 600.2 [M-H]⁻.

[0901] Step 9: Synthesis of compound F001_10

5 [0902] F001_9 (65 mg, 108 μmol) was dissolved in N-methylpyrrolidone (11 mL), followed by addition of potassium *tert*-butoxide (18.2 mg, 162 μmol). The reaction mixture was heated to 50°C and stirred for 16 hours. The reaction mixture was cooled to room temperature, then quenched with water (50 mL), and extracted with ethyl acetate (20 mL × 3). The organic phase was washed with brine (30 mL × 3), dried over anhydrous
10 sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain F001_10 (30 mg).

[0903] MS (ESI) M/Z: 580.2 [M-H]⁻.

[0904] Step 10: Synthesis of compound F001

[0905] F001_10 (15 mg, 25.8 μmol) was dissolved in ethyl acetate (1 mL), followed by
15 addition of 4 M HCl in ethyl acetate (2 mL). The reaction mixture was stirred at 20°C for 1 hour. The reaction mixture was directly concentrated under reduced pressure to obtain F001 (13 mg, hydrochloride salt) as a crude product, which was directly used in the next step.

[0906] MS (ESI) M/Z: 480.2 [M-H]⁻.

20 [0907] Step 11: Synthesis of compound F002

[0908] F001 (13 mg, 25.1 μmol, hydrochloride salt) and triethylamine (5.08 mg, 50.2 μmol)

were dissolved in N,N-dimethylformamide (1 mL), followed by addition of dimethylcarbamoyl chloride (5.40 mg, 50.2 μ mol). The reaction mixture was stirred at 25°C for 1 hour. The reaction mixture was quenched with water (0.1 mL). The residue was purified by preparative chromatography (neutral conditions, chromatographic column:

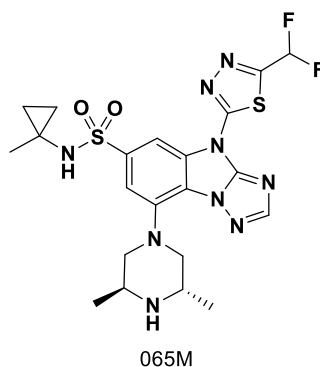
5 Waters Xbridge Prep OBD C18) to obtain F001 (7.29 mg).

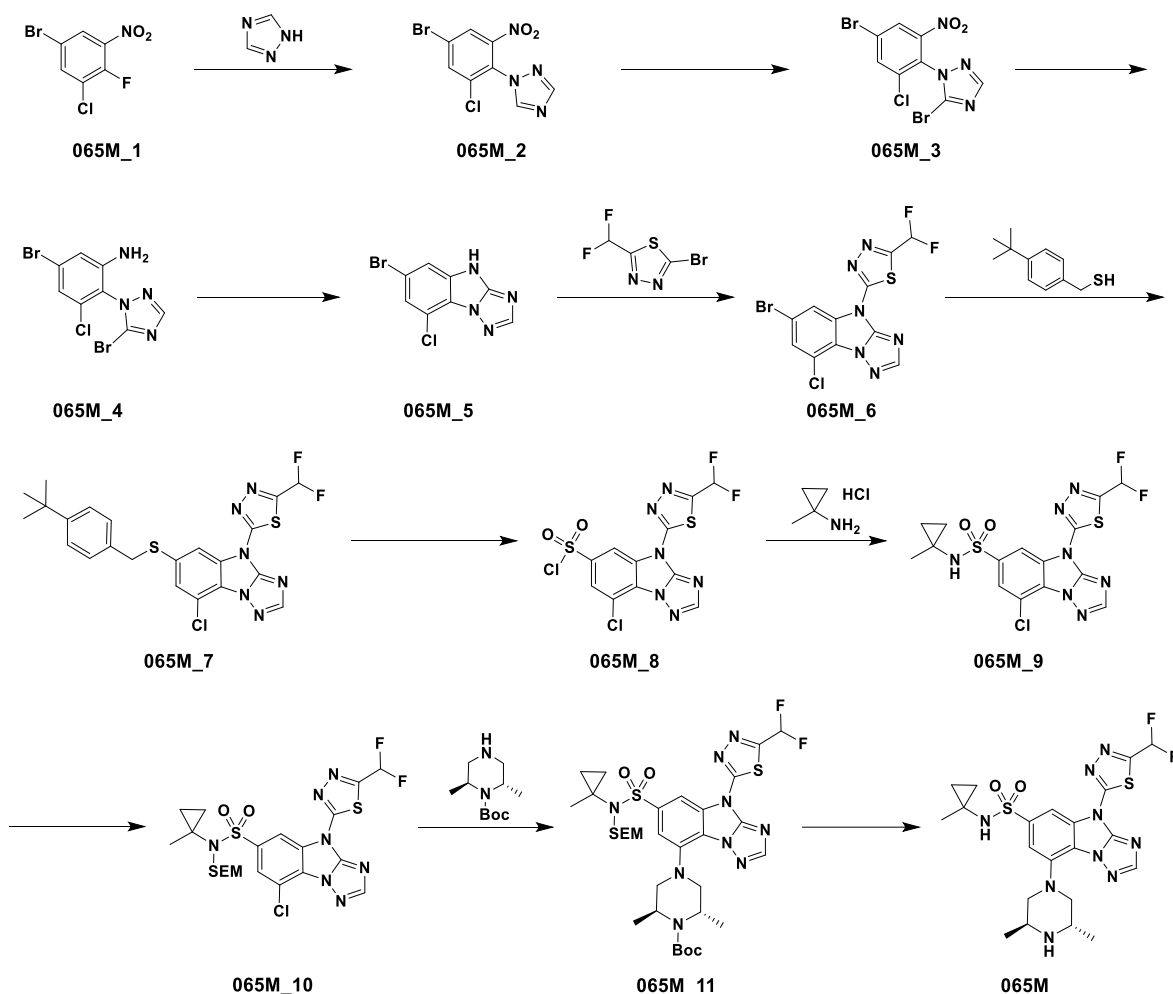
[0909] MS (ESI) M/Z: 553.1 $[M+H]^+$.

[0910] ^1H NMR (400 MHz, DMSO- d_6): δ 9.28 (s, 1H), 8.37 (d, J = 1.6 Hz, 1H), 7.77 (t, J = 52.8 Hz, 1H), 7.51 (d, J = 1.6 Hz, 1H), 3.50 - 3.48 (m, 4H), 3.40 - 3.37 (m, 4H), 2.81 (s, 6H), 1.46 - 1.43 (m, 2H), 1.34 - 1.30 (m, 2H).

10

[0911] Example 065M





[0912] Step 1: Synthesis of compound 065M_2

[0913] 065M_1 (5.00 g, 19.7 mmol), 1,2,4-triazole (1.63 g, 23.6 mmol), and potassium carbonate (4.07 g, 29.5 mmol) were dissolved in dimethyl sulfoxide (50 mL). The mixture was heated to 60°C and stirred for 1 hour. The reaction mixture was cooled to room temperature, then quenched with water (150 mL), and extracted with ethyl acetate (100 mL × 2). The combined organic phases were washed with brine (100 mL × 3), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 065M_2 (5.60 g).

[0914] MS (ESI) M/Z: 302.7, 304.7 [M+H]⁺.

[0915] ^1H NMR (400 MHz, DMSO- d_6): δ 9.07 (s, 1H), 8.56 (s, 1H), 8.53 (s, 1H), 8.35 (s, 1H).

[0916] Step 2: Synthesis of compound 065M_3

[0917] 065M_2 (5.60 g, 18.5 mmol), N-bromosuccinimide (6.57 g, 36.9 mmol), and
5 benzoyl peroxide (447 mg, 1.85 mmol) were dissolved in chlorobenzene (80 mL). The
reaction mixture was heated to 110°C and stirred for 16 hours. The reaction mixture was
cooled to room temperature, then quenched with water (100 mL), and extracted with
dichloromethane (100 mL $\times$ 2). The combined organic phases were washed with saturated
brine (100 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was
10 concentrated by rotary evaporation. The residue was purified by column chromatography
to obtain 065M_3 (5.35 g).

[0918] ^1H NMR (400 MHz, DMSO- d_6): δ 8.67 (s, 1H), 8.60 (d, J = 2.4 Hz, 1H), 8.44 (s, 1H).

[0919] Step 3: Synthesis of compound 065M_4

15 [0920] 065M_3 (5.35 g, 14.0 mmol) and ammonium chloride (3.74 g, 70.0 mmol) were
dissolved in ethanol (80 mL) and water (10 mL). The reaction mixture was heated to 75°C,
followed by portionwise addition of iron powder (2.34 g, 42.0 mmol). The resulting
mixture was stirred at 75°C for 1 hour. The reaction mixture was filtered through diatomite
while hot. The filtrate was concentrated by rotary evaporation to remove most of the
20 ethanol, followed by addition of ethyl acetate (300 mL). The resulting mixture was washed
with water (200 mL $\times$ 1) and saturated brine (200 mL $\times$ 1), dried over anhydrous sodium

sulfate, filtered, and the filtrate was concentrated by rotary evaporation to obtain 065M_4 (4.70 g) as a crude product, which was directly used in the next step without further purification.

[0921] MS (ESI) M/Z: 350.7, 352.7, 354.7 [M+H]⁺.

5 [0922] ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.32 (s, 1H), 7.00 (d, *J* = 1.6 Hz, 1H), 6.96 (d, *J* = 1.6 Hz, 1H), 5.96 (s, 2H).

[0923] Step 4: Synthesis of compound 065M_5

[0924] 065M_4 (4.70 g, 13.3 mmol) and cesium carbonate (13.0 g, 40.0 mmol) were dissolved in N,N-dimethylacetamide (60.0 mL). The reaction mixture was heated to 110°C and stirred for 16 hours. The reaction mixture was cooled to room temperature, quenched with water (200 mL), added with dilute hydrochloric acid (4 N) to adjust the pH to approximately neutral, and extracted with ethyl acetate (100 mL × 2). The combined organic phases were washed with brine (100 mL × 1), dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by triturating with ethyl acetate (10 mL) to obtain 065M_5 (3.60 g).

[0925] MS (ESI) M/Z: 270.7, 272.7 [M+H]⁺.

[0926] ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.90 (s, 1H), 8.17 (s, 1H), 7.69 (d, *J* = 1.2 Hz, 1H), 7.60 (s, 1H).

[0927] Step 5: Synthesis of compound 065M_6

20 [0928] 065M_5 (3.60 g, 13.3 mmol), 2-bromo-5-(difluoromethyl)-1,3,4-thiadiazole (4.28 g, 19.9 mmol), and cesium carbonate (6.48 g, 19.9 mmol) were dissolved in N,N-

dimethylformamide (40.0 mL). The reaction mixture was heated to 80°C and stirred for 16 hours. The reaction mixture was cooled to room temperature, quenched with water (80 mL), resulting in precipitation of a large amount of solid, followed by filtration. The filter cake was washed with water and dried under reduced pressure. The residue was triturated
5 with ethyl acetate (50 mL) at room temperature and filtered to obtain 065M_6 (3.50 g).

[0929] MS (ESI) M/Z: 405.1, 407.0 [M+H]⁺.

[0930] ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.73 (s, 1H), 8.50 (s, 1H), 8.03 (d, *J* = 1.2 Hz, 1H), 7.67 (t, *J* = 53.2 Hz, 1H).

[0931] Step 6: Synthesis of compound 065M_7

10 **[0932]** 065M_6 (3.30 g, 8.14 mmol), 4-*tert*-butylbenzyl mercaptan (2.20 g, 12.2 mmol), and N,N-diisopropylethylamine (3.15 g, 24.4 mmol) were dissolved in 1,4-dioxane (100 mL). The system was purged with nitrogen three times, followed by addition of Pd₂(dba)₃ (373 mg, 407 μmol) and Xantphos (471 mg, 814 μmol), and purged with nitrogen three additional times. The reaction mixture was heated to 90°C and stirred for 1 hour. 200 mg batches
15 were combined for work-up. The reaction mixture was cooled to room temperature and filtered through diatomite. The filtrate was concentrated by rotary evaporation. The crude product was purified by column chromatography to obtain 065M_7 (4.4 g).

[0933] MS (ESI) M/Z: 505.0 [M+H]⁺.

[0934] ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.47 (s, 1H), 8.43 (s, 1H), 7.66 (t, *J* = 53.2 Hz, 1H), 7.65 (d, *J* = 1.2 Hz, 1H), 7.34 - 7.33 (m, 4H), 4.37 (s, 2H), 1.23 (s, 9H).
20

[0935] Step 7: Synthesis of compound 065M_8

[0936] 065M_7 (400 mg, 792 μ mol) was dissolved in acetic acid (1 mL), water (1 mL), and acetonitrile (10 mL). The mixture was cooled to 0°C, and 1,3-dichloro-5,5-dimethylhydantoin (281 mg, 1.43 mmol) was added in portions. After the addition was completed, the reaction mixture was warmed to 20°C and stirred for 1 hour. The reaction mixture was quenched with water (50 mL) and extracted with dichloromethane (50 mL $\times$ 2). The combined organic phases were washed with brine (50 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure at room temperature to obtain 065M_8 (336 mg) as a crude product, which was directly used in the next step without further purification.

10 [0937] MS (ESI) M/Z: 404.9, 406.9 [M-Cl+OH-H]⁻.

[0938] Step 8: Synthesis of compound 065M_9

[0939] 1-Methylcyclopropanamine hydrochloride (170 mg, 1.58 mmol) and N,N-diisopropylethylamine (306 mg, 2.37 mmol) were dissolved in dichloromethane (10.0 mL). A solution of 065M_8 (336 mg, 790 μ mol) in dichloromethane (5 mL) was added dropwise to the reaction mixture. After the addition was completed, the reaction mixture was stirred at 20°C for 20 minutes. The reaction mixture was quenched with water (10 mL) and extracted with dichloromethane (10 mL $\times$ 2). The organic phase was washed with saturated brine (20 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by column chromatography to obtain 065M_9 (320 mg).

20 [0940] MS (ESI) M/Z: 460.2 [M+H]⁺.

[0941] ¹H NMR (400 MHz, DMSO-*d*₆): δ 9.02 (d, *J* = 1.2 Hz, 1H), 8.55 (s, 1H), 8.52 (s,

1H), 8.02 (d, $J = 1.2$ Hz, 1H), 7.69 (t, $J = 53.2$ Hz, 1H), 1.13 (s, 3H), 0.65 - 0.64 (m, 2H), 0.45 - 0.42 (m, 2H).

[0942] Step 9: Synthesis of compound 065M_10

[0943] 065M_9 (320 mg, 696 μ mol) and N,N-diisopropylethylamine (270 mg, 2.09 mmol) were dissolved in dichloromethane (8.00 mL). 2-(Trimethylsilyl)ethoxymethyl chloride (SEM-Cl) (139 mg, 835 μ mol) was added in one portion at 20°C. The reaction mixture was stirred at 20°C for 30 minutes. The reaction mixture was quenched with water (20 mL) and extracted with dichloromethane (20 mL $\times$ 2). The organic phase was washed with brine (30 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain 065M_10 (230 mg).

[0944] MS (ESI) M/Z: 471.9 [M+H-118]⁺.

[0945] ¹H NMR (400 MHz, DMSO-*d*₆): δ 9.07 (d, $J = 1.6$ Hz, 1H), 8.55 (s, 1H), 8.09 (s, 1H), 7.66 (t, $J = 53.2$ Hz, 1H), 4.91 (s, 2H), 3.55 (t, $J = 8.0$ Hz, 2H), 1.27 (s, 3H), 0.93 - 0.86 (m, 4H), 0.61 - 0.59 (m, 2H), -0.03 (s, 9H).

[0946] Step 10: Synthesis of compound 065M_11

[0947] 065M_10 (220 mg, 373 μ mol), *tert*-butyl (2S,6S)-2,6-dimethylpiperazine-1-carboxylate (240 mg, 1.12 mmol), and potassium carbonate (155 mg, 1.12 mmol) were dissolved in 1,4-dioxane (8 mL). The system was purged with nitrogen three times, followed by addition of RuPhos (69.6 mg, 149 μ mol) and RuPhos Pd G3 (125 mg, 149 μ mol), and purged with nitrogen three additional times. The reaction mixture was heated to 90°C

and stirred for 3 hours. The reaction mixture was cooled to room temperature and filtered through diatomite. The filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 065M_11 (130 mg) as a crude product.

[0948] MS (ESI) M/Z: 650.1 [M+H-118]⁺.

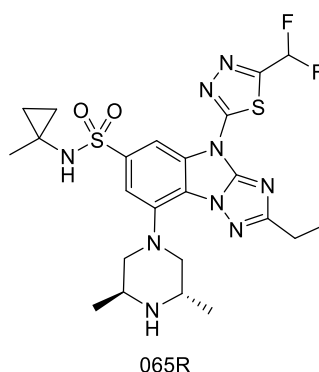
5 **[0949]** Step 11: Synthesis of compound 065M

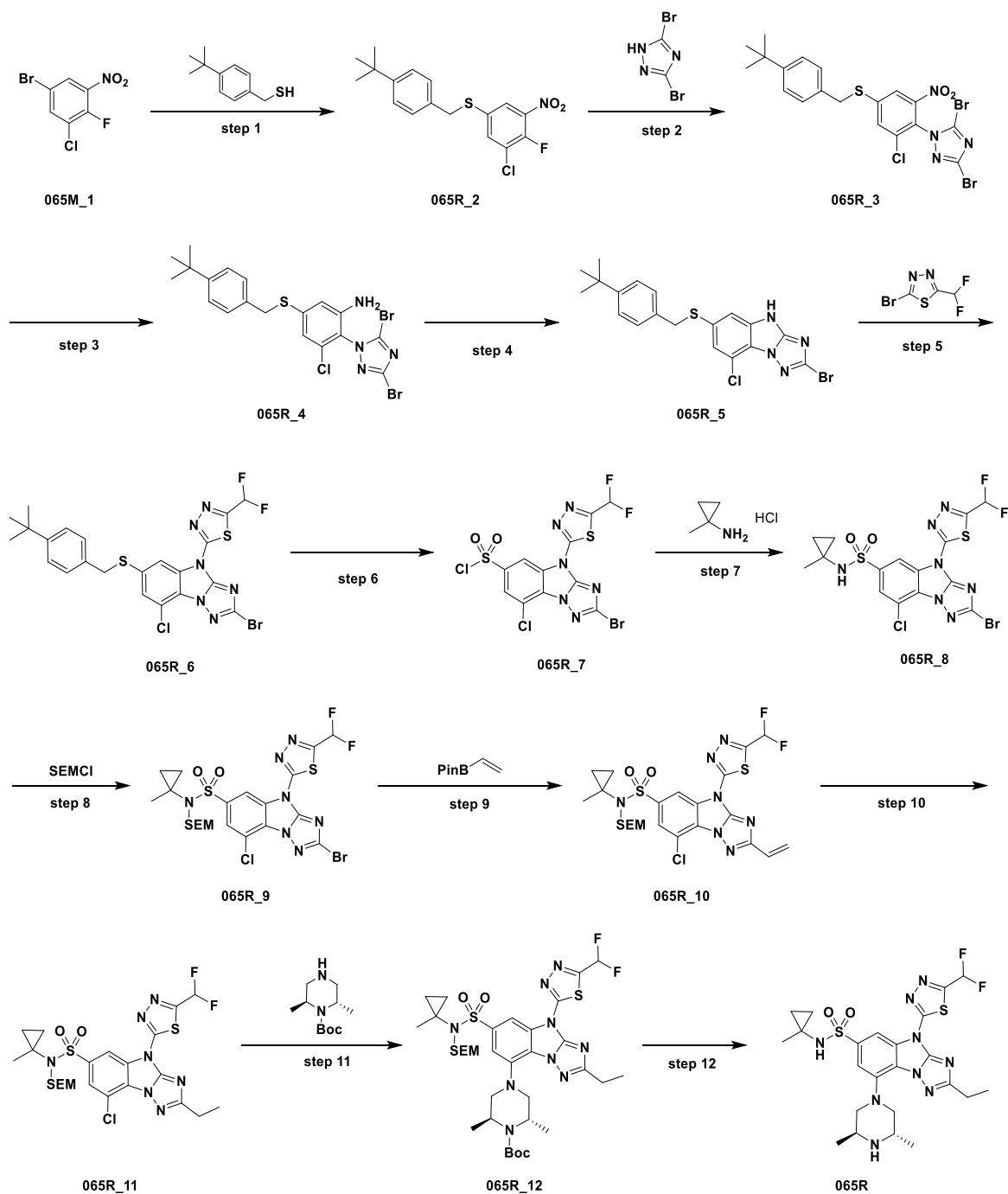
[0950] 065M_11 (130 mg, 169 μ mol) was dissolved in dichloromethane (3 mL), followed by dropwise addition of trifluoroacetic acid (0.5 mL). The reaction mixture was stirred at 20°C for 1 hour. After concentration at room temperature, the residue was purified by preparative chromatography to obtain 065M (34.27 mg).

10 **[0951]** MS (ESI) M/Z: 538.3 [M+H]⁺.

[0952] ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.72 (d, *J* = 1.2 Hz, 1H), 8.48 (s, 1H), 8.33 (s, 1H), 7.68 (t, *J* = 53.2 Hz, 1H), 7.47 (d, *J* = 1.2 Hz, 1H), 3.41 - 3.32 (m, 4H), 2.89 - 2.85 (m, 2H), 1.19 (d, *J* = 6.8 Hz, 6H), 1.09 (s, 3H), 0.67 - 0.64 (m, 2H), 0.42 - 0.39 (m, 2H).

[0953] Example 065R





[0954] Step 1: Synthesis of compound 065R_2

[0955] 065M_1 (5.00 g, 19.7 mmol), 4-*tert*-butylbenzyl mercaptan (3.54 g, 19.7 mmol), and N,N-diisopropylethylamine (5.08 g, 39.3 mmol) were dissolved in 1,4-dioxane (80 mL).

5 The system was purged with nitrogen three times, followed by addition of Pd₂(dba)₃ (900

mg, 983 μ mol) and Xantphos (1.14 g, 1.97 mmol), and purged with nitrogen three additional times. The reaction mixture was heated to 80°C and stirred for 1 hour. Three batches were combined for work-up. The reaction mixture was cooled to room temperature and filtered through diatomite. The filtrate was concentrated by rotary evaporation. The
 5 crude product was purified by column chromatography to obtain 065R_2 (13.0 g).

[0956] ^1H NMR (400 MHz, DMSO- d_6): δ 7.99 - 7.96 (m, 1H), 7.79 - 7.77 (m, 1H), 7.35 - 7.23 (m, 4H), 4.35 (s, 2H), 1.25 (s, 9H).

[0957] Step 2: Synthesis of compound 065R_3

[0958] 065R_2 (12.0 g, 33.9 mmol), 3,5-dibromo-1,2,4-triazole (9.23 g, 40.7 mmol), and
 10 potassium carbonate (7.03 g, 50.9 mmol) were dissolved in dimethyl sulfoxide (100 mL). The mixture was heated to 60°C and stirred for 1 hour. The reaction mixture was cooled to room temperature, then quenched with water (200 mL), and extracted with ethyl acetate (200 mL $\times$ 2). The combined organic phases were washed with brine (300 mL $\times$ 1), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was
 15 purified by column chromatography to obtain 065R_3 (11.0 g).

[0959] MS (ESI) M/Z: 560.8, 562.8 $[\text{M}+\text{H}]^+$.

[0960] ^1H NMR (400 MHz, CDCl_3): δ 7.92 (d, J = 2.0 Hz, 1H), 7.65 (d, J = 2.0 Hz, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 4.28 (s, 2H), 1.33 (s, 9H).

[0961] Step 3: Synthesis of compound 065R_4

[0962] 065R_3 (11.0 g, 19.6 mmol) and ammonium chloride (5.25 g, 98.1 mmol) were
 20 dissolved in ethanol (120 mL) and water (20 mL). The reaction mixture was heated to

70°C, followed by portionwise addition of iron powder (3.29 g, 58.9 mmol). The resulting mixture was stirred at 70°C for 1 hour. The reaction mixture was filtered through diatomite while hot. The filtrate was concentrated under reduced pressure to remove most of the ethanol. The resulting mixture was then diluted with water (100 mL) and extracted with ethyl acetate (100 mL × 2). The combined organic phases were washed with saturated brine (200 mL × 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation to obtain 065R_4 (9.30 g) as a crude product, which was directly used in the next step without further purification.

[0963] ¹H NMR (400 MHz, CDCl₃): δ 7.37 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 6.81 (d, *J* = 1.6 Hz, 1H), 6.62 (d, *J* = 1.6 Hz, 1H), 4.16 (s, 2H), 3.81 (s, 2H), 1.33 (s, 9H).

[0964] Step 4: Synthesis of compound 065R_5

[0965] 065R_4 (9.30 g, 17.5 mmol) and cesium carbonate (11.4 g, 35.0 mmol) were dissolved in N,N-dimethylacetamide (100 mL). The reaction mixture was heated to 110°C and stirred for 2 hours. The reaction mixture was cooled to room temperature, quenched with water (200 mL), added with dilute hydrochloric acid (4 M) to adjust the pH to 6, and extracted with ethyl acetate (200 mL × 2). The combined organic phases were washed with brine (300 mL), dried over anhydrous sodium sulfate, filtered, and concentrated to obtain 065R_5 (8.60 g) as a crude product, which was directly used in the next step without further purification.

[0966] MS (ESI) *M/Z*: 448.9, 450.9 [*M*+*H*]⁺.

[0967] ¹H NMR (400 MHz, DMSO-*d*₆): δ 7.44 (d, *J* = 0.8 Hz, 1H), 7.36 (s, 1H), 7.32 (d, *J*

= 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 4.31 (s, 2H), 1.24 (s, 9H).

[0968] Step 5: Synthesis of compound 065R_6

[0969] 065R_5 (8.60 g, 19.1 mmol) and cesium carbonate (9.34 g, 28.7 mmol) were dissolved in N,N-dimethylacetamide (100 mL), followed by addition of 2-bromo-5-(difluoromethyl)-1,3,4-thiadiazole (6.17 g, 28.7 mmol). The reaction mixture was heated to 80°C and stirred for 16 hours. The reaction mixture was cooled to room temperature, quenched with water (250 mL), resulting in precipitation of a large amount of solid, followed by filtration. The filter cake was washed with water and dried under reduced pressure. The residue was triturated with ethyl acetate/petroleum ether (1/1, 100 mL) at room temperature and filtered to obtain 065R_6 (7.40 g).

[0970] MS (ESI) M/Z : 583.2, 585.2 $[M+H]^+$.

[0971] ^1H NMR (400 MHz, DMSO- d_6): δ 8.43 (d, J = 1.2 Hz, 1H), 7.78 - 7.52 (m, 2H), 7.34 - 7.32 (m, 4H), 4.36 (s, 2H), 1.22 (s, 9H).

[0972] Step 6: Synthesis of compound 065R_7

[0973] 065R_6 (4.50 g, 7.71 mmol) was dissolved in acetic acid (1 mL), water (1 mL), and acetonitrile (40 mL). The mixture was cooled to 0°C, followed by portionwise addition of 1,3-dichloro-5,5-dimethylhydantoin (2.73 g, 13.8 mmol), and stirred at 20°C for 0.5 hours. The reaction mixture was quenched with H₂O (100 mL) and extracted with dichloromethane (100 mL $\times$ 2). The combined organic phases were washed with brine (200 mL $\times$ 1), dried over anhydrous sodium sulfate, and concentrated under reduced pressure at room temperature to obtain 065R_7 (4.20 g).

[0974] MS (ESI) M/Z: 482.8, 484.8 [M-Cl+OH-H]⁻.

[0975] Step 7: Synthesis of compound 065R_8

[0976] 1-Methylcyclopropanamine hydrochloride (1.79 g, 16.7 mmol) and N,N-diisopropylethylamine (4.31 g, 33.3 mmol) were dissolved in dichloromethane (50.0 mL).

5 A solution of 065R_7 (4.20 g, 8.33 mmol) in dichloromethane (5 mL) was added dropwise to the reaction mixture. After the addition was completed, the reaction mixture was stirred at 20°C for 20 minutes. The reaction mixture was quenched with water (80 mL) and extracted with dichloromethane (80 mL × 2). The combined organic phases were washed with saturated brine (100 mL × 1), dried, and concentrated under reduced pressure. The
10 residue was purified by column chromatography to obtain 065R_8 (4.00 g).

[0977] MS (ESI) M/Z: 537.9, 539.8 [M+H]⁺.

[0978] ¹H NMR (400 MHz, DMSO-*d*₆): δ 9.01 (s, 1H), 8.55 (s, 1H), 8.05 (d, *J* = 1.2 Hz, 1H), 7.68 (t, *J* = 53.2 Hz, 1H), 1.12 (s, 3H), 0.66 - 0.62 (m, 2H), 0.46 - 0.42 (m, 2H).

[0979] Step 8: Synthesis of compound 065R_9

15 [0980] 065R_8 (4.00 g, 7.42 mmol) and N,N-diisopropylethylamine (2.88 g, 22.2 mmol) were dissolved in dichloromethane (40.0 mL) and DMF (5 mL). 2-(Trimethylsilyl)ethoxymethyl chloride (1.86 g, 11.1 mmol) was added in one portion at 20°C. The reaction mixture was stirred at 20°C for 1 hour. The reaction mixture was quenched with water (100 mL) and extracted with dichloromethane (100 mL × 2). The combined
20 organic phases were washed with water (200 mL) and brine (100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was

purified by triturating with petroleum ether (100 mL), followed by purification by column chromatography to obtain 065R_9 (2.90 g).

[0981] MS (ESI) M/Z: 550.1, 552.1 [M+H-118]⁺.

[0982] ¹H NMR (400 MHz, DMSO-*d*₆): δ 9.07 (d, *J* = 1.2 Hz, 1H), 8.12 (d, *J* = 1.6 Hz, 1H), 7.66 (t, *J* = 53.2 Hz, 1H), 4.92 (s, 2H), 3.56 (t, *J* = 8.4 Hz, 2H), 1.28 (s, 3H), 0.93 - 0.86 (m, 4H), 0.62 - 0.59 (m, 2H), -0.01 (s, 9H)

[0983] Step 9: Synthesis of compound 065R_10

[0984] 065R_9 (0.80 g, 1.20 mmol), vinylboronic acid pinacol ester (920 mg, 5.98 mmol), and cesium carbonate (1.17 g, 3.59 mmol) were dissolved in 1,4-dioxane (10.0 mL) and water (2.00 mL), and the system was purged with nitrogen three times. Pd(dppf)Cl₂·CH₂Cl₂ (292 mg, 358 μmol) was added thereto under nitrogen atmosphere, and the system was purged with nitrogen three times. The reaction mixture was stirred at 80°C for 16 hours. The reaction mixture was cooled to room temperature, then filtered through diatomite, added with water (50.0 mL), and extracted with ethyl acetate (20 mL × 3). The combined organic phases were washed with brine (20 mL × 3), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain 065R_10 (0.30 g).

[0985] MS (ESI) M/Z: 516.1 [M+H-100]⁺.

[0986] ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.05 (d, *J* = 1.2 Hz, 1H), 8.08 (d, *J* = 1.6 Hz, 1H), 7.67 (t, *J* = 53.2 Hz, 1H), 6.93 - 6.86 (m, 1H), 6.43 - 6.38 (m, 1H), 5.80 - 5.77 (m, 1H),

4.91 (s, 2H), 3.57 - 3.53 (m, 2H), 1.29 (s, 3H), 0.92 - 0.87 (m, 4H), 0.62 - 0.59 (m, 2H), - 0.02 (s, 9H).

[0987] Step 10: Synthesis of compound 065R_11

[0988] Platinum dioxide (36.8 mg, 146 μmol) was added to methanol (10.0 mL), followed
 5 by addition of 065R_10 (200 mg, 325 μmol). The system was purged with hydrogen five times. The reaction mixture was stirred at 25°C for 0.5 hours. The reaction mixture was filtered through diatomite and concentrated under reduced pressure. The residue was purified by column chromatography to obtain 065R_11 (0.10 g).

[0989] MS (ESI) M/Z: 618.3, 620.2 $[\text{M}+\text{H}]^+$.

10 **[0990]** ^1H NMR (400 MHz, DMSO- d_6) δ 9.04 (d, J = 1.6 Hz, 1H), 8.06 (d, J = 1.6 Hz, 1H), 7.66 (t, J = 53.2 Hz, 1H), 4.91 (s, 2H), 3.57 - 3.52 (m, 2H), 2.94 - 2.88 (m, 2H), 1.36 (t, J = 7.6 Hz, 3H), 1.28 (s, 3H), 0.92 - 0.87 (m, 4H), 0.60 - 0.58 (m, 2H), -0.03 (s, 9H).

[0991] Step 11: Synthesis of compound 065R_12

[0992] 065R_11 (0.09 g, 145 μmol), *tert*-butyl (2S,6S)-2,6-dimethylpiperazine-1-carboxylate (93.6 mg, 436 μmol), and cesium carbonate (142 mg, 436 μmol) were dissolved
 15 in 1,4-dioxane (1.00 mL). RuPhos (13.5 mg, 29.1 μmol) and RuPhos Pd G3 (24.3 mg, 29.1 μmol) were added thereto under nitrogen atmosphere, and the system was purged with nitrogen three times. The reaction mixture was stirred at 90°C for 5 hours. The reaction mixture was cooled to room temperature, added with water (10.0 mL), and extracted with
 20 ethyl acetate (10 mL $\times$ 3). The combined organic phases were washed with brine (10 mL $\times$ 3), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure.

The residue was purified by column chromatography to obtain 065R_12 (50 mg).

[0993] MS (ESI) M/Z: 796.2 [M+H]⁺.

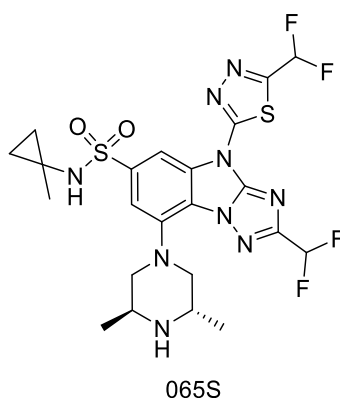
[0994] Step 4: Synthesis of compound 065R

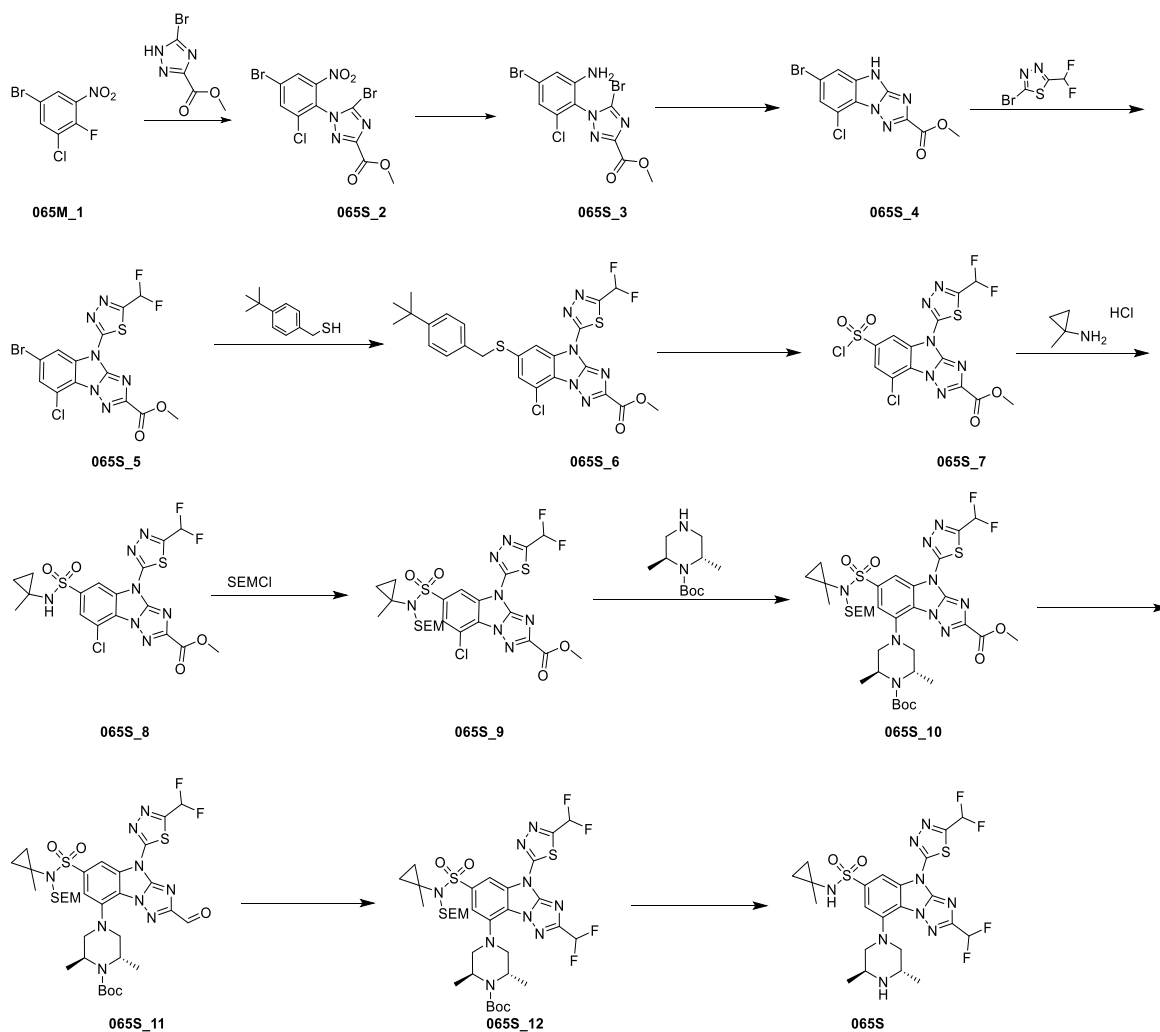
[0995] 065R_12 (50.0 mg, 62.8 μmol) was dissolved in dichloromethane (1.00 mL),
 5 followed by addition of trifluoroacetic acid (1 mL) at 25°C. The reaction mixture was
 stirred at 25°C for 1 hour. After concentration at room temperature, the residue was
 purified by preparative chromatography to obtain 065R (8.89 mg).

[0996] MS (ESI) M/Z: 566.3 [M+H]⁺.

[0997] ¹H NMR (400 MHz, DMSO-*d*₆+D₂O) δ 8.74 (s, 1H), 7.72 - 7.46 (m, 2H), 3.86 -
 10 3.81 (m, 2H), 3.52 - 3.49 (m, 2H), 3.26 - 3.22 (m, 2H), 2.89 (q, *J* = 7.6 Hz, 2H), 1.43 (d, *J*
 = 6.4 Hz, 6H), 1.35 (t, *J* = 7.6 Hz, 3H), 1.06 (s, 3H), 0.65 - 0.59 (m, 2H), 0.41 - 0.38 (m,
 2H).

[0998] Example 065S





[0999] Step 1: Synthesis of compound 065S_2

[1000] Compound 065M_1 (30.0 g, 0.118 mol) and methyl 5-bromo-1,2,4-triazole-3-carboxylate (26.7 g, 0.130 mol) were dissolved in dimethyl sulfoxide (400 mL), followed by addition of potassium carbonate (24.5 g, 0.177 mol). The reaction mixture was stirred at room temperature for 12 hours. The reaction mixture was extracted three times with dichloromethane. The organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, concentrated, and purified by silica gel column chromatography to obtain product 065S_2 (35.6 g).

[1001] MS (ESI) M/Z: 438.8 [M+H]⁺.

[1002] Step 2: Synthesis of compound 065S_3

[1003] 065S_2 (35.6 g, 81.1 mmol), iron powder (45.3 g, 0.811 mol), and acetic acid (500 mL) were added to a flask. The system was purged with nitrogen and stirred at room temperature for 2 hours. The reaction mixture was extracted three times with
5 dichloromethane. The organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, concentrated, and purified by silica gel column chromatography to obtain 065S_3 (29.0 g).

[1004] MS (ESI) M/Z: 408.8 [M+H]⁺.

[1005] Step 3: Synthesis of compound 065S_4

10 **[1006]** Compound 065S_3 (18 g, 43.85 mmol) was dissolved in N,N-dimethylacetamide (200 mL), followed by addition of cesium carbonate (28.57 g, 87.7 mmol). The reaction mixture was stirred at 100°C for 3 hours under nitrogen atmosphere. The reaction mixture was cooled to room temperature and directly used in the next step.

[1007] MS (ESI) M/Z: 329.0 [M+H]⁺.

15 **[1008]** Step 4: Synthesis of compound 065S_5

[1009] Cesium carbonate (14.83 g, 45.52 mmol) and 2-bromo-5-(difluoromethyl)-1,3,4-thiadiazole (7.34 g, 34.14 mmol) were added to the reaction mixture containing 065S_4 (7.5 g, 22.76 mmol) from the previous step. The system was purged with nitrogen. The reaction mixture was stirred at 100°C for 36 hours. The reaction mixture was cooled to
20 room temperature, added with dichloromethane (1000 mL), resulting in precipitation of a solid, followed by filtration to obtain a filter cake. The filtrate was extracted with

dichloromethane (1000 mL $\times$ 3) and saturated brine (500 mL $\times$ 1). The organic phase was dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 065S_5 (9.8 g).

5 **[1010]** MS (ESI) M/Z: 462.0 [M+H]⁺.

[1011] Step 3: Synthesis of compound 065S_6

[1012] 065S_5 (9.8 g, 21.57 mmol) was dissolved in 1,4-dioxane (100 mL), followed by addition of 4-*tert*-butylbenzyl mercaptan (3.89 g, 21.57 mmol), N,N-diisopropylethylamine (6.97 g, 53.92 mmol), Xantphos (0.75 g, 1.29 mmol), and Pd₂(dba)₃ (0.59 g, 0.65 mmol).

10 The system was thoroughly purged with nitrogen. The reaction mixture was stirred at 90°C for 4 hours under nitrogen atmosphere. The reaction mixture was cooled to room temperature, mixed with silica gel, and purified by column chromatography to obtain 065S_6 (10.6 g).

[1013] MS (ESI) M/Z: 563.0 [M+H]⁺.

15 **[1014]** Step 4: Synthesis of compound 065S_7

[1015] 065S_6 (10.6 g, 18.83 mmol) was dissolved in a mixture of acetonitrile/acetic acid/water (7/2/1, 100 mL), followed by portionwise addition of 1,3-dichloro-5,5-dimethylhydantoin (7.42 g, 37.66 mmol) in an ice bath. The reaction mixture was then stirred at room temperature for 3 hours under nitrogen atmosphere. The reaction mixture
20 was extracted with dichloromethane (1500 mL $\times$ 3) and saturated brine (1000 mL $\times$ 1). The organic phase was dried over anhydrous sodium sulfate, filtered, and the filtrate was

concentrated by rotary evaporation to obtain 065S_7 (9 g).

[1016] MS (ESI) M/Z: 482.9 [M+H]⁺.

[1017] Step 5: Synthesis of compound 065S_8

[1018] 065S_7 (9 g, 18.62 mmol) was dissolved in dichloromethane (100 mL), followed
5 by addition of 1-methylcyclopropanamine hydrochloride (6.01 g, 55.86 mmol) and triethylamine (5.65 g, 55.86 mmol) in an ice bath. The reaction mixture was then stirred in an ice bath for 2 hours under nitrogen atmosphere. The reaction mixture was directly mixed with silica gel without further work-up, and purified by column chromatography to obtain 065S_8 (8.3 g).

10 **[1019]** MS (ESI) M/Z: 518.0 [M+H]⁺.

[1020] Step 6: Synthesis of compound 065S_9

[1021] 065S_8 (9 g, 17.38 mmol) was dissolved in N,N-dimethylformamide (100 mL), followed by addition of cesium carbonate (16.99 g, 52.14 mmol) and 2-(trimethylsilyl)ethoxymethyl chloride (SEMCl) (14.49 g, 86.90 mmol) in an ice bath. The
15 reaction mixture was stirred at room temperature for 5 hours under nitrogen atmosphere. The reaction mixture was extracted with ethyl acetate (1000 mL × 3) and water (500 mL). The organic phase was then washed with saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 065S_9 (8.3 g).

20 **[1022]** MS (ESI) M/Z: 648.1 [M+H]⁺.

[1023] Step 7: Synthesis of compound 065S_10

[1024] 065S_9 (5 g, 7.71 mmol) was dissolved in 1,4-dioxane (100 mL), followed by addition of *tert*-butyl (2S,6S)-2,6-dimethylpiperazine-1-carboxylate (3.30 g, 15.42 mmol), cesium carbonate (7.54 g, 23.13 mmol), RuPhos (0.72 g, 1.54 mmol), and RuPhos Pd G3 (0.64 g, 0.77 mmol). The reaction mixture was stirred at 90°C for 3 hours under nitrogen atmosphere. The reaction mixture was cooled to room temperature, and extracted with ethyl acetate (300 mL × 3) and water (500 mL). The organic phase was then washed with saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 065S_10 (3.16 g).

10 [1025] MS (ESI) M/Z: 608.2 [M-118-100+H]⁺.

[1026] Step 8: Synthesis of compound 065S_11

[1027] 065S_10 (1.6 g, 1.94 mmol) was dissolved in dichloromethane (20 mL). The mixture was then cooled to -78°C in a dry ice-ethanol bath, and diisobutylaluminum hydride (0.83 g, 5.82 mmol, 1 mol/L) was slowly added dropwise thereto. The reaction mixture was stirred at -78°C for 2 hours under nitrogen atmosphere. The reaction mixture was slowly quenched with methanol (10 mL) at -78°C and filtered through diatomite. The filter cake was washed with dichloromethane (100 mL × 3). The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography to obtain 065S_11 (1.1 g).

20 [1028] MS (ESI) M/Z: 578.2 [M-118-100+H]⁺.

[1029] Step 9: Synthesis of compound 065S_12

[1030] 065S_11 (1.1 g, 1.38 mmol) was dissolved in dichloromethane (30 mL). The mixture was then cooled to -78°C in a dry ice-ethanol bath, and bis(2-methoxyethyl)aminosulfur trifluoride (1.53 g, 6.90 mmol, 1 mol/L) was slowly added dropwise thereto. The reaction mixture was stirred at room temperature for 3 hours under
5 nitrogen atmosphere. The reaction mixture was slowly quenched with saturated sodium bicarbonate solution (10 mL) in an ice bath, and extracted with dichloromethane (100 mL × 3) and water (100 mL). The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography to obtain 065S_12 (0.79 g).

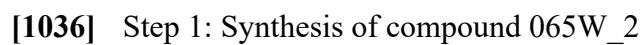
[1031] MS (ESI) M/Z: 700.2 [M-118+H]⁺.

10 [1032] Step 10: Synthesis of compound 065S

[1033] 065S_12 (1 g, 1.22 mmol) was dissolved in dichloromethane (20 mL), followed by addition of trifluoroacetic acid (2 mL) and water (0.5 mL). The reaction mixture was stirred at room temperature for 2 hours under nitrogen atmosphere. The reaction mixture was concentrated under reduced pressure to remove the solvent. The residue was purified
15 by preparative chromatography to obtain 065S (0.33 g).

[1034] MS (ESI) M/Z: 588.2 [M+H]⁺.

[1035] Example 065W



[1037] 065W_1 (5 g, 32.88 mmol) and water (50 mL) were added to a 500 mL single-necked flask, stirred thoroughly, followed by addition of sulfuric acid (2.8 mL, 52.52 mmol). The mixture was then cooled to 0°C, and a solution of sodium nitrite (3.4 g, 49.32 mmol) in water (20 mL) was added dropwise thereto. After the addition was completed, the reaction mixture was stirred for 1 hour, resulting in precipitation of a white solid. Copper(I) bromide (1.41 g, 9.86 mmol) was added thereto at 0°C, followed by dropwise addition of a 48% hydrobromic acid aqueous solution (7.44 mL). The reaction mixture was stirred at room temperature for 3 hours. The reaction mixture was poured into saturated sodium bicarbonate solution and extracted with ethyl acetate (200 mL × 5). The organic phases were combined, washed with saturated brine (100 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain 065W_2 (7.3 g) as a crude product, which was directly used in the next step without further purification.

[1038] MS (ESI) M/Z: 216.0, 218.0 [M+H]⁺.

[1039] Step 2: Synthesis of compound 065W_3

[1040] The crude product 065W_2 from the previous step was dissolved in dimethyl sulfoxide (50 mL), stirred thoroughly, followed by addition of 065M_1 (8.37 g, 32.88 mmol) and potassium carbonate (5 g, 98.64 mmol). The reaction mixture was stirred at 70°C for 9 hours. The reaction mixture was cooled to room temperature, quenched with water (200 mL), and extracted with ethyl acetate (200 mL × 3). The organic phases were combined, washed with saturated brine (100 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain a crude product, which was purified by flash

silica gel column chromatography to obtain 065W_3 (6.60 g).

[1041] MS (ESI) M/Z: 448.8, 450.8, 452.8 $[M+H]^+$.

[1042] Step 3: Synthesis of compound 065W_4

[1043] 065W_3 (17 g, 37.75 mmol) and acetic acid (50 mL) were added to a 500 mL single-necked flask, stirred thoroughly, followed by addition of iron powder (21.08 g, 377.5 mmol).

The reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was filtered through diatomite and washed with ethyl acetate (200 mL). The filtrate was concentrated under reduced pressure to obtain a crude product. The residue was purified by flash silica gel column chromatography to obtain 065W_4 (15 g).

[1044] MS (ESI) M/Z: 418.8, 420.8, 422.8 $[M+H]^+$.

[1045] Step 4: Synthesis of compound 065W_5

[1046] 065W_4 (380 mg, 0.9 mmol) and N,N-dimethylacetamide (5 mL) were added to a 100 mL single-necked flask, stirred thoroughly, followed by addition of cesium carbonate (0.59 g, 1.8 mmol). The reaction mixture was stirred at 100°C for 3 hours. After completion of the reaction, 2-bromo-5-(difluoromethyl)-1,3,4-thiadiazole (0.39 g, 1.8 mmol) and cesium carbonate (0.59 g, 1.8 mmol) were added thereto. The reaction mixture was stirred at 100°C for another 16 hours. The reaction mixture was cooled to room temperature, quenched with water (50 mL), and extracted with ethyl acetate (50 mL $\times$ 3). The organic phases were combined, washed with saturated brine (50 mL $\times$ 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain a crude product, which was purified by flash silica gel column chromatography to obtain 065W_5 (260 mg).

[1047] MS (ESI) M/Z: 472.8, 474.8 [M+H]⁺.

[1048] Step 5: Synthesis of compound 065W_6

[1049] 065W_5 (3 g, 6.33 mmol), Pd₂(dba)₃ (580 mg, 0.63 mmol), Xantphos (732 mg), and 1,4-dioxane (60 mL) were added to a 100 mL single-necked flask. After thorough stirring, the mixture was placed under nitrogen atmosphere. 4-*tert*-Butylbenzyl mercaptan (1.48 g, 8.23 mmol) and N,N-diisopropylethylamine (2.62 mL, 15.82 mmol) were added thereto. The reaction mixture was stirred at 90°C for 1 hour. The reaction mixture was filtered through diatomite and washed with ethyl acetate (100 mL). The filtrate was concentrated under reduced pressure to obtain a crude product. The residue was purified by flash silica gel column chromatography to obtain 065W_6 (3 g).

[1050] MS (ESI) M/Z: 573.0 [M+H]⁺.

[1051] Step 6: Synthesis of compound 065W_7

[1052] 065W_6 (340 mg, 0.59 mmol) and acetonitrile (5 mL) were added to a 50 mL single-necked flask. After thorough stirring, the mixture was cooled to 0°C. Acetic acid (300 µL) and water (600 µL) were added thereto, followed by portionwise addition of 1,3-dichloro-5,5-dimethylhydantoin (230 mg, 1.18 mmol). The reaction mixture was stirred for 1 hour. After completion of the reaction, the reaction mixture was concentrated under reduced pressure to remove most of the solvent, and extracted with ethyl acetate (30 mL × 3). The organic phases were combined, washed with saturated brine (30 mL × 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain a crude product. The crude product was dissolved in dichloromethane (5 mL) and cooled to 0°C,

followed by addition of 1-methylcyclopropanamine hydrochloride (190 mg, 1.77 mmol) and triethylamine (330 μ L, 2.36 mmol). After stirring for 1 hour, the solvent was removed under reduced pressure. The residue was purified by flash silica gel column chromatography to obtain 065W_7 (200 mg).

5 [1053] MS (ESI) M/Z: 528.0 $[M+H]^+$.

[1054] Step 7: Synthesis of compound 065W_8

[1055] 065W_7 (200 mg, 0.38 mmol) and N,N-dimethylacetamide (5 mL) were added to a 50 mL single-necked flask. After thorough stirring, the mixture was cooled to 0°C. Cesium carbonate (389 mg, 1.14 mmol) was added thereto, followed by dropwise addition
10 of 2-(trimethylsilyl)ethoxymethyl chloride (200 μ L). The reaction mixture was warmed to room temperature and stirred for 12 hours. The reaction mixture was quenched with water (20 mL) and extracted with ethyl acetate (30 mL $\times$ 3). The organic phases were combined, washed with saturated brine (30 mL $\times$ 2), dried over anhydrous sodium sulfate, and concentrated under reduced pressure to obtain a crude product. The residue was purified
15 by flash silica gel column chromatography to obtain 065W_8 (190 mg).

[1056] Step 8: Synthesis of compound 065W_9

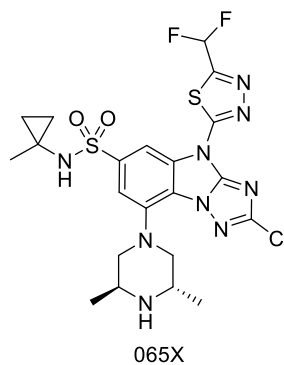
[1057] 065W_8 (190 mg, 0.29 mmol), cesium carbonate (280 mg, 0.87 mmol), RuPhos Pd G3 (24 mg, 0.029 mmol), and RuPhos (20 mg, 0.043 mmol) were added to a 50 mL single-necked flask, followed by addition of 1,4-dioxane (5 mL). After thorough stirring, the
20 mixture was placed under nitrogen atmosphere. *tert*-Butyl (2S,6S)-2,6-dimethylpiperazine-1-carboxylate (87 mg, 0.41 mmol) was then added thereto. The

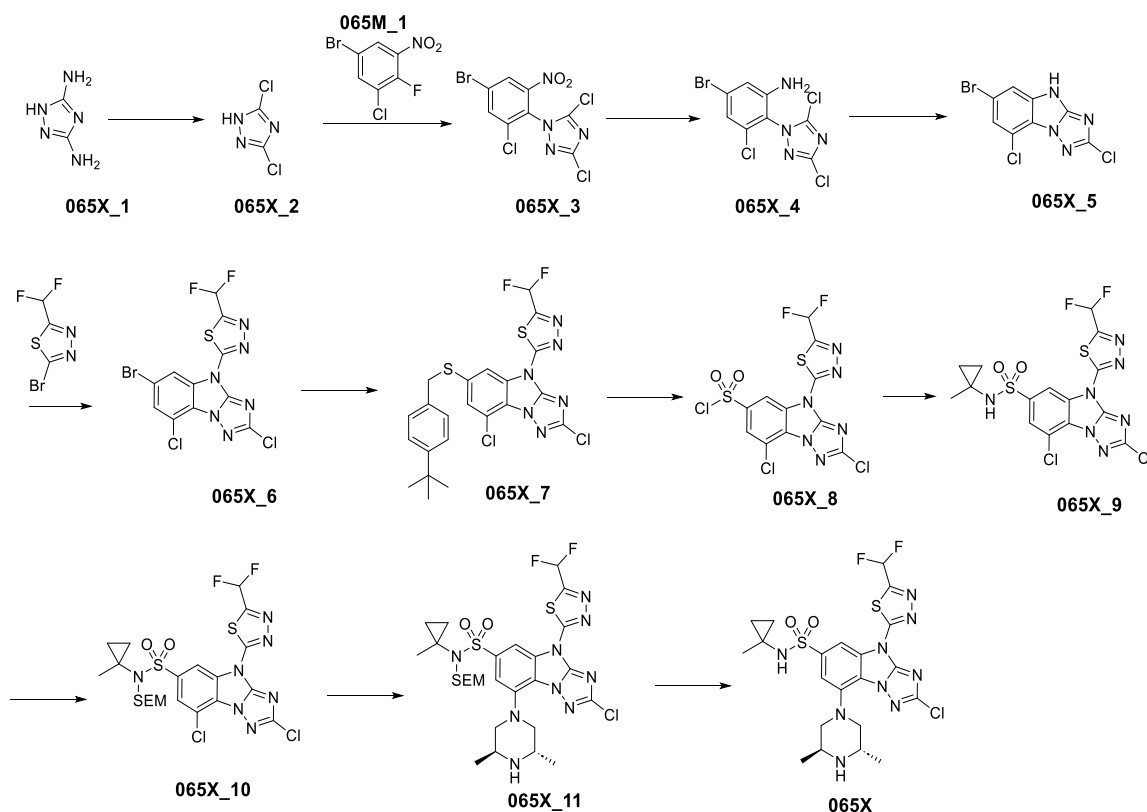
reaction mixture was heated to 90°C and stirred for 3 hours. The reaction mixture was cooled to room temperature, filtered, and concentrated under reduced pressure to obtain a crude product. The residue was purified by flash silica gel column chromatography to obtain 065W_9 (100 mg).

5 **[1058]** Step 11: Synthesis of compound 065W

[1059] 065W_9 (100 mg, 0.12 mmol) and dichloromethane (3 mL) were added to a 50 mL single-necked flask, stirred thoroughly, followed by addition of trifluoroacetic acid (1 mL) and water (0.2 mL). The reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure to obtain a crude product, which
10 was purified by preparative chromatography to obtain 065W (41 mg).

[1060] Example 065X





[1061] Step 1: Synthesis of compound 065X_2

[1062] 065X_1 (12.6 g, 0.127 mol) and hydrochloric acid (100 mL) were added to a two-necked flask. Sodium nitrite (26.4 g, 0.383 mol) was slowly added thereto in an ice bath.

5 After the addition was completed, the reaction mixture was gradually warmed to room temperature and stirred for 60 minutes. The reaction mixture was extracted three times with ethyl acetate. The organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and concentrated to obtain 065X_2 (11.2 g).

[1063] Step 2: Synthesis of compound 065X_3

10 **[1064]** 065X_2 (4.2 g, 30.6 mmol), 5-bromo-1-chloro-2-fluoro-3-nitrobenzene (065M_1, 5.2 g, 20.4 mmol), potassium carbonate (5.6 g, 40.8 mmol), and dimethyl sulfoxide (50 mL) were sequentially added to a round-bottomed flask. The mixture was stirred at room

temperature for 12 hours. The reaction mixture was extracted three times with ethyl acetate. The organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and concentrated to obtain 065X_3, which was directly used in the next step.

[1065] Step 3: Synthesis of compound 065X_4

5 **[1066]** Acetic acid (100 mL) was added to 065X_3 from the previous step, followed by addition of iron powder (11.4 g, 0.204 mol). The system was purged with nitrogen and stirred at room temperature for 2 hours. The reaction mixture was extracted three times with ethyl acetate. The organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, concentrated, and purified by silica gel column chromatography
10 to obtain 065X_4 (5.0 g).

[1067] MS (ESI) M/Z: 340.8 [M+H]⁺.

[1068] Step 4: Synthesis of compound 065X_5

[1069] 065X_4 (3.7 g, 10.8 mmol), cesium carbonate (7.0 g, 21.5 mmol), and N,N-dimethylacetamide (50 mL) were sequentially added to a round-bottomed flask. The
15 mixture was stirred in an oil bath at 100°C for 3 hours. The reaction mixture was cooled to room temperature and directly used in the next step.

[1070] MS (ESI) M/Z: 305.0 [M+H]⁺.

[1071] Step 5: Synthesis of compound 065X_6

[1072] Cesium carbonate (3.5 g, 10.7 mmol) and 2-bromo-5-(difluoromethyl)-1,3,4-thiadiazole (4.6 g, 21.5 mmol) were added to the reaction mixture containing 065X_5 from
20 the previous step. The reaction mixture was stirred in an oil bath at 100°C for 8 hours.

The reaction mixture was extracted three times with a large amount of dichloromethane. The organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, and concentrated to obtain a dark brown solid, which was triturated with ethyl acetate and petroleum ether to obtain 065X_6 (4.2 g).

5 [1073] MS (ESI) M/Z: 438.8 [M+H]⁺.

[1074] Step 6: Synthesis of compound 065X_7

[1075] 065X_6 (0.290 g, 0.66 mmol) was dissolved in 1,4-dioxane (10 mL), followed by addition of 4-*tert*-butylbenzyl mercaptan (0.119 g, 0.66 mmol), N,N-diisopropylethylamine (0.256 g, 1.98 mmol), Xantphos (38.2 mg, 66.0 μmol), and Pd₂(dba)₃ (30.2 mg, 33.0 μmol).

10 The system was thoroughly purged with nitrogen. The reaction mixture was stirred at 90°C for 3 hours under nitrogen atmosphere. The reaction mixture was concentrated and purified by silica gel column chromatography to obtain 065X_7 (0.259 g).

[1076] MS (ESI) M/Z: 539.0 [M+H]⁺.

[1077] Step 7: Synthesis of compound 065X_8

15 [1078] 065X_7 (0.259 g, 0.481 mmol) was dissolved in a mixture of acetonitrile/acetic acid/water (7/2/1, 10 mL), followed by portionwise addition of 1,3-dichloro-5,5-dimethylhydantoin (0.189 g, 0.962 mmol) in an ice bath. The reaction mixture was stirred in an ice bath for 3 hours. The reaction mixture was extracted three times with dichloromethane. The organic phase was washed with saturated brine, dried over
20 anhydrous sodium sulfate, and concentrated to obtain 065X_8, which was directly used in the next step without purification.

[1079] Step 8: Synthesis of compound 065X_9

[1080] The crude product 065X_8 from the previous step was dissolved in dichloromethane (20 mL), followed by addition of 1-methylcyclopropanamine hydrochloride (0.259 g, 2.41 mmol) and triethylamine (0.244 g, 2.41 mmol) in an ice bath.

5 The reaction mixture was then stirred in an ice bath for 2 hours under nitrogen atmosphere. The reaction mixture was extracted three times with dichloromethane. The organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, concentrated, and purified by silica gel column chromatography to obtain 065X_9 (0.130 g).

[1081] MS (ESI) M/Z: 494.0 [M+H]⁺.

10 **[1082]** Step 9: Synthesis of compound 065X_10

[1083] 065X_9 (0.130 g, 0.252 mmol) was dissolved in N,N-dimethylformamide (10 mL), followed by addition of cesium carbonate (0.165 g, 0.505 mmol). 2-(Trimethylsilyl)ethoxymethyl chloride (84.2 mg, 0.505 mmol) was added dropwise thereto in an ice bath. After the addition was completed, the reaction mixture was gradually
15 warmed to room temperature and stirred for 5 hours. The reaction mixture was extracted three times with ethyl acetate. The organic phase was sequentially washed with water and saturated brine, dried over anhydrous sodium sulfate, concentrated, and purified by silica gel column chromatography to obtain 065X_10 (90 mg).

[1084] MS (ESI) M/Z: 506.0 [M+H-118]⁺.

20 **[1085]** Step 10: Synthesis of compound 065X_11

[1086] 065X_10 (90.0 mg, 0.140 mmol), RuPhos Pd G3 (11.7 mg, 14.0 μmol), RuPhos

(13.1 mg, 28.0 μ mol), cesium carbonate (91.2 mg, 0.280 mmol), *tert*-butyl (2S,6S)-2,6-dimethylpiperazine-1-carboxylate (60.0 mg, 0.280 mmol), and 1,4-dioxane (10 mL) were sequentially added to a round-bottomed flask. The reaction mixture was stirred in an oil bath at 90°C for 3 hours. The reaction mixture was extracted three times with ethyl acetate.

5 The organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, concentrated, and purified by silica gel column chromatography to obtain 065X_11 (30.0 mg).

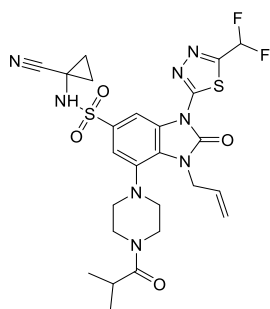
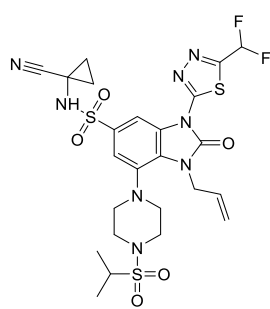
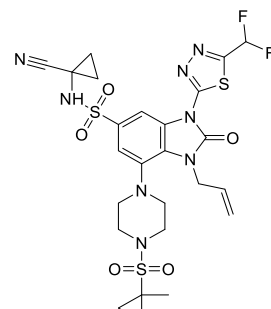
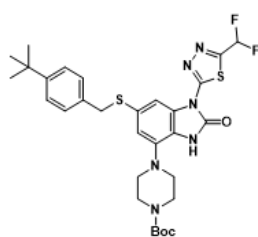
[1087] Step 11: Synthesis of compound 065X

[1088] 065X_11 (30.0 mg, 42.7 μ mol) and dichloromethane (5.0 mL) were added to a
10 reaction flask, followed by addition of trifluoroacetic acid (2.0 mL) in an ice bath. After the addition was completed, the reaction mixture was warmed to room temperature and stirred for 8 hours. The reaction mixture was extracted three times with dichloromethane. The organic phase was washed with saturated brine, dried over anhydrous sodium sulfate, concentrated, and purified by preparative chromatography to obtain compound 065X (10
15 mg).

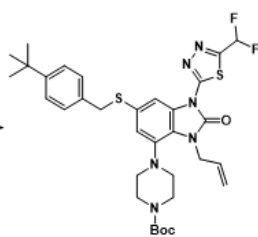
[1089] ^1H NMR (400 MHz, DMSO- d_6 +D $_2$ O) δ 8.72 (d, J = 1.4 Hz, 1H), 7.65 (t, J = 53.1 Hz, 1H), 7.50 (d, J = 1.6 Hz, 1H), 3.42 - 3.38 (m, 2H), 3.28 (dd, J = 11.1, 3.2 Hz, 2H), 2.93 (dd, J = 11.1, 6.0 Hz, 2H), 1.22 (d, J = 6.5 Hz, 6H), 1.09 (s, 3H), 0.67 - 0.65 (m, 2H), 0.56 - 0.31 (m, 2H).

20 **[1090]** MS (ESI) M/Z : 572.0 $[\text{M}+\text{H}]^+$.

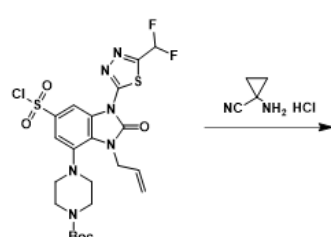
[1091] Examples 067C, 067D, and 074B

**067C****067D****074B**

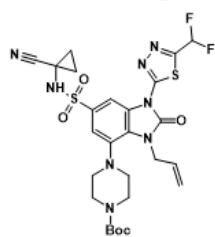
A001_6



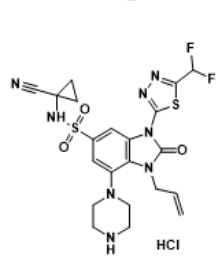
067_1



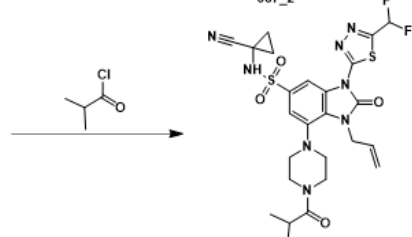
067_2



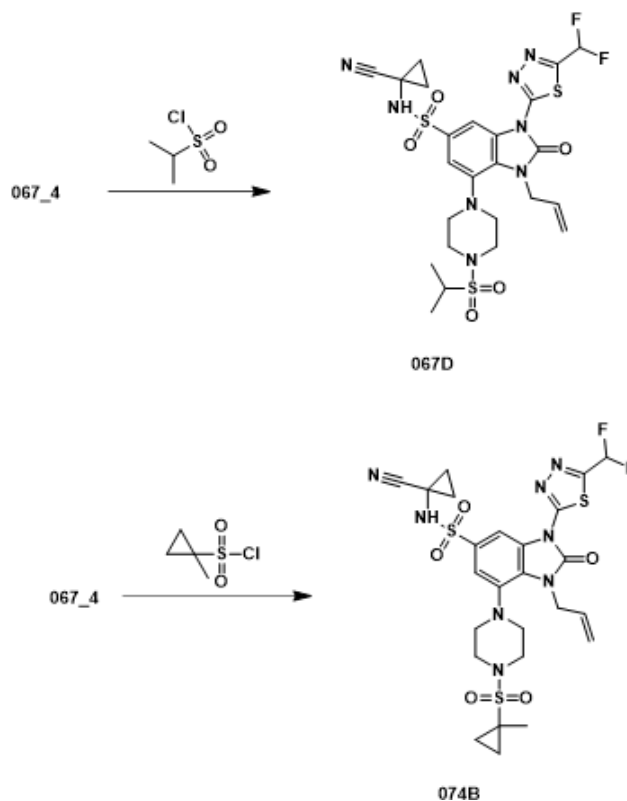
067_3



067_4



067C



[1092] Step 1: Synthesis of compound 067_1

[1093] A001_6 (15.0 g, 23.7 mmol) and potassium carbonate (9.86 g, 71.3 mmol) were dissolved in N,N-dimethylformamide (150 mL), followed by addition of 3-bromopropene (5.75 g, 47.5 mmol) at room temperature. The reaction mixture was heated to 50°C and stirred for 12 hours. The reaction mixture was cooled to room temperature, then quenched with water (500 mL), and extracted with ethyl acetate (200 mL × 3). The combined organic phases were washed with brine (200 mL × 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 067_1 (13.0 g).

[1094] MS (ESI) M/Z: 671.4 [M+H]⁺.

[1095] ^1H NMR (400 MHz, DMSO- d_6) δ 8.28 (d, J = 1.6 Hz, 1H), 7.62 (t, J = 52.8 Hz, 1H), 7.29 - 7.27 (m, 2H), 7.22 - 7.20 (m, 2H), 7.02 (d, J = 1.6 Hz, 1H), 6.05 - 5.97 (m, 1H), 5.11 (d, J = 10.4 Hz, 1H), 5.00 (d, J = 17.2 Hz, 1H), 4.83 - 4.82 (m, 2H), 4.17 (s, 2H), 3.97 - 3.85 (m, 2H), 3.08 - 2.96 (m, 2H), 2.86 - 2.77 (m, 2H), 2.66 - 2.59 (m, 2H), 1.43 (s, 9H),
 5 1.23 (s, 9H).

[1096] Step 3: Synthesis of compound 067_2

[1097] 067_1 (3.00 g, 4.47 mmol) was dissolved in a mixed solvent of acetonitrile (21 mL), acetic acid (3 mL), and water (6 mL), followed by addition of 1,3-dichloro-5,5-dimethylhydantoin (1.76 g, 8.94 mmol) at 0°C. The reaction mixture was slowly warmed
 10 to 25°C and stirred for 2 hours. Four parallel batches were performed and combined for work-up. The reaction mixture was quenched at 0°C with water (100 mL), and extracted with dichloromethane (100 mL $\times$ 3). The combined organic phases were washed with brine (100 mL $\times$ 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation at low temperature to obtain 067_2 (10.0 g) as a crude product, which
 15 was directly used in the next step without purification.

[1098] MS (ESI) M/Z : 571.1 $[\text{M}-\text{Cl}+\text{OH}-\text{H}]^-$.

[1099] Step 4: Synthesis of compound 067_3

[1100] 1-Aminocyclopropanecarbonitrile hydrochloride (4.01 g, 33.8 mmol) was dissolved in pyridine (20 mL), followed by dropwise addition of a solution of 067_2 (5.00 g, 8.46
 20 mmol) in dichloromethane (10 mL). The reaction mixture was stirred at 25°C for 1 hour. Two parallel batches were performed and combined for work-up. The reaction mixture was

quenched with water (100 mL) and extracted with dichloromethane (100 mL $\times$ 3). The combined organic phases were washed with brine (100 mL $\times$ 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 067_3 (4.00 g).

5 **[1101]** MS (ESI) M/Z: 637.1 [M+H]⁺.

[1102] ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.21 (s, 1H), 8.76 (d, *J* = 1.6 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.10 - 6.01 (m, 1H), 5.12 (d, *J* = 10.4 Hz, 1H), 5.03 (d, *J* = 17.6 Hz, 1H), 4.94 - 4.91 (m, 2H), 3.99 - 3.93 (m, 1H), 3.08 - 2.96 (m, 3H), 2.90 - 2.88 (m, 2H), 2.83 - 2.78 (m, 2H), 1.45 - 1.41 (m, 11H), 1.30 - 1.27 (m, 2H).

10 **[1103]** Step 5: Synthesis of compound 067_4

[1104] 067_3 (4.00 g, 6.28 mmol) was dissolved in ethyl acetate (20 mL), followed by addition of hydrochloric acid/ethyl acetate (4 M, 20.0 mL). The reaction mixture was stirred at 25°C for 0.5 hours. The reaction mixture was directly concentrated under reduced pressure. The crude product was triturated with methyl *tert*-butyl ether (30 mL) at room temperature and filtered to obtain 067_4 (3.3 g).

15 **[1105]** MS (ESI) M/Z: 537.4 [M+H]⁺.

[1106] ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.36 (s, 1H), 9.26 (s, 2H), 8.80 (d, *J* = 1.6 Hz, 1H), 7.78 - 7.52 (m, 2H), 6.13 - 6.04 (m, 1H), 5.13 (d, *J* = 11.6 Hz, 1H), 5.03 (d, *J* = 17.6 Hz, 1H), 4.91 - 4.86 (m, 2H), 3.43 - 3.34 (m, 2H), 3.24 - 3.10 (m, 6H), 1.44 - 1.41 (m, 2H), 1.32 - 1.26 (m, 2H).

20 **[1107]** Step 6: Synthesis of compound 074B

[1108] 067_4 (0.15 g, 261 μ mol) was dissolved in N,N-dimethylformamide (4 mL), followed by addition of triethylamine (106 mg, 1.05 mmol) and 1-methylcyclopropane-1-sulfonyl chloride (44.5 mg, 287 μ mol). The reaction mixture was stirred at 25°C for 1 hour.

After concentration, the residue was purified by preparative chromatography to obtain 074B

5 (53.73 mg).

[1109] MS (ESI) M/Z: 655.1 $[M+H]^+$.

[1110] ^1H NMR (400 MHz, DMSO- d_6) δ 9.21 (s, 1H), 8.78 (d, J = 1.6 Hz, 1H), 7.80 - 7.51 (m, 2H), 6.12 - 6.02 (m, 1H), 5.14 (d, J = 10.8 Hz, 1H), 5.03 (d, J = 17.6 Hz, 1H), 4.94 - 4.90 (m, 2H), 3.74 - 3.71 (m, 2H), 3.24 - 3.14 (m, 2H), 3.09 - 3.07 (m, 2H), 2.96 - 2.90 (m, 2H), 1.47 (s, 3H), 1.45 - 1.41 (m, 2H), 1.31 - 1.28 (m, 2H), 1.22 - 1.19 (m, 2H), 0.90 - 0.88 (m, 2H).

[1111] Step 7: Synthesis of compound 067C

[1112] 067_4 (0.28 g, 0.48 mmol) and triethylamine (158 mg, 1.56 mmol) were dissolved in N,N-dimethylformamide (2.00 mL), followed by addition of isobutyryl chloride (45.8 mg, 429 μ mol). The reaction mixture was stirred at 25°C for 1 hour. The reaction mixture was quenched with water (0.3 mL). The residue was purified by preparative chromatography to obtain 067C (70 mg).

[1113] MS (ESI) M/Z: 607.2 $[M+H]^+$.

[1114] ^1H NMR (400 MHz, DMSO- d_6) δ 8.75 (d, J = 1.6 Hz, 1H), 8.39 (s, 1H), 7.78 - 7.51 (m, 2H), 6.11 - 6.04 (m, 1H), 5.13 (d, J = 10.4 Hz, 1H), 5.04 (d, J = 17.2 Hz, 1H), 4.96 - 4.94 (m, 2H), 4.49 - 4.46 (m, 1H), 4.08 - 4.04 (m, 1H), 3.39 - 3.36 (m, 1H), 3.06 - 3.03 (m,

2H), 2.96 - 2.93 (m, 1H), 2.89 - 2.83 (m, 3H), 1.44 - 1.41 (m, 2H), 1.28 - 1.25 (m, 2H), 1.05 - 1.02 (m, 6H).

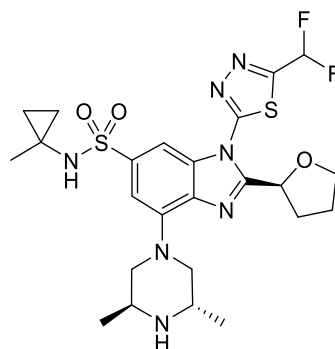
[1115] Step 8: Synthesis of compound 067D

[1116] 067_4 (2.00 g, 3.49 mmol) was dissolved in a mixed solvent of tetrahydrofuran (20 mL) and water (5 mL), followed by addition of sodium carbonate (1.11 g, 10.5 mmol) and isopropylsulfonyl chloride (995 mg, 6.98 mmol). The reaction mixture was stirred at 20°C for 1 hour. One 800 mg batch was combined for a single work-up. The reaction mixture was diluted with water (30 mL) and extracted with ethyl acetate (30 mL × 3). The combined organic phases were washed with brine (50 mL × 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The crude product was purified by column chromatography to obtain 067D (942.64 mg).

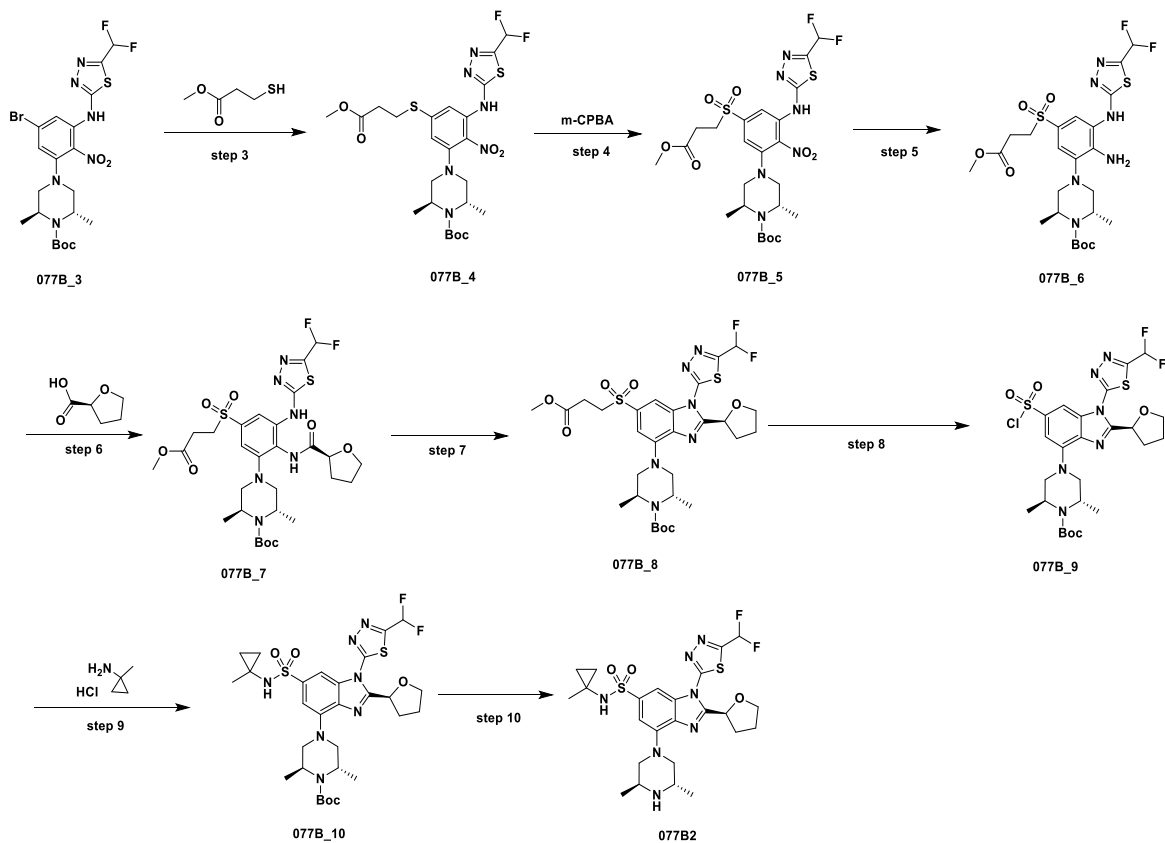
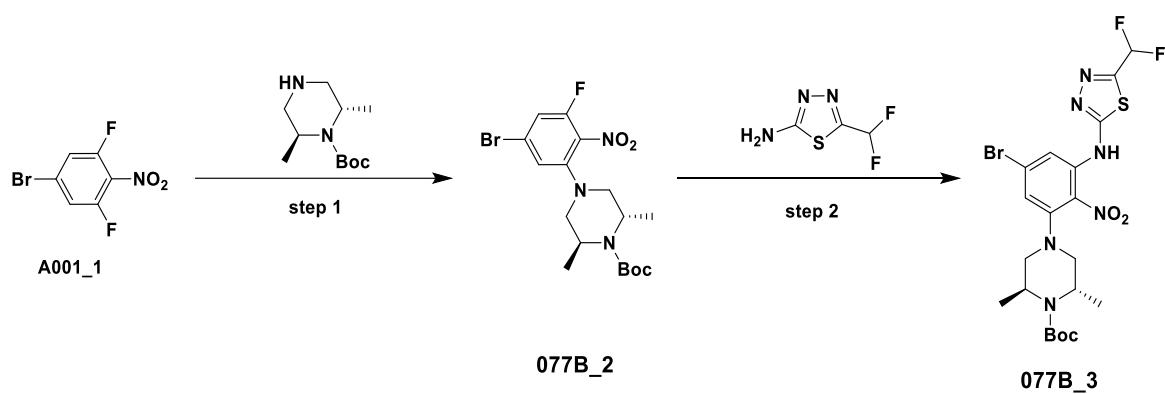
[1117] MS (ESI) M/Z: 643.3 [M+H]⁺.

[1118] ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.21 (s, 1H), 8.77 (d, *J* = 1.6 Hz, 1H), 7.79 (s, 1H), 7.64 (t, *J* = 53.2 Hz, 1H), 6.11 - 6.02 (m, 1H), 5.13 (d, *J* = 10.8 Hz, 1H), 5.02 (d, *J* = 17.6 Hz, 1H), 4.93 - 4.91 (m, 2H), 3.71 - 3.67 (m, 2H), 3.46 - 3.41 (m, 1H), 3.18 - 3.15 (m, 2H), 3.08 - 3.05 (m, 2H), 2.94 - 2.91 (m, 2H), 1.44 - 1.42 (m, 2H), 1.29 - 1.27 (m, 8H).

[1119] Example 077B2



077B2



[1120] Step 1: Synthesis of compound 077B_2

[1121] A001_1 (3.00 g, 12.6 mmol) and N,N-diisopropylethylamine (8.15 g, 63.0 mmol) were dissolved in N,N-dimethylacetamide (30 mL), followed by addition of *tert*-butyl (2S,6S)-2,6-dimethylpiperazine-1-carboxylate (2.70 g, 12.6 mmol). The reaction mixture was heated to 110°C and stirred for 3 hours. The reaction mixture was cooled to room temperature, then quenched with water (100 mL), and extracted with ethyl acetate (30 mL × 3). The organic phase was washed with brine (50 mL × 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 077B_2 (5.06 g).

[1122] MS (ESI) M/Z: 332.2, 334.2 [M-Boc]⁺.

[1123] ¹H NMR (400 MHz, DMSO-*d*₆): δ 7.21 - 7.18 (m, 1H), 7.14 (s, 1H), 4.06 - 4.03 (m, 2H), 3.79 - 3.75 (m, 2H), 2.99 - 2.96 (m, 2H), 1.42 (s, 9H), 1.15 (d, *J* = 6.4 Hz, 6H).

[1124] Step 2: Synthesis of compound 077B_3

[1125] Cesium carbonate (11.4 g, 35.1 mmol) and 5-(difluoromethyl)-1,3,4-thiadiazol-2-amine (2.65 g, 17.6 mmol) were added to a solution of 077B_2 (5.06 g, 11.7 mmol) in N,N-dimethylacetamide (50 mL). The reaction mixture was heated to 110°C and stirred for 16 hours. The reaction mixture was cooled to room temperature, then quenched with water (100 mL), and extracted with ethyl acetate (30 mL × 3). The organic phase was washed with brine (50 mL × 3), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 077B_3 (3.65 g).

[1126] MS (ESI) M/Z: 561.1, 563.1 [M-H]⁻.

[1127] Step 3: Synthesis of compound 077B_4

[1128] 077B_3 (10 g, 17.7 mmol) and methyl 3-mercaptopropionate (2.35 g, 19.5 mmol) were dissolved in 1,4-dioxane (100 mL), followed by addition of N,N-diisopropylethylamine (7.34 g, 56.8 mmol) and Xantphos (2.05 g, 3.55 mmol). The reaction mixture was purged with nitrogen three times at 25°C. Pd₂(dba)₃ (1.63 g, 1.77 mmol) was then added thereto. The reaction mixture was purged with nitrogen three times at 25°C, then heated to 85°C, and stirred for 2 hours. The reaction mixture was cooled to room temperature, then quenched with water (100 mL), and extracted with ethyl acetate (50 mL × 3). The organic phase was washed with brine (50 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 077B_4 (8 g).

[1129] MS (ESI) M/Z: 603.4 [M+H]⁺.

[1130] Step 4: Synthesis of compound 077B_5

[1131] 077B_4 (8 g, 13.2 mmol) was dissolved in dichloromethane (80.0 mL). The mixture was cooled to 0°C, and *m*-chloroperoxybenzoic acid (8.08 g, 39.8 mmol, 85% purity) was added in portions. The reaction mixture was stirred at 0°C for 1 hour. The reaction mixture was quenched with water (100 mL) and extracted with dichloromethane (50 mL × 3). The organic phase was washed with sodium sulfite aqueous solution (30 mL) and brine (30 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 077B_5 (5.7 g).

[1132] MS (ESI) M/Z: 657.1 [M+Na]⁺.

[1133] Step 5: Synthesis of compound 077B_6

[1134] 077B_5 (5.7 g, 8.98 mmol) was dissolved in ethanol (52.0 mL) and water (13.0 mL).

The mixture was heated to 60°C, followed by portionwise addition of iron powder (2.51 g, 44.9 mmol) and ammonium chloride (2.40 g, 44.9 mmol). The reaction mixture was heated to 80°C and stirred for 2 hours. The reaction mixture was filtered through diatomite while hot. The filtrate was diluted with water (30 mL) and extracted with ethyl acetate (50 mL × 3). The organic phase was washed with brine (50 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 077B_6 (4.1 g).

[1135] MS (ESI) M/Z: 603.1 [M-H]⁻.

[1136] ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.95 (s, 1H), 7.78 (s, 1H), 7.48 - 7.21 (m, 2H), 5.65 (s, 2H), 4.03 - 4.00 (m, 2H), 3.54 (s, 3H), 3.45 (t, *J* = 7.2 Hz, 2H), 3.20 - 3.17 (m, 2H), 2.64 - 2.58 (m, 4H), 1.43 (s, 9H), 1.32 (d, *J* = 6.4 Hz, 6H).

[1137] Step 6: Synthesis of compound 077B_7S

[1138] 077B_6 (4.00 g, 6.61 mmol), S-(-)-tetrahydrofuran-2-carboxylic acid (921 mg, 7.94 mmol), HATU (3.02 g, 7.94 mmol), and N,N-diisopropylethylamine (2.56 g, 19.8 mmol) were dissolved in N,N-dimethylformamide (40.0 mL). The reaction mixture was stirred at 25°C for 1 hour. The reaction mixture was added with water (200 mL) and extracted with ethyl acetate (100 mL × 3). The combined organic phases were washed with brine (100 mL × 6), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced

pressure to obtain 077B_7 (5.00 g) as a crude product, which was directly used in the next step without further purification.

[1139] MS (ESI) M/Z : 703.4 $[M+H]^+$.

[1140] Step 7: Synthesis of compound 077B_8

5 **[1141]** 077B_7S (5.00 g, 7.11 mmol) was dissolved in toluene (80.0 mL) and acetic acid (40.0 mL). The reaction mixture was stirred at 50°C for 12 hours. The reaction mixture was cooled to room temperature, added with water (200 mL), and extracted with ethyl acetate (100 mL $\times$ 3). The combined organic phases were washed with brine (100 mL $\times$ 6), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The
10 residue was purified by column chromatography to obtain 077B_8 (3.20 g).

[1142] MS (ESI) M/Z : 685.1 $[M+H]^+$.

[1143] ^1H NMR (400 MHz, DMSO- d_6) δ 7.67 (t, J = 53.2 Hz, 1H), 7.52 (d, J = 1.2 Hz, 1H), 6.89 (d, J = 1.2 Hz, 1H), 5.40 - 5.37 (m, 1H), 4.19 - 4.14 (m, 2H), 4.05 - 4.01 (m, 4H), 3.82 - 3.76 (m, 1H), 3.72 - 3.66 (m, 1H), 3.57 (t, J = 7.2 Hz, 2H), 3.52 (s, 3H), 2.76 - 2.68
15 (m, 1H), 2.63 (t, J = 7.2 Hz, 2H), 2.31 - 2.22 (m, 1H), 2.09 - 2.00 (m, 1H), 1.96 - 1.92 (m, 1H), 1.45 (s, 9H), 1.25 (d, J = 6.4 Hz, 6H).

[1144] Step 8: Synthesis of compound 077B_9

[1145] 077B_8 (1.60 g, 2.34 mmol) was dissolved in tetrahydrofuran (16.0 mL), followed by addition of sodium methoxide (378 mg, 7.01 mmol) at 0°C. The reaction mixture was
20 stirred at 0°C for 30 minutes. The solvent was removed by rotary evaporation at room temperature, and the residue was dried under oil pump vacuum for 15 minutes. The

remaining solid was dissolved in dichloromethane (16.0 mL), followed by addition of N-chlorosuccinimide (312 mg, 2.34 mmol) in an ice bath. Two parallel batches were performed. The reaction mixture was warmed to 25°C and stirred for 1 hour. The reaction mixture was quenched with water (100 mL) and extracted with dichloromethane (100 mL × 3). The organic phase was washed with brine (100 mL × 3), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 077B_9 (2.90 g) as a crude product, which was directly used in the next step without further purification.

[1146] MS (ESI) M/Z: 633.2 [M+H]⁺.

10 [1147] Step 9: Synthesis of compound 077B_10

[1148] 1-Methylcyclopropanamine hydrochloride (1.97 g, 18.3 mmol) and N,N-diisopropylethylamine (4.74 g, 36.6 mmol) were dissolved in dichloromethane (30.0 mL), followed by addition of 077B_9 (2.90 g, 4.58 mmol). The reaction mixture was stirred at 25°C for 1 hour. The reaction mixture was quenched with water (100 mL) and extracted with dichloromethane (50 mL × 3). The organic phase was washed with brine (100 mL × 3), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain 077B_10S (1.47 g).

[1149] MS (ESI) M/Z: 668.4 [M+H]⁺.

[1150] ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.02 (s, 1H), 7.67 (t, *J* = 53.2 Hz, 1H), 7.50 (d, *J* = 1.2 Hz, 1H), 6.93 (d, *J* = 1.2 Hz, 1H), 5.38 - 5.35 (m, 1H), 4.19 - 4.15 (m, 2H), 3.99 - 3.95 (m, 4H), 3.82 - 3.77 (m, 1H), 3.74 - 3.68 (m, 1H), 2.77 - 2.69 (m, 1H), 2.29 - 2.22 (m, 1H),

2.09 - 2.01 (m, 1H), 1.96 - 1.90 (m, 1H), 1.45 (s, 9H), 1.24 (d, $J = 6.4$ Hz, 6H), 1.04 (s, 3H),
0.64 - 0.61 (m, 2H), 0.36 - 0.34 (m, 2H)

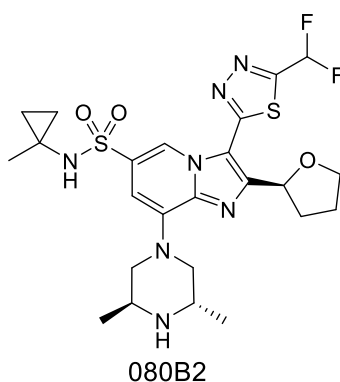
[1151] Step 10: Synthesis of compound 077B2

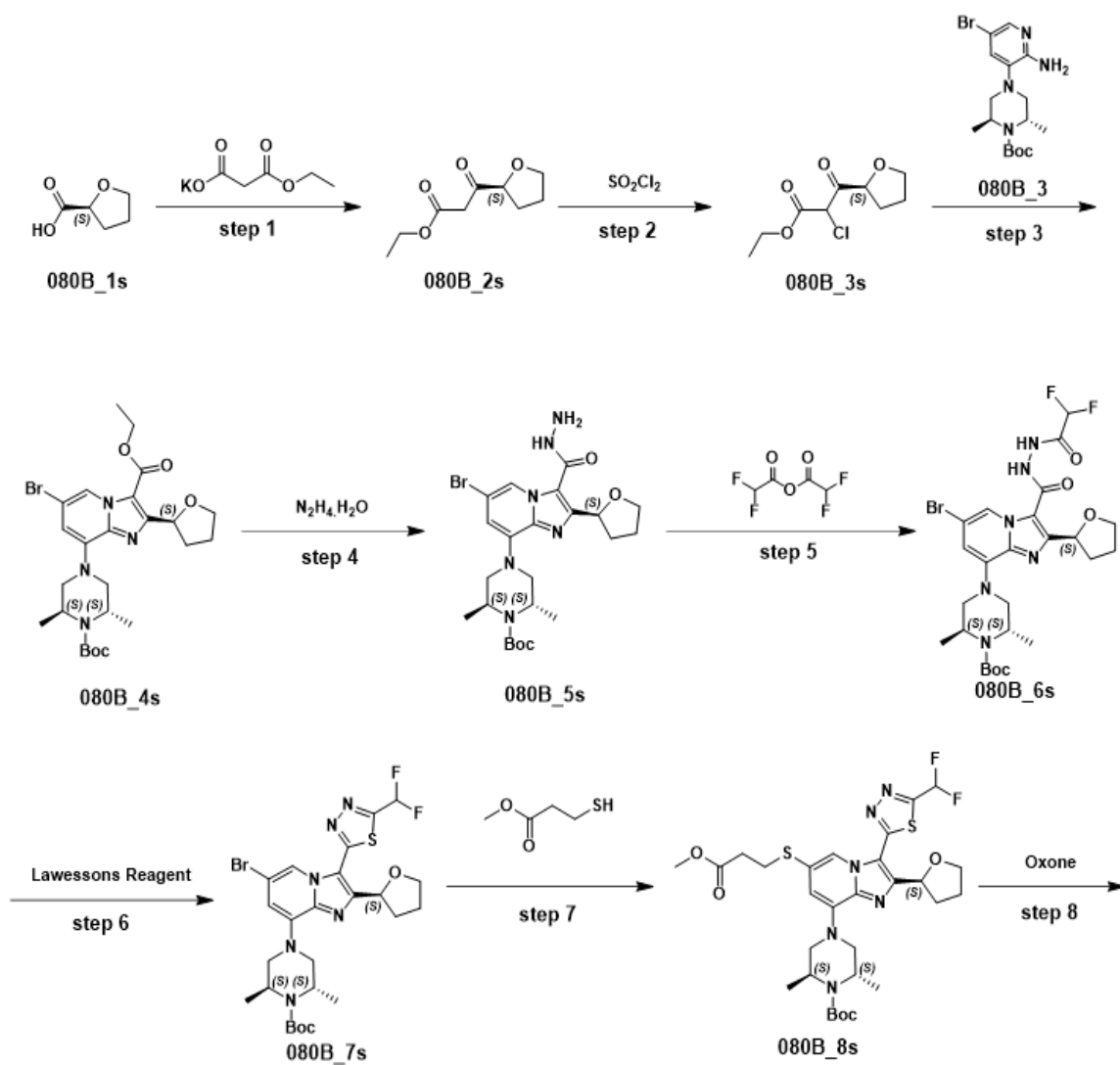
[1152] 077B_10 (1.47 g, 2.20 mmol) was dissolved in 1,4-dioxane (10.0 mL), followed by
5 addition of 4 M HCl in dioxane (20 mL) at 25°C. The reaction mixture was stirred at 25°C
for 0.5 hours. The reaction mixture was concentrated under reduced pressure. The
residue was purified by preparative chromatography to obtain 077B2 (900 mg).

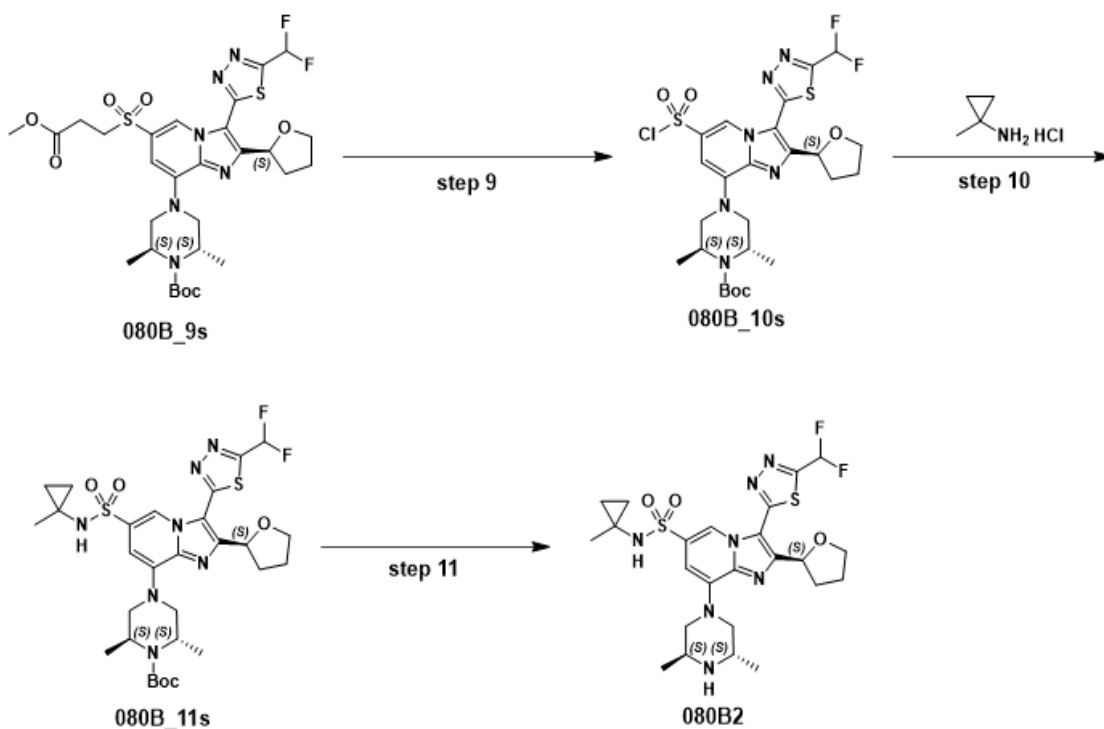
[1153] MS (ESI) M/Z : 568.1 $[M+H]^+$.

[1154] ^1H NMR (400 MHz, DMSO- d_6) δ 8.06 (s, 1H), 7.80 - 7.54 (m, 2H), 7.09 (d, $J = 1.2$
10 Hz, 1H), 5.40 - 5.37 (m, 1H), 3.83 - 3.74 (m, 2H), 3.45 - 3.39 (m, 4H), 3.28 - 3.22 (m, 2H),
2.75 - 2.67 (m, 1H), 2.33 - 2.23 (m, 1H), 2.12 - 2.03 (m, 1H), 2.01 - 1.93 (m, 1H), 1.17 (d, J
= 6.4 Hz, 6H), 1.03 (s, 3H), 0.65 - 0.58 (m, 2H), 0.37 - 0.33 (m, 2H).

[1155] Example 080B2







[1156] Step 1: Synthesis of compound 080B_{2s}

[1157] 080B_{1s} (60.0 g, 517 mmol) was dissolved in tetrahydrofuran (600 mL), followed by portionwise addition of 1,1-carbonyldiimidazole (CDI, 101 g, 620 mmol). After the

5 addition was completed, the reaction mixture was stirred at 20°C for 1.5 hours. Magnesium chloride (48.2 g, 506 mmol) and ethyl potassium malonate (132 g, 775 mmol) were added in portions. The reaction mixture was stirred at 20°C for another 3 hours. The reaction mixture was quenched with water (600 mL), added with dilute hydrochloric acid (4 M) to adjust the pH to approximately 5, and extracted with ethyl acetate (500 mL × 2). The

10 extract was washed with saturated brine (500 mL × 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The crude product was purified by column chromatography to obtain 080B_{2s} (86.8 g).

[1158] MS (ESI) M/Z: 186.9 [M+H]⁺.

[1159] ^1H NMR (400 MHz, CDCl_3): δ 4.40 - 4.36 (m, 1H), 4.19 (q, $J = 7.2$ Hz, 2H), 3.93 - 3.89 (m, 2H), 3.57 (s, 2H), 2.23 - 2.19 (m, 1H), 2.04 - 2.01 (m, 1H), 1.94 - 1.88 (m, 2H), 1.27 (t, $J = 7.2$ Hz, 3H).

[1160] Step 2: Synthesis of compound 080B_3s

5 **[1161]** 080B_2s (28.5 g, 153 mmol) was dissolved in dichloromethane (500 mL). The mixture was cooled to 0°C , followed by dropwise addition of sulfonyl chloride (20.6 g, 153 mmol). After the addition was completed, the reaction mixture was slowly warmed to 25°C and stirred for 2 hours. The reaction mixture was quenched with water (500 mL) and extracted with dichloromethane ($400\text{ mL} \times 2$). The combined organic phases were washed
10 with brine ($400\text{ mL} \times 1$), dried over anhydrous sodium sulfate, and concentrated under reduced pressure at room temperature to obtain 080B_3s (100 g) as a crude product, which was directly used in the next step without further purification.

[1162] MS (ESI) M/Z : 218.9, 220.9 $[\text{M}-\text{H}]^-$.

[1163] ^1H NMR (400 MHz, CDCl_3): δ 5.19 - 5.15 (m, 1H), 4.63 - 4.60 (m, 1H), 4.28 - 4.25
15 (m, 2H), 3.96 - 3.82 (m, 2H), 2.25 - 2.12 (m, 2H), 1.95 - 1.85 (m, 2H), 1.33 - 1.28 (m, 3H).

[1164] Step 3: Synthesis of compound 080B_4s

[1165] 080B_3s (23.7 g, 107 mmol), 080B_3 (13.8 g, 35.8 mmol), and $4\text{\AA}$ molecular sieves (14 g) were added to isopropanol (150 mL). The reaction mixture was heated to 100°C and stirred for 36 hours. The reaction mixture was cooled to room temperature and filtered.
20 The filtrate was concentrated under reduced pressure at room temperature. The residue was dissolved in ethyl acetate (300 mL), washed with water ($200\text{ mL} \times 1$) and saturated brine

(200 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The crude product was purified by column chromatography to obtain 080B_4s (9.8 g).

[1166] MS (ESI) M/Z: 551.4, 553.3 $[M+H]^+$.

5 **[1167]** ^1H NMR (400 MHz, CDCl_3): δ 8.96 (s, 1H), 6.38 (s, 1H), 5.76 - 5.73 (m, 1H), 4.47 - 4.41 (m, 2H), 4.24 - 4.20 (m, 3H), 4.02 - 3.99 (m, 5H), 2.31 - 2.19 (m, 4H), 1.51 (s, 9H), 1.43 (t, $J = 7.2$ Hz, 3H), 1.30 (d, $J = 7.2$ Hz, 6H).

[1168] Step 4: Synthesis of compound 080B_5s

[1169] 080B_4s (9.80 g, 17.8 mmol) was dissolved in ethanol (90 mL), followed by
10 addition of hydrazine hydrate (37.0 g, 591 mmol, 80%). The reaction mixture was heated to 80°C and stirred for 16 hours. The reaction mixture was cooled to room temperature, quenched with water (150 mL), and extracted with ethyl acetate (100 mL $\times$ 3). The extract was washed with brine (100 mL $\times$ 2), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation to obtain 080B_5s (7 g) as a crude product,
15 which was directly used in the next step without further purification.

[1170] MS (ESI) M/Z: 537.3, 539.3 $[M+H]^+$.

[1171] ^1H NMR (400 MHz, CDCl_3): δ 9.58 (s, 1H), 9.05 (s, 1H), 6.32 (d, $J = 1.2$ Hz, 1H), 5.17 (t, $J = 7.2$ Hz, 1H), 4.23 - 4.21 (m, 2H), 4.14 - 4.11 (m, 2H), 4.02 - 3.95 (m, 6H), 2.86 - 2.81 (m, 1H), 2.27 - 2.24 (m, 1H), 2.16 - 2.07 (m, 2H), 1.50 (s, 9H), 1.30 (d, $J = 6.4$ Hz,
20 6H).

[1172] Step 5: Synthesis of compound 080B_6s

[1173] 080B_5s (7.00 g, 12.7 mmol) and triethylamine (3.84 g, 37.9 mmol) were dissolved in a mixed solvent of tetrahydrofuran (50.0 mL) and dichloromethane (50.0 mL). The mixture was cooled to 0°C, followed by dropwise addition of difluoroacetic anhydride (2.64 g, 15.2 mmol). The reaction mixture was naturally warmed to 25°C and stirred for 1 hour.

5 The reaction mixture was quenched with water (100 mL) and extracted with dichloromethane (100 mL $\times$ 3). The extract was washed with brine (100 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The crude product was purified by column chromatography to obtain 080B_6s (6.90 g).

10 **[1174]** MS (ESI) M/Z: 615.3, 617.3 [M+H]⁺.

[1175] ¹H NMR (400 MHz, CDCl₃): δ 11.82 (s, 1H), 9.26 (s, 1H), 9.12 (d, J = 1.6 Hz, 1H), 6.39 (d, J = 1.2 Hz, 1H), 6.10 (t, J = 53.6 Hz, 1H), 5.26 (t, J = 7.2 Hz, 1H), 4.25 - 4.23 (m, 3H), 4.06 - 3.96 (m, 5H), 2.71 - 2.68 (m, 1H), 2.35 - 2.34 (m, 1H), 2.17 - 2.08 (m, 2H), 1.51 (s, 9H), 1.31 (d, J = 6.4 Hz, 6H).

15 **[1176]** Step 6: Synthesis of compound 080B_7s

[1177] 080B_6s (6.90 g, 10.9 mmol) and pyridine (4.32 g, 54.6 mmol) were dissolved in dioxane (70.0 mL). Lawesson's reagent (8.84 g, 21.9 mmol) was added in one portion at 25°C. The reaction mixture was heated to 80°C and stirred for 2 hours. The reaction mixture was cooled to room temperature, quenched with water (100 mL), and filtered. The
20 filtrate was extracted with ethyl acetate (100 mL $\times$ 2), washed with brine (100 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The

crude product was purified by column chromatography to obtain 080B_7s (4.6 g).

[1178] MS (ESI) M/Z: 613.3, 615.3 [M+H]⁺.

[1179] ¹H NMR (400 MHz, CDCl₃): δ 9.40 (d, *J* = 1.2 Hz, 1H), 7.09 (t, *J* = 53.6 Hz, 1H), 6.43 (d, *J* = 1.2 Hz, 1H), 5.26 (t, *J* = 6.4 Hz, 1H), 4.27 - 4.25 (m, 2H), 4.05 - 3.97 (m, 6H),
5 2.78 - 2.73 (m, 1H), 2.33 - 2.29 (m, 2H), 2.24 - 2.22 (m, 1H), 1.51 (s, 9H), 1.33 (d, *J* = 6.4 Hz, 1H).

[1180] Step 7: Synthesis of compound 080B_8s

[1181] 080B_7s (4.6 g, 7.50 mmol), methyl 3-mercaptopropionate (991 mg, 8.25 mmol), and N,N-diisopropylethylamine (DIEA, 2.91 g, 22.5 mmol) were dissolved in dioxane (50.0
10 mL), and the system was purged with nitrogen three times. Xantphos (868 mg, 1.50 mmol) and Pd₂(dba)₃ (687 mg, 750 μmol) were added to the reaction mixture in one portion, and the system was purged with nitrogen three times. The reaction mixture was heated to 85°C and stirred for 2 hours. The reaction mixture was cooled to room temperature and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by column
15 chromatography to obtain 080B_8s (4.6 g).

[1182] MS (ESI) M/Z: 653.4 [M+H]⁺.

[1183] ¹H NMR (400 MHz, CDCl₃): δ 9.34 (s, 1H), 7.09 (t, *J* = 54.0 Hz, 1H), 6.41 (d, *J* = 0.8 Hz, 1H), 5.28 (t, *J* = 6.8 Hz, 1H), 4.26 - 4.24 (m, 2H), 4.07 - 3.97 (m, 6H), 3.70 (s, 3H), 3.16 (t, *J* = 3.2 Hz, 2H), 2.75 - 2.74 (m, 1H), 2.66 (t, *J* = 7.2 Hz, 2H), 2.31 - 2.27 (m, 2H),
20 2.13 - 2.07 (m, 1H), 1.52 (s, 9H), 1.33 (d, *J* = 6.8 Hz, 6H).

[1184] Step 8: Synthesis of compound 080B_9s

[1185] 080B_8s (4.60 g, 7.05 mmol) was dissolved in methanol (150 mL), followed by portionwise addition of potassium peroxymonosulfate (oxone, 8.66 g, 14.1 mmol) at 25°C. The reaction mixture was stirred at 25°C for 1 hour. The reaction mixture was quenched with saturated sodium sulfite aqueous solution (100 mL) and extracted with ethyl acetate (100 mL × 3). The organic phase was washed with brine (200 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography to obtain 080B_9s (2.9 g).

[1186] MS (ESI) M/Z: 685.2 [M+H]⁺.

[1187] ¹H NMR (400 MHz, CDCl₃): δ 9.76 (d, *J* = 1.6 Hz, 1H), 7.11 (t, *J* = 53.6 Hz, 1H), 6.58 (s, 1H), 5.30 (t, *J* = 6.4 Hz, 1H), 4.30 - 4.28 (m, 2H), 4.12 - 4.00 (m, 6H), 3.67 (s, 3H), 3.55 (t, *J* = 7.6 Hz, 2H), 2.86 (t, *J* = 6.4 Hz, 2H), 2.73 - 2.72 (m, 1H), 2.37 - 2.34 (m, 1H), 2.22 - 2.21 (m, 1H), 2.15 - 2.14 (m, 1H), 1.52 (s, 9H), 1.34 (d, *J* = 6.8 Hz, 6H).

[1188] Step 9: Synthesis of compound 080B_10s

[1189] 080B_9s (2.90 g, 4.23 mmol) was dissolved in tetrahydrofuran (100 mL). The mixture was cooled to 0°C, and sodium methoxide (1.14 g, 21.2 mmol) was added in one portion. The reaction mixture was stirred at 0°C for 30 minutes. The reaction mixture was concentrated under reduced pressure at room temperature. The crude product was dissolved in dichloromethane (30 mL). The mixture was cooled to 0°C, and N-chlorosuccinimide (NCS, 566 mg, 4.24 mmol) was added in one portion. The reaction mixture was warmed to 25°C and stirred for 30 minutes. The reaction mixture was quenched with water (100 mL) and extracted with dichloromethane (50 mL × 3). The

combined organic phases were washed with brine (100 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure at room temperature to obtain 080B_10s (2.68 g) as a crude product, which was directly used in the next step without further purification.

5 **[1190]** MS (ESI) M/Z: 633.2 [M+H]⁺.

[1191] Step 10: Synthesis of compound 080B_11s

[1192] 1-Methylcyclopropanamine hydrochloride (911 mg, 8.47 mmol) and N,N-diisopropylethylamine (DIEA, 1.64 g, 12.7 mmol) were dissolved in dichloromethane (30.0 mL), followed by addition of 080B_10s (2.68 g, 4.23 mmol). After the addition was
10 completed, the reaction mixture was stirred at 25°C for 30 minutes. The reaction mixture was quenched with water (50 mL) and extracted with dichloromethane (50 mL $\times$ 2). The organic phase was washed with saturated brine (100 mL $\times$ 1), dried, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain 080B_11s (1.20 g).

15 **[1193]** MS (ESI) M/Z: 668.5 [M+H]⁺.

[1194] ¹H NMR (400 MHz, CDCl₃): δ 9.76 (d, J = 1.2 Hz, 1H), 7.10 (t, J = 53.6 Hz, 1H), 6.64 (d, J = 1.6 Hz, 1H), 5.29 (t, J = 6.8 Hz, 1H), 5.15 (s, 1H), 4.28 - 4.26 (m, 2H), 4.12 - 4.00 (m, 6H), 2.77 - 2.72 (m, 1H), 2.35 - 2.12 (m, 3H), 1.52 (s, 9H), 1.34 - 1.33 (m, 9H), 0.94 - 0.92 (m, 2H), 0.59 - 0.56 (m, 2H).

20 **[1195]** Step 11: Synthesis of compound 080B2

[1196] 080B_11s (1.20 g, 1.80 mmol) was dissolved in dioxane (5 mL), followed by

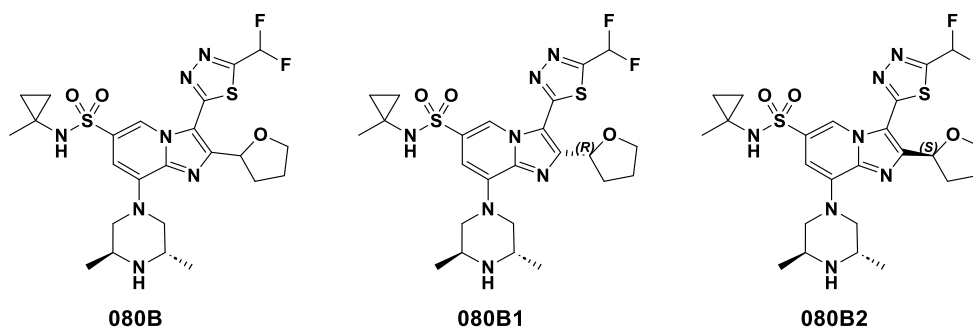
addition of 4 M HCl in dioxane (5 mL). The reaction mixture was stirred at 20°C for 0.5 hours. After concentration, the crude product was purified by preparative chromatography (neutral conditions, column: Waters Xbridge Prep OBD C18) to obtain compound 080B2 (784.6 mg).

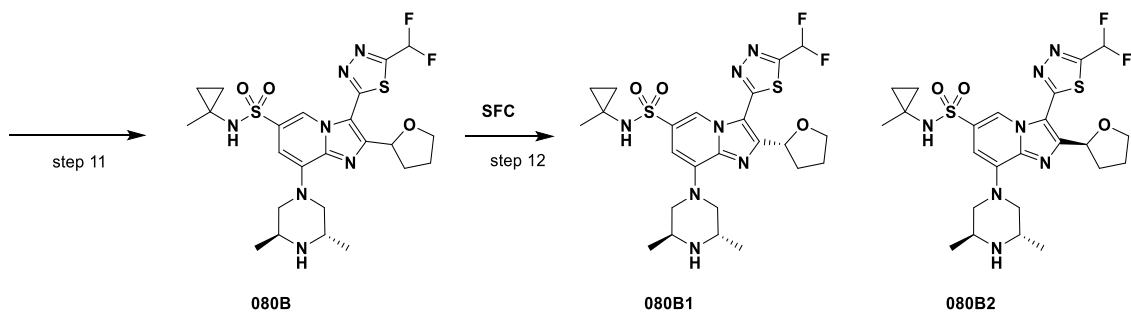
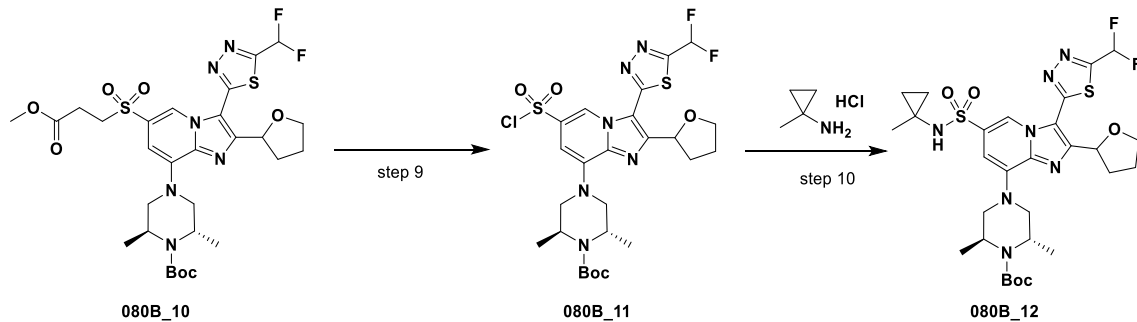
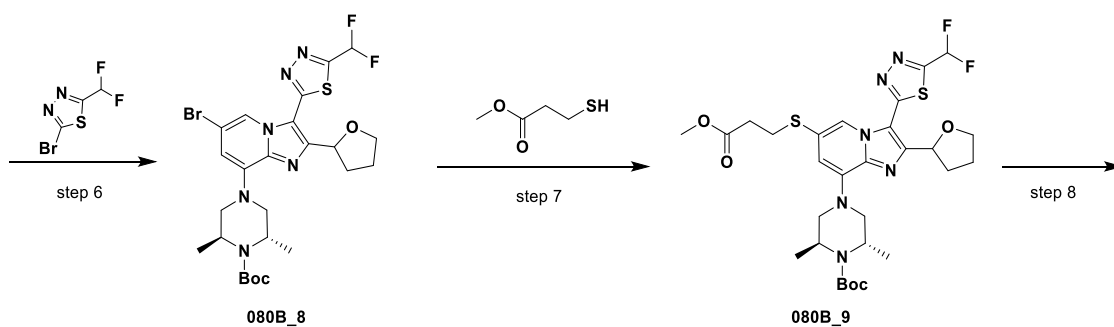
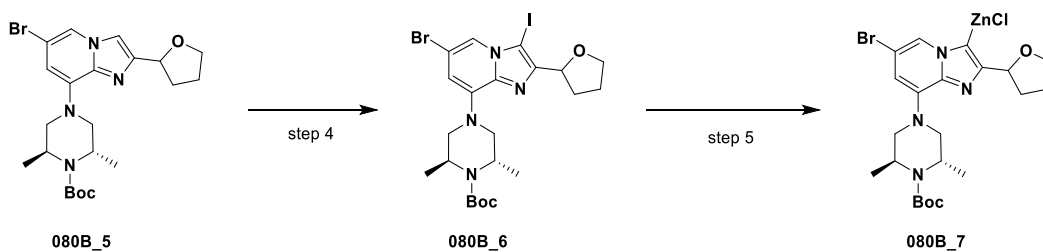
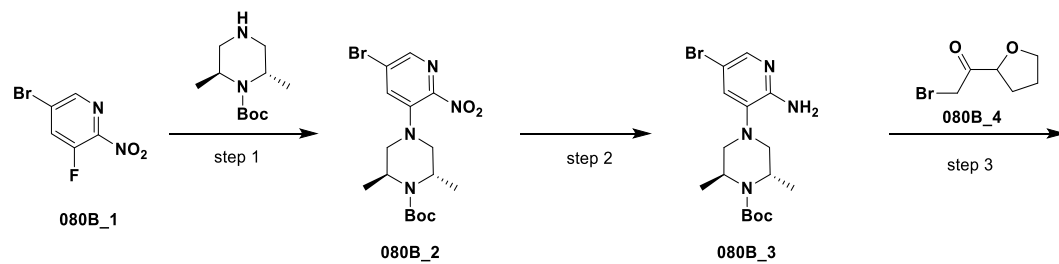
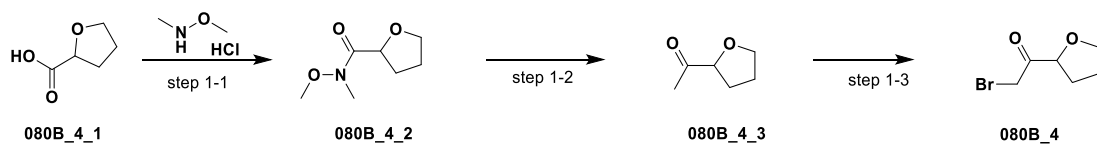
5 [1197] MS (ESI) M/Z : 568.2 $[M+H]^+$.

[1198] ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 9.65 (s, 1H), 8.36 (s, 1H), 7.70 (t, $J = 53.2$ Hz, 1H), 6.94 (d, $J = 1.2$ Hz, 1H), 5.30 (t, $J = 6.8$ Hz, 1H), 3.91 - 3.88 (m, 2H), 3.50 - 3.46 (m, 2H), 3.37 - 3.36 (m, 2H), 3.30 - 3.27 (m, 2H), 2.59 - 2.53 (m, 1H), 2.30 - 2.25 (m, 1H), 2.12 - 2.06 (m, 2H), 1.19 (d, $J = 6.4$ Hz, 6H), 1.12 (s, 3H), 0.73 - 0.65 (m, 2H), 0.46 - 0.43 (m, 2H).

10 2H).

[1199] Examples 080B, 080B1, and 080B2





[1200] Step 1-1: Synthesis of compound 080B_4_2

[1201] 080B_4_1 (30.0 g, 258 mmol) and triethylamine (TEA, 131 g, 1.29 mol) were dissolved in tetrahydrofuran (500 mL), followed by addition of methoxymethylamine (15.7 g, 258 mmol) and butyl phosphate anhydride (50% solution in ethyl acetate, 372 g, 516 mmol). After the addition was completed, the reaction mixture was stirred at 20°C for 1 hour. The reaction mixture was quenched with water (1 L) and extracted with dichloromethane (500 mL × 6). The combined organic phases were washed with saturated brine (400 mL × 2), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain 080B_4_2 (17.0 g).

[1202] MS (ESI) M/Z: 160.4 [M+H]⁺.

[1203] ¹H NMR (400 MHz, CDCl₃-d): δ 4.77 (s, 1H), 4.05 - 4.00 (m, 1H), 3.96 - 3.88 (m, 1H), 3.72 (s, 3H), 3.20 (s, 3H), 2.23 - 2.15 (m, 1H), 2.02 - 1.84 (m, 3H).

[1204] Step 1-2: Synthesis of compound 080B_4_3

[1205] 080B_4_2 (5 g, 31.4 mmol) was dissolved in tetrahydrofuran (50 mL), and the system was purged with nitrogen three times. The mixture was cooled to 0°C, followed by dropwise addition of methylmagnesium bromide (3 M in diethyl ether, 15.71 mL). After the addition was completed, the reaction mixture was stirred at 0°C for 1 hour. After completion of the reaction, the reaction mixture was quenched with ammonium chloride aqueous solution (30 mL) and extracted with dichloromethane (15 mL × 6). The combined organic phases were washed with saturated brine (25 mL), dried over anhydrous sodium

sulfate, filtered, and concentrated under reduced pressure to obtain 080B_4_3 (4.80 g) as a crude product, which was directly used in the next step without further purification.

[1206] Step 1-3: Synthesis of compound 080B_4

[1207] 080B_4_3 (3.60 g, 31.5 mmol) was dissolved in dichloromethane (40 mL), and the
5 system was purged with nitrogen three times. The mixture was cooled to 0°C, followed by dropwise addition of triethylamine (3.83 g, 37.8 mmol) and trimethylsilyl trifluoromethanesulfonate (7.71 g, 34.7 mmol). After the addition was completed, the reaction mixture was stirred at 0°C for 0.5 hours. N-bromosuccinimide (6.17 g, 34.6 mmol) was then added thereto. The reaction mixture was stirred at 0°C for another 0.5 hours.
10 The reaction mixture was quenched with water (30 mL) and extracted with dichloromethane (25 mL × 3). The combined organic phases were washed with saturated brine (25 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain 080B_4 (7.00 g) as a crude product, which was directly used in the next step without further purification.

15 **[1208]** Step 1: Synthesis of compound 080B_2

[1209] 080B_1 (10 g, 45.2 mmol), *tert*-butyl (2S,6S)-2,6-dimethylpiperazine-1-carboxylate (9.70 g, 45.2 mmol), and N,N-diisopropylethylamine (29.2 g, 226 mmol) were dissolved in N,N-dimethylacetamide (100 mL). The mixture was heated to 110°C and stirred for 6 hours. The reaction mixture was cooled to room temperature, then quenched
20 with water (150 mL), and extracted with ethyl acetate (100 mL × 2). The combined organic phases were washed with brine (100 mL × 1), dried over anhydrous sodium sulfate, and

concentrated under reduced pressure at room temperature. The residue was purified by column chromatography to obtain 080B_2 (18 g).

[1210] MS (ESI) M/Z: 315.2, 317.2 [M-Boc+H]⁺.

[1211] ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.02 (d, *J* = 1.6 Hz, 1H), 7.93 (d, *J* = 2.0 Hz, 1H), 4.13 - 4.03 (m, 2H), 3.82 - 3.78 (m, 2H), 2.97 - 2.94 (m, 2H), 1.42 (s, 9H), 1.16 (d, *J* = 6.4 Hz, 6H).

[1212] Step 2: Synthesis of compound 080B_3

[1213] 080B_2 (18.0 g, 43.3 mmol) and ammonium chloride (11.6 g, 216 mmol) were dissolved in ethanol (200 mL) and water (50 mL). The reaction mixture was heated to 60°C, followed by portionwise addition of iron powder (12.1 g, 216 mmol). The resulting mixture was stirred at 85°C for 1 hour. The reaction mixture was filtered through diatomite while hot. The filtrate was concentrated under reduced pressure to remove most of the ethanol. The resulting mixture was diluted with water (100 mL) and extracted with ethyl acetate (150 mL × 3). The combined organic phases were washed with saturated brine (200 mL × 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 080B_3 (15.2 g).

[1214] MS (ESI) M/Z: 385.2, 387.2 [M+H]⁺.

[1215] ¹H NMR (400 MHz, DMSO-*d*₆): δ 7.70 (d, *J* = 2.0 Hz, 1H), 7.21 (d, *J* = 2.0 Hz, 1H), 5.78 (s, 2H), 4.00 - 3.95 (m, 2H), 3.28 - 3.24 (m, 2H), 2.63 - 2.59 (m, 2H), 1.42 (s, 9H), 1.26 (d, *J* = 6.4 Hz, 6H).

[1216] Step 3: Synthesis of compound 080B_5

[1217] 080B_3 (6 g, 15.6 mmol) and 080B_4 (6.01 g, 31.1 mmol) were dissolved in tetrahydrofuran (60 mL), followed by addition of sodium carbonate (908 mg, 8.56 mmol). The mixture was heated to 70°C and stirred for 16 hours. The reaction mixture was cooled
5 to room temperature, then quenched with water (100 mL), and extracted with ethyl acetate (50 mL × 3). The combined organic phases were washed with saturated brine (50 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 080B_5 (3.40 g).

10 **[1218]** MS (ESI) M/Z: 479.3, 481.3 [M+H]⁺.

[1219] ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.16 (d, *J* = 1.2 Hz, 1H), 7.71 (d, *J* = 1.6 Hz, 1H), 6.17 (s, 1H), 4.95 (t, *J* = 7.2 Hz, 1H), 4.13 - 4.00 (m, 4H), 3.94 - 3.85 (m, 3H), 3.78 - 3.73 (m, 1H), 2.24 - 2.19 (m, 1H), 2.05 - 1.89 (m, 3H), 1.43 (s, 9H), 1.20 (d, *J* = 6.4 Hz, 6H).

[1220] Step 4: Synthesis of compound 080B_6

15 **[1221]** 080B_5 (2.90 g, 6.05 mmol) was dissolved in N,N-dimethylformamide (30.0 mL), followed by addition of N-iodosuccinimide (1.63 g, 7.26 mmol). The reaction mixture was stirred at 25°C for 16 hours. The reaction mixture was quenched with water (100 mL) and extracted with ethyl acetate (20 mL × 3). The combined organic phases were washed with saturated brine (50 mL × 3), dried, and concentrated. The residue was purified by column
20 chromatography to obtain 080B_6 (2.00 g).

[1222] MS (ESI) M/Z: 605.2, 607.2 [M+H]⁺.

[1223] ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 7.81 (s, 1H), 6.33 (s, 1H), 4.96 - 4.92 (m, 1H), 4.10 - 4.07 (m, 2H), 4.04 - 4.01 (m, 1H), 3.93 - 3.88 (m, 4H), 3.80 - 3.74 (m, 1H), 2.26 - 2.20 (m, 1H), 2.18 - 2.09 (m, 2H), 1.98 - 1.93 (m, 1H), 1.43 (s, 9H), 1.20 (d, $J = 6.8$ Hz, 6H).

[1224] Steps 5 and 6: Synthesis of compound 080B_8

5 **[1225]** 080B_6 (200 mg, 330 μmol) was dissolved in tetrahydrofuran (2.00 mL), and the system was purged with nitrogen three times. The mixture was cooled to -65°C , followed by dropwise addition of isopropylmagnesium chloride (2.0 M in tetrahydrofuran, 185 μL). The reaction mixture was stirred at 0°C for 0.5 hours. A solution of dichloro(N,N,N,N -tetramethylethylenediamine)zinc (91.7 mg, 363 μmol) in tetrahydrofuran (1 mL) was added

10 dropwise thereto at the same temperature. The reaction mixture was slowly warmed to room temperature and stirred for 0.5 hours. The reaction mixture was cooled again to 0°C , followed by dropwise addition of a solution of 2-bromo-5-(difluoromethyl)-1,3,4-thiadiazole (355 mg, 1.65 mmol) and tetrakis(triphenylphosphine)palladium (190 mg, 165 μmol) in tetrahydrofuran (1 mL). The reaction mixture was slowly warmed to 25°C and

15 stirred for 1 hour. The reaction mixture was quenched with ammonium chloride aqueous solution (3 mL) and extracted with ethyl acetate (5 mL $\times$ 3). The combined organic phases were washed with brine (5 mL $\times$ 2), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by thin-layer chromatography to obtain 080B_8 (50 mg).

20 **[1226]** MS (ESI) M/Z : 613.2, 615.2 $[\text{M}+\text{H}]^+$.

[1227] ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 9.22 - 9.20 (m, 1H), 7.68 (t, $J = 53.6$ Hz, 1H),

6.63 (s, 1H), 5.26 - 5.22 (m, 1H), 4.15 - 4.10 (m, 3H), 4.02 - 3.98 (m, 2H), 3.90 - 3.85 (m, 3H), 2.64 - 2.57 (m, 1H), 2.29 - 2.20 (m, 1H), 2.17 - 2.00 (m, 2H), 1.44 (s, 9H), 1.24 (d, $J = 6.8$ Hz, 6H).

[1228] Step 7: Synthesis of compound 080B_9

5 **[1229]** 080B_8 (260 mg, 424 μmol), methyl 3-mercaptopropionate (56.0 mg, 466 μmol), and N,N-diisopropylethylamine (175 mg, 1.36 mmol) were dissolved in 1,4-dioxane (3 mL). The system was purged with nitrogen three times, followed by addition of $\text{Pd}_2(\text{dba})_3$ (38.8 mg, 42.3 μmol) and Xantphos (49.0 mg, 84.7 μmol), and purged with nitrogen three additional times. The reaction mixture was heated to 85°C and stirred for 2 hours. The
10 reaction mixture was cooled to room temperature, then quenched with water (10 mL), and extracted with ethyl acetate (15 mL $\times$ 3). The combined organic phases were washed with brine (20 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The crude product was purified by column chromatography to obtain 080B_9 (167 mg).

15 **[1230]** MS (ESI) M/Z : 653.2 $[\text{M}+\text{H}]^+$.

[1231] Step 8: Synthesis of compound 080B_10

[1232] 080B_9 (100 mg, 153 μmol) was dissolved in methanol (4 mL), followed by addition of potassium peroxymonosulfate complex (188 mg, 306 μmol). The reaction mixture was stirred at 25°C for 2 hours. Two parallel batches were performed and
20 combined for work-up. The reaction mixture was quenched with sodium sulfite aqueous solution (5 mL) and extracted with ethyl acetate (5 mL $\times$ 3). The combined organic phases

were washed with brine (5 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure at room temperature. The residue was purified by thin-layer chromatography to obtain 080B_10 (103 mg).

[1233] MS (ESI) M/Z : 685.2 $[M+H]^+$.

5 **[1234]** ^1H NMR (400 MHz, $\text{DMSO-}d_6$): δ 9.54 - 9.52 (m, 1H), 7.70 (t, $J = 53.2$ Hz, 1H), 6.72 - 6.70 (m, 1H), 5.32 - 5.28 (m, 1H), 4.17 - 4.12 (m, 2H), 4.08 - 4.03 (m, 3H), 3.92 - 3.85 (m, 3H), 3.70 (t, $J = 7.2$ Hz, 2H), 3.52 (s, 3H), 2.71 (t, $J = 7.2$ Hz, 2H), 2.30 - 2.23 (m, 1H), 2.18 - 2.00 (m, 3H), 1.44 (s, 9H), 1.26 (d, $J = 6.8$ Hz, 6H).

[1235] Step 9: Synthesis of compound 080B_11

10 **[1236]** 080B_10 (80.0 mg, 116 μmol) was dissolved in tetrahydrofuran (2 mL), and the system was purged with nitrogen three times. The reaction mixture was then cooled to 0°C , followed by addition of sodium methoxide (18.9 mg, 350 μmol), and stirred at room temperature for 30 minutes. The solvent was removed by rotary evaporation at room temperature, and the residue was dried under oil pump vacuum for 15 minutes. The solid
15 was dissolved in dichloromethane (2 mL). The mixture was cooled to 0°C , followed by addition of N-chlorosuccinimide (15.6 mg, 116 μmol). The reaction mixture was slowly warmed to room temperature and stirred for 1 hour. The reaction mixture was quenched with water (10 mL) and extracted with dichloromethane ($5\text{ mL} \times 3$). The combined organic phases were washed with brine (5 mL), dried over anhydrous sodium sulfate, filtered, and
20 the filtrate was concentrated by rotary evaporation to obtain 080B_11 (74 mg) as a crude product, which was directly used in the next step without further purification.

[1237] MS (ESI) M/Z: 633.1 [M+H]⁺.

[1238] Step 10: Synthesis of compound 080B_12

[1239] 1-Methylcyclopropanamine hydrochloride (50.3 mg, 467 μ mol) and N,N-diisopropylethylamine (121 mg, 934 μ mol) were dissolved in dichloromethane (2.00 mL).

5 A solution of 080B_11 (74.0 mg, 117 μ mol) in dichloromethane (1 mL) was added dropwise to the reaction mixture. After the addition was completed, the reaction mixture was stirred at 20°C for 20 minutes. After completion of the reaction, the reaction mixture was quenched with water (10 mL) and extracted with dichloromethane (10 mL $\times$ 2). The combined organic phases were washed with saturated brine (10 mL $\times$ 1), dried over
10 anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain 080B_12 (46.0 mg).

[1240] MS (ESI) M/Z: 668.2 [M+H]⁺.

[1241] Step 11: Synthesis of compound 080B

[1242] 080B_12 (45.0 mg, 67.4 μ mol) was dissolved in 1,4-dioxane (0.5 mL), followed by
15 addition of HCl in dioxane (0.5 mL). The reaction mixture was stirred at 25°C for 1 hour. After concentration, the residue was purified by preparative chromatography to obtain 080B (14.67 mg).

[1243] MS (ESI) M/Z: 568.4 [M+H]⁺.

[1244] ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.65 (s, 1H), 8.35 (s, 1H), 7.70 (t, *J* = 53.2 Hz, 1H), 6.94 (s, 1H), 5.34 - 5.29 (m, 1H), 3.93 - 3.86 (m, 2H), 3.51 - 3.47 (m, 2H), 3.36 - 3.35
20 (m, 2H), 3.28 - 3.26 (m, 2H), 2.65 - 2.56 (m, 1H), 2.30 - 2.23 (m, 1H), 2.17 - 2.01 (m, 2H),

1.18 (d, $J = 6.4$ Hz, 6H), 1.12 (s, 3H), 0.74 - 0.66 (m, 2H), 0.46 - 0.39 (m, 2H).

[1245] Step 12: Synthesis of compounds 080B1 and 080B2

[1246] 080B (60.0 mg, 89.8 μ mol) was separated by preparative chromatography (SFC, column: DAICEL CHIRALCEL OD (250 mm $\times$ 30 mm, 10 μ m); mobile phase), and purified
5 by column chromatography (neutral conditions, column: WePure Biotech XP tC18) to obtain 080B1 (6.50 mg, peak 1, $t = 1.647$ min) and 080B2 (8.47 mg, peak 2, $t = 1.896$ min).

[1247] 080B1:

[1248] MS (ESI) M/Z : 568.0 $[M+H]^+$.

[1249] ^1H NMR (400 MHz, DMSO- d_6): δ 9.64 (d, $J = 1.6$ Hz, 1H), 8.34 (s, 1H), 7.70 (t, J
10 = 53.2 Hz, 1H), 6.94 (d, $J = 1.2$ Hz, 1H), 5.34 - 5.31 (m, 1H), 3.88 (t, $J = 6.8$ Hz, 2H), 3.50 - 3.46 (m, 2H), 3.37 - 3.34 (m, 2H), 3.28 - 3.24 (m, 2H), 2.67 - 2.61 (m, 1H), 2.30 - 2.24 (m, 1H), 2.15 - 2.03 (m, 2H), 1.19 (d, $J = 6.4$ Hz, 6H), 1.12 (s, 3H), 0.74 - 0.66 (m, 2H), 0.46 - 0.40 (m, 2H).

[1250] 080B2:

15 **[1251]** MS (ESI) M/Z : 568.1 $[M+H]^+$.

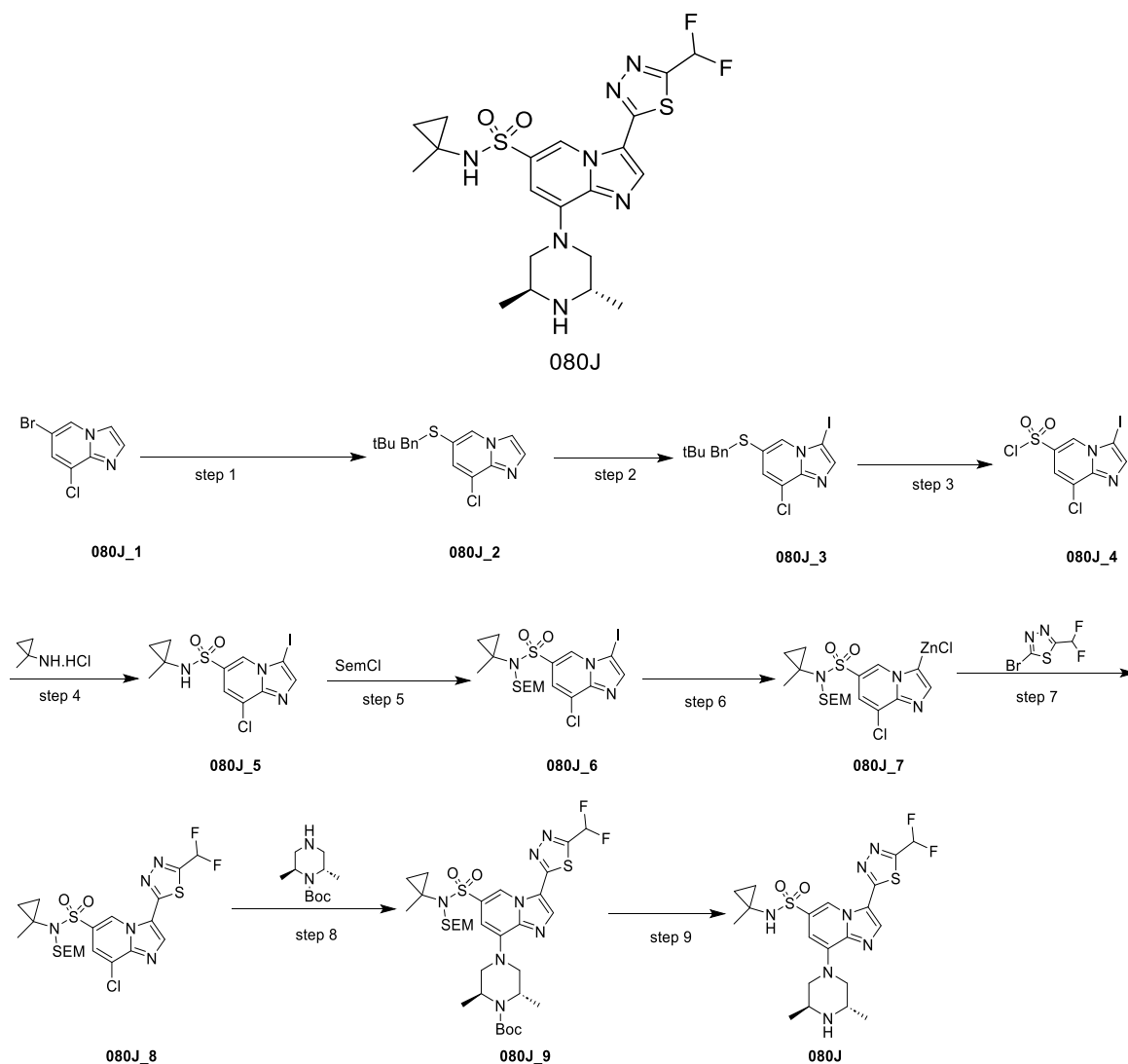
[1252] ^1H NMR (400 MHz, DMSO- d_6): δ 9.65 (s, 1H), 8.35 (s, 1H), 7.70 (t, $J = 53.6$ Hz, 1H), 6.94 (s, 1H), 5.30 (t, $J = 6.4$ Hz, 1H), 3.95 - 3.85 (m, 2H), 3.50 - 3.46 (m, 2H), 3.36 - 3.32 (m, 2H), 3.28 - 3.26 (m, 2H), 2.65 - 2.56 (m, 1H), 2.32 - 2.23 (m, 1H), 2.17 - 2.02 (m, 2H), 1.19 (d, $J = 6.4$ Hz, 6H), 1.12 (s, 3H), 0.74 - 0.66 (m, 2H), 0.47 - 0.40 (m, 2H).

20 **[1253]** The retention time, PARG enzyme activity, or KURAMOCHI cell activity of compound 080B2 prepared in this example were essentially identical to those of example

080B2 prepared by chiral synthesis, confirming that the configuration of compound 080B2 prepared in this example is identical to that of example 080B2 prepared by chiral synthesis, both being the S configuration.

[1254] Other chiral compounds disclosed herein, such as 079J1 and 079J2, 083A1 and 083A2, were confirmed for their chiral structures by referring to the synthesis of 077B2 or 080B2 and PARG enzyme activity or KURAMOCHI cell activity data. The currently recorded structures correspond one-to-one with their retention times.

[1255] Example 080J



[1256] Step 1: Synthesis of compound 080J_2

[1257] Compound 080J_1 (3 g, 12.96 mmol) was dissolved in 1,4-dioxane (30 mL), followed by addition of 4-*tert*-butylbenzyl mercaptan (3.51 g, 19.44 mmol), N,N-diisopropylethylamine (5.02 g, 38.88 mmol), Xantphos (1.50 g, 2.59 mmol), and Pd₂(dba)₃ (1.19 g, 1.30 mmol). The system was thoroughly purged with nitrogen. The reaction mixture was stirred at 100°C for 5 hours under nitrogen atmosphere. The reaction mixture was cooled to room temperature, then quenched with water, and extracted with ethyl acetate (200 mL × 3). The combined organic phases were washed with saturated brine (100 mL × 2), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 080J_2 (3 g).

[1258] MS (ESI) M/Z: 331.1 [M+H]⁺.

[1259] Step 2: Synthesis of compound 080J_3

[1260] 080J_2 (1 g, 3.02 mmol) was dissolved in acetonitrile (10 mL), followed by addition of N-iodosuccinimide (0.75 g, 3.32 mmol) and trifluoroacetic acid (0.69 g, 6.04 mmol). The system was purged with nitrogen. The reaction mixture was stirred at room temperature for 1 hour. LCMS indicated complete conversion of the starting material, and the target product was detected by MS. The reaction mixture was quenched with water and extracted with ethyl acetate (100 mL × 3). The organic phase was washed with saturated brine (100 mL × 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 080J_3 (1.2 g).

[1261] MS (ESI) M/Z: 457.0 [M+H]⁺.

[1262] Step 3: Synthesis of compound 080J_4

[1263] 080J_3 (1.1 g, 2.41 mmol) was dissolved in a mixture of acetonitrile/acetic acid/water (7/2/1, 10 mL), followed by portionwise addition of 1,3-dichloro-5,5-dimethylhydantoin (0.95 g, 4.82 mmol) in an ice bath. The system was thoroughly purged with nitrogen. The reaction mixture was stirred at room temperature for 2 hours under nitrogen atmosphere. The reaction mixture was quenched with water and extracted with ethyl acetate (100 mL × 3). The organic phase was washed with saturated brine (30 mL × 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 080J_4 (0.9 g) as a crude product.

[1264] MS (ESI) M/Z: 376.9 [M+H]⁺.

[1265] Step 4: Synthesis of compound 080J_5

[1266] 080J_4 (0.9 g, 2.39 mmol) was dissolved in dichloromethane (10 mL), followed by addition of 1-methylcyclopropanamine hydrochloride (0.77 g, 7.17 mmol) in an ice bath, and triethylamine (0.73 g, 2.39 mmol) was slowly added thereto. The system was thoroughly purged with nitrogen. The reaction mixture was stirred in an ice bath for 2 hours. The reaction mixture was quenched with water and extracted with dichloromethane (100 mL × 3). The organic phase was washed with saturated brine (50 mL × 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 080J_5 (0.65 g) as a crude

product.

[1267] MS (ESI) M/Z: 412.0 [M+H]⁺.

[1268] Step 5: Synthesis of compound 080J_6

[1269] 080J_5 (1.8 g, 4.37 mmol) was dissolved in N,N-dimethylformamide (20 mL),
5 followed by addition of cesium carbonate (2.85 g, 8.74 mmol) in an ice bath, and 2-(trimethylsilyl)ethoxymethyl chloride (0.87 g, 5.24 mmol) was slowly added thereto. The system was thoroughly purged with nitrogen. The reaction mixture was stirred at room temperature for 16 hours. The reaction mixture was quenched with water and extracted with ethyl acetate (100 mL × 3). The organic phase was washed with saturated brine (100
10 mL × 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 080J_6 (2.1 g) as a crude product.

[1270] MS (ESI) M/Z: 542.0 [M+H]⁺.

[1271] Steps 6 and 7: Synthesis of compound 080J_8

15 **[1272]** 080J_6 (2.1 g, 3.88 mmol) was dissolved in tetrahydrofuran (20 mL). The system was thoroughly purged with nitrogen. The reaction mixture was then cooled to -78°C in a dry ice-ethanol bath. Isopropylmagnesium chloride-lithium chloride complex (0.85 g, 5.82 mmol, 1.3 mol/L) was slowly added dropwise thereto, and the mixture was stirred for 30 minutes. Dichloro(N,N,N',N'-tetramethylethylenediamine)zinc (1.47 g, 5.82 mmol) was
20 added thereto, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was then cooled in an ice bath, followed by addition of 2-bromo-5-

(difluoromethyl)-1,3,4-thiadiazole (1.25 g, 5.82 mmol) and tetrakis(triphenylphosphine)palladium (1.35 g, 1.16 mmol), and stirred at room temperature for 1 hour. The reaction mixture was added with saturated ammonium chloride solution (10 mL) in an ice bath and extracted with ethyl acetate (150 mL $\times$ 3). The organic phase
 5 was washed with saturated brine (100 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 080J_8 (0.45 g).

[1273] MS (ESI) M/Z: 550.1 $[M+H]^+$.

[1274] Step 8: Synthesis of compound 080J_9

10 **[1275]** 080J_8 (2.1 g, 3.88 mmol) was dissolved in 1,4-dioxane (10 mL), followed by addition of *tert*-butyl (2S,6S)-2,6-dimethylpiperazine-1-carboxylate (0.35 g, 1.64 mmol), cesium carbonate (0.8 g, 2.46 mmol), RuPhos (0.077 g, 0.16 mmol), and RuPhos Pd G3 (0.069 g, 0.082 mmol). The system was thoroughly purged with nitrogen. The reaction mixture was then stirred at 90°C for 3 hours. The reaction mixture was then cooled to room
 15 temperature, quenched with water, and extracted with ethyl acetate (150 mL $\times$ 3). The organic phase was washed with saturated brine (100 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation. The residue was purified by column chromatography to obtain 080J_9 (0.35 g).

[1276] MS (ESI) M/Z: 728.2 $[M+H]^+$.

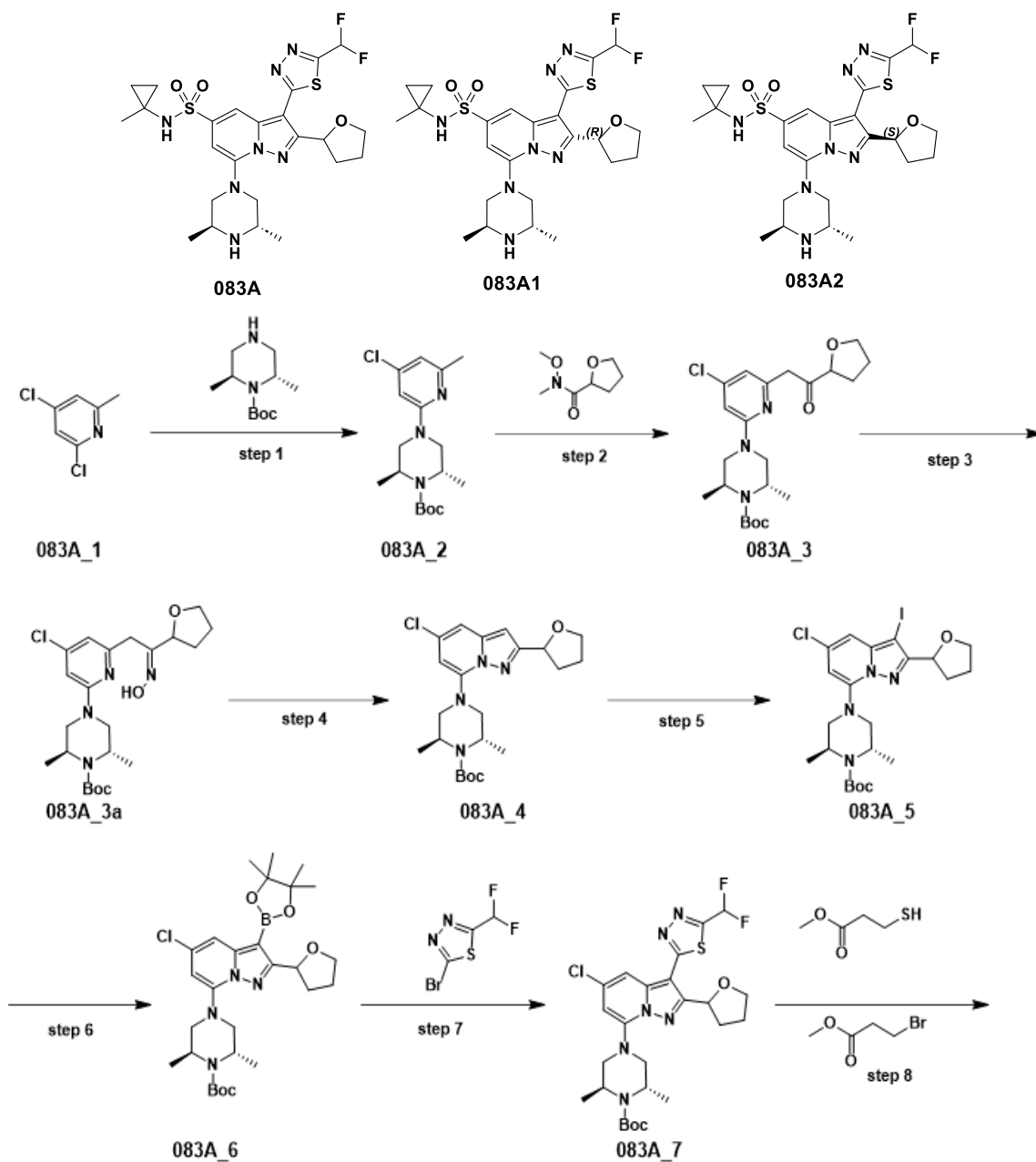
20 **[1277]** Step 9: Synthesis of compound 080J

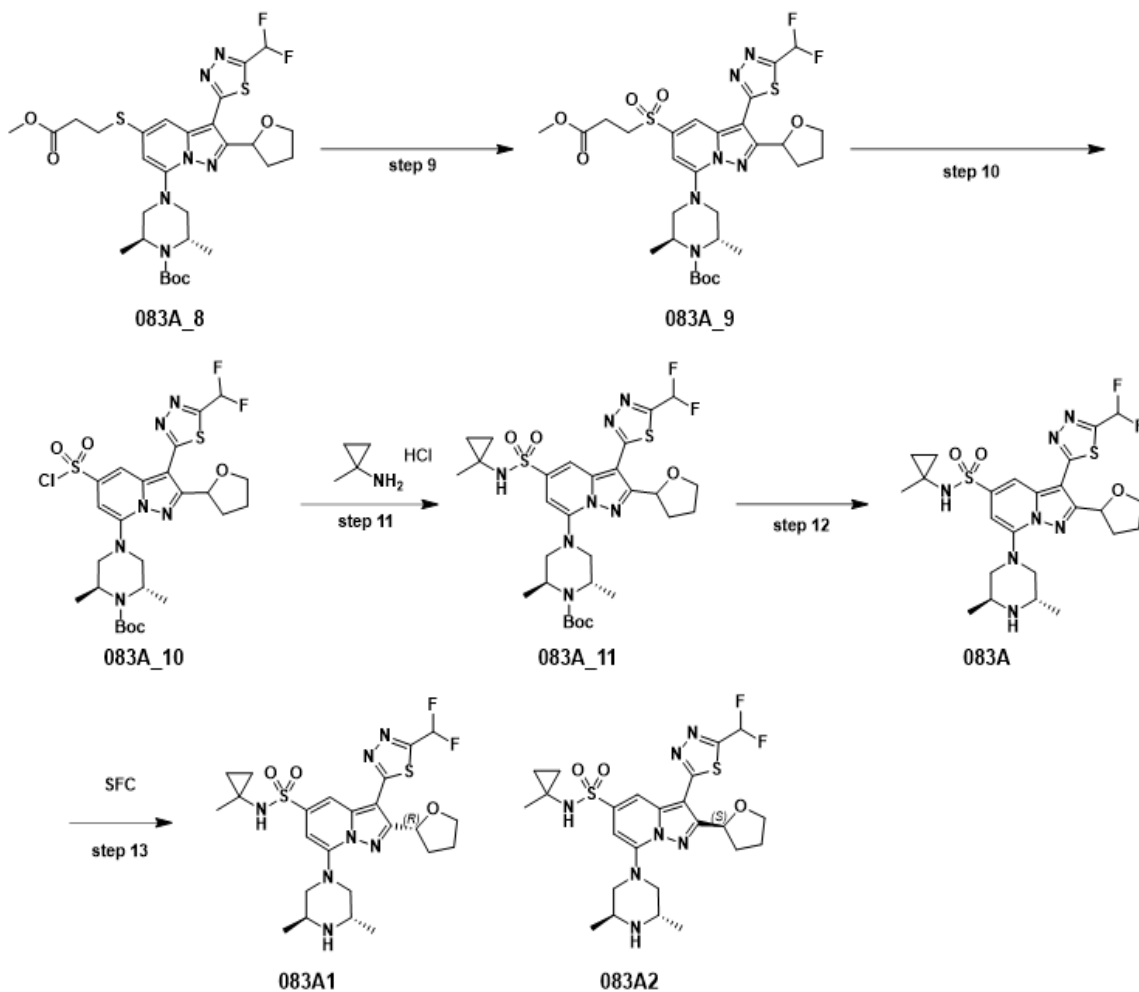
[1278] 080J_9 (87 mg, 0.12 mmol) was dissolved in dichloromethane (10 mL), followed

by addition of trifluoroacetic acid (1 mL) and water (0.5 mL). The system was thoroughly purged with nitrogen. The reaction mixture was then stirred at room temperature for 3 hours. The reaction mixture was concentrated under reduced pressure to remove the solvent. The residue was purified by preparative chromatography to obtain 080J (0.043 g).

5 [1279] MS (ESI) M/Z : 498.2 $[M+H]^+$.

[1280] Examples 083A, 083A1, and 083A2





[1281] Step 1: Synthesis of compound 083A_2

[1282] 083A_1 (20.0 g, 123 mmol), *tert*-butyl (2*S*,6*S*)-2,6-dimethylpiperazine-1-carboxylate (26.5 g, 123 mmol), and anhydrous potassium phosphate (78.6 g, 370 mmol) were dissolved in 1,4-dioxane (500 mL). The system was purged with nitrogen three times, followed by addition of $\text{Pd}(\text{OAc})_2$ (2.77 g, 12.3 mmol) and 1,1'-bis(diphenylphosphino)ferrocene (DPPF, 27.4 g, 49.4 mmol), and purged with nitrogen three additional times. The reaction mixture was heated to 85°C and stirred for 16 hours. The reaction mixture was cooled to room temperature and filtered through diatomite. The filtrate was concentrated by rotary evaporation. The crude product was purified by column

chromatography to obtain 083A_2 (15.8 g).

[1283] MS (ESI) M/Z: 340.3 [M+H]⁺.

[1284] ¹H NMR (400 MHz, DMSO-*d*₆): δ 6.57 (s, 1H), 6.42 (s, 1H), 4.10 - 4.08 (m, 2H), 3.82 - 3.79 (m, 2H), 3.56 - 3.52 (m, 2H), 2.30 (s, 3H), 1.43 (s, 9H), 1.14 (d, *J* = 6.4 Hz, 6H).

5 [1285] Step 2: Synthesis of compound 083A_3

[1286] 083A_2 (6.00 g, 17.7 mmol) was dissolved in tetrahydrofuran (60 mL). The system was purged with nitrogen three times, then cooled to -70°C, and LDA (2 M in tetrahydrofuran, 17.7 mL, 35.4 mmol) was added dropwise thereto. After the addition was completed, the reaction mixture was stirred at -70°C for 2 hours. A solution of N-methoxy-
10 N-methyltetrahydrofuran-2-carboxamide (4.22 g, 26.5 mmol) in tetrahydrofuran (5 mL) was then added dropwise thereto. The reaction mixture was stirred at -70°C for another 1 hour. The reaction mixture was warmed to 0°C, quenched with saturated ammonium chloride aqueous solution (100 mL), and extracted with ethyl acetate (60 mL × 3). The combined organic phases were washed with brine (100 mL × 1), dried over anhydrous sodium sulfate,
15 filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain 083A_3 (6.1 g).

[1287] MS (ESI) M/Z: 438.3 [M+H]⁺.

[1288] Step 3: Synthesis of compound 083A_3a

[1289] 083A_3 (4.00 g, 9.13 mmol), potassium acetate (1.79 g, 18.3 mmol), and
20 hydroxylamine hydrochloride (1.27 g, 18.3 mmol) were dissolved in ethanol (40 mL) and water (5 mL). The reaction mixture was stirred at 25°C for 16 hours. The reaction

mixture was quenched with water (70 mL) and extracted with ethyl acetate (50 mL $\times$ 2). The combined organic phases were washed with saturated brine (100 mL), dried over anhydrous sodium sulfate, filtered, and the filtrate was concentrated by rotary evaporation to obtain 083A_3a (4.00 g).

5 **[1290]** MS (ESI) M/Z: 453.3 $[M+H]^+$.

[1291] ^1H NMR (400 MHz, CDCl_3): δ 9.34 (s, 1H), 6.59 (s, 1H), 6.32 (d, $J = 1.2$ Hz, 1H), 4.55 (t, $J = 7.2$ Hz, 1H), 4.25 (s, 2H), 3.94 - 3.90 (m, 2H), 3.72 - 3.62 (m, 6H), 2.05 - 1.94 (m, 4H), 1.50 (s, 9H), 1.25 - 1.21 (m, 6H).

[1292] Step 4: Synthesis of compound 083A_4

10 **[1293]** 083A_3a (3.00 g, 6.62 mmol), triphenylphosphine (2.61 g, 9.93 mmol), imidazole (902 mg, 13.3 mmol), and elemental iodine (2.52 g, 9.93 mmol) were dissolved in tetrahydrofuran (100 mL). The reaction mixture was heated to 35°C and stirred for 0.5 hours under air atmosphere. The reaction mixture was cooled to room temperature, quenched with saturated sodium sulfite aqueous solution (100 mL), and extracted with ethyl
15 acetate (100 mL $\times$ 2). The combined organic phases were washed with brine (100 mL $\times$ 2), dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by reverse-phase chromatography to obtain 083A_4 (540 mg).

[1294] MS (ESI) M/Z: 435.1 $[M+H]^+$.

[1295] ^1H NMR (400 MHz, CDCl_3): δ 7.02 (d, $J = 1.6$ Hz, 1H), 6.38 (d, $J = 2.4$ Hz, 1H),
20 5.90 (d, $J = 1.6$ Hz, 1H), 5.14 (t, $J = 6.8$ Hz, 1H), 4.22 - 4.20 (m, 2H), 4.01 - 3.93 (m, 4H), 3.57 - 3.53 (m, 2H), 2.34 - 2.32 (m, 1H), 2.25 - 2.23 (m, 1H), 2.09 - 2.01 (m, 2H), 1.51 (s,

9H), 1.38 - 1.35 (m, 6H).

[1296] Step 5: Synthesis of compound 083A_5

[1297] 083A_4 (720 mg, 1.66 mmol) was dissolved in N,N-dimethylformamide (10.0 mL).

N-Iodosuccinimide (372 mg, 1.66 mmol) was added in one portion at 25°C. The reaction
5 mixture was stirred at 25°C for 1 hour. The reaction mixture was quenched with water (20 mL) and extracted with ethyl acetate (15 mL × 2). The extract was washed with saturated sodium sulfite aqueous solution (20 mL) and brine (10 mL × 1), dried over anhydrous sodium sulfate, filtered, and concentrated. The crude product was purified by column chromatography to obtain 083A_5 (800 mg).

10 **[1298]** MS (ESI) M/Z: 561.2 [M+H]⁺.

[1299] ¹H NMR (400 MHz, CDCl₃): δ 7.01 (d, *J* = 1.6 Hz, 1H), 5.96 (d, *J* = 2.0 Hz, 1H), 5.20 - 5.15 (m, 1H), 4.22 - 4.21 (m, 2H), 4.10 - 4.08 (m, 1H), 4.05 - 3.97 (m, 3H), 3.56 - 3.52 (m, 2H), 2.40 - 2.37 (m, 1H), 2.30 - 2.19 (m, 2H), 2.09 - 2.05 (m, 1H), 1.51 (s, 9H), 1.36 - 1.34 (m, 6H).

15 **[1300]** Step 6: Synthesis of compound 083A_6

[1301] 083A_5 (900 mg, 1.60 mmol) and 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (896 mg, 4.81 mmol) were dissolved in tetrahydrofuran (10.0 mL). The system was purged with nitrogen three times. The reaction mixture was cooled to 0°C, followed by dropwise addition of isopropylmagnesium chloride (2 M, 2.41 mL), then
20 warmed to 25°C, and stirred for 0.5 hours. The reaction mixture was quenched with saturated ammonium chloride aqueous solution (10 mL) and extracted with ethyl acetate (10

mL $\times$ 2). The combined organic phases were washed with brine (10 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography to obtain 083A_6 (600 mg).

[1302] MS (ESI) M/Z: 561.2 [M+H]⁺.

5 **[1303]** ¹H NMR (400 MHz, CDCl₃): δ 7.49 (t, *J* = 2.0 Hz, 1H), 5.97 (t, *J* = 2.0 Hz, 1H), 5.58 - 5.53 (m, 1H), 4.21 - 4.18 (m, 2H), 4.01 - 3.97 (m, 4H), 3.57 - 3.53 (m, 2H), 2.32 - 2.23 (m, 3H), 2.21 - 2.04 (m, 1H), 1.51 (s, 9H), 1.38 - 1.34 (m, 6H), 1.29 (s, 12H).

[1304] Step 7: Synthesis of compound 083A_7

[1305] 083A_6 (600 mg, 1.07 mmol), 2-bromo-5-(difluoromethyl)-1,3,4-thiadiazole (690
10 mg, 3.21 mmol), and sodium carbonate (340 mg, 3.21 mmol) were dissolved in 1,4-dioxane (5.00 mL) and water (1.00 mL). The system was purged with nitrogen three times, followed by addition of XPhos (51.0 mg, 107 μ mol) and XPhos Pd G2 (42.1 mg, 53.5 μ mol), and purged with nitrogen three additional times. The reaction mixture was heated to 80°C and stirred for 4 hours. The reaction mixture was cooled to room temperature, then
15 quenched with water (15 mL), and extracted with ethyl acetate (15 mL $\times$ 2). The combined organic phases were washed with saturated brine (20 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography to obtain 083A_7 (200 mg).

[1306] MS (ESI) M/Z: 569.3 [M+H]⁺.

20 **[1307]** ¹H NMR (400 MHz, CDCl₃): δ 8.10 - 8.09 (m, 1H), 7.07 (t, *J* = 54.0 Hz, 1H), 6.17 (d, *J* = 1.6 Hz, 1H), 5.39 - 5.34 (m, 1H), 4.26 - 4.25 (m, 2H), 4.14 - 4.07 (m, 4H), 3.59 - 3.55

(m, 2H), 2.63 - 2.62 (m, 1H), 2.37 - 2.35 (m, 1H), 2.19 - 2.13 (m, 2H), 1.51 (s, 9H), 1.38 (d, $J = 6.4$ Hz, 6H).

[1308] Step 8: Synthesis of compound 083A_8

[1309] Methyl 3-mercaptopropionate (127 mg, 1.05 mmol) was dissolved in N,N-dimethylacetamide (5.00 mL). The system was purged with nitrogen three times. The reaction mixture was cooled to 0°C in an ice-water bath, followed by addition of sodium hydride (56.2 mg, 1.41 mmol, 60% purity), and stirred at 0°C for 10 minutes. 083A_7 (200 mg, 351 μ mol) was then added thereto. After the addition was completed, the reaction mixture was slowly warmed to 25°C and stirred for another 1 hour. Methyl 3-bromopropionate (294 mg, 1.76 mmol) was added thereto, and the mixture was stirred for 30 minutes. The reaction mixture was quenched with saturated ammonium chloride aqueous solution (10 mL) and extracted with ethyl acetate (10 mL $\times$ 2). The combined organic phases were washed with brine (20 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain 083A_8 (200 mg).

[1310] MS (ESI) M/Z: 653.4 $[M+H]^+$.

[1311] ^1H NMR (400 MHz, CDCl_3): δ 7.93 (d, $J = 2.0$ Hz, 1H), 7.06 (t, $J = 54.0$ Hz, 1H), 6.09 (d, $J = 1.6$ Hz, 1H), 5.40 - 5.35 (m, 1H), 4.24 - 4.23 (m, 2H), 4.07 - 4.03 (m, 4H), 3.73 (s, 3H), 3.55 - 3.51 (m, 2H), 3.36 (t, $J = 7.2$ Hz, 2H), 2.79 (t, $J = 7.2$ Hz, 2H), 2.64 - 2.62 (m, 1H), 2.37 - 2.35 (m, 1H), 2.17 - 2.12 (m, 2H), 1.52 (s, 9H), 1.38 (d, $J = 6.4$ Hz, 6H).

[1312] Step 9: Synthesis of compound 083A_9

[1313] 083A_8 (200 mg, 306 μ mol) was dissolved in methanol (10.0 mL), followed by addition of potassium peroxymonosulfate (oxone, 377 mg, 613 μ mol) at room temperature.

The reaction mixture was stirred at 25°C for 0.5 hours. The reaction mixture was quenched with sodium sulfite aqueous solution (15 mL) and extracted with ethyl acetate (15 mL $\times$ 2).

5 The combined organic phases were washed with brine (30 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography to obtain 083A_9 (160 mg).

[1314] MS (ESI) M/Z : 685.4 $[M+H]^+$.

[1315] ^1H NMR (400 MHz, $CDCl_3$): δ 8.55 (d, J = 1.6 Hz, 1H), 7.09 (t, J = 54.0 Hz, 1H),
10 6.56 (s, 1H), 5.43 - 5.38 (m, 1H), 4.30 - 4.20 (m, 4H), 4.10 - 3.95 (m, 2H), 3.67 - 3.62 (m, 5H), 3.56 - 3.52 (m, 2H), 2.88 - 2.83 (m, 2H), 2.75 - 2.55 (m, 1H), 2.45 - 2.35 (m, 1H), 2.20 - 2.10 (m, 2H), 1.53 (s, 9H), 1.39 (d, J = 6.4 Hz, 6H).

[1316] Step 10: Synthesis of compound 083A_10

[1317] 083A_9 (150 mg, 219 μ mol) was dissolved in tetrahydrofuran (10 mL). The
15 reaction mixture was cooled to 0°C, and sodium methoxide (59.2 mg, 1.10 mmol) was added in one portion. The reaction mixture was stirred at 0°C for 30 minutes. After concentration under reduced pressure at room temperature, the crude product was dissolved in dichloromethane (5 mL). The reaction mixture was cooled to 0°C, followed by addition of N-chlorosuccinimide (48.6 mg, 364 μ mol), then slowly warmed to 25°C, and stirred for
20 another 30 minutes. The reaction mixture was quenched with H_2O (10 mL) and extracted with dichloromethane (10 mL $\times$ 2). The combined organic phases were washed with

saturated brine (20 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure at room temperature to obtain 083A_10 (230 mg) as a crude product, which was directly used in the next step without further purification.

[1318] MS (ESI) M/Z : 633.3 $[M+H]^+$.

5 **[1319]** Step 11: Synthesis of compound 083A_11

[1320] 1-Methylcyclopropanamine hydrochloride (78.2 mg, 727 μ mol) and N,N -diisopropylethylamine (141 mg, 1.09 mmol) were dissolved in dichloromethane (5.00 mL). A solution of 083A_10 (230 mg, 363 mmol) in dichloromethane (1 mL) was added dropwise to the reaction mixture. After the addition was completed, the reaction mixture was stirred
10 at 25°C for 10 minutes. The reaction mixture was quenched with water (10 mL) and extracted with dichloromethane (10 mL $\times$ 2). The combined organic phases were washed with saturated brine (10 mL $\times$ 1), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to obtain 083A_11 (125 mg).

15 **[1321]** MS (ESI) M/Z : 668.1 $[M+H]^+$.

[1322] ^1H NMR (400 MHz, CDCl_3): δ 8.53 - 8.52 (m, 1H), 7.08 (t, J = 53.6 Hz, 1H), 6.61 (d, J = 1.6 Hz, 1H), 5.40 (q, J = 6.8 Hz, 1H), 5.12 (s, 1H), 4.29 - 4.26 (m, 2H), 4.19 - 4.15 (m, 2H), 4.13 - 3.95 (m, 2H), 3.63 - 3.59 (m, 2H), 2.66 - 2.63 (m, 1H), 2.40 - 2.38 (m, 1H), 2.19 - 2.15 (m, 2H), 1.52 (s, 9H), 1.38 (d, J = 6.8 Hz, 6H), 1.33 (s, 3H), 0.93 - 0.90 (m, 2H),
20 0.59 - 0.55 (m, 2H).

[1323] Step 12: Synthesis of compound 083A

[1324] 083A_11 (120 mg, 180 μ mol) was dissolved in dioxane (1 mL), followed by addition of 4 M HCl in dioxane (1 mL). The reaction mixture was stirred at 20°C for 0.5 hours. After concentration, the residue was purified by preparative chromatography to obtain 083A (80.0 mg).

5 **[1325]** MS (ESI) M/Z: 568.1 $[M+H]^+$.

[1326] ^1H NMR (400 MHz, DMSO- d_6): δ 8.48 (d, J = 1.6 Hz, 1H), 8.45 (s, 1H), 7.65 (t, J = 53.2 Hz, 1H), 6.80 (s, 1H), 5.43 - 5.38 (m, 1H), 3.92 - 3.85 (m, 2H), 3.37 - 3.23 (m, 6H), 2.62 - 2.60 (m, 1H), 2.33 - 2.31 (m, 1H), 2.11 - 2.05 (m, 2H), 1.26 (d, J = 4.2 Hz, 6H), 1.11 (s, 3H), 0.74 - 0.65 (m, 2H), 0.48 - 0.44 (m, 2H).

10 **[1327]** Step 13: Synthesis of compounds 083A1 and 083A2

[1328] 083A (65 mg, 115 μ mol) was separated by SFC (column: DAICEL CHIRALPAK IG) to obtain 083A1 (25.50 mg, peak 1, t = 1.590 min) and 083A2 (24.22 mg, peak 2, t = 1.898 min).

[1329] 083A2:

15 **[1330]** MS (ESI) M/Z: 568.1 $[M+H]^+$.

[1331] ^1H NMR (400 MHz, DMSO- d_6): δ 8.48 (d, J = 1.6 Hz, 1H), 8.45 (s, 1H), 7.65 (t, J = 53.2 Hz, 1H), 6.80 (s, 1H), 5.42 (t, J = 6.4 Hz, 1H), 3.93 - 3.85 (m, 2H), 3.42 - 3.40 (m, 4H), 3.28 - 3.25 (m, 2H), 2.64 - 2.62 (m, 1H), 2.35 - 2.29 (m, 1H), 2.09 - 2.05 (m, 2H), 1.27 (d, J = 5.6 Hz, 6H), 1.11 (s, 3H), 0.74 - 0.65 (m, 2H), 0.48 - 0.44 (m, 2H).

20 **[1332] 083A1:**

[1333] MS (ESI) M/Z: 568.1 $[M+H]^+$.

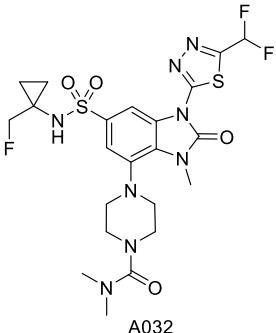
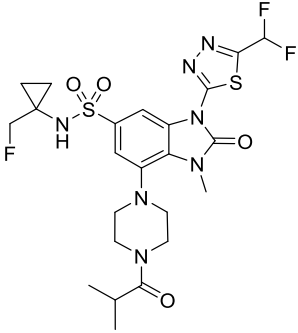
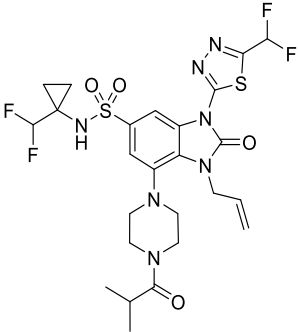
[1334] ^1H NMR (400 MHz, DMSO- d_6): δ 8.49 (d, J = 1.6 Hz, 1H), 8.45 (s, 1H), 7.66 (t, J = 53.2 Hz, 1H), 6.81 (s, 1H), 5.40 (t, J = 6.4 Hz, 1H), 3.93 - 3.89 (m, 2H), 3.46 - 3.40 (m, 4H), 3.28 - 3.25 (m, 2H), 2.59 - 2.50 (m, 1H), 2.33 - 2.30 (m, 1H), 2.11 - 2.04 (m, 2H), 1.29 (d, J = 5.2 Hz, 6H), 1.11 (s, 3H), 0.75 - 0.66 (m, 2H), 0.48 - 0.44 (m, 2H).

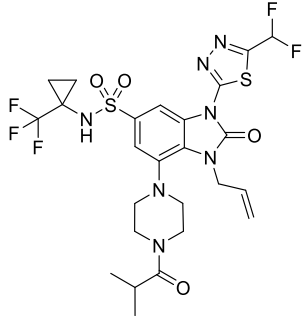
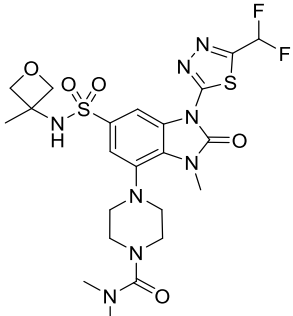
- 5 **[1335]** The compounds listed in Table 14 below can be synthesized according to the synthetic methods described in the above examples, or according to the synthetic schemes of Example 5, Example 14, Example 23, Example 27, Example 29, Example 36, Example 40, Reference Example 1, and comparative compound, or according to methods reported in the prior literature.

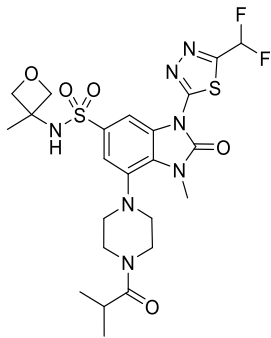
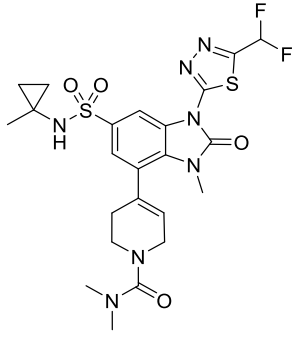
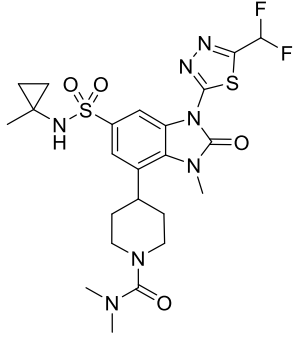
10

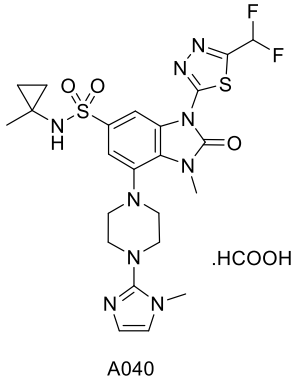
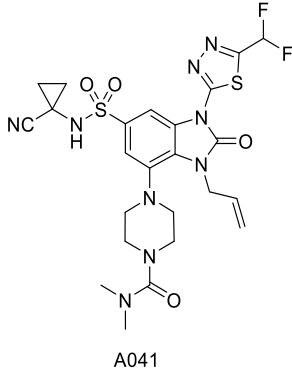
[1336] Table 14

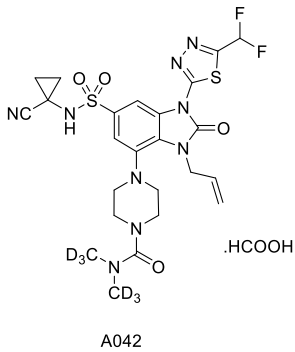
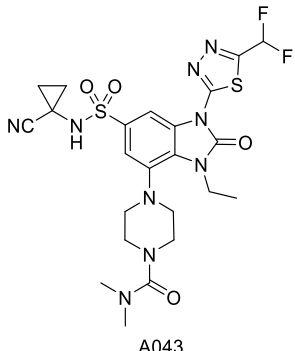
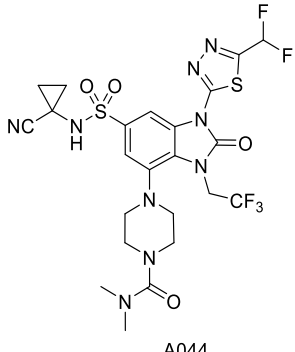
Example	Structural formula	Structural characterization
A031	A031	^1H NMR (400 MHz, DMSO-d_6) δ 9.25 (s, br. 1H), 8.93 (s, br. 1H), 8.68 (d, J = 1.6 Hz, 1H), 8.65 (s, 1H), 7.77 - 7.51 (m, 2H), 4.25 (s, 1H), 4.13 (s, 1H), 3.78 (s, 3H), 3.41 - 3.38 (m, 2H), 3.31 - 3.26 (m, 4H), 3.12 - 3.09 (m, 2H), 0.73 - 0.71 (m, 4H). MS (ESI) M/Z: 518.1 $[\text{M}+\text{H}]^+$.

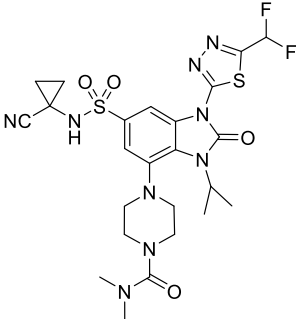
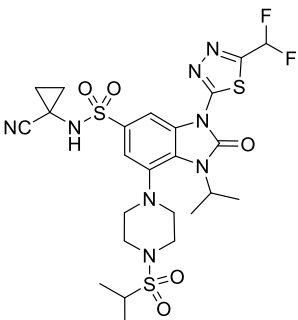
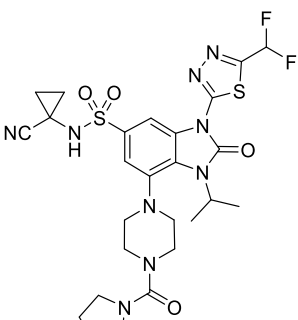
A032	 A032	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.64 (d, <i>J</i> = 1.6 Hz, 1H), 8.51 (s, 1H), 7.77 - 7.50 (m, 2H), 4.24 (s, 1H), 4.12 (s, 1H), 3.79 (s, 3H), 3.65 - 3.56 (m, 2H), 3.15 - 3.05 (m, 4H), 2.92 - 2.84 (m, 2H), 2.80 (s, 6H), 0.72 - 0.69 (m, 4H). MS (ESI) M/Z: 589.2 [M+H]⁺.
A033	 A033	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.65 (d, <i>J</i> = 1.6 Hz, 1H), 8.51 (s, 1H), 7.77 - 7.50 (m, 2H), 4.55 - 4.48 (m, 1H), 4.24 (s, 1H), 4.12 (s, 1H), 4.10 - 4.05 (m, 1H), 3.80 (s, 3H), 3.42 - 3.35 (m, 1H), 3.18 - 3.15 (m, 2H), 3.00 - 2.90 (m, 2H), 2.86 - 2.76 (m, 1H), 2.68 - 2.66 (m, 1H), 1.08 - 1.03 (m, 6H), 0.72 - 0.70 (m, 4H). MS (ESI) M/Z: 588.1 [M+H]⁺.
A034	 A034	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.75 (s, 1H), 8.70 (d, <i>J</i> = 1.6 Hz, 1H), 7.79 - 7.50 (m, 2H), 6.12 - 6.05 (m, 1H), 5.83 (t, <i>J</i> = 56.8 Hz, 1H), 5.17 - 5.08 (m, 2H), 4.95 - 4.92 (m, 2H), 4.52 - 4.42 (m, 1H), 4.10 - 4.00 (m, 1H), 3.37 - 3.35 (m, 1H), 3.08 - 2.99 (m, 2H), 2.98 - 2.90 (m, 1H), 2.88 -

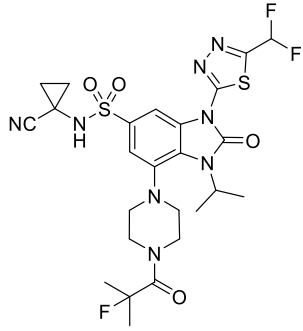
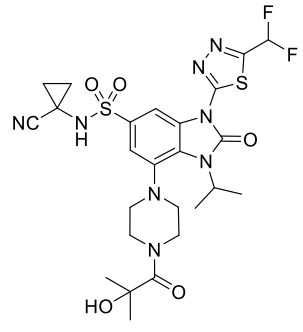
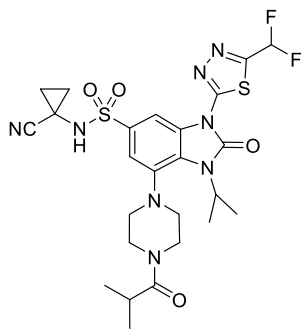
		2.77 (m, 2H), 2.75 - 2.64 (m, 1H), 1.10 - 0.99 (m, 6H), 0.94 - 0.88 (m, 2H), 0.78 - 0.75 (m, 2H). MS (ESI) M/Z: 632.2 [M+H]⁺.
A035	 A035	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.16 (s, 1H), 8.70 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.12 - 6.05 (m, 1H), 5.17 - 5.08 (m, 2H), 4.94 - 4.92 (m, 2H), 4.53 - 4.41 (m, 1H), 4.11 - 3.98 (m, 1H), 3.37 - 3.35 (m, 1H), 3.09 - 2.99 (m, 2H), 2.98 - 2.90 (m, 1H), 2.87 - 2.77 (m, 2H), 2.74 - 2.64 (m, 1H), 1.21 - 1.17 (m, 2H), 1.10 - 0.99 (m, 8H). MS (ESI) M/Z: 650.3 [M+H]⁺.
A036	 A036	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.66 (d, <i>J</i> = 1.6 Hz, 1H), 8.42 (s, 1H), 7.64 - 7.50 (m, 2H), 4.53 (d, <i>J</i> = 6.0 Hz, 2H), 4.09 (d, <i>J</i> = 6.4 Hz, 2H), 3.79 (s, 3H), 3.70 - 3.51 (m, 2H), 3.18 - 3.01 (m, 4H), 2.95 - 2.83 (m, 2H), 2.80 (s, 6H), 1.43 (s, 3H). MS (ESI) M/Z: 587.1 [M+H]⁺.

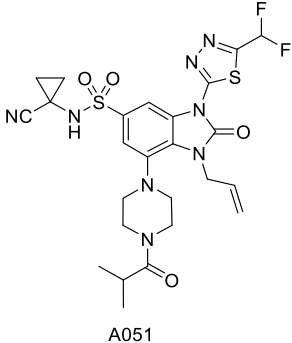
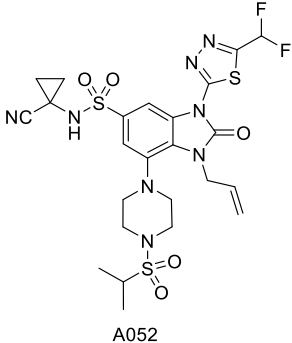
A037	 A037	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.67 (d, <i>J</i> = 1.6 Hz, 1H), 8.40 (s, 1H), 7.77 - 7.50 (m, 2H), 4.53 (d, <i>J</i> = 6.0 Hz, 2H), 4.51 - 4.41 (m, 1H), 4.09 (d, <i>J</i> = 6.0 Hz, 2H), 4.07 - 3.95 (m, 1H), 3.80 (s, 3H), 3.47 - 3.36 (m, 1H), 3.24 - 3.09 (m, 2H), 3.03 - 2.88 (m, 2H), 2.88 - 2.77 (m, 1H), 2.76 - 2.62 (m, 1H), 1.43 (s, 3H), 1.04 (s, 6H). MS (ESI) M/Z: 586.1 [M+H]⁺.
A038	 A038	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.78 (s, 1H), 8.16 (s, 1H), 7.64 (t, <i>J</i> = 53.2 Hz, 1H), 7.53 (s, 1H), 5.84 (s, 1H), 3.89 - 3.87 (m, 2H), 3.47 (s, 3H), 3.44 - 3.41 (m, 2H), 2.80 (s, 6H), 2.48 - 2.46 (m, 2H), 1.09 (s, 3H), 0.64 - 0.61 (m, 2H), 0.40 - 0.36 (m, 2H). MS (ESI) M/Z: 568.2 [M+H]⁺.
A039	 A039	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.78 (d, <i>J</i> = 1.6 Hz, 1H), 8.19 (s, 1H), 7.72 (d, <i>J</i> = 1.6 Hz, 1H), 7.64 (t, <i>J</i> = 53.2 Hz, 1H), 3.78 (s, 3H), 3.73 - 3.69 (m, 2H), 3.56 (t, <i>J</i> = 12.0 Hz, 1H), 2.95 (t, <i>J</i> = 12.0 Hz, 2H), 2.78 (s, 6H), 1.88 - 1.85 (m,

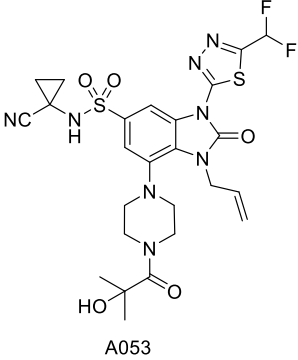
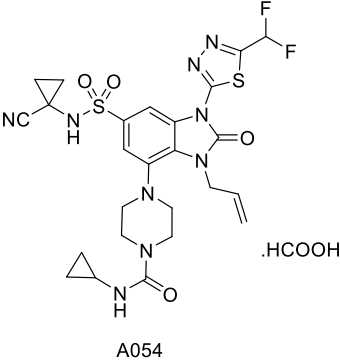
		2H), 1.76 - 1.68 (m, 2H), 1.05 (s, 3H), 0.63 - 0.60 (m, 2H), 0.39 - 0.35 (m, 2H). MS (ESI) M/Z: 570.2 [M+H]⁺.
A040	 A040	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.67 (d, <i>J</i> = 1.6 Hz, 1H), 8.17 (s, 1H), 7.77 - 7.51 (m, 2H), 6.91 (d, <i>J</i> = 1.2 Hz, 1H), 6.64 (d, <i>J</i> = 1.6 Hz, 1H), 3.82 (s, 3H), 3.51 (s, 3H), 3.21 - 3.12 (m, 8H), 1.09 (s, 3H), 0.66 - 0.63 (m, 2H), 0.41 - 0.38 (m, 2H). MS (ESI) M/Z: 580.1 [M+H]⁺.
A041	 A041	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.14 (s, 1H), 8.76 (d, <i>J</i> = 0.8 Hz, 1H), 7.78 - 7.52 (m, 2H), 6.09 - 6.02 (m, 1H), 5.15 - 5.12 (m, 1H), 5.07 - 5.02 (m, 1H), 4.94 - 4.93 (m, 2H), 3.59 - 3.56 (m, 2H), 3.04 - 2.91 (m, 6H), 2.80 (s, 6H), 1.44 - 1.40 (m, 2H), 1.30 - 1.26 (m, 2H). MS (ESI) M/Z: 608.1 [M+H]⁺.

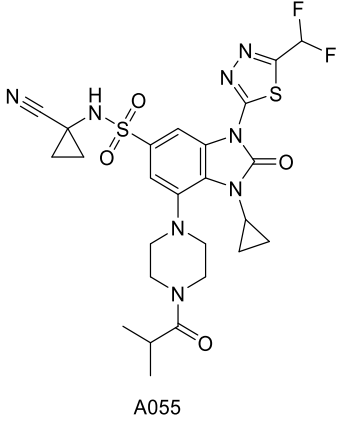
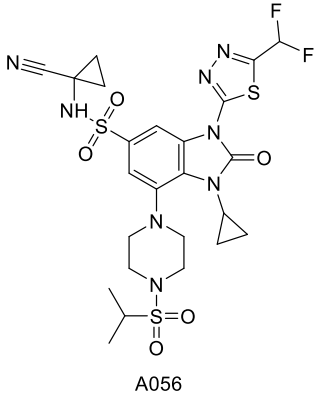
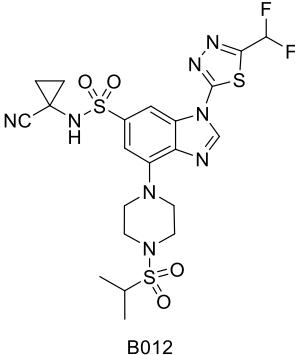
A042	 A042	¹H NMR (400 MHz, CDCl₃-<i>d</i>) δ 8.99 (s, 1H), 7.88 (s, 1H), 7.06 (t, <i>J</i> = 53.6 Hz, 1H), 6.00 - 5.95 (m, 1H), 5.90 (s, 1H), 5.24 - 5.22 (m, 1H), 5.15 - 5.11 (m, 1H), 5.05 - 5.04 (m, 2H), 3.71 - 3.69 (m, 2H), 3.15 - 3.05 (m, 6H), 1.69 - 1.65 (m, 2H), 1.46 - 1.43 (m, 2H). MS (ESI) M/Z: 614.2 [M+H]⁺.
A043	 A043	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.73 (s, 1H), 7.77 - 7.51 (m, 2H), 4.31 - 4.29 (m, 2H), 3.64 - 3.61 (m, 2H), 3.07 - 2.95 (m, 6H), 2.81 (s, 6H), 1.43 - 1.41 (m, 2H), 1.34 - 1.30 (m, 3H), 1.27 - 1.23 (m, 2H). MS (ESI) M/Z: 596.1 [M+H]⁺.
A044	 A044	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.28 (s, 1H), 8.80 (d, <i>J</i> = 1.2 Hz, 1H), 7.92 (d, <i>J</i> = 1.6 Hz, 1H), 7.66 (t, <i>J</i> = 52.8 Hz, 1H), 5.22 - 5.15 (m, 2H), 3.63 - 3.60 (m, 2H), 3.00 - 2.93 (m, 6H), 2.81 (s, 6H), 1.46 - 1.42 (m, 2H), 1.32 - 1.28 (m, 2H). MS (ESI) M/Z: 650.2 [M+H]⁺.

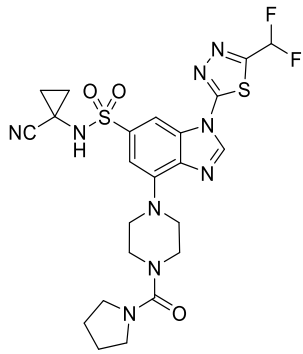
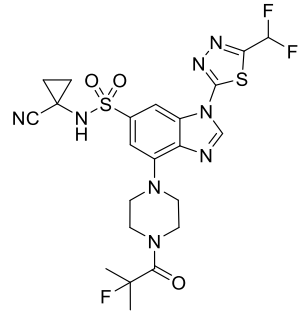
A045	 A045	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.18 (s, 1H), 8.73 (d, <i>J</i> = 1.6 Hz, 1H), 7.80 - 7.50 (m, 2H), 5.92 - 5.82 (m, 1H), 3.65 - 3.61 (m, 2H), 3.13 - 3.00 (m, 4H), 2.97 - 2.86 (m, 2H), 2.81 (s, 6H), 1.56 (d, <i>J</i> = 6.8 Hz, 6H), 1.45 - 1.39 (m, 2H), 1.31 - 1.24 (m, 2H). MS (ESI) M/Z: 610.3 [M+H]⁺.
A046	 A046	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.16 (s, 1H), 8.76 - 8.71 (m, 1H), 7.78 - 7.50 (m, 2H), 5.88 - 5.76 (m, 1H), 3.76 - 3.73 (m, 2H), 3.48 - 3.39 (m, 1H), 3.27 - 3.12 (m, 4H), 2.95 - 2.85 (m, 2H), 1.56 (d, <i>J</i> = 6.8 Hz, 6H), 1.46 - 1.40 (m, 2H), 1.30 - 1.27 (m, 8H) MS (ESI) M/Z: 645.1 [M+H]⁺.
A047	 A047	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.14 (s, 1H), 8.73 (d, <i>J</i> = 1.6 Hz, 1H), 7.80 - 7.49 (m, 2H), 5.93 - 5.82 (m, 1H), 3.77 - 3.73 (m, 2H), 3.35 - 3.33 (m, 3H), 3.31 - 3.30 (m, 1H), 3.12 - 2.98 (m, 4H), 2.95 - 2.84 (m, 2H), 1.81 - 1.74 (m, 4H), 1.57 (d, <i>J</i> = 6.8 Hz, 6H), 1.44 - 1.39 (m, 2H), 1.30 - 1.24 (m, 2H).

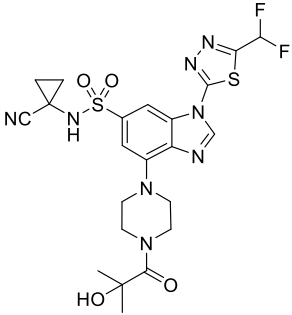
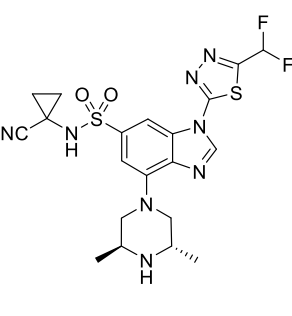
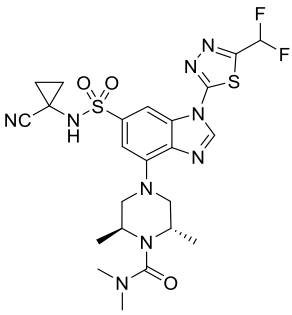
		MS (ESI) M/Z: 636.1 [M+H] ⁺ .
A048	 A048	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.13 (s, 1H), 8.74 (d, <i>J</i> = 1.6 Hz, 1H), 7.79 - 7.47 (m, 2H), 5.94 - 5.82 (m, 1H), 4.48 - 4.44 (m, 2H), 3.56 - 3.39 (m, 1H), 3.20 - 3.17 (m, 2H), 3.09 - 2.96 (m, 1H), 2.93 - 2.78 (m, 2H), 1.63 (s, 3H), 1.60 - 1.55 (m, 9H), 1.46 - 1.39 (m, 2H), 1.30 - 1.25 (m, 2H). MS (ESI) M/Z: 627.1 [M+H]⁺.
A049	 A049	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.14 (s, 1H), 8.73 (d, <i>J</i> = 1.6 Hz, 1H), 7.77 - 7.51 (m, 2H), 5.93 - 5.86 (m, 1H), 5.51 - 3.61 (m, 2H), 5.20 - 4.35 (m, 2H), 3.23 - 3.07 (m, 2H), 3.01 (s, 6H), 1.58 (d, <i>J</i> = 6.8 Hz, 6H), 1.45 - 1.39 (m, 2H), 1.29 - 1.24 (m, 2H). MS (ESI) M/Z: 625.2 [M+H]⁺.
A050	 A050	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.18 (s, 1H), 8.74 (d, <i>J</i> = 1.6 Hz, 1H), 7.80 - 7.48 (m, 2H), 5.97 - 5.80 (m, 1H), 4.55 - 4.50 (m, 1H), 4.14 - 4.08 (m, 1H), 3.44 - 3.34 (m, 1H), 3.18 - 3.13 (m, 2H), 3.00 - 2.93 (m, 1H), 2.92 - 2.82 (m, 2H), 2.79 -

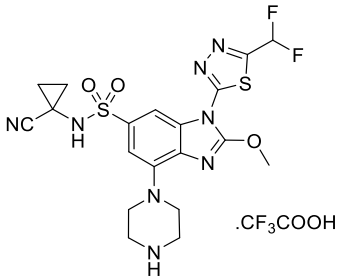
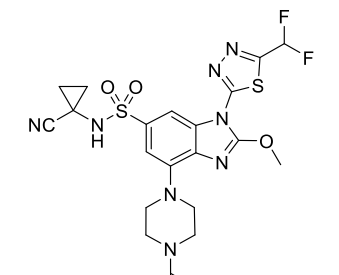
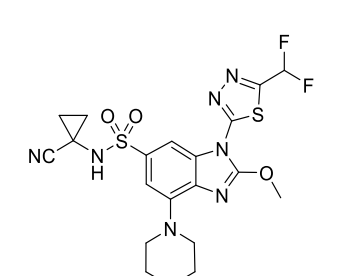
		2.69 (m, 1H), 1.57 (d, $J = 6.8$ Hz, 6H), 1.48 - 1.39 (m, 2H), 1.30 - 1.25 (m, 2H), 1.11 - 0.96 (m, 6H). MS (ESI) M/Z: 609.2 $[M+H]^+$.
A051	 A051	¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 8.76 (d, $J = 1.6$ Hz, 1H), 8.56 (s, 1H), 7.78 - 7.52 (m, 2H), 6.11 - 6.04 (m, 1H), 5.15 - 5.02 (m, 2H), 4.95 - 4.92 (m, 2H), 4.49 - 4.45 (m, 1H), 4.08 - 4.04 (m, 1H), 3.06 - 3.03 (m, 2H), 2.96 - 2.83 (m, 5H), 1.42 - 1.40 (m, 2H), 1.28 - 1.26 (m, 2H), 1.07 - 1.02 (m, 6H). MS (ESI) M/Z: 607.1 $[M+H]^+$.
A052	 A052	¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 9.21 (s, 1H), 8.77 (s, 1H), 7.80 (s, 1H), 7.65 (t, $J = 52.8$ Hz, 1H), 6.11 - 6.03 (m, 1H), 5.14 - 5.12 (m, 1H), 5.05 - 5.00 (m, 1H), 4.93 - 4.91 (m, 2H), 3.71 - 3.68 (m, 2H), 3.45 - 3.41 (m, 1H), 3.25 - 3.15 (m, 2H), 3.08 - 3.05 (m, 2H), 2.94 - 2.85 (m, 2H), 1.44 - 1.41 (m, 2H), 1.31 - 1.27 (m, 8H). MS (ESI) M/Z: 643.1 $[M+H]^+$.

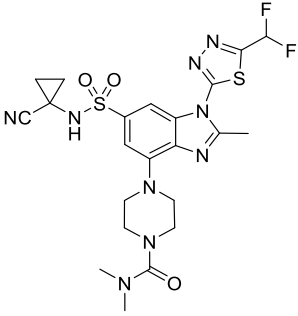
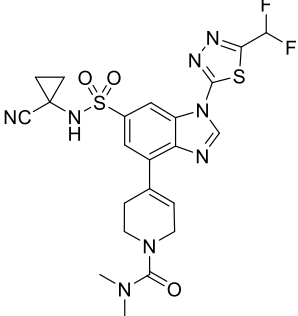
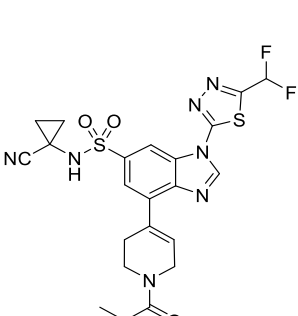
A053	 A053	¹H NMR (400 MHz, CDCl₃-<i>d</i>) δ 8.98 (s, 1H), 7.85 (s, 1H), 7.06 (t, <i>J</i> = 53.6 Hz, 1H), 6.08 - 5.93 (m, 2H), 5.27 - 5.25 (m, 1H), 5.15 - 5.11 (m, 1H), 5.06 - 5.05 (m, 2H), 4.63 - 4.60 (m, 2H), 3.87 - 3.77 (m, 1H), 3.19 - 3.15 (m, 1H), 3.14 - 3.10 (m, 2H), 3.04 - 2.98 (m, 2H), 1.69 - 1.65 (m, 2H), 1.57 (s, 6H), 1.46 - 1.43 (m, 2H). MS (ESI) M/Z: 623.1 [M+H]⁺.
A054	 A054	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.20 (s, 1H), 8.76 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.70 (d, <i>J</i> = 2.4 Hz, 1H), 6.08 - 6.01 (m, 1H), 5.14 - 5.02 (m, 2H), 4.94 - 4.92 (m, 2H), 4.00 - 3.96 (m, 2H), 3.00 - 2.93 (m, 4H), 2.81 - 2.77 (m, 2H), 2.55 - 2.52 (m, 1H), 1.44 - 1.41 (m, 2H), 1.31 - 1.29 (m, 2H), 0.57 - 0.55 (m, 2H), 0.41 - 0.39 (m, 2H). MS (ESI) M/Z: 620.1 [M+H]⁺.

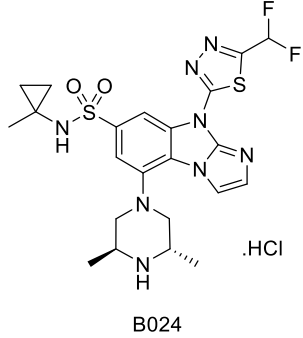
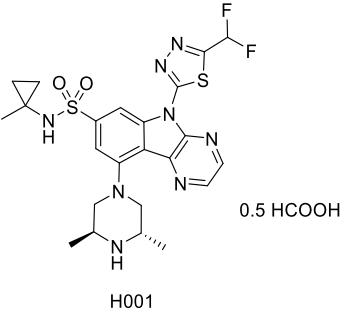
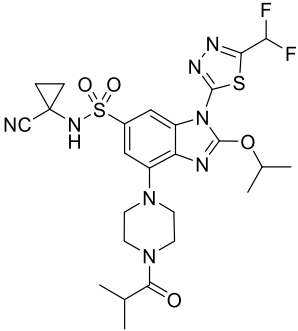
A055	 A055	¹H NMR (400 MHz, CDCl₃-d) δ 8.87 (d, <i>J</i> = 1.2 Hz, 1H), 7.73 (d, <i>J</i> = 1.2 Hz, 1H), 7.03 (t, <i>J</i> = 53.6 Hz, 1H), 6.02 (s, 1H), 4.68 - 4.64 (m, 1H), 3.98 - 3.96 (m, 1H), 3.85 - 3.84 (m, 1H), 3.48 - 3.47 (m, 1H), 3.32 - 3.27 (m, 1H), 3.20 - 2.85 (m, 4H), 2.87 - 2.82 (m, 1H), 1.64 - 1.62 (m, 2H), 1.42 - 1.41 (m, 2H), 1.24 - 1.20 (m, 4H), 1.18 - 1.17 (m, 6H). MS (ESI) M/Z: 607.2 [M+H]⁺.
A056	 A056	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.16 (s, 1H), 8.67 (d, <i>J</i> = 1.6 Hz, 1H), 7.77 - 7.50 (m, 2H), 3.67 - 3.52 (m, 2H), 3.45 - 3.34 (m, 4H), 3.28 - 3.19 (m, 2H), 3.00 - 2.78 (m, 2H), 1.44 - 1.41 (m, 2H), 1.28 - 1.26 (m, 8H), 1.17 - 1.15 (m, 2H), 1.03 - 1.01 (m, 2H). MS (ESI) M/Z: 643.2 [M+H]⁺.
B012	 B012	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.18 (s, 1H), 9.10 (s, 1H), 8.32 (d, <i>J</i> = 1.6 Hz, 1H), 7.68 (t, <i>J</i> = 53.2 Hz, 1H), 7.24 (d, <i>J</i> = 1.6 Hz, 1H), 3.73 - 3.64 (m, 4H), 3.55 - 3.47 (m, 4H), 3.46 - 3.37 (m,

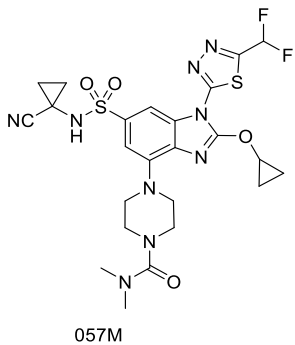
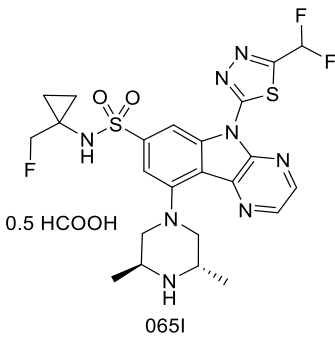
		1H), 1.47 - 1.39 (m, 2H), 1.31 - 1.28 (m, 2H), 1.27 (d, $J = 6.8$ Hz, 6H). MS (ESI) M/Z: 587.3 $[M+H]^+$.
B013	 B013	^1H NMR (400 MHz, DMSO-d_6) δ 9.17 (s, 1H), 9.08 (s, 1H), 8.30 (d, $J = 1.2$ Hz, 1H), 7.69 (t, $J = 53.2$ Hz, 1H), 7.22 (d, $J = 0.8$ Hz, 1H), 3.68 - 3.58 (m, 4H), 3.42 - 3.41 (m, 4H), 3.34 - 3.33 (m, 2H), 3.31 - 3.29 (m, 2H), 1.81 - 1.73 (m, 4H), 1.46 - 1.38 (m, 2H), 1.32 - 1.24 (m, 2H). MS (ESI) M/Z: 578.2 $[M+H]^+$.
B014	 B014	^1H NMR (400 MHz, DMSO-d_6) δ 9.17 (s, 1H), 9.10 (s, 1H), 8.31 (d, $J = 1.2$ Hz, 1H), 7.69 (t, $J = 53.2$ Hz, 1H), 7.23 (d, $J = 1.2$ Hz, 1H), 4.03 - 3.72 (m, 4H), 3.67 - 3.65 (m, 4H), 1.62 (s, 3H), 1.57 (s, 3H), 1.45 - 1.38 (m, 2H), 1.31 - 1.24 (m, 2H). MS (ESI) M/Z: 569.2 $[M+H]^+$.

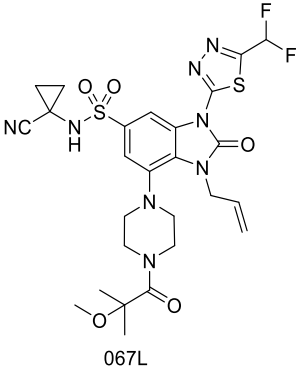
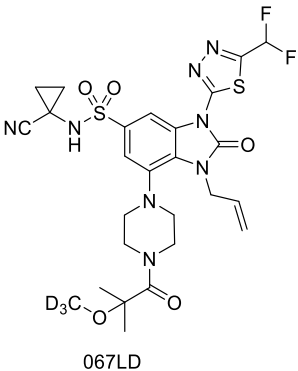
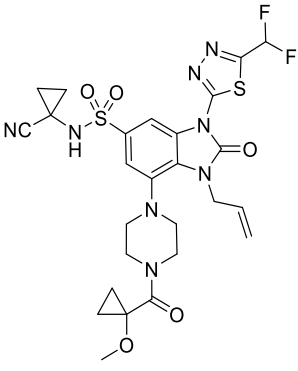
B015	 B015	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.16 (s, 1H), 9.09 (s, 1H), 8.30 (d, <i>J</i> = 1.6 Hz, 1H), 7.68 (t, <i>J</i> = 53.2 Hz, 1H), 7.23 (d, <i>J</i> = 1.2 Hz, 1H), 5.51 (s, 1H), 4.31 - 3.71 (m, 4H), 3.64 - 3.62 (m, 4H), 1.45 - 1.39 (m, 2H), 1.36 (s, 6H), 1.31 - 1.23 (m, 2H). MS (ESI) M/Z: 567.2 [M+H]⁺.
B016	 B016	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.04 (s, 1H), 8.21 (d, <i>J</i> = 1.2 Hz, 1H), 7.68 (t, <i>J</i> = 52.8 Hz, 1H), 7.16 (d, <i>J</i> = 1.6 Hz, 1H), 3.56 - 3.53 (m, 2H), 3.38 - 3.34 (m, 2H), 3.33 - 3.29 (m, 2H), 1.40 - 1.38 (m, 2H), 1.28 - 1.24 (m, 2H), 1.16 (d, <i>J</i> = 6.4 Hz, 6H). MS (ESI) M/Z: 509.1 [M+H]⁺.
B017	 B017	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.07 (s, 1H), 8.25 (s, 1H), 7.68 (t, <i>J</i> = 53.2 Hz, 1H), 7.21 (s, 1H), 3.65 - 3.63 (m, 2H), 3.60 - 3.52 (m, 4H), 2.90 (s, 6H), 1.42 - 1.40 (m, 2H), 1.29 - 1.26 (m, 2H), 1.23 (d, <i>J</i> = 6.0 Hz, 6H). MS (ESI) M/Z: 580.2 [M+H]⁺.

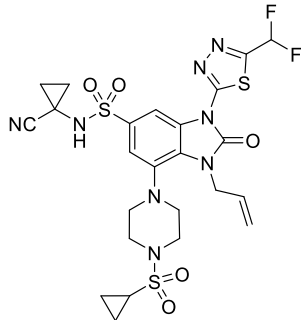
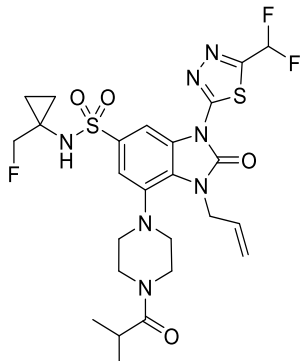
B018	 B018	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.16 (s, 1H), 8.80 (s, 1H), 8.51 (d, <i>J</i> = 1.6 Hz, 1H), 7.66 (t, <i>J</i> = 53.2 Hz, 1H), 7.29 (d, <i>J</i> = 1.6 Hz, 1H), 4.37 (s, 3H), 3.72 - 3.70 (m, 4H), 3.36 - 3.35 (m, 4H), 1.44 - 1.38 (m, 2H), 1.32 - 1.27 (m, 2H). MS (ESI) M/Z: 511.1 [M+H]⁺.
B019	 B019	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.97 (s, 1H), 8.45 (d, <i>J</i> = 1.6 Hz, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 7.25 (d, <i>J</i> = 1.2 Hz, 1H), 4.36 (s, 3H), 3.53 - 3.49 (m, 4H), 3.35 - 3.32 (m, 4H), 2.80 (s, 6H), 1.42 - 1.38 (m, 2H), 1.27 - 1.22 (m, 2H). MS (ESI) M/Z: 582.1 [M+H]⁺.
B020	 B020	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.09 (s, 1H), 8.46 (d, <i>J</i> = 1.2 Hz, 1H), 7.66 (t, <i>J</i> = 53.6 Hz, 1H), 7.25 (d, <i>J</i> = 1.6 Hz, 1H), 4.37 (s, 3H), 3.77 - 3.68 (m, 4H), 3.56 - 3.51 (m, 2H), 3.49 - 3.43 (m, 2H), 2.98 - 2.94 (m, 1H), 1.44 - 1.35 (m, 2H), 1.29 - 1.23 (m, 2H), 1.04 (d, <i>J</i> = 6.4 Hz, 6H). MS (ESI) M/Z: 581.1 [M+H]⁺.

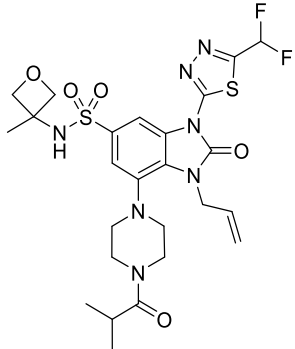
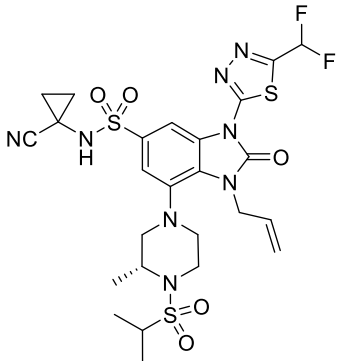
B021	 B021	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.05 (s, 1H), 7.88 (d, <i>J</i> = 1.2 Hz, 1H), 7.69 (t, <i>J</i> = 52.8 Hz, 1H), 7.18 (d, <i>J</i> = 1.2 Hz, 1H), 3.65 - 3.55 (m, 4H), 3.42 - 3.32 (m, 4H), 2.80 (s, 6H), 2.78 (s, 3H), 1.42 - 1.37 (m, 2H), 1.28 - 1.22 (m, 2H). MS (ESI) M/Z: 566.1 [M+H]⁺.
B022	 B022	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.23 (s, 1H), 8.98 (s, 1H), 8.71 (s, 1H), 7.84 (s, 1H), 7.69 (t, <i>J</i> = 53.2 Hz, 1H), 6.96 (s, 1H), 3.97 (d, <i>J</i> = 2.4 Hz, 2H), 3.44 (t, <i>J</i> = 5.6 Hz, 2H), 2.81 - 2.79 (m, 8H), 1.44 - 1.40 (m, 2H), 1.30 - 1.26 (m, 2H). MS (ESI) M/Z: 549.0 [M+H]⁺.
B023	 B023	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.26 (s, 1H), 9.24 (s, 1H), 8.72 (s, 1H), 7.84 (s, 1H), 7.70 (t, <i>J</i> = 52.8 Hz, 1H), 6.95 (s, 1H), 4.37 - 4.23 (m, 2H), 3.80 - 3.77 (m, 2H), 3.03 - 2.91 (m, 1H), 2.84 - 2.72 (m, 2H), 1.43 - 1.41 (m, 2H), 1.30 - 1.27 (m, 2H), 1.07 - 1.03 (m, 6H). MS (ESI) M/Z: 548.1 [M+H]⁺.

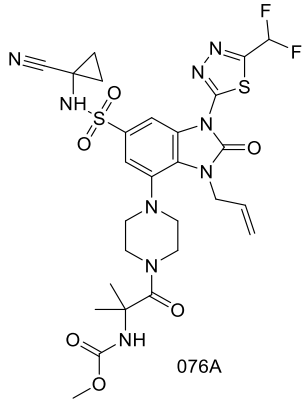
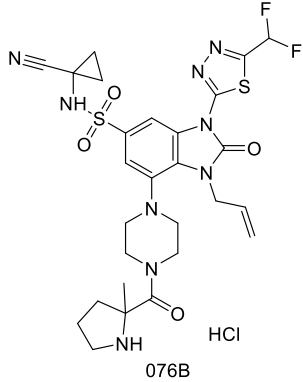
B024	 B024	¹H NMR (400 MHz, CDCl₃-<i>d</i>) δ 10.25 (s, 2H), 9.12 (s, 1H), 7.82 (s, 1H), 7.54 - 7.53 (m, 1H), 7.42 - 7.41 (m, 1H), 7.09 (t, <i>J</i> = 53.6 Hz, 1H), 5.34 (s, 1H), 4.12 - 4.02 (m, 2H), 3.68 - 3.66 (m, 2H), 3.23 - 3.18 (m, 2H), 1.78 - 1.75 (m, 6H), 1.29 (s, 3H), 0.85 - 0.83 (m, 2H), 0.57 - 0.54 (m, 2H). MS (ESI) M/Z: 537.2 [M+H]⁺.
H001	 H001	¹H NMR (400 MHz, CD₃CN-<i>d</i>₃) δ 9.17 (s, 1H), 8.84 (d, <i>J</i> = 2.4 Hz, 1H), 8.58 (d, <i>J</i> = 2.4 Hz, 1H), 8.23 (s, 0.5H, HCOOH), 7.48 (s, 1H), 7.28 (t, <i>J</i> = 53.2 Hz, 1H), 6.37 (s, 1H), 3.75 - 3.74 (m, 2H), 3.65 (d, <i>J</i> = 10.4 Hz, 2H), 3.15 - 3.12 (m, 2H), 1.34 (d, <i>J</i> = 6.0 Hz, 6H), 1.15 (s, 3H), 0.78 - 0.77 (m, 2H), 0.48 - 0.47 (m, 2H). MS (ESI) M/Z: 549.4 [M+H]⁺.
057L	 057L	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.03 (s, 1H), 8.48 (d, <i>J</i> = 1.6 Hz, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 7.24 (d, <i>J</i> = 1.2 Hz, 1H), 5.51 - 5.45 (m, 1H), 3.74 - 3.70 (m, 4H), 3.53 - 3.44 (m, 4H), 2.96 - 2.90 (m, 1H), 1.58 (d, <i>J</i> = 6.4 Hz, 6H), 1.41 - 1.38

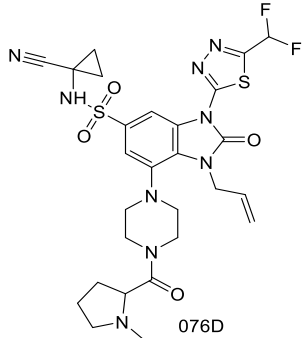
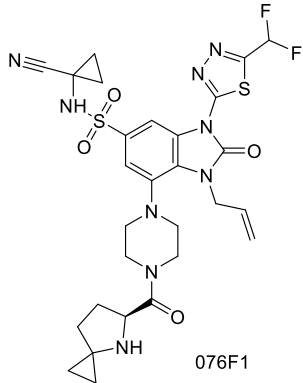
		(m, 2H), 1.27 - 1.23 (m, 2H), 1.04 (d, $J = 6.8$ Hz, 6H). MS (ESI) M/Z: 609.1 $[M+H]^+$.
057M	 057M	^1H NMR (400 MHz, DMSO-d_6) δ 9.06 (s, 1H), 8.46 (d, $J = 1.6$ Hz, 1H), 7.64 (t, $J = 52.8$ Hz, 1H), 7.26 (d, $J = 1.2$ Hz, 1H), 4.80 - 4.75 (m, 1H), 3.54 - 3.52 (m, 4H), 3.36 - 3.33 (m, 4H), 2.80 (s, 6H), 1.42 - 1.38 (m, 2H), 1.27 - 1.24 (m, 2H), 1.13 - 1.08 (m, 2H), 0.97 - 0.94 (m, 2H). MS (ESI) M/Z: 608.4 $[M+H]^+$.
065I	 0.5 HCOOH 065I	^1H NMR (400 MHz, DMSO-d_6) δ 9.08 (s, 1H), 8.92 (d, $J = 2.8$ Hz, 1H), 8.81 (s, 1H), 8.69 (d, $J = 2.4$ Hz, 1H), 8.27 (s, 0.5H), 7.70 (t, $J = 53.2$ Hz, 1H), 7.47 (s, 1H), 4.21 (d, $J = 50.0$ Hz, 2H), 3.64 - 3.62 (m, 2H), 3.54 - 3.52 (m, 2H), 3.10 - 3.06 (m, 2H), 1.27 (d, $J = 6.0$ Hz, 6H), 0.77 - 0.75 (m, 4H). MS (ESI) M/Z: 567.4 $[M+H]^+$.

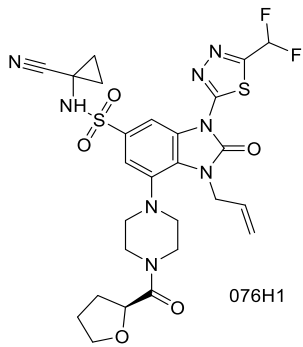
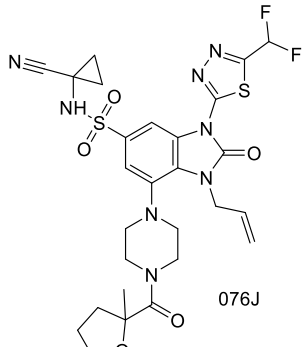
067L	 067L	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.16 (s, 1H), 8.77 (s, 1H), 7.76 (s, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 6.12 - 6.05 (m, 1H), 5.16 - 5.13 (m, 1H), 5.07 - 5.03 (m, 1H), 4.96 - 4.94 (m, 2H), 4.83 - 4.79 (m, 1H), 4.51 - 4.49 (m, 1H), 3.20 (s, 3H), 3.09 - 3.06 (m, 2H), 3.07 - 2.70 (m, 4H), 1.44 - 1.41 (m, 2H), 1.37 (s, 6H), 1.30 - 1.27 (m, 2H). MS (ESI) M/Z: 637.2 [M+H]⁺.
067LD	 067LD	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.77 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.12 - 6.05 (m, 1H), 5.15 - 5.03 (m, 2H), 4.96 - 4.95 (m, 2H), 4.87 - 4.70 (m, 1H), 4.58 - 4.40 (m, 1H), 3.36 - 3.33 (m, 1H), 3.11 - 3.06 (m, 2H), 2.92 - 2.84 (m, 3H), 1.45 - 1.41 (m, 2H), 1.37 (s, 6H), 1.30 - 1.27 (m, 2H). MS (ESI) M/Z: 640.4 [M+H]⁺.
067N	 067N	¹H NMR (400 MHz, CDCl₃) δ 8.90 (s, 1H), 7.85 (d, <i>J</i> = 2.0 Hz, 1H), 7.05 (t, <i>J</i> = 53.6 Hz, 1H), 6.41 (s, 1H), 6.05 - 5.97 (m, 1H), 5.27 - 5.24 (m, 1H), 5.16 - 5.12 (m, 1H), 5.07 - 5.06 (m, 2H), 4.67 - 4.64 (m, 2H), 3.39 (s, 3H), 3.15 - 2.97 (m,

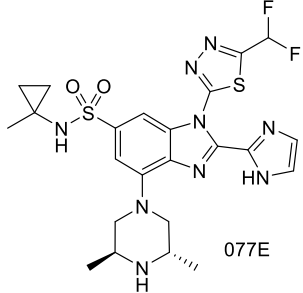
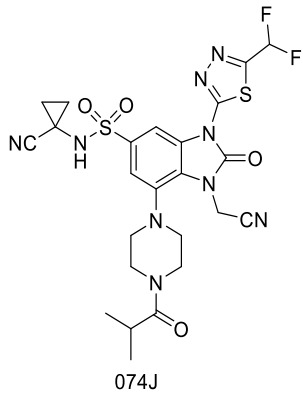
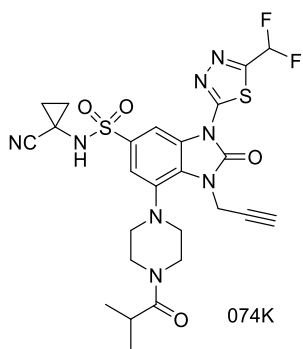
		6H), 1.66 - 1.63 (m, 2H), 1.43 - 1.42 (m, 2H), 1.18 - 1.16 (m, 2H), 1.01 - 0.99 (m, 2H). MS (ESI) M/Z: 635.2 [M+H] ⁺ .
067R	 067R	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.22 (s, 1H), 8.78 (d, <i>J</i> = 2.0 Hz, 1H), 7.80 (d, <i>J</i> = 1.6 Hz, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 6.10 - 6.03 (m, 1H), 5.16 - 5.13 (m, 1H), 5.08 - 5.03 (m, 1H), 4.92 - 4.91 (m, 2H), 3.67 - 3.65 (m, 2H), 3.16 - 3.10 (m, 4H), 3.01 - 2.98 (m, 2H), 2.76 - 2.72 (m, 1H), 1.46 - 1.43 (m, 2H), 1.32 - 1.30 (m, 2H), 1.06 - 1.03 (m, 2H), 0.99 - 0.97 (m, 2H). MS (ESI) M/Z: 641.2 [M+H]⁺.
068A	 068A	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.71 (d, <i>J</i> = 1.2 Hz, 1H), 8.51 (s, 1H), 7.78 - 7.51 (m, 2H), 6.13 - 6.05 (m, 1H), 5.16 - 5.07 (m, 2H), 4.94 - 4.93 (m, 2H), 4.51 - 4.46 (m, 1H), 4.25 (s, 1H), 4.13 (s, 1H), 4.07 - 4.04 (m, 1H), 3.34 - 3.33 (m, 1H), 3.04 - 3.01 (m, 2H), 2.96 - 2.92 (m, 1H), 2.85 - 2.79 (m, 2H), 2.69 - 2.67 (m, 1H), 1.07 - 1.01 (m, 6H), 0.72 - 0.70 (m, 4H). MS (ESI) M/Z: 614.2 [M+H]⁺.

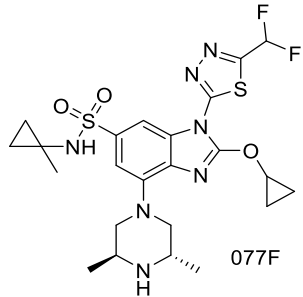
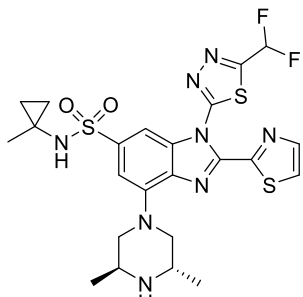
068B	 068B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.74 (d, <i>J</i> = 1.6 Hz, 1H), 8.42 (s, 1H), 7.72 (d, <i>J</i> = 1.6 Hz, 1H), 7.64 (t, <i>J</i> = 53.2 Hz, 1H), 6.12 - 6.05 (m, 1H), 5.17 - 5.08 (m, 2H), 4.94 - 4.93 (m, 2H), 4.54 - 4.46 (m, 3H), 4.10 - 4.04 (m, 3H), 3.36 - 3.33 (m, 1H), 3.04 - 2.96 (m, 2H), 2.94 - 2.91 (m, 1H), 2.87 - 2.82 (m, 2H), 2.73 - 2.67 (m, 1H), 1.44 (s, 3H), 1.04 (d, <i>J</i> = 5.6 Hz, 6H). MS (ESI) M/Z: 612.2 [M+H]⁺.
069B	 069B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.95 (d, <i>J</i> = 1.6 Hz, 1H), 7.91 (d, <i>J</i> = 1.6 Hz, 1H), 7.64 (t, <i>J</i> = 53.2 Hz, 1H), 6.08 - 5.94 (m, 1H), 5.13 (d, <i>J</i> = 10.4 Hz, 1H), 5.05 (d, <i>J</i> = 17.6 Hz, 1H), 5.01 - 4.87 (m, 2H), 4.13 - 4.07 (m, 1H), 2.98 - 2.83 (m, 5H), 2.81 - 2.72 (m, 1H), 2.42 - 2.37 (m, 1H), 2.05 - 1.93 (m, 1H), 1.91 - 1.83 (m, 2H), 1.66 - 1.54 (m, 1H), 1.51 - 1.30 (m, 6H), 0.98 (d, <i>J</i> = 6.0 Hz, 3H). MS (ESI) M/Z: 657.1 [M+H]⁺.

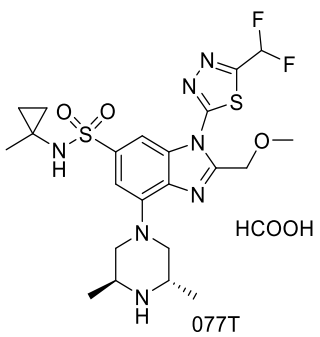
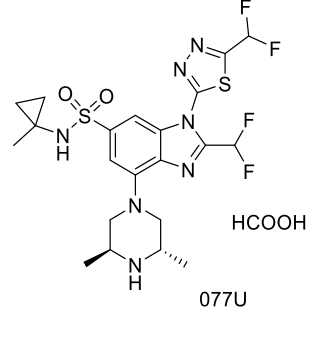
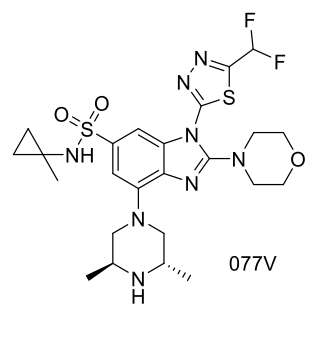
076A	 076A	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.24 (s, 1H), 8.76 (s, 1H), 7.77 - 7.51 (m, 3H), 6.00 - 5.99 (m, 1H), 5.13 (d, <i>J</i> = 10.8 Hz, 1H), 5.04 (d, <i>J</i> = 17.6 Hz, 1H), 4.95 - 4.94 (m, 2H), 4.48 - 4.45 (m, 2H), 3.57 (s, 3H), 3.15 - 2.98 (m, 4H), 2.74 - 2.68 (m, 2H), 1.40 - 1.37 (m, 8H), 1.29 - 1.25 (m, 2H). MS (ESI) M/Z: 680.1 [M+H]⁺.
076B	 076B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.44 - 9.41 (m, 1H), 9.28 (s, 1H), 8.92 - 8.88 (m, 1H), 8.78 (d, <i>J</i> = 1.6 Hz, 1H), 7.84 (d, <i>J</i> = 1.6 Hz, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 6.12 - 6.05 (m, 1H), 5.14 (d, <i>J</i> = 10.8 Hz, 1H), 5.06 (d, <i>J</i> = 17.2 Hz, 1H), 4.96 - 4.95 (m, 2H), 4.52 - 4.38 (m, 1H), 4.03 - 3.95 (m, 1H), 3.50 - 3.43 (m, 1H), 3.24 - 2.87 (m, 7H), 2.39 - 2.19 (m, 2H), 2.13 - 1.88 (m, 2H), 1.65 (s, 3H), 1.44 - 1.40 (m, 2H), 1.31 - 1.28 (m, 2H). MS (ESI) M/Z: 648.3 [M+H]⁺.

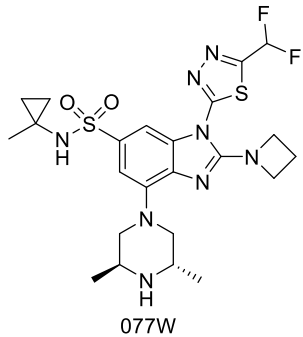
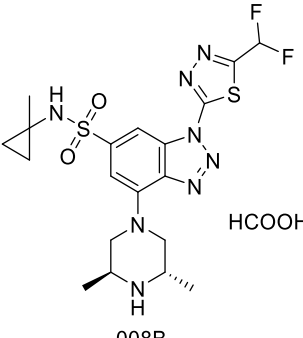
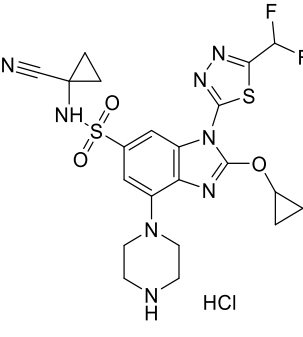
076D		¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.19 (s, 1H), 8.76 (s, 1H), 7.78 - 7.51 (m, 2H), 6.10 - 6.03 (m, 1H), 5.13 (d, <i>J</i> = 10.8 Hz, 1H), 5.04 (d, <i>J</i> = 16.8 Hz, 1H), 4.95 - 4.94 (m, 2H), 4.47 - 4.31 (m, 2H), 3.26 - 3.11 (m, 2H), 3.05 - 2.96 (m, 3H), 2.90 - 2.72 (m, 3H), 2.25 (s, 3H), 2.21 - 2.06 (m, 2H), 1.77 - 1.71 (m, 3H), 1.42 - 1.40 (m, 2H), 1.26 - 1.23 (m, 2H). MS (ESI) M/Z: 648.2 [M+H]⁺.
076F1		¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.76 (s, 1H), 7.78 (s, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 6.12 - 6.03 (m, 1H), 5.13 (d, <i>J</i> = 10.0 Hz, 1H), 5.04 (d, <i>J</i> = 17.6 Hz, 1H), 4.96 - 4.95 (m, 2H), 4.46 - 4.43 (m, 1H), 4.13 - 3.96 (m, 2H), 3.05 - 2.99 (m, 2H), 2.95 - 2.90 (m, 2H), 2.82 - 2.76 (m, 1H), 2.46 - 2.36 (m, 1H), 2.28 - 2.17 (m, 1H), 1.94 - 1.70 (m, 2H), 1.57 - 1.54 (m, 1H), 1.43 - 1.40 (m, 2H), 1.29 - 1.26 (m, 2H), 0.73 - 0.68 (m, 1H), 0.59 - 0.54 (m, 1H), 0.49 - 0.44 (m, 1H), 0.37 - 0.32 (m, 1H). MS (ESI) M/Z: 660.2 [M+H]⁺.

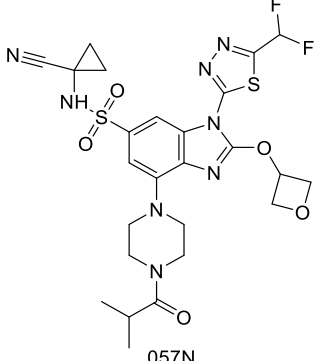
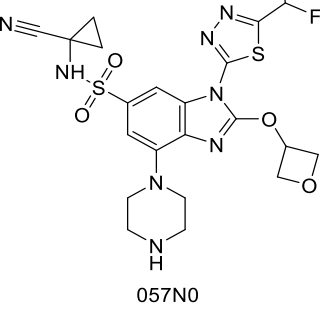
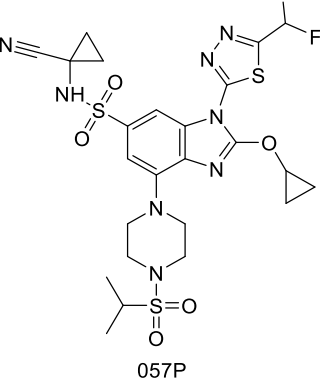
076H1	 076H1	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.76 (d, <i>J</i> = 1.6 Hz, 1H), 8.40 (s, 1H), 7.78 - 7.51 (m, 2H), 6.12 - 6.03 (m, 1H), 5.13 (d, <i>J</i> = 10.4 Hz, 1H), 5.04 (d, <i>J</i> = 17.6 Hz, 1H), 4.96 - 4.94 (m, 2H), 4.75 - 4.72 (m, 1H), 4.43 - 4.39 (m, 1H), 4.12 - 4.09 (m, 1H), 3.84 - 3.72 (m, 2H), 3.31 - 3.26 (m, 1H), 3.04 - 3.02 (m, 2H), 2.91 - 2.82 (m, 2H), 2.80 - 2.73 (m, 1H), 2.12 - 2.01 (m, 2H), 1.87 - 1.82 (m, 2H), 1.41 - 1.38 (m, 2H), 1.27 - 1.25 (m, 2H). MS (ESI) M/Z: 635.2 [M+H]⁺.
076J	 076J	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.18 (s, 1H), 8.77 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.12 - 6.03 (m, 1H), 5.13 (d, <i>J</i> = 10.4 Hz, 1H), 5.05 (d, <i>J</i> = 17.2 Hz, 1H), 4.96 - 4.95 (m, 2H), 4.81 - 4.60 (m, 1H), 4.56 - 4.35 (m, 1H), 3.92 - 3.84 (m, 1H), 3.82 - 3.72 (m, 1H), 3.31 - 3.18 (m, 1H), 3.17 - 3.04 (m, 2H), 2.94 - 2.76 (m, 3H), 2.70 - 2.66 (m, 1H), 1.92 - 1.82 (m, 1H), 1.81 - 1.72 (m, 1H), 1.62 - 1.57 (m, 1H), 1.42 - 1.40 (m, 5H), 1.30 - 1.26 (m, 2H).

		MS (ESI) M/Z: 649.2 [M+H] ⁺ .
077E		¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.03 (s, 1H), 7.67 (t, <i>J</i> = 53.2 Hz, 1H), 7.49 - 7.26 (m, 2H), 7.09 - 7.05 (m, 2H), 3.64 - 3.61 (m, 2H), 3.46 - 3.42 (m, 2H), 3.38 - 3.34 (m, 2H), 1.20 (d, <i>J</i> = 6.4 Hz, 6H), 1.04 (s, 3H), 0.62 - 0.59 (m, 2H), 0.37 - 0.34 (m, 2H). MS (ESI) M/Z: 564.3 [M+H]⁺.
074J		¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.73 (d, <i>J</i> = 1.6 Hz, 1H), 7.85 (d, <i>J</i> = 1.7 Hz, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 5.40 (s, 2H), 4.56 - 4.42 (m, 1H), 4.15 - 4.10 (m, 1H), 3.55 - 3.40 (m, 1H), 3.14 - 3.07 (m, 2H), 3.01 - 2.91 (m, 3H), 2.86 - 2.78 (m, 1H), 1.39 (q, <i>J</i> = 5.3, 4.6 Hz, 2H), 1.30 - 1.25 (m, 2H), 1.06 (s, 6H). MS (ESI) M/Z: 606.2 [M+H]⁺.
074K		¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.25 (s, 1H), 8.75 (d, <i>J</i> = 1.7 Hz, 1H), 7.80 (d, <i>J</i> = 1.7 Hz, 1H), 7.64 (t, <i>J</i> = 53.2 Hz, 1H), 5.17 (d, <i>J</i> = 6.7 Hz, 2H), 4.56 - 4.39 (m, 1H), 4.16 - 4.02 (m, 1H), 3.50 - 3.38 (m, 2H), 3.20 - 3.10 (m, 2H), 3.02 -

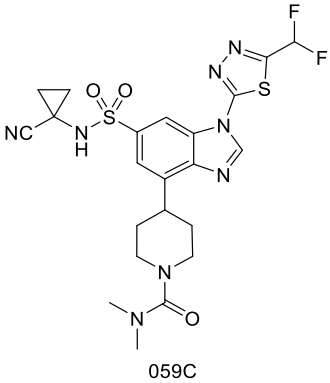
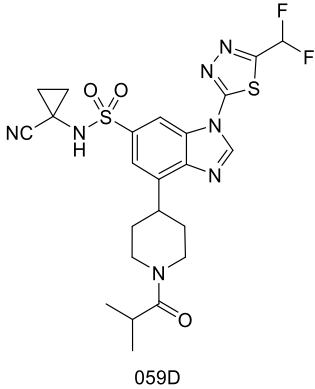
		2.90 (m, 3H), 2.84 - 2.74 (m, 1H), 1.47 - 1.39 (m, 2H), 1.31 - 1.26 (m, 2H), 1.05 (s, 6H). MS (ESI) M/Z: 605.2 [M+H]⁺.
077F	 077F	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.42 (d, <i>J</i> = 1.5 Hz, 1H), 8.08 (s, 1H), 7.64 (t, <i>J</i> = 53.0 Hz, 1H), 7.24 (d, <i>J</i> = 1.7 Hz, 1H), 4.72 (tt, <i>J</i> = 6.1, 2.8 Hz, 1H), 3.78 - 3.70 (m, 2H), 3.66 - 3.58 (m, 2H), 3.55 - 3.47 (m, 2H), 1.42 (d, <i>J</i> = 6.4, 6H), 1.12 - 1.07 (m, 2H), 1.05 (s, 3H), 0.96 - 0.92 (m, 2H), 0.68 - 0.58 (m, 2H), 0.42 - 0.32 (m, 2H). MS (ESI) M/Z: 554.2 [M+H]⁺.
077S	 077S	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.10 (s, 1H), 8.06 (d, <i>J</i> = 3.2 Hz, 1H), 7.94 (d, <i>J</i> = 3.2 Hz, 1H), 7.70 (t, <i>J</i> = 53.1 Hz, 1H), 7.32 (d, <i>J</i> = 1.4 Hz, 1H), 7.19 (d, <i>J</i> = 1.5 Hz, 1H), 3.88 - 3.62 (m, 6H), 1.24 (d, <i>J</i> = 6.1 Hz, 6H), 1.04 (s, 3H), 0.68 - 0.58 (m, 2H), 0.42 - 0.33 (m, 2H). MS (ESI) M/Z: 581.2 [M+H]⁺.

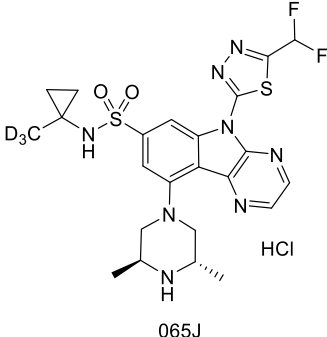
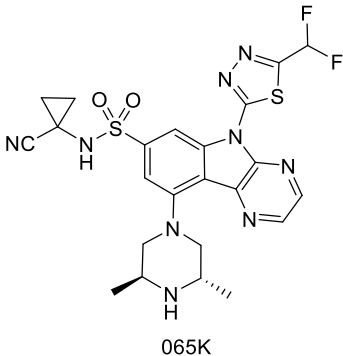
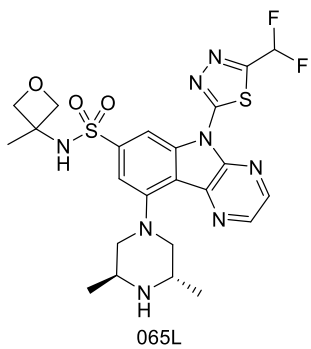
077T	 077T	¹H NMR (400 MHz, DMSO-<i>d</i>₆+D₂O) δ 8.39 (s, 1H), 7.88 (d, <i>J</i> = 1.4 Hz, 1H), 7.61 (t, <i>J</i> = 53.1 Hz, 1H), 7.19 (d, <i>J</i> = 1.6 Hz, 1H), 4.86 (s, 2H), 3.77 - 3.51 (m, 6H), 3.35 (s, 3H), 1.36 (d, <i>J</i> = 6.1 Hz, 6H), 1.05 (s, 3H), 0.68 - 0.58 (m, 2H), 0.51 - 0.32 (m, 2H). MS (ESI) M/Z: 542.2 [M+H]⁺.
077U	 077U	¹H NMR (400 MHz, DMSO-<i>d</i>₆+D₂O) δ 8.38 (s, 1H), 7.69 - 7.25 (m, 3H), 7.25 (s, 1H), 7.40 (d, <i>J</i> = 1.4 Hz, 1H), 7.25 (d, <i>J</i> = 1.5 Hz, 1H), 3.90 - 3.65 (m, 6H), 1.42 (d, <i>J</i> = 6.2 Hz, 6H), 1.06 (s, 3H), 0.68 - 0.59 (m, 2H), 0.50 - 0.39 (m, 2H). MS (ESI) M/Z: 548.2 [M+H]⁺.
077V	 077V	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.43 (s, 1H), 8.25 (d, <i>J</i> = 1.5 Hz, 1H), 7.59 (t, <i>J</i> = 53.2 Hz, 1H), 7.18 (d, <i>J</i> = 1.6 Hz, 1H), 3.90 - 3.80 (m, 4H), 3.57 - 3.40 (m, 6H), 3.33 - 3.21 (m, 4H), 1.33 (d, <i>J</i> = 5.4 Hz, 6H), 1.05 (s, 3H), 0.69 - 0.57 (m, 2H), 0.42 - 0.33 (m, 2H). MS (ESI) M/Z: 583.2 [M+H]⁺.

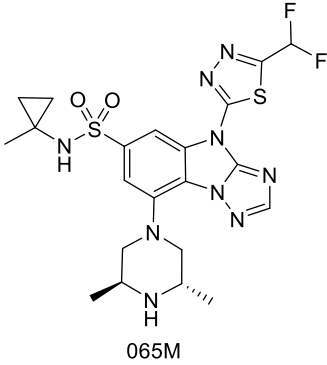
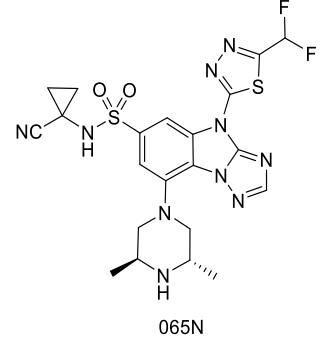
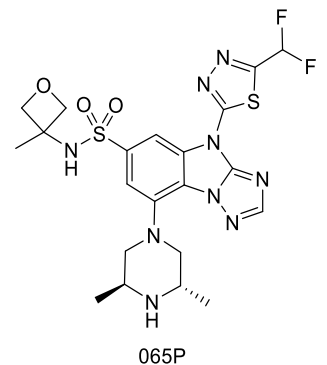
077W	 077W	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.41 (s, 1H), 7.78 (d, <i>J</i> = 1.5 Hz, 1H), 7.59 (t, <i>J</i> = 53.2 Hz, 1H), 7.13 (d, <i>J</i> = 1.6 Hz, 1H), 4.12 (t, <i>J</i> = 7.7 Hz, 4H), 3.60 - 3.53 (m, 2H), 3.50 - 3.43 (m, 4H), 2.43 - 2.34 (m, 2H), 1.34 (d, <i>J</i> = 6.5 Hz, 6H), 1.03 (s, 3H), 0.66 - 0.56 (m, 2H), 0.42 - 0.32 (m, 2H). MS (ESI) M/Z: 553.2 [M+H]⁺.
008B	 008B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.42 - 8.31 (m, 1H), 8.07 (d, <i>J</i> = 6.0 Hz, 1H), 7.84 - 7.51 (m, 1H), 7.14 (d, <i>J</i> = 5.2 Hz, 1H), 3.88 - 3.79 (m, 2H), 3.66 - 3.56 (m, 2H), 2.61 - 2.54 (m, 2H), 1.18 - 1.02 (m, 9H), 0.72 - 0.61 (m, 2H), 0.45 - 0.35 (m, 2H). ¹⁹F NMR (376 MHz, DMSO-<i>d</i>₆) δ -110.28. MS (ESI) M/Z: 499.1 [M+H]⁺.
057M0	 057M0	¹H NMR (400 MHz, MeOD-<i>d</i>₄) δ 8.74 - 8.73 (m, 1H), 7.43 - 7.16 (m, 2H), 4.95 - 4.85 (m, 1H), 3.86 - 3.84 (m, 4H), 3.51 - 3.48 (m, 4H), 1.51 - 1.47 (m, 2H), 1.41 - 1.37 (m, 2H), 1.16 - 1.11 (m, 2H), 1.03 - 1.00 (m, 2H). MS (ESI) M/Z: 537.4 [M+H]⁺.

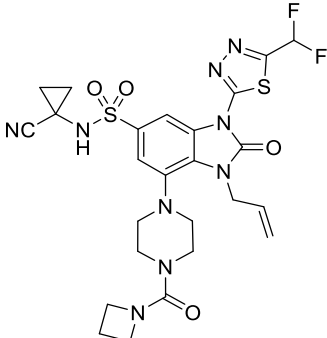
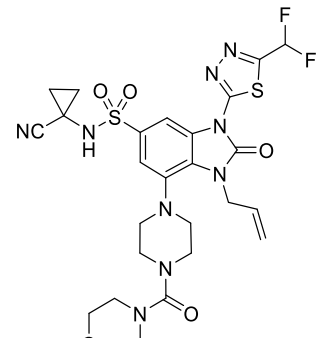
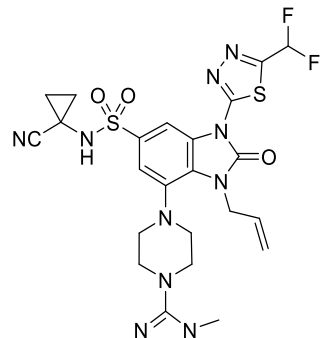
057N	 057N	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.08 (s, 1H), 8.46 (d, <i>J</i> = 1.2 Hz, 1H), 7.67 (t, <i>J</i> = 53.2 Hz, 1H), 7.23 (d, <i>J</i> = 1.2 Hz, 1H), 5.99 - 5.93 (m, 1H), 5.04 - 5.00 (m, 2H), 4.91 - 4.87 (m, 2H), 3.73 - 3.68 (m, 4H), 3.52 - 3.38 (m, 4H), 2.98 - 2.91 (m, 1H), 1.41 - 1.38 (m, 2H), 1.27 - 1.23 (m, 2H), 1.04 (d, <i>J</i> = 6.8 Hz, 6H). MS (ESI) M/Z: 623.3 [M+H]⁺.
057N0	 057N0	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.40 (s, 1H), 7.66 (t, <i>J</i> = 53.2 Hz, 1H), 7.18 (s, 1H), 6.11 - 6.07 (m, 1H), 5.96 - 5.91 (m, 1H), 5.00 - 4.97 (m, 2H), 4.89 - 4.86 (m, 2H), 3.53 - 3.47 (m, 5H), 2.91 - 2.89 (m, 3H), 1.33 - 1.29 (m, 2H), 1.23 (s, 1H), 1.19 - 1.15 (m, 2H). MS (ESI) M/Z: 553.3 [M+H]⁺.
057P	 057P	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.07 (s, 1H), 8.47 (d, <i>J</i> = 0.8 Hz, 1H), 7.63 (t, <i>J</i> = 52.8 Hz, 1H), 7.27 (s, 1H), 4.79 - 4.75 (m, 1H), 3.62 - 3.55 (m, 4H), 3.54 - 3.47 (m, 4H), 3.44 - 3.38 (m, 1H), 1.42 - 1.38 (m, 2H), 1.30 - 1.23 (m, 8H), 1.11 - 1.07 (m, 2H), 0.97 - 0.92 (m, 2H).

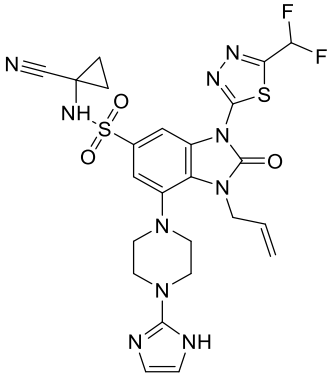
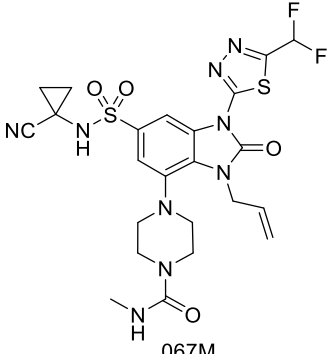
		MS (ESI) M/Z: 643.3 [M+H] ⁺ .
057Q	057Q	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.06 (s, 1H), 8.46 (s, 1H), 7.63 (t, <i>J</i> = 53.6 Hz, 1H), 7.25 (s, 1H), 4.83 - 4.78 (m, 1H), 3.80 - 3.65 (m, 4H), 3.55 - 3.48 (m, 4H), 2.98 - 2.94 (m, 1H), 1.39 - 1.35 (m, 2H), 1.26 - 1.22 (m, 2H), 1.10 - 0.94 (m, 10H). MS (ESI) M/Z: 607.4 [M+H]⁺.
058B	058B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 12.51 (s, 1H), 8.73 (d, <i>J</i> = 1.6 Hz, 1H), 7.77 - 7.50 (m, 2H), 6.08 - 6.06 (m, 1H), 5.86 - 5.79 (m, 1H), 5.37 - 5.33 (m, 1H), 5.25 - 5.23 (m, 1H), 3.99 - 3.97 (m, 2H), 3.90 - 3.89 (m, 2H), 3.41 - 3.38 (m, 2H), 2.79 (s, 6H), 2.55 - 2.51 (m, 2H), 1.59 - 1.57 (m, 4H). MS (ESI) M/Z: 605.2 [M+H]⁺.
058E	058E	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 12.53 (s, 1H), 8.74 (s, 1H), 7.77 - 7.50 (m, 2H), 6.10 - 6.08 (m, 1H), 5.85 - 5.77 (m, 1H), 5.37 - 5.33 (m, 1H), 5.25 - 5.23 (m, 1H), 4.26 - 4.16 (m, 2H), 3.99 - 3.97 (m, 2H), 3.75 - 3.74 (m, 2H), 2.99 - 2.96 (m,

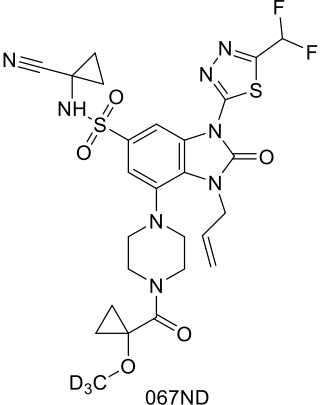
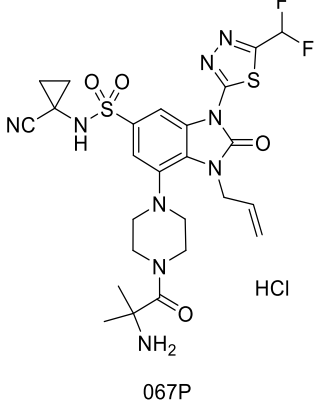
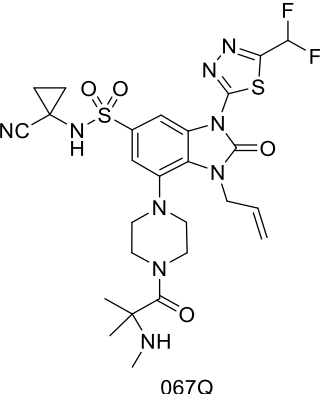
		1H), 2.60 - 2.58 (m, 2H), 1.59 - 1.57 (m, 4H), 1.05 (d, $J = 6.8$ Hz, 6H). MS (ESI) M/Z: 604.2 $[M+H]^+$.
059C	 059C	^1H NMR (400 MHz, DMSO-d_6) δ 9.20 (s, 1H), 8.66 - 8.65 (m, 2H), 7.78 (s, 1H), 7.69 (t, $J = 53.2$ Hz, 1H), 3.75 - 3.72 (m, 2H), 3.58 - 3.50 (m, 1H), 2.95 - 2.92 (m, 2H), 2.78 (s, 6H), 1.90 - 1.78 (m, 4H), 1.42 - 1.38 (m, 2H), 1.29 - 1.25 (m, 2H). MS (ESI) M/Z: 551.1 $[M+H]^+$.
059D	 059D	^1H NMR (400 MHz, DMSO-d_6) δ 9.21 (s, 1H), 8.66 (s, 1H), 8.43 (s, 1H), 7.77 (s, 1H), 7.69 (t, J $= 53.2$ Hz, 1H), 4.66 - 4.62 (m, 1H), 4.17 - 4.13 (m, 1H), 3.63 (t, $J = 12.0$ Hz, 1H), 3.25 (t, $J =$ 12.8 Hz, 1H), 2.97 - 2.92 (m, 1H), 2.74 - 2.70 (m, 1H), 2.02 - 1.97 (m, 2H), 1.80 - 1.65 (m, 2H), 1.41 - 1.39 (m, 2H), 1.30 - 1.27 (m, 2H), 1.07 - 1.01 (m, 6H). MS (ESI) M/Z: 550.1 $[M+H]^+$.

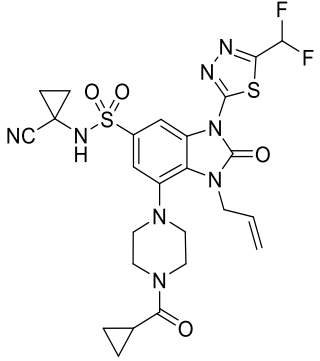
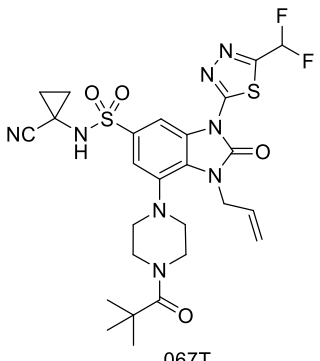
065J	 065J	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.29 (s, 2H), 9.17 (s, 1H), 8.95 (d, <i>J</i> = 2.8 Hz, 1H), 8.74 (d, <i>J</i> = 2.4 Hz, 1H), 8.45 (s, 1H), 7.70 (t, <i>J</i> = 53.2 Hz, 1H), 7.53 (s, 1H), 4.09 - 3.90 (m, 2H), 3.80 - 3.65 (m, 2H), 3.37 - 3.33 (m, 2H), 1.46 (d, <i>J</i> = 6.8 Hz, 6H), 0.72 - 0.65 (m, 2H), 0.45 - 0.41 (m, 2H). MS (ESI) M/Z: 552.1 [M+H]⁺.
065K	 065K	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.12 (s, 1H), 8.93 (d, <i>J</i> = 2.4 Hz, 1H), 8.70 (d, <i>J</i> = 2.8 Hz, 1H), 7.70 (t, <i>J</i> = 53.2 Hz, 1H), 7.49 (s, 1H), 3.54 - 3.49 (m, 4H), 3.07 - 3.02 (m, 2H), 1.44 - 1.42 (m, 2H), 1.33 - 1.29 (m, 2H), 1.23 (d, <i>J</i> = 6.4 Hz, 6H). MS (ESI) M/Z: 560.0 [M+H]⁺.
065L	 065L	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.08 (d, <i>J</i> = 1.2 Hz, 1H), 8.90 (d, <i>J</i> = 2.8 Hz, 1H), 8.68 (d, <i>J</i> = 2.8 Hz, 1H), 7.69 (t, <i>J</i> = 53.2 Hz, 1H), 7.46 (s, 1H), 4.60 (d, <i>J</i> = 4.8 Hz, 2H), 4.14 (d, <i>J</i> = 6.0 Hz, 2H), 3.49 - 3.46 (m, 4H), 3.02 - 2.97 (m, 2H), 1.48 (s, 3H), 1.21 (d, <i>J</i> = 6.4 Hz, 6H). MS (ESI) M/Z: 565.4 [M+H]⁺.

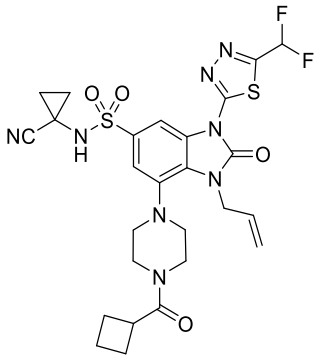
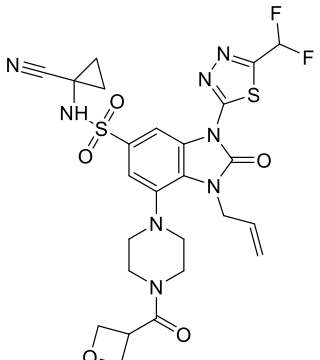
065M	 065M	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.72 (d, <i>J</i> = 1.2 Hz, 1H), 8.48 (s, 1H), 8.33 (s, 1H), 7.68 (t, <i>J</i> = 53.2 Hz, 1H), 7.47 (d, <i>J</i> = 1.2 Hz, 1H), 3.41 - 3.32 (m, 4H), 2.89 - 2.85 (m, 2H), 1.19 (d, <i>J</i> = 6.8 Hz, 6H), 1.09 (s, 3H), 0.67 - 0.64 (m, 2H), 0.42 - 0.39 (m, 2H). MS (ESI) M/Z: 538.3 [M+H]⁺.
065N	 065N	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.76 (s, 1H), 8.51 (s, 1H), 7.68 (t, <i>J</i> = 53.2 Hz, 1H), 7.51 (s, 1H), 3.43 - 3.35 (m, 4H), 2.93 - 2.89 (m, 2H), 1.44 - 1.41 (m, 2H), 1.29 - 1.27 (m, 2H), 1.20 (d, <i>J</i> = 6.4 Hz, 6H). MS (ESI) M/Z: 549.0 [M+H]⁺.
065P	 065P	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.72 (d, <i>J</i> = 1.2 Hz, 1H), 8.64 (s, 1H), 8.49 (s, 1H), 7.67 (t, <i>J</i> = 53.2 Hz, 1H), 7.46 (d, <i>J</i> = 1.2 Hz, 1H), 4.57 - 4.55 (m, 2H), 4.12 (d, <i>J</i> = 6.4 Hz, 2H), 3.41 - 3.32 (m, 4H), 2.89 - 2.84 (m, 2H), 1.46 (s, 3H), 1.18 (d, <i>J</i> = 6.4 Hz, 6H). MS (ESI) M/Z: 554.0 [M+H]⁺.

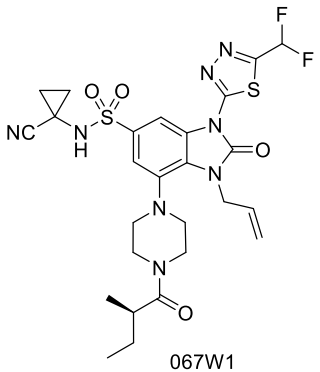
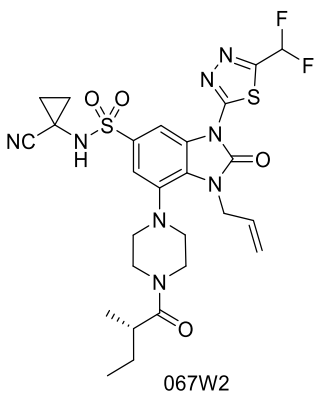
067B	 067B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.06 (s, 1H), 8.75 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.09 - 6.02 (m, 1H), 5.14 - 5.02 (m, 2H), 4.93 - 4.89 (m, 2H), 3.94 (t, <i>J</i> = 7.6 Hz, 4H), 3.79 - 3.76 (m, 2H), 3.02 - 2.96 (m, 4H), 2.85 - 2.80 (m, 2H), 2.19 - 2.15 (m, 2H), 1.42 - 1.39 (m, 2H), 1.28 - 1.25 (m, 2H). MS (ESI) M/Z: 620.1 [M+H]⁺.
067G	 067G	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.17 (s, 1H), 8.76 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.09 - 6.02 (m, 1H), 5.15 - 5.12 (m, 1H), 5.07 - 5.02 (m, 1H), 4.94 - 4.93 (m, 2H), 3.65 - 3.58 (m, 6H), 3.22 - 3.20 (m, 4H), 3.06 - 2.91 (m, 6H), 1.43 - 1.40 (m, 2H), 1.29 - 1.26 (m, 2H). MS (ESI) M/Z: 650.2 [M+H]⁺.
067J	 067J	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.14 (s, 1H), 8.77 (d, <i>J</i> = 1.6 Hz, 1H), 7.83 (d, <i>J</i> = 2.0 Hz, 1H), 7.66 (t, <i>J</i> = 53.2 Hz, 1H), 6.91 (d, <i>J</i> = 1.6 Hz, 1H), 6.63 (d, <i>J</i> = 1.2 Hz, 1H), 6.11 - 6.02 (m, 1H), 5.16 - 5.14 (m, 1H), 5.09 - 5.05 (m, 1H), 4.98 - 4.97 (m, 2H), 3.50 (s, 3H), 3.26 - 3.23 (m, 2H),

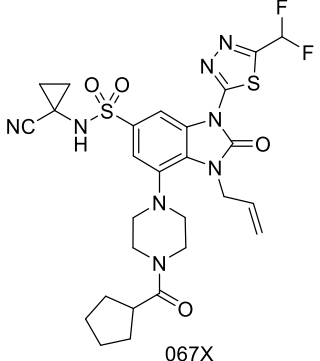
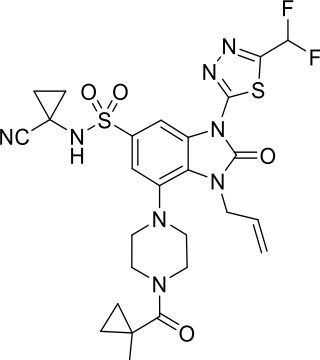
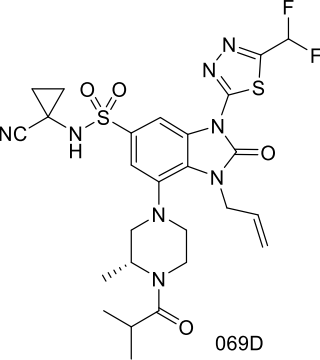
		3.17 - 3.02 (m, 6H), 1.45 - 1.38 (m, 2H), 1.31 - 1.28 (m, 2H). MS (ESI) M/Z: 617.2 [M+H]⁺.
067JD	 067JD	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.77 (d, <i>J</i> = 1.6 Hz, 1H), 8.20 (s, 1H), 7.79 - 7.52 (m, 2H), 6.65 (s, 2H), 6.10 - 6.01 (m, 1H), 5.14 - 5.12 (m, 1H), 5.07 - 5.02 (m, 1H), 4.96 - 4.95 (m, 2H), 3.84 - 3.81 (m, 2H), 3.09 - 3.05 (m, 2H), 3.02 - 2.97 (m, 4H), 1.45 - 1.42 (m, 2H), 1.31 - 1.28 (m, 2H). MS (ESI) M/Z: 603.2 [M+H]⁺.
067M	 067M	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.18 (s, 1H), 8.75 (d, <i>J</i> = 1.2 Hz, 1H), 7.78 - 7.52 (m, 2H), 6.58 - 6.56 (m, 1H), 6.09 - 6.02 (m, 1H), 5.14 - 5.11 (m, 1H), 5.06 - 5.02 (m, 1H), 4.93 - 4.92 (m, 2H), 4.00 - 3.96 (m, 2H), 3.00 - 2.92 (m, 4H), 2.81 - 2.78 (m, 2H), 2.60 (d, <i>J</i> = 4.0 Hz, 3H), 1.42 - 1.40 (m, 2H), 1.28 - 1.26 (m, 2H). MS (ESI) M/Z: 594.1 [M+H]⁺.

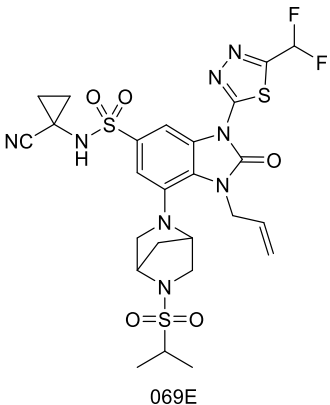
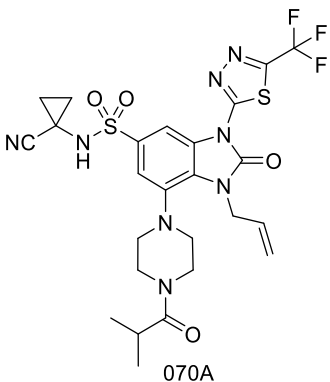
067ND	 067ND	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.17 (s, 1H), 8.77 (s, 1H), 7.78 - 7.51 (m, 2H), 6.13 - 6.05 (m, 1H), 5.14 (d, <i>J</i> = 10.8 Hz, 1H), 5.05 (d, <i>J</i> = 17.2 Hz, 1H), 4.96 - 4.95 (m, 2H), 4.45 - 4.39 (m, 2H), 3.30 - 3.07 (m, 4H), 2.90 - 2.85 (m, 2H), 1.44 - 1.41 (m, 2H), 1.30 - 1.26 (m, 2H), 1.04 - 1.02 (m, 2H), 0.93 - 0.92 (m, 2H). MS (ESI) M/Z: 638.2 [M+H]⁺.
067P	 067P	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.29 (s, 1H), 8.78 (s, 1H), 8.27 (s, 3H), 7.83 (s, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 6.13 - 6.05 (m, 1H), 5.15 - 5.12 (m, 1H), 5.07 - 5.03 (m, 1H), 4.95 - 4.94 (m, 2H), 4.34 - 4.31 (m, 2H), 3.30 - 3.19 (m, 2H), 3.08 - 3.06 (m, 2H), 2.91 - 2.89 (m, 2H), 1.62 (s, 6H), 1.44 - 1.40 (m, 2H), 1.31 - 1.29 (m, 2H). MS (ESI) M/Z: 622.2 [M+H]⁺.
067Q	 067Q	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.17 (s, 1H), 8.76 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.52 (m, 2H), 6.11 - 6.03 (m, 1H), 5.15 - 5.13 (m, 1H), 5.07 - 5.03 (m, 1H), 4.96 - 4.95 (m, 2H), 3.35 - 3.33 (m, 2H), 3.06 - 2.98 (m, 4H), 2.86 - 2.82 (m, 2H), 2.22 (s,

		3H), 1.43 - 1.40 (m, 2H), 1.30 - 1.27 (m, 8H). MS (ESI) M/Z: 636.4 [M+H]⁺.
067S	 067S	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.83 (s, 1H), 8.77 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.52 (m, 2H), 6.13 - 6.04 (m, 1H), 5.15 - 5.03 (m, 2H), 4.96 - 4.95 (m, 2H), 4.42 - 4.39 (m, 2H), 3.38 - 3.36 (m, 1H), 3.07 - 3.05 (m, 2H), 2.90 - 2.79 (m, 3H), 2.07 - 2.04 (m, 1H), 1.44 - 1.41 (m, 2H), 1.30 - 1.27 (m, 2H), 0.76 - 0.73 (m, 4H). MS (ESI) M/Z: 605.1 [M+H]⁺.
067T	 067T	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.18 (s, 1H), 8.76 (d, <i>J</i> = 1.2 Hz, 1H), 7.78 - 7.52 (m, 2H), 6.11 - 6.04 (m, 1H), 5.15 - 5.02 (m, 2H), 4.95 - 4.94 (m, 2H), 4.40 - 4.37 (m, 2H), 3.12 - 3.03 (m, 4H), 2.85 - 2.79 (m, 2H), 1.44 - 1.40 (m, 2H), 1.30 - 1.27 (m, 2H), 1.25 (s, 9H). MS (ESI) M/Z: 621.2 [M+H]⁺.

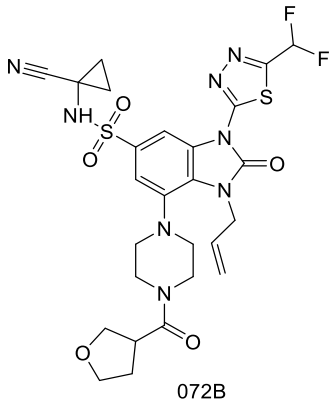
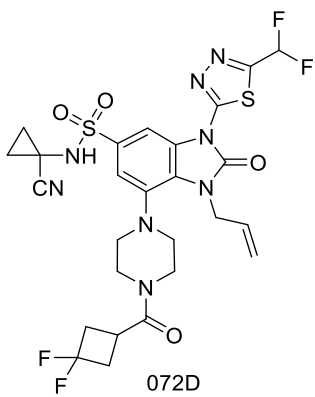
067U	 067U	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.17 (s, 1H), 8.76 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.10 - 6.02 (m, 1H), 5.14 - 5.12 (m, 1H), 5.06 - 5.02 (m, 1H), 4.94 - 4.92 (m, 2H), 4.44 - 4.41 (m, 1H), 3.79 - 3.76 (m, 1H), 3.43 - 3.37 (m, 1H), 3.24 (t, <i>J</i> = 11.6 Hz, 1H), 3.01 - 2.99 (m, 2H), 2.84 - 2.72 (m, 3H), 2.27 - 2.07 (m, 4H), 1.95 - 1.88 (m, 1H), 1.80 - 1.75 (m, 1H), 1.44 - 1.40 (m, 2H), 1.30 - 1.26 (m, 2H). MS (ESI) M/Z: 619.1 [M+H]⁺.
067V	 067V	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.16 (s, 1H), 8.75 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.52 (m, 2H), 6.11 - 6.05 (m, 1H), 5.14 - 5.02 (m, 2H), 4.94 - 4.93 (m, 2H), 4.76 - 4.66 (m, 3H), 4.46 - 4.44 (m, 1H), 4.20 - 4.16 (m, 1H), 3.47 - 3.44 (m, 1H), 3.27 - 3.21 (m, 1H), 3.05 - 2.79 (m, 6H), 1.39 - 1.37 (m, 2H), 1.25 - 1.23 (m, 2H). MS (ESI) M/Z: 621.1 [M+H]⁺.

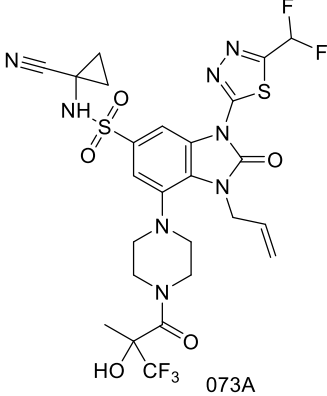
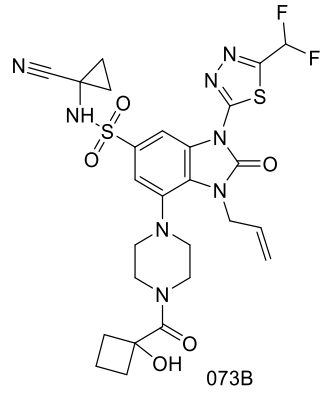
067W1	 067W1	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.18 (s, 1H), 8.77 (s, 1H), 7.78 - 7.52 (m, 2H), 6.12 - 6.03 (m, 1H), 5.15 - 5.12 (m, 1H), 5.07 - 5.02 (m, 1H), 4.95 - 4.94 (m, 2H), 4.53 - 4.49 (m, 1H), 4.11 - 4.08 (m, 1H), 3.36 - 3.34 (m, 1H), 3.07 - 3.04 (m, 2H), 2.90 - 2.74 (m, 4H), 1.62 - 1.59 (m, 1H), 1.43 - 1.40 (m, 2H), 1.34 - 1.26 (m, 3H), 1.05 - 1.00 (m, 3H), 0.87 - 0.83 (m, 3H). MS (ESI) M/Z: 621.1 [M+H]⁺.
067W2	 067W2	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.18 (s, 1H), 8.76 (d, <i>J</i> = 1.2 Hz, 1H), 7.78 - 7.52 (m, 2H), 6.11 - 6.04 (m, 1H), 5.15 - 5.02 (m, 2H), 4.95 - 4.94 (m, 2H), 4.52 - 4.49 (m, 1H), 4.11 - 4.08 (m, 1H), 3.36 - 3.34 (m, 1H), 3.06 - 3.03 (m, 2H), 2.87 - 2.74 (m, 4H), 1.62 - 1.59 (m, 1H), 1.39 - 1.26 (m, 5H), 1.06 - 0.99 (m, 3H), 0.87 - 0.83 (m, 3H). MS (ESI) M/Z: 621.2 [M+H]⁺.

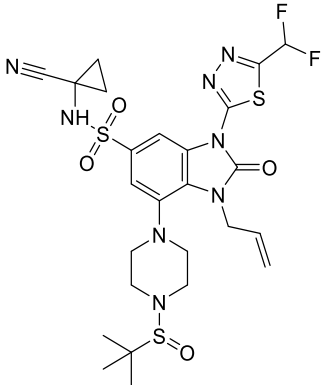
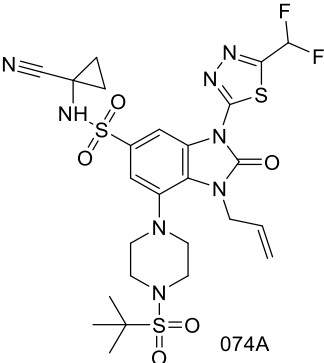
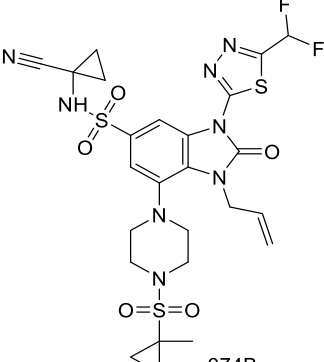
067X	 067X	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.18 (s, 1H), 8.77 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.11 - 6.04 (m, 1H), 5.15 - 5.03 (m, 2H), 4.95 - 4.94 (m, 2H), 4.49 - 4.46 (m, 1H), 4.10 - 4.07 (m, 1H), 3.34 - 3.31 (m, 1H), 3.07 - 3.03 (m, 3H), 2.90 - 2.75 (m, 3H), 1.80 - 1.54 (m, 8H), 1.43 - 1.41 (m, 2H), 1.30 - 1.28 (m, 2H). MS (ESI) M/Z: 633.1 [M+H]⁺.
067Y	 067Y	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.18 (s, 1H), 8.77 (s, 1H), 7.79 (d, <i>J</i> = 0.8 Hz, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 6.12 - 6.04 (m, 1H), 5.15 - 5.13 (m, 1H), 5.07 - 5.03 (m, 1H), 4.96 - 4.95 (m, 2H), 4.34 - 4.31 (m, 2H), 3.15 - 3.03 (m, 4H), 2.89 - 2.84 (m, 2H), 1.44 - 1.41 (m, 2H), 1.30 - 1.26 (m, 5H), 0.87 - 0.85 (m, 2H), 0.59 - 0.56 (m, 2H). MS (ESI) M/Z: 619.2 [M+H]⁺.
069D	 069D	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.13 (s, 1H), 8.77 (s, 1H), 7.76 (s, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 6.12 - 6.05 (m, 1H), 5.14 (d, <i>J</i> = 9.6 Hz, 1H), 5.10 (m, 0.5H), 5.02 (d, <i>J</i> = 17.2 Hz, 1H), 4.94 - 4.92 (m, 1H), 4.79 - 4.78 (m, 0.5H), 4.43 - 4.42

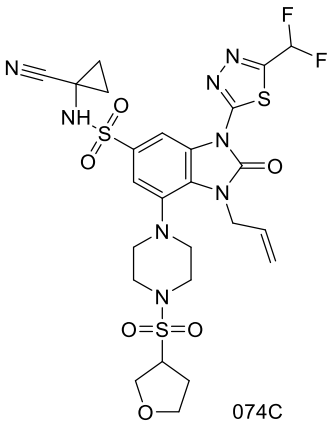
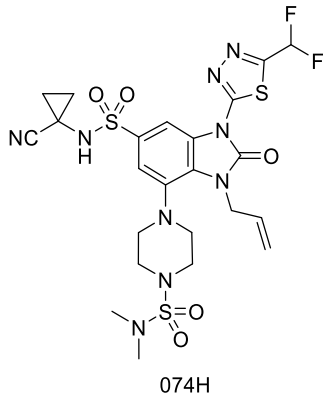
		(m, 0.5H), 4.33 - 4.32 (m, 0.5H), 3.88 - 3.87 (m, 0.5H), 3.51 - 3.49 (m, 0.5H), 3.21 - 2.88 (m, 5H), 2.67 - 2.66 (m, 0.5H), 2.51 - 2.50 (m, 0.5H), 1.38 (s, 3H), 1.30 - 1.22 (m, 4H), 1.08 - 0.98 (m, 6H). MS (ESI) M/Z: 621.4 [M+H]⁺.
069E	 069E	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.25 (s, 1H), 8.73 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.03 - 5.94 (m, 1H), 5.14 (d, <i>J</i> = 10.0 Hz, 1H), 5.09 - 5.00 (m, 2H), 4.79 - 4.74 (m, 1H), 4.47 - 4.46 (m, 1H), 4.05 - 4.04 (m, 1H), 3.59 - 3.56 (m, 1H), 3.41 - 3.35 (m, 3H), 3.26 - 3.22 (m, 1H), 2.21 - 2.18 (m, 1H), 1.97 - 1.94 (m, 1H), 1.46 - 1.39 (m, 2H), 1.35 - 1.26 (m, 8H). MS (ESI) M/Z: 655.1 [M+H]⁺.
070A	 070A	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.12 (s, 1H), 8.75 (d, <i>J</i> = 1.6 Hz, 1H), 7.79 (d, <i>J</i> = 1.6 Hz, 1H), 6.11 - 6.04 (m, 1H), 5.15 - 5.13 (m, 1H), 5.08 - 5.03 (m, 1H), 4.96 - 4.95 (m, 2H), 4.49 - 4.46 (m, 1H), 4.07 - 4.05 (m, 1H), 3.34 - 3.31 (m, 1H), 3.06 - 3.03 (m, 2H), 2.96 - 2.83 (m, 4H), 1.44 -

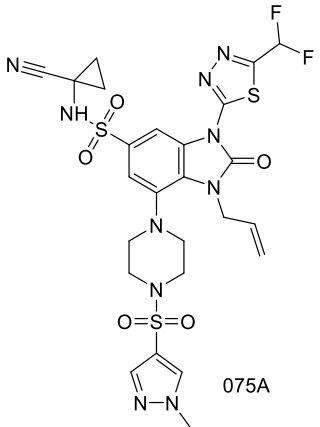
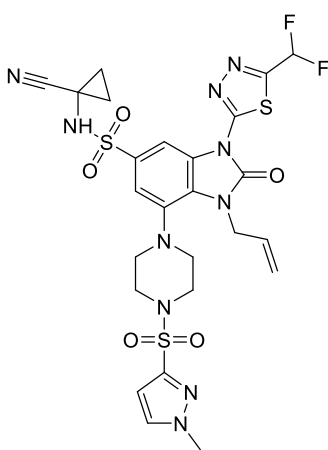
		1.41 (m, 2H), 1.30 - 1.27 (m, 2H), 1.05 - 1.03 (m, 6H). MS (ESI) M/Z: 625.2 [M+H]⁺.
070B	070B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.20 (s, 1H), 8.75 (d, <i>J</i> = 1.6 Hz, 1H), 7.77 (d, <i>J</i> = 1.6 Hz, 1H), 6.12 - 6.05 (m, 1H), 5.50 (s, 1H), 5.16 - 5.14 (m, 1H), 5.08 - 5.04 (m, 1H), 4.96 - 4.95 (m, 2H), 4.89 - 4.25 (m, 2H), 3.14 - 2.96 (m, 3H), 2.95 - 2.71 (m, 3H), 1.44 - 1.40 (m, 2H), 1.36 (s, 6H), 1.29 - 1.26 (m, 2H). MS (ESI) M/Z: 641.2 [M+H]⁺.
071C2	071C2	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.78 (s, 1H), 8.60 (s, 1H), 7.76 (s, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 6.12 - 6.05 (m, 1H), 5.51 - 5.48 (m, 0.5H), 5.30 - 5.29 (m, 0.5H), 5.16 - 5.14 (m, 1H), 5.11 - 5.10 (m, 0.5H), 5.05 - 5.00 (m, 1H), 4.95 - 4.90 (m, 1H), 4.81 - 4.80 (m, 0.5H), 4.76 - 4.75 (m, 0.5H), 4.30 - 4.29 (m, 0.5H), 3.47 - 3.45 (m, 0.5H), 3.25 - 3.23 (m, 0.5H), 3.10 - 2.96 (m, 2H), 2.95 - 2.85 (m, 1H), 2.75 - 2.73 (m, 0.5H), 2.52 - 2.51 (m, 0.5H), 1.50 - 1.48 (m, 3H), 1.40 - 1.36

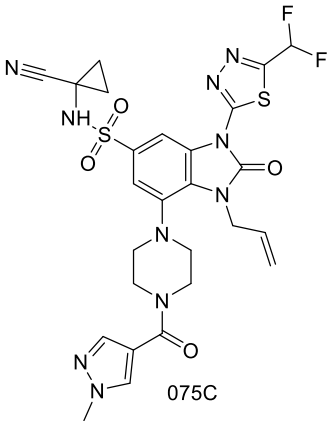
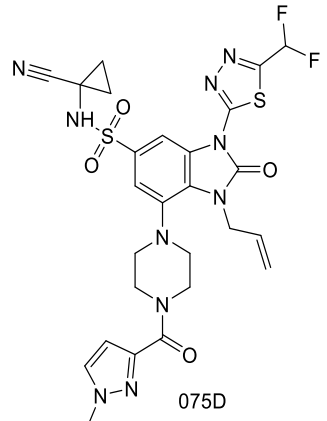
		(m, 6H), 1.30 - 1.27 (m, 4H). MS (ESI) M/Z: 637.4 [M+H]⁺.
072B	 072B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.18 (s, 1H), 8.77 (d, <i>J</i> = 1.2 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.11 - 6.04 (m, 1H), 5.13 (d, <i>J</i> = 10.4 Hz, 1H), 5.05 (d, <i>J</i> = 17.2 Hz, 1H), 4.95 - 4.90 (m, 2H), 4.53 - 4.45 (m, 1H), 4.18 - 4.05 (m, 1H), 3.96 - 3.84 (m, 1H), 3.82 - 3.68 (m, 3H), 3.45 - 3.39 (m, 1H), 3.05 - 2.99 (m, 2H), 2.90 - 2.78 (m, 4H), 2.08 - 1.98 (m, 2H), 1.41 - 1.39 (m, 2H), 1.30 - 1.26 (m, 2H). MS (ESI) M/Z: 635.2 [M+H]⁺.
072D	 072D	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.21 (s, 1H), 8.76 (d, <i>J</i> = 1.6 Hz, 1H), 7.79 - 7.52 (m, 2H), 6.10 - 6.03 (m, 1H), 5.14 - 5.02 (m, 2H), 4.94 - 4.93 (m, 2H), 4.45 - 4.42 (m, 1H), 3.87 - 3.84 (m, 1H), 3.30 - 3.26 (m, 2H), 3.04 - 2.98 (m, 2H), 2.93 - 2.77 (m, 7H), 1.44 - 1.41 (m, 2H), 1.30 - 1.26 (m, 2H). MS (ESI) M/Z: 655.0 [M+H]⁺.

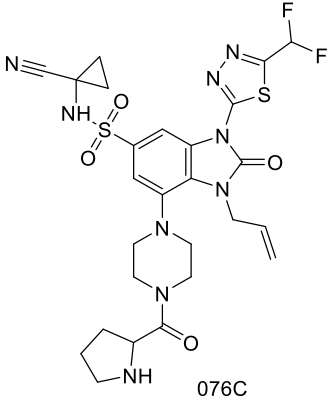
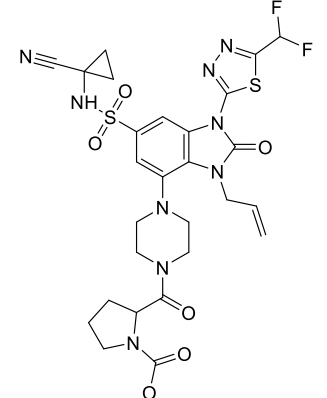
073A	 073A	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.93 (s, 1H), 8.77 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.52 (m, 2H), 7.20 (s, 1H), 6.12 - 6.04 (m, 1H), 5.14 (d, <i>J</i> = 11.2 Hz, 1H), 5.05 (d, <i>J</i> = 17.6 Hz, 1H), 4.96 - 4.95 (m, 2H), 4.86 - 4.83 (m, 1H), 4.47 - 4.45 (m, 1H), 3.05 - 2.87 (m, 6H), 1.58 (s, 3H), 1.43 - 1.40 (m, 2H), 1.30 - 1.26 (m, 2H). MS (ESI) M/Z: 677.3 [M+H]⁺.
073B	 073B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.02 (s, 1H), 8.76 (d, <i>J</i> = 1.6 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.11 - 6.02 (m, 2H), 5.14 (d, <i>J</i> = 10.0 Hz, 1H), 5.05 (d, <i>J</i> = 18.0 Hz, 1H), 4.96 - 4.95 (m, 2H), 4.45 - 4.42 (m, 1H), 4.18 - 4.15 (m, 1H), 3.30 - 3.25 (m, 1H), 3.06 - 2.87 (m, 5H), 2.65 - 2.55 (m, 2H), 2.09 - 2.07 (m, 2H), 1.77 - 1.75 (m, 1H), 1.45 - 1.40 (m, 3H), 1.30 - 1.26 (m, 2H). MS (ESI) M/Z: 635.4 [M+H]⁺.

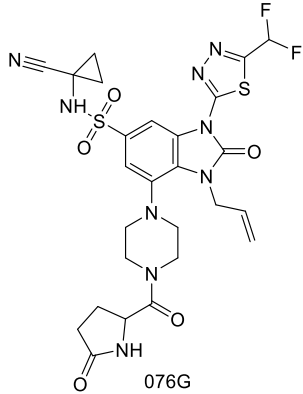
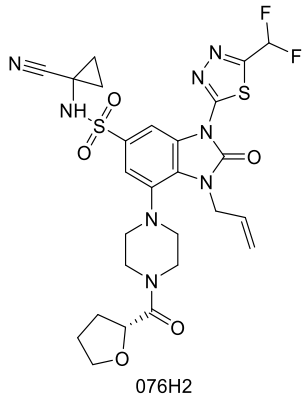
074A-11	 074A-11	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.20 (s, 1H), 8.76 (d, <i>J</i> = 1.6 Hz, 1H), 7.79 - 7.51 (m, 2H), 6.10 - 6.00 (m, 1H), 5.12 (d, <i>J</i> = 11.2 Hz, 1H), 5.02 (d, <i>J</i> = 18.4 Hz, 1H), 4.93 - 4.91 (m, 2H), 3.38 - 3.34 (m, 2H), 3.20 - 3.15 (m, 1H), 3.06 - 2.91 (m, 5H), 1.44 - 1.40 (m, 2H), 1.30 - 1.27 (m, 2H), 1.15 (s, 9H). MS (ESI) M/Z: 641.1 [M+H]⁺.
074A	 074A	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.12 (s, 1H), 8.77 (s, 1H), 7.81 - 7.51 (m, 2H), 6.14 - 6.01 (m, 1H), 5.12 (d, <i>J</i> = 9.2 Hz, 1H), 5.02 (d, <i>J</i> = 17.2 Hz, 1H), 4.93 - 4.91 (m, 2H), 3.71 - 3.65 (m, 2H), 3.32 - 3.30 (m, 2H), 3.05 - 2.92 (m, 4H), 1.44 - 1.40 (m, 2H), 1.36 - 1.27 (m, 11H). MS (ESI) M/Z: 657.0 [M+H]⁺.
074B	 074B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.20 (s, 1H), 8.78 (d, <i>J</i> = 1.6 Hz, 1H), 7.80 - 7.51 (m, 2H), 6.12 - 6.04 (m, 1H), 5.14 (d, <i>J</i> = 10.4 Hz, 1H), 5.03 (d, <i>J</i> = 18.0 Hz, 1H), 4.93 - 4.91 (m, 2H), 3.74 - 3.71 (m, 2H), 3.23 - 3.14 (m, 2H), 3.10 - 3.06 (m, 2H), 2.96 - 2.91 (m, 2H), 1.48 (s, 3H), 1.44 - 1.38

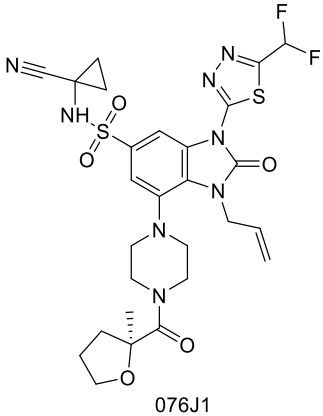
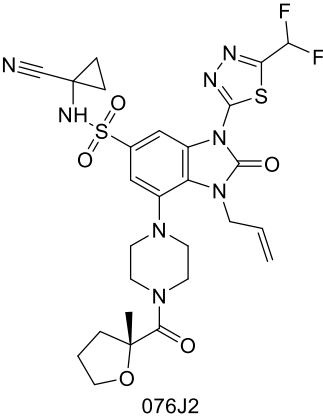
		(m, 2H), 1.31 - 1.27 (m, 2H), 1.22 - 1.19 (m, 2H), 0.91 - 0.89 (m, 2H). MS (ESI) M/Z: 655.0 [M+H]⁺.
074C		¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.14 (s, 1H), 8.78 (d, <i>J</i> = 1.2 Hz, 1H), 7.79 - 7.51 (m, 2H), 6.12 - 6.04 (m, 1H), 5.13 (<i>J</i> = 10.8 Hz, 1H), 5.03 (d, <i>J</i> = 17.2 Hz, 1H), 4.92 - 4.90 (m, 2H), 4.19 - 4.10 (m, 1H), 4.03 - 3.97 (m, 1H), 3.94 - 3.83 (m, 2H), 3.72 - 3.64 (m, 3H), 3.20 - 3.03 (m, 4H), 2.99 - 2.86 (m, 2H), 2.36 - 2.23 (m, 1H), 2.19 - 2.09 (m, 1H), 1.45 - 1.41 (m, 2H), 1.31 - 1.27 (m, 2H). MS (ESI) M/Z: 671.2 [M+H]⁺.
074H		¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.24 (s, 1H), 8.78 (d, <i>J</i> = 2.0 Hz, 1H), 7.81 (d, <i>J</i> = 1.6 Hz, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 6.12 - 6.01 (m, 1H), 5.14 (dd, <i>J</i> = 10.4 Hz, 0.8 Hz, 1H), 5.03 (dd, <i>J</i> = 17.6 Hz, 1.2 Hz, 1H), 4.94 - 4.89 (m, 2H), 3.63 - 3.54 (m, 2H), 3.14 - 3.03 (m, 4H), 3.02 - 2.91 (m, 2H), 2.82 (s, 6H), 1.45 - 1.42 (m, 2H), 1.32 - 1.28 (m, 2H). ¹⁹F NMR (376 MHz, DMSO-<i>d</i>₆) δ -109.76.

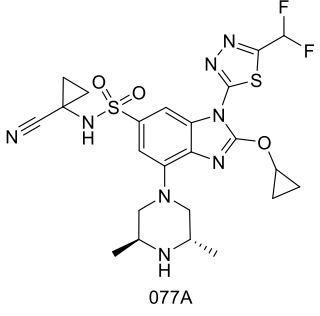
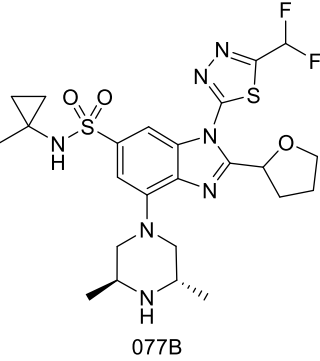
		MS (ESI) M/Z: 643.9 [M+H] ⁺ .
075A	 075A	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.20 (s, 1H), 8.76 (s, 1H), 8.41 (s, 1H), 7.86 (s, 1H), 7.78 - 7.51 (m, 2H), 5.88 - 5.80 (m, 1H), 5.04 (d, <i>J</i> = 10.4 Hz, 1H), 4.89 (d, <i>J</i> = 17.2 Hz, 1H), 4.77 - 4.75 (m, 2H), 3.94 (s, 3H), 3.63 - 3.60 (m, 2H), 3.08 - 3.01 (m, 4H), 2.56 - 2.52 (m, 2H), 1.45 - 1.42 (m, 2H), 1.32 - 1.27 (m, 2H). MS (ESI) M/Z: 681.1 [M+H]⁺.
075B	 075B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.19 (s, 1H), 8.76 (d, <i>J</i> = 1.2 Hz, 1H), 8.01 (d, <i>J</i> = 2.0 Hz, 1H), 7.79 - 7.51 (m, 2H), 6.74 (d, <i>J</i> = 2.0 Hz, 1H), 5.93 - 5.81 (m, 1H), 5.07 (d, <i>J</i> = 10.8 Hz, 1H), 4.94 (d, <i>J</i> = 17.6 Hz, 1H), 4.78 - 4.77 (m, 2H), 4.00 (s, 3H), 3.70 - 3.66 (m, 2H), 3.12 - 2.96 (m, 4H), 2.79 - 2.74 (m, 2H), 1.47 - 1.38 (m, 2H), 1.33 - 1.25 (m, 2H). MS (ESI) M/Z: 681.2 [M+H]⁺.

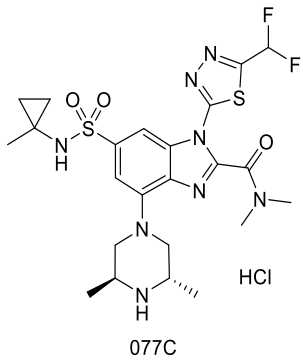
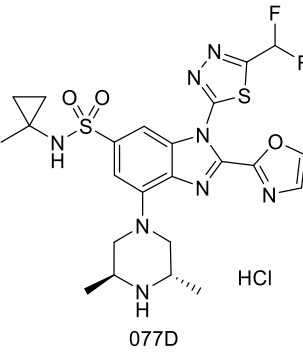
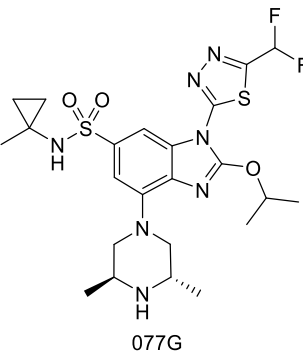
075C	 075C	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.17 (s, 1H), 8.77 (d, <i>J</i> = 1.6 Hz, 1H), 8.12 (s, 1H), 7.79 - 7.51 (m, 3H), 6.12 - 6.05 (m, 1H), 5.14 (d, <i>J</i> = 10.4 Hz, 1H), 5.06 (d, <i>J</i> = 18.0 Hz, 1H), 4.97 - 4.95 (m, 2H), 4.37 - 4.33 (m, 2H), 3.87 (s, 3H), 3.26 - 3.15 (m, 2H), 3.07 - 3.05 (m, 2H), 2.93 - 2.88 (m, 2H), 1.43 - 1.40 (m, 2H), 1.29 - 1.25 (m, 2H). MS (ESI) M/Z: 645.4 [M+H]⁺.
075D	 075D	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.17 (s, 1H), 8.76 (d, <i>J</i> = 1.6 Hz, 1H), 7.79 - 7.51 (m, 3H), 6.60 (d, <i>J</i> = 2.4 Hz, 1H), 6.14 - 6.05 (m, 1H), 5.14 (d, <i>J</i> = 10.4 Hz, 1H), 5.06 (d, <i>J</i> = 17.6 Hz, 1H), 4.97 - 4.95 (m, 2H), 4.92 - 4.87 (m, 1H), 4.62 - 4.53 (m, 1H), 3.90 (s, 3H), 3.42 - 3.37 (m, 1H), 3.12 - 3.05 (m, 3H), 2.92 - 2.86 (m, 2H), 1.44 - 1.40 (m, 2H), 1.30 - 1.26 (m, 2H). MS (ESI) M/Z: 645.1 [M+H]⁺.

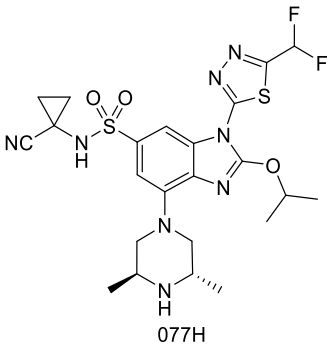
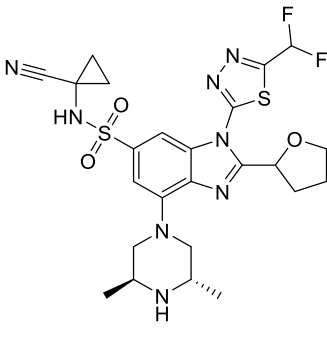
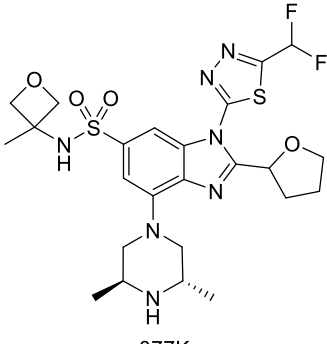
076C	 076C	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.76 (d, <i>J</i> = 1.2 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.12 - 6.03 (m, 1H), 5.13 (d, <i>J</i> = 10.8 Hz, 1H), 5.05 (d, <i>J</i> = 17.6 Hz, 1H), 4.95 - 4.93 (m, 2H), 4.46 - 4.43 (m, 1H), 4.09 - 4.01 (m, 1H), 3.95 - 3.86 (m, 1H), 3.05 - 2.99 (m, 3H), 2.93 - 2.87 (m, 2H), 2.81 - 2.72 (m, 1H), 2.69 - 2.63 (m, 1H), 2.10 - 1.93 (m, 2H), 1.75 - 1.54 (m, 3H), 1.41 - 1.38 (m, 2H), 1.27 - 1.24 (m, 2H). MS (ESI) M/Z: 634.3 [M+H]⁺.
076E	 076E	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.13 (s, 1H), 8.77 (s, 1H), 7.79 - 7.51 (m, 2H), 6.13 - 6.05 (m, 1H), 5.14 (d, <i>J</i> = 10.8 Hz, 1H), 5.07 - 5.01 (m, 1H), 4.96 - 4.94 (m, 2H), 4.80 - 4.68 (m, 1H), 4.42 - 4.37 (m, 1H), 4.15 - 4.03 (m, 1H), 3.59 - 3.51 (m, 3H), 3.40 - 3.36 (m, 3H), 3.11 - 2.97 (m, 2H), 2.90 - 2.71 (m, 3H), 2.30 - 2.08 (m, 1H), 1.93 - 1.75 (m, 3H), 1.47 - 1.37 (m, 2H), 1.28 - 1.23 (m, 2H). MS (ESI) M/Z: 692.3 [M+H]⁺.

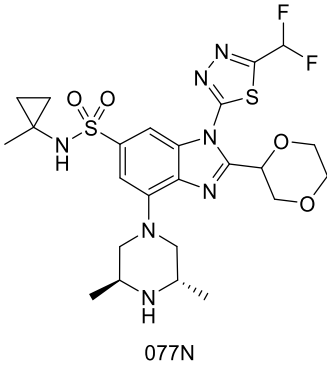
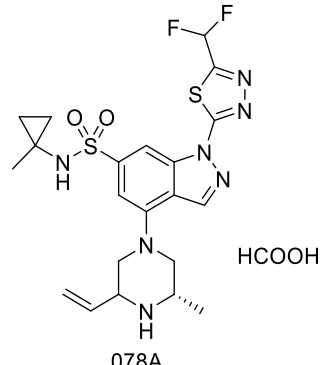
076G	 076G	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.20 (s, 1H), 8.76 (d, <i>J</i> = 1.6 Hz, 1H), 7.80 - 7.52 (m, 3H), 6.11 - 6.04 (m, 1H), 5.13 (d, <i>J</i> = 10.8 Hz, 1H), 5.05 (d, <i>J</i> = 16.8 Hz, 1H), 4.96 - 4.94 (m, 2H), 4.66 - 4.56 (m, 1H), 4.45 - 4.41 (m, 1H), 4.02 - 3.95 (m, 1H), 3.39 - 3.35 (m, 1H), 3.08 - 3.03 (m, 2H), 2.93 - 2.77 (m, 3H), 2.37 - 2.32 (m, 1H), 2.15 - 2.09 (m, 2H), 2.04 - 1.90 (m, 1H), 1.44 - 1.40 (m, 2H), 1.30 - 1.26 (m, 2H). MS (ESI) M/Z: 648.2 [M+H]⁺.
076H2	 076H2	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.18 (s, 1H), 8.76 (s, 1H), 7.78 - 7.51 (m, 2H), 6.12 - 6.03 (m, 1H), 5.13 (d, <i>J</i> = 10.8 Hz, 1H), 5.04 (d, <i>J</i> = 16.8 Hz, 1H), 4.95 - 4.93 (m, 2H), 4.75 - 4.71 (m, 1H), 4.43 - 4.39 (m, 1H), 4.13 - 4.08 (m, 1H), 3.84 - 3.76 (m, 2H), 3.30 - 3.27 (m, 1H), 3.05 - 3.02 (m, 2H), 2.91 - 2.76 (m, 3H), 2.14 - 2.00 (m, 2H), 1.88 - 1.82 (m, 2H), 1.44 - 1.40 (m, 2H), 1.29 - 1.27 (m, 2H). MS (ESI) M/Z: 635.0 [M+H]⁺.

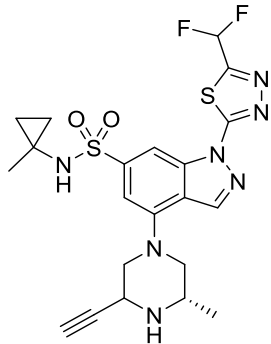
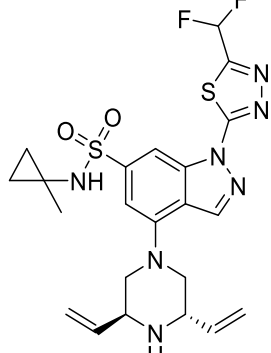
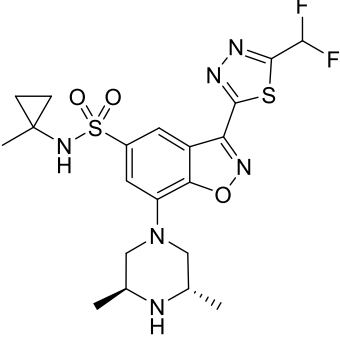
076J1	 076J1	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.13 (s, 1H), 8.77 (d, <i>J</i> = 1.2 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.12 - 6.03 (m, 1H), 5.13 (d, <i>J</i> = 10.8 Hz, 1H), 5.05 (d, <i>J</i> = 17.2 Hz, 1H), 4.96 - 4.95 (m, 2H), 4.81 - 4.60 (m, 1H), 4.56 - 4.35 (m, 1H), 3.92 - 3.84 (m, 1H), 3.82 - 3.72 (m, 1H), 3.25 - 3.22 (m, 1H), 3.07 - 3.04 (m, 2H), 2.94 - 2.76 (m, 3H), 2.70 - 2.66 (m, 1H), 1.92 - 1.82 (m, 1H), 1.81 - 1.75 (m, 1H), 1.62 - 1.57 (m, 1H), 1.43 (s, 3H), 1.41 - 1.40 (m, 2H), 1.30 - 1.26 (m, 2H). MS (ESI) M/Z: 649.3 [M+H]⁺.
076J2	 076J2	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.13 (s, 1H), 8.75 (d, <i>J</i> = 1.2 Hz, 1H), 7.78 - 7.51 (m, 2H), 6.12 - 6.03 (m, 1H), 5.13 (d, <i>J</i> = 10.8 Hz, 1H), 5.05 (d, <i>J</i> = 17.2 Hz, 1H), 4.96 - 4.95 (m, 2H), 4.81 - 4.60 (m, 1H), 4.56 - 4.35 (m, 1H), 3.92 - 3.84 (m, 1H), 3.82 - 3.72 (m, 1H), 3.25 - 3.22 (m, 1H), 3.07 - 3.04 (m, 2H), 2.94 - 2.80 (m, 3H), 2.70 - 2.66 (m, 1H), 1.87 - 1.85 (m, 1H), 1.77 - 1.75 (m, 1H), 1.62 - 1.57 (m, 1H), 1.43 (s, 3H), 1.42 - 1.40 (m, 2H), 1.30 - 1.26 (m, 2H).

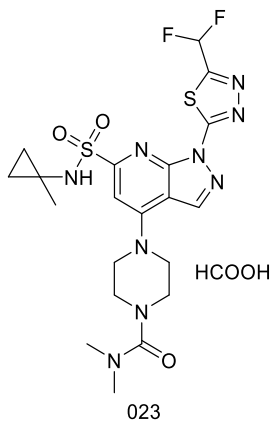
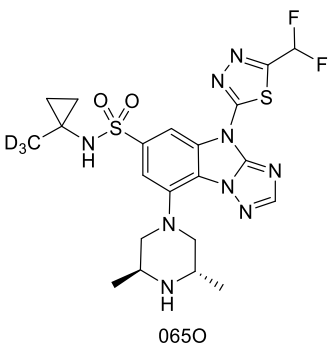
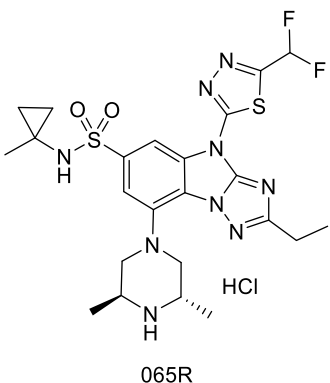
		MS (ESI) M/Z: 649.3 [M+H] ⁺ .
077A		¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.38 (d, <i>J</i> = 1.6 Hz, 1H), 7.63 (t, <i>J</i> = 52.8 Hz, 1H), 7.18 (d, <i>J</i> = 1.6 Hz, 1H), 4.73 - 4.69 (m, 1H), 3.29 - 3.26 (m, 6H), 1.39 - 1.37 (m, 2H), 1.26 - 1.22 (m, 2H), 1.20 (d, <i>J</i> = 6.4 Hz, 6H), 1.10 - 1.08 (m, 2H), 0.96 - 0.90 (m, 2H). MS (ESI) M/Z: 565.3 [M+H]⁺.
077B		¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.05 (s, 1H), 7.80 - 7.53 (m, 2H), 7.08 (s, 1H), 5.42 - 5.37 (m, 1H), 3.84 - 3.79 (m, 1H), 3.78 - 3.72 (m, 1H), 3.45 - 3.38 (m, 4H), 3.29 - 3.25 (m, 2H), 2.77 - 2.66 (m, 1H), 2.32 - 2.23 (m, 1H), 2.13 - 2.05 (m, 1H), 2.03 - 1.93 (m, 1H), 1.17 (d, <i>J</i> = 6.4 Hz, 6H), 1.03 (s, 3H), 0.63 - 0.58 (m, 2H), 0.38 - 0.33 (m, 2H). MS (ESI) M/Z: 568.4 [M+H]⁺.

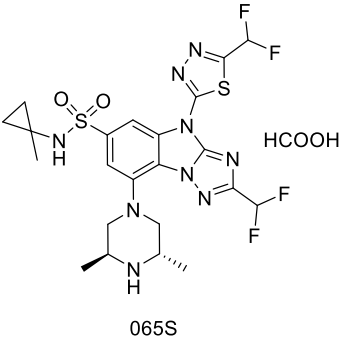
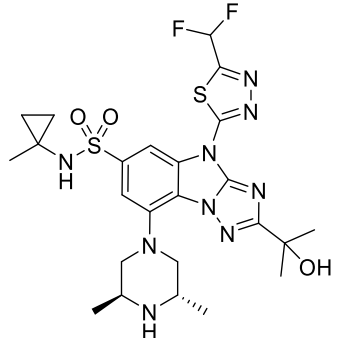
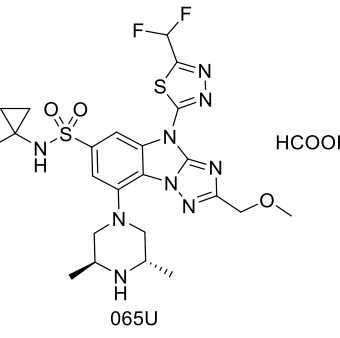
077C	 077C	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.21 (s, 2H), 8.19 (s, 1H), 7.77 (s, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 7.24 (s, 1H), 3.78 - 3.67 (m, 6H), 3.35 (s, 3H), 3.08 (s, 3H), 1.43 (d, <i>J</i> = 6.0 Hz, 6H), 1.06 (s, 3H), 0.71 - 0.58 (m, 2H), 0.45 - 0.35 (m, 2H). MS (ESI) M/Z: 569.1 [M+H]⁺.
077D	 077D	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.29 (s, 2H), 8.47 (s, 1H), 8.15 (s, 1H), 7.70 (t, <i>J</i> = 53.2 Hz, 1H), 7.50 (s, 1H), 7.34 (s, 1H), 7.23 (s, 1H), 3.83 - 3.79 (m, 6H), 1.45 (d, <i>J</i> = 5.6 Hz, 6H), 1.04 (s, 3H), 0.64 - 0.62 (m, 2H), 0.40 - 0.37 (m, 2H). MS (ESI) M/Z: 565.2 [M+H]⁺.
077G	 077G	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.36 (d, <i>J</i> = 1.2 Hz, 1H), 8.02 (s, 1H), 7.64 (t, <i>J</i> = 53.2 Hz, 1H), 7.15 (d, <i>J</i> = 1.6 Hz, 1H), 5.42 - 5.35 (m, 1H), 3.28 - 3.22 (m, 6H), 2.01 (s, 1H), 1.58 - 1.56 (m, 6H), 1.18 (d, <i>J</i> = 5.6 Hz, 6H), 1.04 (s, 3H), 0.66 - 0.59 (m, 2H), 0.38 - 0.33 (m, 2H). MS (ESI) M/Z: 556.1 [M+H]⁺.

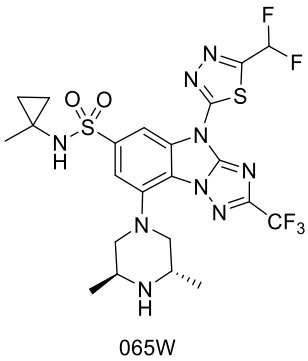
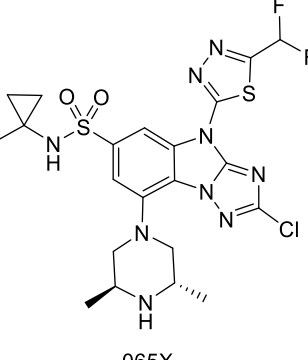
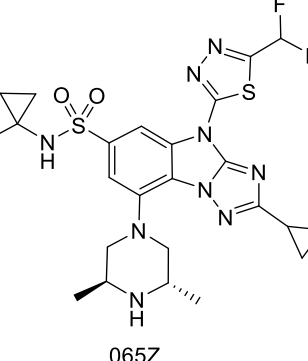
077H	 077H	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.40 (d, <i>J</i> = 1.2 Hz, 1H), 7.64 (t, <i>J</i> = 53.2 Hz, 1H), 7.16 (d, <i>J</i> = 1.2 Hz, 1H), 5.43 - 5.37 (m, 1H), 3.27 - 3.24 (m, 6H), 1.59 - 1.56 (m, 6H), 1.39 - 1.37 (m, 2H), 1.24 - 1.22 (m, 2H), 1.19 (d, <i>J</i> = 5.6 Hz, 6H). MS (ESI) M/Z: 567.3 [M+H]⁺.
077J	 077J	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 7.80 - 7.54 (m, 2H), 7.10 (s, 1H), 5.44 - 5.39 (m, 1H), 3.85 - 3.80 (m, 1H), 3.78 - 3.69 (m, 1H), 3.47 - 3.40 (m, 4H), 3.28 - 3.26 (m, 2H), 2.78 - 2.66 (m, 1H), 2.33 - 2.24 (m, 1H), 2.14 - 1.94 (m, 2H), 1.40 - 1.35 (m, 2H), 1.26 - 1.22 (m, 2H), 1.18 (d, <i>J</i> = 6.0 Hz, 6H). MS (ESI) M/Z: 579.0 [M+H]⁺.
077K	 077K	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.33 (s, 1H), 7.80 - 7.53 (m, 2H), 7.09 (s, 1H), 5.42 - 5.37 (m, 1H), 4.53 - 4.50 (m, 2H), 4.08 - 4.06 (m, 2H), 3.84 - 3.79 (m, 1H), 3.78 - 3.68 (m, 1H), 3.45 - 3.40 (m, 4H), 3.29 - 3.25 (m, 2H), 2.76 - 2.66 (m, 1H), 2.32 - 2.23 (m, 1H), 2.09 - 1.97 (m, 2H), 1.40 (s, 3H), 1.17 (d, <i>J</i> = 6.0 Hz, 6H). MS (ESI) M/Z: 584.1 [M+H]⁺.

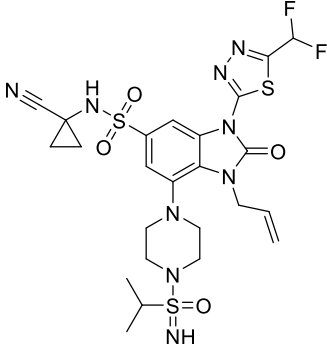
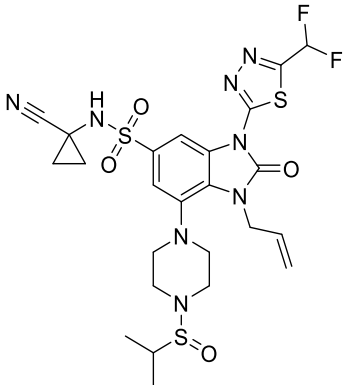
077N	 077N	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.07 (s, 1H), 7.79 (s, 1H), 7.68 (t, <i>J</i> = 53.2 Hz, 1H), 7.10 (s, 1H), 5.07 - 5.04 (m, 1H), 4.19 - 4.14 (m, 2H), 3.78 - 3.75 (m, 3H), 3.66 - 3.65 (m, 1H), 3.42 - 3.39 (m, 4H), 3.28 - 3.25 (m, 2H), 2.17 (s, 1H), 1.17 (d, <i>J</i> = 6.4 Hz, 6H), 1.02 (s, 3H), 0.65 - 0.58 (m, 2H), 0.36 - 0.35 (m, 2H). MS (ESI) M/Z: 584.4 [M+H]⁺.
078A	 078A	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.92 (s, 1H), 8.45 (s, 1H), 8.33 (s, 1H), 7.74 - 7.47 (m, 1H), 7.15 (d, <i>J</i> = 0.8 Hz, 1H), 5.95 - 5.87 (m, 1H), 5.39 (d, <i>J</i> = 17.6 Hz, 1H), 5.19 (d, <i>J</i> = 10.8 Hz, 1H), 3.72 - 3.69 (m, 2H), 3.62 - 3.58 (m, 1H), 3.14 - 3.10 (m, 1H), 2.69 - 2.55 (m, 2H), 1.13 (d, <i>J</i> = 6.0 Hz, 3H), 1.07 (s, 3H), 0.67 - 0.64 (m, 2H), 0.41 - 0.39 (m, 2H). MS (ESI) M/Z: 510.1 [M+H]⁺.

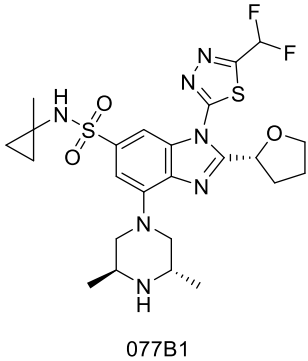
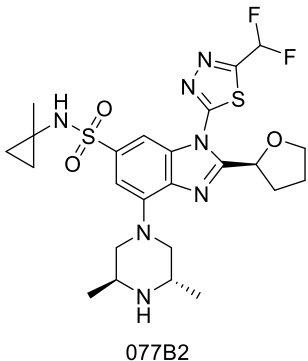
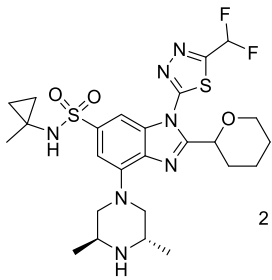
078B	 078B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.92 (s, 1H), 8.47 (s, 1H), 8.34 (s, 1H), 7.60 (t, <i>J</i> = 53.2 Hz, 1H), 7.15 (s, 1H), 3.83 - 3.74 (m, 2H), 3.66 (d, <i>J</i> = 11.2 Hz, 1H), 3.31 (d, <i>J</i> = 2.4 Hz, 1H), 2.99 - 2.96 (m, 1H), 2.87 (t, <i>J</i> = 10.8 Hz, 1H), 2.57 (t, <i>J</i> = 11.2 Hz, 1H), 1.07 (d, <i>J</i> = 6.0 Hz, 3H), 1.06 (s, 3H), 0.69 - 0.63 (m, 2H), 0.42 - 0.40 (m, 2H). MS (ESI) M/Z: 508.1 [M+H]⁺.
078C	 078C	¹H NMR (400 MHz, CD₃OD) δ 8.65 (s, 1H), 8.51 - 8.47 (m, 2H), 7.37 - 7.10 (m, 2H), 6.24 - 6.18 (m, 2H), 5.42 - 5.38 (m, 2H), 5.30 - 5.27 (m, 2H), 3.89 - 3.87 (m, 2H), 3.54 - 3.50 (m, 2H), 3.38 - 3.35 (m, 2H), 1.15 (s, 3H), 0.77 - 0.75 (m, 2H), 0.46 - 0.43 (m, 2H). ¹⁹F NMR (377 MHz, CD₃OD) δ -110.87. MS (ESI) M/Z: 522.6 [M+H]⁺.
021B	 021B	¹H NMR (400 MHz, DMSO-<i>d</i>₆+D₂O) δ 8.22 (s, 1H), 7.69 (t, <i>J</i> = 53.2 Hz, 1H), 7.40 (s, 1H), 3.38 - 3.35 (m, 2H), 3.29 - 3.25 (m, 2H), 3.16 - 3.11 (m, 2H), 1.16 (d, <i>J</i> = 6.4 Hz, 6H), 1.03 (s, 3H), 0.66 - 0.59 (m, 2H), 0.42 - 0.37 (m, 2H).

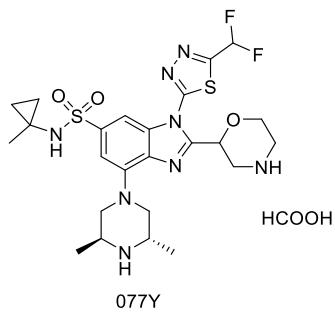
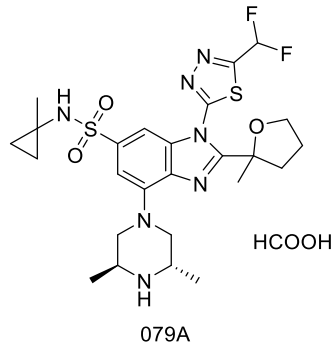
		MS (ESI) M/Z: 499.3 [M+H] ⁺ .
023	 023	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.72 (s, 1H), 8.47 (s, 1H), 8.31 (s, 1H), 7.63 (t, <i>J</i> = 53.0 Hz, 1H), 6.78 (s, 1H), 3.89 - 3.79 (m, 4H), 3.59 - 3.39 (m, 4H), 2.80 (s, 6H), 1.16 (s, 3H), 0.78 - 0.70 (m, 2H), 0.47 - 0.36 (m, 2H). MS (ESI) M/Z: 542.2 [M+H]⁺.
065O	 065O	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.72 (s, 1H), 8.48 (s, 1H), 8.32 (s, 1H), 7.68 (t, <i>J</i> = 52.8 Hz, 1H), 7.47 (s, 1H), 3.41 - 3.37 (m, 2H), 3.30 - 3.31 (m, 2H), 2.89 - 2.86 (m, 2H), 1.18 (d, <i>J</i> = 6.4 Hz, 6H), 0.66 - 0.64 (m, 2H), 0.41 - 0.39 (m, 2H). MS (ESI) M/Z: 541.3 [M+H]⁺.
065R	 065R	¹H NMR (400 MHz, DMSO-<i>d</i>₆+D₂O) δ 8.74 (s, 1H), 7.72 - 7.46 (m, 2H), 3.86 - 3.81 (m, 2H), 3.52 - 3.49 (m, 2H), 3.26 - 3.22 (m, 2H), 2.89 (q, <i>J</i> = 7.6 Hz, 2H), 1.43 (d, <i>J</i> = 6.4 Hz, 6H), 1.35 (t, <i>J</i> = 7.6 Hz, 3H), 1.06 (s, 3H), 0.65 - 0.59 (m, 2H), 0.41 - 0.38 (m, 2H). MS (ESI) M/Z: 566.3 [M+H]⁺.

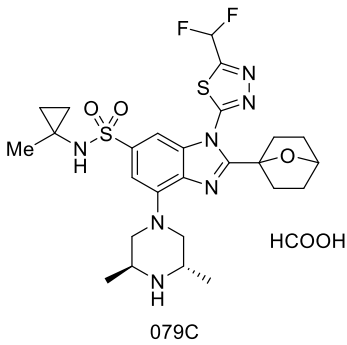
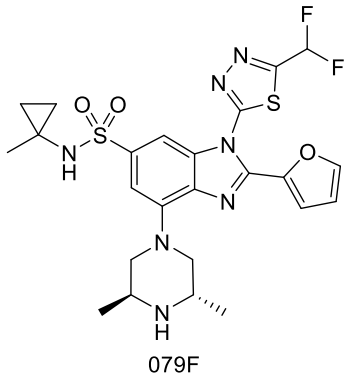
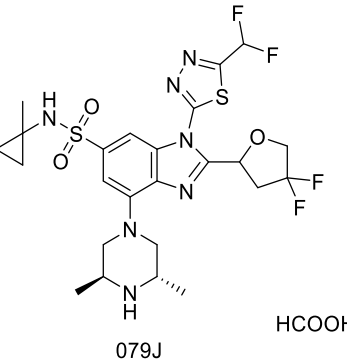
065S	 065S	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.73 (d, <i>J</i> = 1.4 Hz, 1H), 8.38 (s, 1H), 8.31 (s, 1H), 7.68 (t, <i>J</i> = 53.0 Hz, 1H), 7.51 (d, <i>J</i> = 1.6 Hz, 1H), 7.34 (t, <i>J</i> = 52.6 Hz, 1H), 3.41 - 3.25 (m, 4H), 3.01 - 2.92 (m, 2H), 1.24 (d, <i>J</i> = 6.4 Hz, 6H), 1.10 (s, 3H), 0.66 (q, <i>J</i> = 4.2 Hz, 2H), 0.46 - 0.38 (m, 2H). MS (ESI) M/Z: 588.1 [M+H]⁺.
065T	 065T	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.76 (d, <i>J</i> = 1.4 Hz, 1H), 8.42 (s, 1H), 7.68 (t, <i>J</i> = 53.1 Hz, 1H), 7.54 (d, <i>J</i> = 1.6 Hz, 1H), 3.65 - 3.04 (m, 6H), 1.26 - 1.21 (m, 12H), 1.11 (s, 3H), 0.67 (q, <i>J</i> = 3.3 Hz, 2H), 0.54 - 0.30 (m, 2H). MS (ESI) M/Z: 596.2 [M+H]⁺.
065U	 065U	¹H NMR (400 MHz, DMSO-<i>d</i>₆+D₂O) δ 8.73 (d, <i>J</i> = 1.5 Hz, 1H), 8.30 (s, 1H), 7.66 (t, <i>J</i> = 53.1 Hz, 1H), 7.49 (d, <i>J</i> = 1.6 Hz, 1H), 4.62 (d, <i>J</i> = 1.3 Hz, 2H), 3.54 - 3.46 (m, 2H), 3.41 (s, 3H), 3.37 - 3.30 (m, 2H), 3.01 (dd, <i>J</i> = 11.2, 6.0 Hz, 2H), 1.27 (d, <i>J</i> = 6.5 Hz, 6H), 1.09 (s, 3H), 0.66 (d, <i>J</i> = 4.8 Hz, 2H), 0.49 - 0.37 (m, 2H). MS (ESI) M/Z: 582.2 [M+H]⁺.

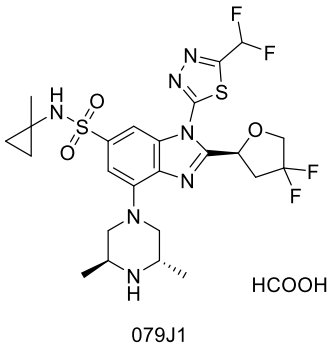
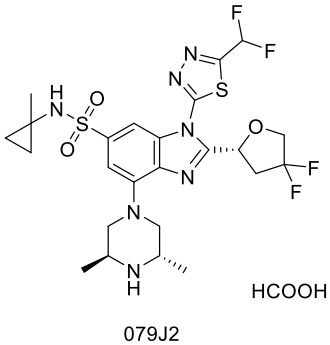
065W	 065W	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.76 (s, 1H), 8.29 (s, 1H), 7.97 - 7.36 (m, 2H), 3.61 - 3.55 (m, 2H), 3.35 - 3.33 (m, 2H), 3.12 - 3.05 (m, 2H), 1.31 (s, 6H), 1.10 (s, 3H), 0.69 - 0.63 (m, 2H), 0.46 - 0.39 (m, 2H). MS (ESI) M/Z: 606.0 [M+H]⁺.
065X	 065X	¹H NMR (400 MHz, DMSO-<i>d</i>₆+D₂O) δ 8.72 (d, <i>J</i> = 1.4 Hz, 1H), 7.65 (t, <i>J</i> = 53.1 Hz, 1H), 7.50 (d, <i>J</i> = 1.6 Hz, 1H), 3.42 - 3.38 (m, 2H), 3.28 (dd, <i>J</i> = 11.1, 3.2 Hz, 2H), 2.93 (dd, <i>J</i> = 11.1, 6.0 Hz, 2H), 1.22 (d, <i>J</i> = 6.5 Hz, 6H), 1.09 (s, 3H), 0.67 - 0.65 (m, 2H), 0.56 - 0.31 (m, 2H). MS (ESI) M/Z: 572.0 [M+H]⁺.
065Z	 065Z	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.67 (d, <i>J</i> = 1.6 Hz, 1H), 8.29 (s, 1H), 7.66 (t, <i>J</i> = 53.2 Hz, 1H), 7.42 (d, <i>J</i> = 1.6 Hz, 1H), 3.39 - 3.37 (m, 2H), 3.26 - 3.23 (m, 2H), 2.92 - 2.88 (m, 2H), 2.20 - 2.18 (m, 1H), 1.20 (d, <i>J</i> = 6.4 Hz, 6H), 1.12 - 1.09 (m, 2H), 1.07 (s, 3H), 1.03 - 0.99 (m, 2H), 0.66 - 0.63 (m, 2H), 0.41 - 0.39 (m, 2H). MS (ESI) M/Z: 578.4 [M+H]⁺.

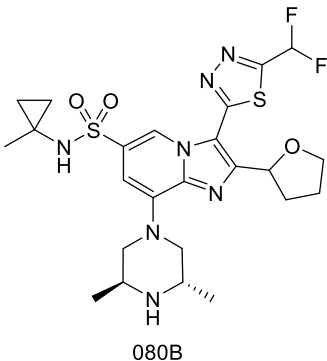
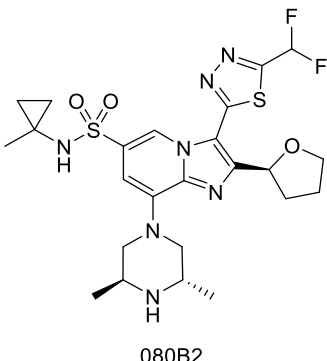
074G	 074G	¹H NMR (400 MHz, CHLOROFORM-d) δ ppm 8.98 (s, 1H), 7.89 (s, 1H), 7.06 (t, $J = 54.00$ Hz, 1H), 6.07 (br s, 1H), 5.91 - 6.03 (m, 1H), 5.24 (d, $J = 10.61$ Hz, 1H), 5.12 (d, $J = 17.05$ Hz, 1H), 5.02 (br d, $J = 4.77$ Hz, 2H), 3.94 - 4.06 (m, 2H), 3.28 - 3.39 (m, 1H), 3.00 - 3.21 (m, 6H), 1.67 - 1.70 (m, 2H), 1.40 - 1.47 (m, 8H). MS (ESI) M/Z: 642.3 $[M+H]^+$.
074M	 074M	¹H NMR (400 MHz, CHLOROFORM-d) δ ppm 8.97 (d, $J = 1.67$ Hz, 1H), 7.89 (d, $J = 1.67$ Hz, 1H), 7.05 (t, $J = 53.60$ Hz, 1H), 6.17 (s, 1H), 5.92 - 6.04 (m, 1H), 5.22 (d, $J = 10.25$ Hz, 1H), 5.08 (d, $J = 16.81$ Hz, 1H), 5.00 - 5.05 (m, 2H), 3.33 - 3.51 (m, 3H), 3.08 - 3.24 (m, 5H), 2.94 - 3.04 (m, 1H), 1.63 - 1.68 (m, 2H), 1.42 - 1.46 (m, 2H), 1.38 (d, $J = 6.91$ Hz, 3H), 1.23 (d, $J = 6.91$ Hz, 3H). MS (ESI) M/Z: 627.3 $[M+H]^+$.

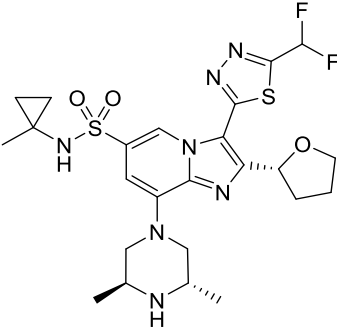
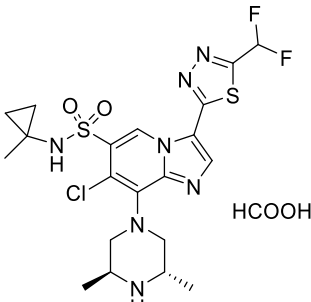
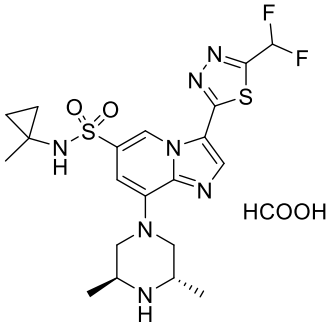
077B1	 077B1	¹H NMR (400 MHz, DMSO-<i>d</i>₆+D₂O) δ 7.62 - 7.35 (m, 2H), 7.07 (s, 1H), 5.34 - 5.31 (m, 1H), 3.78 - 3.76 (m, 1H), 3.68 - 3.65 (m, 1H), 3.50 - 3.48 (m, 4H), 3.41 - 3.38 (m, 2H), 2.67 - 2.65 (m, 1H), 2.29 - 2.26 (m, 1H), 2.01 - 1.95 (m, 2H), 1.21 (d, <i>J</i> = 6.4 Hz, 6H), 0.98 (s, 3H), 0.60 - 0.54 (m, 2H), 0.36 - 0.34 (m, 2H). MS (ESI) M/Z: 568.4 [M+H]⁺.
077B2	 077B2	¹H NMR (400 MHz, DMSO-<i>d</i>₆+D₂O) δ 7.63 (s, 1H), 7.47 (t, <i>J</i> = 52.8 Hz, 1H), 7.09 (s, 1H), 5.33 - 5.29 (m, 1H), 3.78 - 3.75 (m, 1H), 3.72 - 3.68 (m, 1H), 3.54 - 3.50 (m, 6H), 2.62 - 2.59 (m, 1H), 2.28 - 2.26 (m, 1H), 2.02 - 1.95 (m, 2H), 1.26 (d, <i>J</i> = 6.4 Hz, 6H), 0.97 (s, 3H), 0.59 - 0.53 (m, 2H), 0.36 - 0.32 (m, 2H). MS (ESI) M/Z: 568.4 [M+H]⁺.
077X	 077X 2 HCOOH	¹H NMR (400 MHz, DMSO-<i>d</i>₆+D₂O) δ 8.38 (s, 2H), 7.85 (d, <i>J</i> = 3.8 Hz, 1H), 7.64 (t, <i>J</i> = 53.1 Hz, 2H), 7.15 (s, 1H), 4.87 (d, <i>J</i> = 9.9 Hz, 1H), 3.90 - 3.79 (m, 1H), 3.60 - 3.47 (m, 7H), 2.22 - 1.90 (m, 3H), 1.73 - 1.50 (m, 3H), 1.30 (d, <i>J</i> =

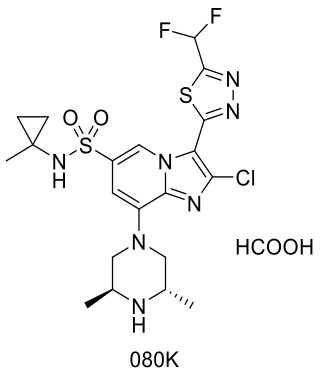
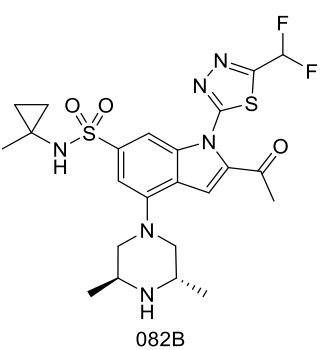
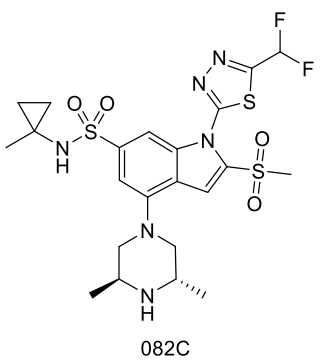
		6.2 Hz, 6H), 1.03 (s, 3H), 0.70 - 0.56 (m, 2H), 0.38 (s, 2H). MS (ESI) M/Z: 582.2 [M+H]⁺.
077Y	 077Y	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.22 (s, 1H), 8.10 (s, 1H), 7.86 (d, <i>J</i> = 2.2 Hz, 1H), 7.69 (t, <i>J</i> = 53.0 Hz, 1H), 7.18 - 7.14 (m, 1H), 4.92 - 4.85 (m, 1H), 3.80 - 3.51 (m, 8H), 3.35 - 3.21 (m, 2H), 2.83 - 2.71 (m, 2H), 1.33 (d, <i>J</i> = 5.4 Hz, 6H), 1.03 (s, 3H), 0.69 - 0.56 (m, 2H), 0.42 - 0.31 (m, 2H). MS (ESI) M/Z: 583.2 [M+H]⁺.
079A	 079A	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.01 (s, 1H), 7.80 - 7.53 (m, 1H), 7.09 - 7.04 (m, 2H), 3.76 - 3.71 (m, 1H), 3.60 - 3.47 (m, 4H), 3.45 - 3.35 (m, 3H), 2.93 - 2.81 (m, 1H), 2.04 - 1.91 (m, 2H), 1.89 - 1.76 (m, 1H), 1.64 (d, <i>J</i> = 6.0 Hz, 3H), 1.26 (d, <i>J</i> = 6.4 Hz, 6H), 1.03 (s, 3H), 0.64 - 0.57 (m, 2H), 0.39 - 0.31 (m, 2H). ¹⁹F NMR (376 MHz, DMSO-<i>d</i>₆) δ -110.85. MS (ESI) M/Z: 581.8 [M+H]⁺.

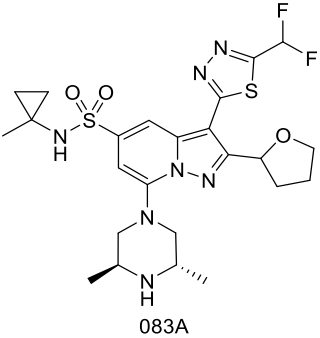
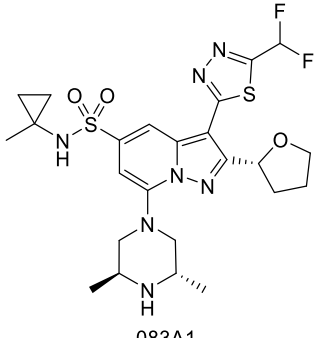
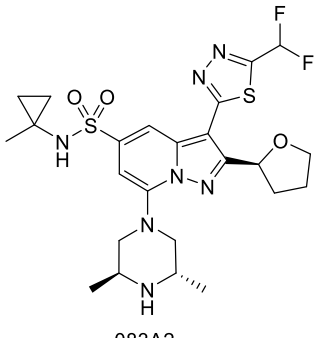
079C	 079C	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.85 (s, 1H), 8.05 (s, 1H), 7.67 (t, <i>J</i> = 56.0 Hz, 1H), 7.40 (d, <i>J</i> = 1.4 Hz, 1H), 7.17 (d, <i>J</i> = 1.5 Hz, 1H), 4.68 (t, <i>J</i> = 4.6 Hz, 1H), 3.80 - 3.76 (m, 4H), 3.60 - 3.66 (d, <i>J</i> = 11.9 Hz, 2H), 2.14 - 2.05 (m, 4H), 1.72 - 1.66 (m, 4H), 1.42 (d, <i>J</i> = 6.1 Hz, 6H), 1.03 (s, 3H), 0.65 - 0.58 (m, 2H), 0.42 - 0.35 (m, 2H). MS (ESI) M/Z: 594.2 [M+H]⁺.
079F	 079F	¹H NMR (400 MHz, DMSO+D₂O-<i>d</i>₆) δ 7.85 (s, 1H), 7.59 (t, <i>J</i> = 53.6 Hz, 1H), 7.32 (d, <i>J</i> = 2.0 Hz, 1H), 7.08 (s, 1H), 7.02 (d, <i>J</i> = 3.2 Hz, 1H), 6.72 - 6.70 (m, 1H), 3.56 - 3.52 (m, 2H), 3.42 - 3.37 (m, 2H), 3.28 - 3.23 (m, 2H), 1.16 (d, <i>J</i> = 6.4 Hz, 6H), 1.01 (s, 3H), 0.62 - 0.56 (m, 2H), 0.36 - 0.33 (m, 2H). MS (ESI) M/Z: 564.1 [M+H]⁺.
079J	 079J	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.10 (s, 1H), 7.82 - 7.55 (m, 2H), 7.15 (s, 1H), 5.86 - 5.81 (m, 1H), 4.19 - 3.92 (m, 2H), 3.69 - 3.50 (m, 6H), 3.07 - 2.88 (m, 2H), 1.38 - 1.20 (m, 6H), 1.04 (s, 3H), 0.70 - 0.56 (m, 2H), 0.43 - 0.31 (m, 2H).

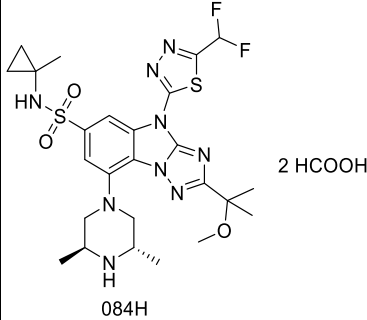
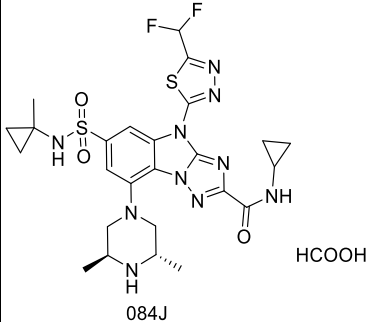
		¹⁹F NMR (376 MHz, DMSO-<i>d</i>₆) δ -96.95 (dd, <i>J</i> = 228.61 Hz, 20.68 Hz, 1 F), -101.50 (dd, <i>J</i> = 228.61 Hz, 34.59 Hz, 1 F), -110.58. MS (ESI) M/Z: 604.1 [M+H]⁺.
079J1	 079J1	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.26 (s, 1H), 8.10 (s, 1H), 7.82 - 7.55 (m, 2H), 7.67 (d, <i>J</i> = 1.6 Hz, 1H), 7.14 (d, <i>J</i> = 1.6 Hz, 1H), 5.84 - 5.80 (m, 1H), 4.17 - 3.98 (m, 2H), 3.54 - 3.47 (m, 6H), 3.05 - 2.89 (m, 2H), 1.24 (d, <i>J</i> = 6.4 Hz, 6H), 1.04 (s, 3H), 0.66 - 0.59 (m, 2H), 0.42 - 0.31 (m, 2H). ¹⁹F NMR (376 MHz, DMSO-<i>d</i>₆) δ -96.68, -97.29, -101.19, -101.80, -110.59. MS (ESI) M/Z: 604.1 [M+H]⁺.
079J2	 079J2	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.32 (s, 1H), 8.10 (s, 1H), 7.82 - 7.55 (m, 2H), 7.67 (s, 1H), 7.14 (s, 1H), 5.86 - 5.83 (m, 1H), 4.14 - 3.92 (m, 2H), 3.55 - 3.48 (m, 6H), 3.06 - 2.88 (m, 2H), 1.24 (d, <i>J</i> = 6.4 Hz, 6H), 1.04 (s, 3H), 0.68 - 0.57 (m, 2H), 0.42 - 0.31 (m, 2H). ¹⁹F NMR (376 MHz, DMSO-<i>d</i>₆) δ -96.61, -97.22, -101.29, -101.90, -110.59.

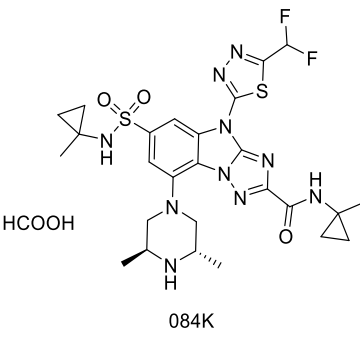
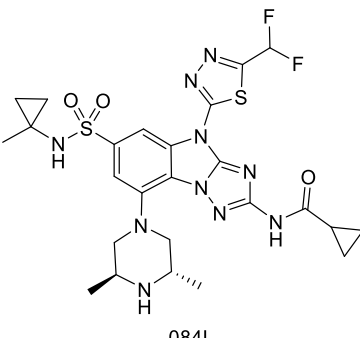
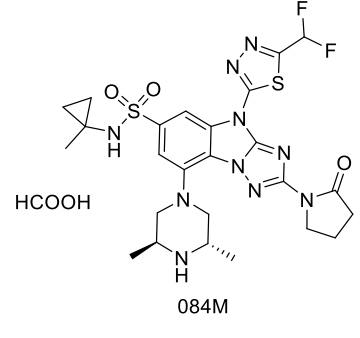
		MS (ESI) M/Z: 604.1 [M+H] ⁺ .
080B	 080B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.65 (s, 1H), 8.35 (s, 1H), 7.70 (t, <i>J</i> = 53.2 Hz, 1H), 6.94 (s, 1H), 5.34 - 5.29 (m, 1H), 3.93 - 3.86 (m, 2H), 3.51 - 3.47 (m, 2H), 3.36 - 3.35 (m, 2H), 3.28 - 3.26 (m, 2H), 2.65 - 2.56 (m, 1H), 2.30 - 2.23 (m, 1H), 2.17 - 2.01 (m, 2H), 1.18 (d, <i>J</i> = 6.4 Hz, 6H), 1.12 (s, 3H), 0.74 - 0.66 (m, 2H), 0.46 - 0.39 (m, 2H). MS (ESI) M/Z: 568.4 [M+H]⁺.
080B2	 080B2	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.65 (d, <i>J</i> = 1.2 Hz, 1H), 8.35 (s, 1H), 7.70 (t, <i>J</i> = 53.6 Hz, 1H), 6.94 (s, 1H), 5.30 (t, <i>J</i> = 6.4 Hz, 1H), 3.95 - 3.85 (m, 2H), 3.50 - 3.46 (m, 2H), 3.36 - 3.32 (m, 2H), 3.28 - 3.26 (m, 2H), 2.65 - 2.56 (m, 1H), 2.32 - 2.23 (m, 1H), 2.17 - 2.02 (m, 2H), 1.19 (d, <i>J</i> = 6.4 Hz, 6H), 1.12 (s, 3H), 0.74 - 0.66 (m, 2H), 0.47 - 0.40 (m, 2H). MS (ESI) M/Z: 568.1 [M+H]⁺.

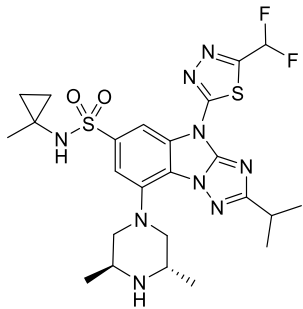
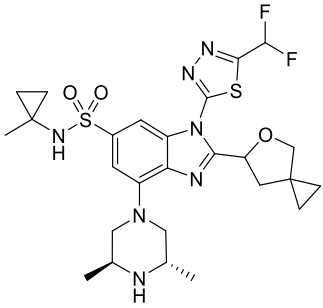
080B1	 080B1	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.64 (d, <i>J</i> = 1.6 Hz, 1H), 8.34 (s, 1H), 7.70 (t, <i>J</i> = 53.2 Hz, 1H), 6.94 (d, <i>J</i> = 1.2 Hz, 1H), 5.34 - 5.31 (m, 1H), 3.88 (t, <i>J</i> = 6.8 Hz, 2H), 3.50 - 3.46 (m, 2H), 3.37 - 3.34 (m, 2H), 3.28 - 3.24 (m, 2H), 2.67 - 2.61 (m, 1H), 2.30 - 2.24 (m, 1H), 2.15 - 2.03 (m, 2H), 1.19 (d, <i>J</i> = 6.4 Hz, 6H), 1.12 (s, 3H), 0.74 - 0.66 (m, 2H), 0.46 - 0.40 (m, 2H). MS (ESI) M/Z: 568.0 [M+H]⁺.
080H	 080H	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 10.01 (s, 1H), 8.69 (s, 2H), 8.30 (s, 1H), 7.71 (t, <i>J</i> = 53.2 Hz, 1H), 3.59 - 3.40 (m, 4H), 3.14 (dd, <i>J</i> = 12.0, 5.9 Hz, 2H), 1.23 (d, <i>J</i> = 6.4 Hz, 6H), 1.22 (s, 3H), 0.81 - 0.69 (m, 2H), 0.52 - 0.41 (m, 2H). MS (ESI) M/Z: 532.2 [M+H]⁺.
080J	 080J	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 9.62 (d, <i>J</i> = 1.5 Hz, 1H), 8.60 (s, 1H), 8.41 (s, 1H), 8.26 (s, 1H), 7.70 (t, <i>J</i> = 53.2 Hz, 1H), 6.97 (d, <i>J</i> = 1.6 Hz, 1H), 3.59 - 3.35 (m, 6H), 1.22 (d, <i>J</i> = 6.3 Hz, 6H), 1.13 (s, 3H), 0.75 - 0.65 (m, 2H), 0.48 - 0.40 (m, 2H).

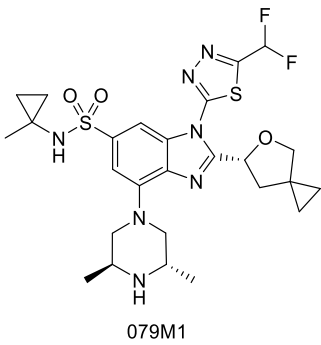
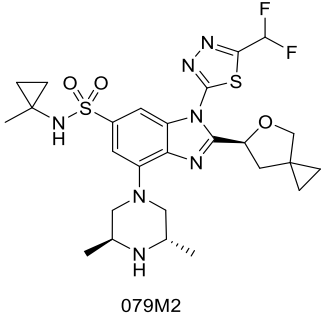
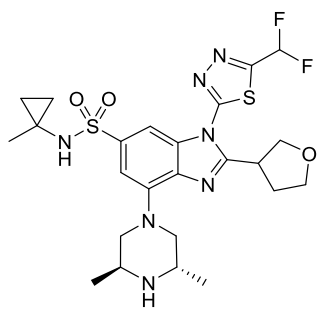
		MS (ESI) M/Z: 498.2 [M+H] ⁺ .
080K	 080K	¹H NMR (400 MHz, DMSO-<i>d</i>₆+D₂O) δ 9.81 (d, <i>J</i> = 1.5 Hz, 1H), 8.34 (s, 2H), 7.73 (t, <i>J</i> = 53.2 Hz, 1H), 7.08 (d, <i>J</i> = 1.6 Hz, 1H), 3.53 - 3.30 (m, 6H), 1.19 (d, <i>J</i> = 6.0 Hz, 6H), 1.13 (s, 3H), 0.77 - 0.66 (m, 2H), 0.52 - 0.34 (m, 2H). MS (ESI) M/Z: 532.0 [M+H]⁺.
082B	 082B	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.12 (s, 1H), 7.79 - 7.52 (m, 2H), 7.26 (s, 1H), 7.06 (s, 1H), 3.38 - 3.33 (m, 2H), 3.27 - 3.24 (m, 2H), 3.03 - 2.93 (m, 2H), 2.65 (s, 3H), 1.22 (d, <i>J</i> = 6.4 Hz, 6H), 1.00 (s, 3H), 0.62 - 0.56 (m, 2H), 0.36 - 0.33 (m, 2H). MS (ESI) M/Z: 539.0 [M+H]⁺.
082C	 082C	¹H NMR (400 MHz, DMSO-<i>d</i>₆+D₂O) δ 7.76 - 7.52 (m, 2H), 7.32 (s, 1H), 7.10 (s, 1H), 3.52 (s, 3H), 3.30 - 3.25 (m, 2H), 3.22 - 3.19 (m, 2H), 3.00 - 2.91 (m, 2H), 1.20 (d, <i>J</i> = 6.4 Hz, 6H), 1.00 (s, 3H), 0.61 - 0.55 (m, 2H), 0.37 - 0.35 (m, 2H). MS (ESI) M/Z: 575.0 [M+H]⁺.

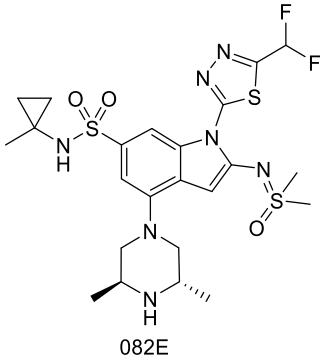
083A	 083A	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.48 (d, <i>J</i> = 1.6 Hz, 1H), 8.45 (s, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 6.80 (s, 1H), 5.43 - 5.38 (m, 1H), 3.92 - 3.85 (m, 2H), 3.37 - 3.23 (m, 6H), 2.62 - 2.60 (m, 1H), 2.33 - 2.31 (m, 1H), 2.11 - 2.05 (m, 2H), 1.26 (d, <i>J</i> = 4.2 Hz, 6H), 1.11 (s, 3H), 0.74 - 0.65 (m, 2H), 0.48 - 0.44 (m, 2H). MS (ESI) M/Z: 568.1 [M+H]⁺.
083A1	 083A1	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.48 (d, <i>J</i> = 1.6 Hz, 1H), 8.45 (s, 1H), 7.65 (t, <i>J</i> = 53.2 Hz, 1H), 6.80 (s, 1H), 5.42 (t, <i>J</i> = 6.4 Hz, 1H), 3.93 - 3.85 (m, 2H), 3.42 - 3.40 (m, 4H), 3.28 - 3.25 (m, 2H), 2.64 - 2.62 (m, 1H), 2.35 - 2.29 (m, 1H), 2.09 - 2.05 (m, 2H), 1.27 (d, <i>J</i> = 5.6 Hz, 6H), 1.11 (s, 3H), 0.74 - 0.65 (m, 2H), 0.48 - 0.44 (m, 2H). MS (ESI) M/Z: 568.1 [M+H]⁺.
083A2	 083A2	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.49 (d, <i>J</i> = 1.6 Hz, 1H), 8.45 (s, 1H), 7.66 (t, <i>J</i> = 53.2 Hz, 1H), 6.81 (s, 1H), 5.40 (t, <i>J</i> = 6.4 Hz, 1H), 3.93 - 3.89 (m, 2H), 3.46 - 3.40 (m, 4H), 3.28 - 3.25 (m, 2H), 2.59 - 2.50 (m, 1H), 2.33 - 2.30 (m, 1H),

		2.11 - 2.04 (m, 2H), 1.29 (d, $J = 5.2$ Hz, 6H), 1.11 (s, 3H), 0.75 - 0.66 (m, 2H), 0.48 - 0.44 (m, 2H). MS (ESI) M/Z: 568.1 $[M+H]^+$.
084H		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆ +D ₂ O) δ 8.71 (d, $J = 1.5$ Hz, 1H), 8.41 (s, 2H), 7.66 (t, $J = 53.0$ Hz, 1H), 7.46 (d, $J = 1.6$ Hz, 1H), 3.55 - 3.27 (m, 4H), 3.11 (s, 3H), 2.92 (dd, $J = 11.1, 5.9$ Hz, 2H), 1.66 (s, 6H), 1.23 (d, $J = 6.4$ Hz, 6H), 1.08 (s, 3H), 0.69 - 0.62 (m, 2H), 0.43 - 0.37 (m, 2H). MS (ESI) M/Z: 610.2 $[M+H]^+$.
084J		¹ H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 8.93 (s, 1H), 8.78 (d, $J = 1.4$ Hz, 1H), 8.72 (d, $J = 4.3$ Hz, 1H), 8.42 (s, 1H), 7.71 (t, $J = 52.0$ Hz, 1H), 7.55 (d, $J = 1.5$ Hz, 1H), 3.99 - 3.87 (m, 2H), 3.57 - 3.47 (m, 2H), 3.41 - 3.30 (m, 2H), 2.90 (td, $J = 7.3, 3.7$ Hz, 1H), 1.49 (d, $J = 6.6$ Hz, 6H), 1.11 (s, 3H), 0.82 - 3.62 (m, 6H), 0.47 - 0.39 (m, 2H). MS (ESI) M/Z: 621.2 $[M+H]^+$.

084K	 084K	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.92 (s, 1H), 8.78 (d, <i>J</i> = 1.4 Hz, 1H), 8.42 (s, 1H), 7.72 (t, <i>J</i> = 53.0 Hz, 1H), 7.55 (d, <i>J</i> = 1.6 Hz, 1H), 3.96 - 3.86 (m, 2H), 3.56 - 3.46 (m, 2H), 3.34 - 3.38 (m, 2H), 1.48 (d, <i>J</i> = 6.6 Hz, 6H), 1.42 (s, 3H), 1.24 (s, 1H), 1.12 (s, 3H), 0.86 - 0.80 (m, 2H), 0.73 - 0.64 (m, 4H), 0.46 - 0.40 (m, 2H). MS (ESI) M/Z: 635.2 [M+H]⁺.
084L	 084L	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 11.11 (s, 1H), 8.68 (s, 1H), 8.29 (s, 1H), 7.69 (t, <i>J</i> = 53.1 Hz, 1H), 7.43 (s, 1H), 3.41 - 3.35 (m, 4H), 2.91 - 2.87 (m, 2H), 2.01 - 1.99 (m, 1H), 1.19 (d, <i>J</i> = 6.5 Hz, 6H), 1.09 (s, 3H), 0.87 - 0.85 (m, 4H), 0.67 - 0.64 (m, 2H), 0.41 - 0.39 (m, 2H). MS (ESI) M/Z: 621.2 [M+H]⁺.
084M	 084M	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.70 (d, <i>J</i> = 1.5 Hz, 1H), 8.32 (s, 1H), 8.29 (s, 1H), 7.68 (t, <i>J</i> = 53.1 Hz, 1H), 7.45 (d, <i>J</i> = 1.6 Hz, 1H), 4.07 - 3.95 (m, 2H), 3.51 - 3.47 (m, 2H), 3.38 - 3.36 (m, 2H), 2.96 (dd, <i>J</i> = 11.2, 5.9 Hz, 2H), 2.60 - 2.50 (m, 2H), 2.17 (p, <i>J</i> = 7.6 Hz, 2H), 1.26 (d, <i>J</i> = 6.4

		Hz, 6H), 1.10 (s, 3H), 0.66 (q, $J = 4.4$ Hz, 2H), 0.45 - 0.33 (m, 2H). MS (ESI) M/Z: 621.2 $[M+H]^+$.
065Y	 065Y	^1H NMR (400 MHz, DMSO-d_6+D$_2$O) δ 8.68 (d, $J = 1.2$ Hz, 1H), 7.70 - 7.43 (m, 2H), 3.49 - 3.47 (m, 2H), 3.36 - 3.33 (m, 2H), 3.20 - 3.14 (m, 1H), 2.99 - 2.96 (m, 2H), 1.37 (d, $J = 6.8$ Hz, 6H), 1.25 (d, $J = 6.4$ Hz, 6H), 1.05 (s, 3H), 0.64 - 0.61 (m, 2H), 0.41 - 0.38 (m, 2H). MS (ESI) M/Z: 580.3 $[M+H]^+$.
079M	 079M	^1H NMR (400 MHz, DMSO-d_6) δ 8.06 (s, 1H), 7.81 - 7.54 (m, 2H), 7.09 (s, 1H), 5.59 - 5.55 (m, 1H), 3.67 - 3.60 (m, 2H), 3.50 - 3.35 (m, 4H), 3.29 - 3.26 (m, 2H), 2.82 - 2.75 (m, 1H), 2.35 - 2.32 (m, 1H), 1.17 (d, $J = 6.4$ Hz, 6H), 1.03 (s, 3H), 0.73 - 0.70 (m, 2H), 0.65 - 0.62 (m, 4H), 0.37 - 0.34 (m, 2H). MS (ESI) M/Z: 594.4 $[M+H]^+$.

079M1	 079M1	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.06 (s, 1H), 7.81 - 7.54 (m, 2H), 7.09 (d, <i>J</i> = 1.2 Hz, 1H), 5.60 - 5.57 (m, 1H), 3.67 - 3.60 (m, 2H), 3.50 - 3.47 (m, 2H), 3.40 - 3.35 (m, 2H), 3.29 - 3.25 (m, 2H), 2.82 - 2.77 (m, 1H), 2.37 - 2.32 (m, 1H), 1.17 (d, <i>J</i> = 6.4 Hz, 6H), 1.03 (s, 3H), 0.75 - 0.71 (m, 2H), 0.65 - 0.60 (m, 4H), 0.37 - 0.34 (m, 2H). MS (ESI) M/Z: 594.4 [M+H]⁺.
079M2	 079M2	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.06 (s, 1H), 7.81 - 7.54 (m, 2H), 7.09 (d, <i>J</i> = 1.2 Hz, 1H), 5.58 - 5.55 (m, 1H), 3.67 - 3.65 (m, 2H), 3.41 - 3.26 (m, 6H), 2.80 - 2.75 (m, 1H), 2.35 - 2.30 (m, 1H), 1.17 (d, <i>J</i> = 6.4 Hz, 6H), 1.04 (s, 3H), 0.75 - 0.72 (m, 2H), 0.68 - 0.59 (m, 4H), 0.39 - 0.34 (m, 2H). MS (ESI) M/Z: 594.4 [M+H]⁺.
079N	 079N	¹H NMR (400 MHz, DMSO-<i>d</i>₆) δ 8.03 (s, 1H), 7.68 (t, <i>J</i> = 53.2 Hz, 1H), 7.50 (s, 1H), 7.08 (s, 1H), 4.05 - 4.03 (m, 2H), 3.97 - 3.87 (m, 2H), 3.85 - 3.80 (m, 1H), 3.47 - 3.40 (m, 4H), 3.29 - 3.26 (m, 2H), 2.39 - 2.33 (m, 1H), 2.29 - 2.20 (m, 1H), 1.19 (d, <i>J</i> = 6.8 Hz, 6H), 1.03 (s, 3H), 0.65

		- 0.59 (m, 2H), 0.37 - 0.34 (m, 2H). MS (ESI) M/Z: 568.4 [M+H]⁺.
082E	 082E	¹H NMR (400 MHz, DMSO-<i>d</i>₆+D₂O) δ 8.76 (s, 1H), 7.46 (t, <i>J</i> = 53.6 Hz, 1H), 7.11 (d, <i>J</i> = 1.6 Hz, 1H), 5.99 (s, 1H), 3.51 - 3.50 (m, 6H), 3.25 - 3.23 (m, 2H), 2.98 - 2.95 (m, 2H), 2.88 - 2.74 (m, 2H), 1.21 (d, <i>J</i> = 6.4 Hz, 6H), 1.00 (s, 3H), 0.63 - 0.55 (m, 2H), 0.36 - 0.29 (m, 2H). MS (ESI) M/Z: 588.2 [M+H]⁺.

[1337] Biological Evaluation

[1338] Test Example 1: Enzymatic inhibitory activity of the compounds of the present disclosure against PARG

[1339] In this experiment, the enzymatic inhibitory activity of the compounds of the present disclosure against PARG was determined using an HTRF (homogeneous time-resolved fluorescence) assay.

[1340] 1. Experimental materials

[1341] HTRF assay reagents were purchased from PerkinElmer (Cat. Nos. 61HISTLB and 610SAXLB). The purified protein was prepared in-house.

10 [1342] PARG enzyme reaction buffer: 50 mM Tris (pH 7.4), 0.1 mg/mL BSA, 3 mM EDTA, 0.4 mM EGTA, 1 mM DTT, 50 mM KCl, and 0.01% Tween 20.

[1343] 2. Experimental methods

[1344] 1) Using an ultra-micro pipette, the compounds of the present disclosure were serially diluted (starting at 10 μ M with 3- to 5-fold serial dilutions) and added to a 384-well reaction plate, with each concentration tested in duplicate wells. Control group 1 was added with 10 μ M control compound (100% inhibition group). Control group 2 was added with
5 DMSO (0% inhibition group). After compound addition, the 384-well plate was centrifuged at 1000 rpm for 1 minute.

[1345] 2) 2.5 μ L of PARG protein was added to each well and incubated with the compounds of the present disclosure at room temperature for 15 minutes, followed by centrifugation at 1000 rpm for 1 minute.

10 [1346] 3) 2.5 μ L of PARylated PARP1 protein was added to each well and incubated at room temperature for 60 minutes, followed by centrifugation at 1000 rpm for 1 minute.

[1347] 4) 5 μ L of His-Tb & SA-XL665 HTRF assay reagents were added to each well and incubated at room temperature for 60 minutes, followed by centrifugation at 1000 rpm for 1 minute.

15 [1348] 5) Luminescence signals were measured using a PHERAstar FSX microplate reader from BMG.

[1349] 6) Data analysis was performed using GraphPad Prism 8. The IC₅₀ values of the compounds of the present disclosure were calculated as follows. The average inhibition rate of control group 1 (100% inhibition group) was set as the relative inhibition rate of 100%.
20 The average value of duplicate wells in control group 2 (0% inhibition group) was set as the relative inhibition rate of 0%. The HTRF signal values were converted into relative

inhibition rates. The IC_{50} values of the compounds were calculated by fitting the data to a four-parameter logistic model. The experimental results are shown in Table 15.

[1350] Table 15: Enzymatic inhibitory activity of the compounds of the present disclosure against PARG

Example compound	IC_{50} against PARG enzyme (nM)
A002	16.4
B002	11.6
A003	5.4
A004	10.7
B003	10.2
B001	44.7
C002	48.2
B004	15.6
B005	11.5
A006	3.7
A005	30.4
B011	9.9
B010	31.4
A013	2.9
A018	34.1
A019	18.1

A023	1.5
A027	3.8
A029	3.0
A030	18.2
A005	30.4
A014	12.3
A028	19.0
B013	21.3
B014	31.4
B015	15.8
A032	2.4
A031	35.2
A033	4.0
A036	6.8
A037	6.8
B016	21.2
B017	31.5
B019	6.3
B020	19.8
B021	25.1
A038	5.2

A039	3.5
B022	18.7
B023	16.7
A040	5.0
A041	4.4
A042	5.1
A043	8.0
A044	7.0
A045	13.9
A046	5.5
A047	15.0
A048	34.8
A049	15.7
A050	22.5
B024	16.5
A051	7.5
A052	1.6
A053	6.7
A054	38.6
H001	1.1
A055	11.9

A056	5.2
008B	9.6
057L	8.6
057M	2.8
057N	8.3
057P	29.3
057Q	5.1
059C	6.5
059D	28.8
065I	1.8
065J	2.4
065K	6.3
065L	5.5
065M	1.4
065N	7.3
065P	5.8
067B	6.9
067G	8.7
067J	7.8
067JD	31.6
067L	4.9

067LD	2.2
067M	29.0
067N	3.1
067ND	2.3
067P	5.2
067Q	5.0
067R	3.4
067S	13.3
067T	16.0
067U	20.0
067V	13.4
067W1	19.7
067W2	13.1
067X	21.1
067Y	21.2
068A	3.5
068B	15.8
069D	23.5
070A	15.3
070B	20.3
071C2	8.9

072B	15.9
073A	30.6
073B	4.5
074A	0.8
074A-11	2.8
074B	2.7
074C	2.9
074H	7.5
074J	10.8
074K	1.9
075B	35.7
076A	13.0
076B	9.7
076C	8.6
076D	14.7
076E	4.9
076F1	30.6
076G	9.0
076H1	14.4
076H2	14.0
076J	7.0

077A	10.4
077B	3.4
077F	9.2
077G	1.6
077H	3.0
077J	10.4
077K	12.8
077N	3.4
077T	27.8
077V	21.7
021B	3.3
065O	3.1
065R	0.4
065S	1.4
065T	1.5
065U	0.5
065W	0.8
065X	0.5
065Z	1.0
074G	3.3
074L	15.0

074M	6.2
077B2	1.6
077X	21.3
077Y	10.3
079J	1.8
079J1	0.6
080B	0.5
080B1	2.2
080B2	0.4
080J	2.4
080K	1.7
083A	2.1
083A1	14.6
083A2	1.0
084H	0.7
084J	0.7
084K	0.7
084L	1.1
084M	0.8
065Y	0.8
079M	3.8

079M2	1.9
079N	6.2
082E	5.5
081G	4.9

[1351] Conclusion: Analysis of the above experimental data indicated that the compounds of the present disclosure exhibited significant inhibitory activity against PARG enzyme.

[1352] Test Example 2: Inhibitory effect of the compounds of the present disclosure on the proliferation of KURAMOCHI cells

5 **[1353]** In this experiment, the inhibitory effect of the compounds of the present disclosure on the proliferation of the cancer cell line KURAMOCHI was evaluated by measuring intracellular ATP levels using a bioluminescent assay, and the half maximal inhibitory concentration (IC₅₀) was determined.

[1354] 1. Experimental materials

10 **[1355]** RPMI 1640 medium (Cat. No. 11875-093), fetal bovine serum (10099-141), and 100× Pen/Strep (15070-063) were purchased from GIBCO. CellTiter-Glo Luminescent Cell Viability Assay reagent (Cat. No. G7573) was purchased from Promega.

[1356] 2. Experimental methods

[1357] 1) Day 1: KURAMOCHI cells were counted using a cell counter and seeded into a
15 96-well culture plate at a density of 4000 cells per well in 100 µL medium. The plate was incubated overnight in an incubator (37°C, 5% CO₂).

[1358] 2) Day 2: Using a D300e digital dispenser (TECAN), 500 nL of serially diluted test

compounds of the present disclosure (starting at 10 μ M, a total of 9 concentrations, 1:4 dilution) were added to the cells in the culture plate. The final concentration of DMSO was 0.5%. The cell culture plate was incubated for 7 days in a cell culture incubator (37°C, 5% CO₂). Control group 1 received only medium and DMSO (100% inhibition group).

5 Control group 2 received only DMSO (0% inhibition group). The final concentration of DMSO in both groups was 0.5%.

[1359] 3) Day 9: 100 μ L of CellTiter-Glo reagent was added to each well. The plate was shaken at 500 rpm for 2 minutes, centrifuged at 1000 rpm for 1 minute, and then incubated at room temperature in the dark for 10 minutes to stabilize the luminescence signal.

10 [1360] 4) Luminescence signals were measured using an EnVision microplate reader (PerkinElmer).

[1361] 5) Data analysis was performed using GraphPad Prism 8. The IC₅₀ values of the compounds of the present disclosure were calculated as follows. The CTG signal values were analyzed. The average inhibition rate of control group 1 (100% inhibition group) was set as the relative inhibition rate of 100%. The average inhibition rate of control group 2 (0% inhibition group) was set as the relative inhibition rate of 0%. The CTG signal values were converted into relative inhibition rates. The inhibition percentage (inhibition%) for each concentration of the compounds of the present disclosure was calculated according to the following formula:

20 [1362] $\text{Inhibition\%} = (b - x) / (b - a) * 100\%$;

[1363] a = CTG value (highest concentration), b = CTG value (blank well), x = CTG value

(test well).

[1364] IC₅₀ was calculated using GraphPad Prism 8.

[1365] (1) The concentration and inhibition rate corresponding to each well were recorded.

Statistical calculation was performed using Log10 (compound concentration).

5 **[1366]** (2) The data were input into GraphPad Prism 8 and Analysis was selected.

[1367] (3) Nonlinear regression (curve fit) was selected.

[1368] (4) Log (inhibitor) vs. response - Variable slope was selected.

[1369] (5) The calculation formula was selected, and the calculation was performed according to the following formula: $Y = \text{Bottom} + (\text{Top} - \text{Bottom}) / (1 + 10^{((\text{LogIC}_{50} - X) * \text{HillSlope}))}$; X: log of dose or concentration; Y: response; Top and Bottom: maximum and minimum response.

[1370] (6) The IC₅₀ values were calculated by fitting the data. The experimental results are shown in Table 16.

15 **[1371]** Table 16: Inhibitory effect of the compounds of the present disclosure on the proliferation of KURAMOCHI cells

Example compound	IC ₅₀ against KURAMOCHI cells (nM)
A002	86
B002	16
A003	13
B003	16
C002	25

D002	85
B001	53
A004	80
F002	49
A008	59
A006	8
A005	45
A018	7
A019	16
A023	4
A027	5
A029	8
A030	10
A013	13
A014	37
A028	48
B010	59
B011	32
B013	53
B014	43
A032	5

A031	63
A033	9
A036	12
A037	14
B016	74
B017	20
B019	19
B020	59
B021	51
A038	7
A039	7
A040	9
A041	11
A042	6
A043	11
A045	16
A046	8
A047	13
A048	27
A049	50
A050	20

A051	12
A052	2
A053	37
008B	9
057L	8
057M	6
057N	9
057Q	7
059C	20
059D	40
065I	5
065J	7
065K	22
065L	18
065M	3
065N	9
065P	7
067B	15
067G	26
067J	21
067L	4

067LD	5
067N	3
067ND	3
067P	74
067Q	13
067R	6
067S	14
067T	11
067U	21
067V	83
067W1	23
067W2	11
067X	23
067Y	34
068A	4
068B	17
069E	55
070A	18
070B	25
071C2	50
072B	53

072D	52
073A	34
073B	22
074A	1
074A-11	4
074B	3
074C	13
074H	12
074K	8
076E	35
076H1	34
076H2	40
076J	9
077A	11
077B	7
077F	9
077G	2
077H	5
077N	8
077S	58
077T	35

077V	37
078A	30
078B	34
078C	15
021B	11
065O	3
065R	2
065S	2
065T	13
065U	2
065W	4
065X	4
065Z	4
074G	40
074M	16
077B2	3
077X	16
079J	4
079J1	2
080B	1
080B1	4

080B2	0.6
080J	5
080K	4
083A	4
083A1	25
083A2	3
084H	3
084J	16
084K	9
084L	29
084M	9
065Y	6
079M	15
081G	25

[1372] Conclusion: Analysis of the above experimental data indicated that the example compounds of the present disclosure exhibited an inhibitory effect on the proliferation of KURAMOCHI cells.

[1373] **Test Example 3: *In vitro* evaluation of PXR activation potential of the compounds of the present disclosure in stably transfected DPX2 cells**

[1374] 1. Experimental purpose

[1375] The purpose of this study was to evaluate the potential of the compounds of the

present disclosure and the comparative compound (WO2023183850A1, compound of formula A) to activate PXR *in vitro*, thereby inducing drug-metabolizing enzymes.

[1376] 2. Experimental materials

[1377] DPX2 cells (HepG2 cell line stably transfected with PXR and a CYP3A4 promoter-driven luciferase reporter gene) were purchased from Puracyp Inc (Carlsbad, CA). Fetal
5 bovine serum was purchased from Acantor.

[1378] 3. Experimental methods

[1379] 1) DPX2 cells were cultured in medium containing 10% fetal bovine serum (FBS).

[1380] 2) DPX2 cells were cultured in a T-75 flask in a cell culture incubator at 37°C with
10 5% CO₂ and 95% relative humidity. The cells were subjected to trypsinization when they reached 80% to 90% confluence.

[1381] 3) The medium was aspirated from the T-75 flask, and the cells were rinsed with 10 mL of PBS. After removing PBS, 3 to 5 mL of trypsin was added. The flask was incubated at 37°C for approximately 5 minutes or until cell detachment and floating were
15 observed. An excess of serum-containing medium was then added to inactivate the trypsin.

[1382] 4) The detached cells were transferred to a 50 mL centrifuge tube and centrifuged at 150 g for 5 minutes. The cell pellet was resuspended in seeding medium to a density of 3.2×10^5 cells/mL. 25 μ L of the cell suspension was then seeded into each well of a 384-well cell culture plate. The 384-well plate was incubated for 24 hours in the cell culture
20 incubator before conducting the PXR activation assay.

[1383] 5) DMSO stock solutions of test compounds, positive control (rifampicin), and

negative control (propranolol) were prepared at 1000× the final incubation concentrations using a Tecan system. The final incubation concentration of positive control (rifampicin) was 1 μ M, 10 μ M, or 20 μ M. The final incubation concentration of negative control (propranolol) was 10 μ M. The final incubation concentrations of test compounds were
5 provided by the client. The final concentration of DMSO in incubation buffer was 0.1%.

[1384] 6) The 384-well plate was removed from the cell culture incubator, and 25 nL of DMSO stock solution containing test or control compounds was dispensed into the corresponding wells using Echo, with each experimental condition tested in triplicate. The 384-well plate was returned to the cell culture incubator and incubated for 24 or 48 hours.

10 **[1385]** 7) Prior to the experiment, cell morphology and monolayer integrity were examined to ensure acceptable quality. After 24 or 48 hours of cell treatment, quantification of PXR activation was performed.

[1386] 8) CellTiter Fluor™ Cell Viability Assay Kit and One-Glo Luciferase Assay Kit were equilibrated to room temperature. GF-AFC substrate (10 μ L) was transferred to assay
15 buffer (10 mL), followed by 1:1 dilution with 10 mL of PBS to prepare a cell viability assay system. One-Glo luciferase assay buffer was mixed with One-Glo luciferase assay substrate to prepare a luciferase assay system.

[1387] 9) The 384-well plate was removed from the cell culture incubator, and the medium was aspirated from the plate. 25 μ L of the prepared cell viability assay system was gently
20 added to each well, followed by incubation for 30 minutes in the cell culture incubator at 37°C.

[1388] 10) The 384-well plate was removed from the cell culture incubator, and fluorescence of individual wells was measured using a microplate reader in fluorescence mode with excitation at 400 nm and emission at 505 nm. Subsequently, 25 µL of the prepared luciferase assay system was gently added to each well, followed by vortexing and incubation at room temperature for 5 minutes, and luminescence of individual wells was measured using a microplate reader.

[1389] 4. Data analysis

[1390] 1) Cell viability

[1391] Cell viability percentage was calculated using the following formula: Cell viability (%) = $I_{\text{sample}} / I_{\text{vehicle}} \times 100$, where I_{sample} is the mean fluorescence intensity of treated wells; I_{vehicle} is the mean fluorescence intensity of cells treated with 0.1% DMSO.

[1392] 2) Fold activation calculation

[1393] All calculations were performed using Microsoft Excel. Normalized luciferase activity was calculated as RLU/RFU, where RLU represents the average of relative light units of triplicate wells for each test compound at each dose, and RFU represents the average of relative fluorescence units of triplicate wells for each test compound at each dose. RLU and RFU for the vehicle represent the average of triplicate wells for the cell samples treated with 0.1% DMSO. Fold activation at the mRNA level was calculated using the following formula: Fold activation = $(RLU_{\text{sample}} / RFU_{\text{sample}}) / (RLU_{\text{vehicle}} / RFU_{\text{vehicle}})$

[1394] Table 17: Fold activation of PXR by the compounds of the present disclosure

Example compound	Fold activation
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Comparative compound	3.16
065R	1.45
065S	1.82
065W	1.11

[1395] Conclusion: As shown in Table 17, the compounds of the present disclosure exhibited weaker activation ability compared to the comparative compound.

[1396] Test Example 4: Pharmacokinetic evaluation of the compounds of the present disclosure in mice

5 **[1397]** Using mice as test animals, the compounds of the present disclosure were administered via intravenous bolus and oral injection. Plasma samples were collected at specific time points. Compound concentrations in plasma were determined by LC-MS/MS, and PK parameters were calculated to characterize the pharmacokinetic behavior of the compounds of the present disclosure in plasma.

10 **[1398]** 1. Experimental protocol

[1399] 1.1 Test compounds:

[1400] Some compounds of the present disclosure.

[1401] 1.2 Experimental animals

[1402] CD-1 mice, male, supplied by Zhejiang Vital River Laboratory Animal Technology
15 Co., Ltd.

[1403] BALB/c nude mice, female, supplied by Jiangsu GemPharmatech Co., Ltd.

[1404] 1.3 Dosing regimen

[1405] Dosing regimen for CD-1 mice: Both the IV (intravenous) and PO (oral) experimental groups consisted of 3 mice. The IV group was administered at a dose of 1 mg/kg and a volume of 5 mL/kg. The PO group was administered at a dose of 30 mg/kg and a volume of 10 mL/kg. The dosing vehicle was 5% (v/v) DMSO/10% (v/v) Solutol/85% (v/v) saline.

[1406] Dosing regimen for BALB/c nude mice: The PO (oral) experimental group consisted of 3 mice, which were administered at a dose of 30 mg/kg and a volume of 10 mL/kg. The dosing vehicle was 5% (v/v) DMSO/10% (v/v) Solutol/85% (v/v) saline.

[1407] 1.4 Experimental equipment

[1408] The centrifuge was purchased from Eppendorf. The pipettes were purchased from Eppendorf.

[1409] 1.5 Sample collection

[1410] Following administration, 0.025 mL of blood was collected via venipuncture at the following time points: 0.0833 (IV), 0.25, 0.5, 1, 2, 4, 8, and 24 hours. Blood samples were collected into EDTA-K2 tubes and centrifuged at 4°C and 2000 g for 10 minutes to separate plasma, which was stored at -80°C.

[1411] 1.6 Sample processing

[1412] Mouse plasma processing:

[1413] 1) 15 µL of plasma was mixed with 200 µL of acetonitrile for protein precipitation. The mixture was vortexed and centrifuged for 15 minutes.

[1414] 2) The supernatant after processing was diluted with water and analyzed by

LC/MS/MS to determine the concentration of the test compound.

[1415] 2. Experimental results

[1416] Pharmacokinetic parameters were calculated using WinNonlin 6.1. The PK parameters following IV and PO administration in CD-1 mice are shown in Table 18. The

5 PK parameters following PO administration in BALB/c nude mice are shown in Table 19.

Specifically, $C_{\max}$ represents maximum plasma concentration, CL represents clearance, V_{ss} represents volume of distribution at steady state, $T_{1/2}$ represents terminal elimination half-life, MRT_{Inf} represents mean residence time, AUC represents area under the plasma concentration-time curve, and F represents bioavailability.

10 **[1417]** Table 18: Pharmacokinetic parameters of the compounds of the present disclosure in CD-1 mice

Compound	Route of administration	Dose (mg/kg)	$C_{\max}$ (nM)	CL (mL/hr/kg)	V_{ss} (L/kg)	$T_{1/2}$ (hr)	MRT_{Inf} (hr)	AUC (hr*nM)
065R	IV	1	/	50	6.8	2.2	2.3	555
	PO	30	1609	/	/	2.4	4.6	11246
065W	IV	1	/	22	7.2	5.2	5.6	1256
	PO	30	1981	/	/	3.3	5.7	18280

[1418] Table 19: Pharmacokinetic parameters of the compounds of the present disclosure in BALB/c nude mice

Compound	Route of administration	Dose (mg/kg)	$C_{\max}$ (nM)	$T_{1/2}$ (hr)	MRT_{Inf} (hr)	AUC (hr*nM)
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065R	PO	30	1616	2.62	4.39	9520
065S	PO	30	1345	2.69	4.80	9210
065W	PO	30	1340	5.28	7.74	16397
080B2	PO	30	1868	2.45	3.27	8349

[1419] Note: “/” indicates not determined.

[1420] Conclusion: As shown in Tables 18 and 19, the compounds of the present disclosure exhibited favorable pharmacokinetic properties in both CD-1 mice and BALB/c nude mice.

[1421] Test Example 5: *In vivo* efficacy study

5 **[1422] 1. Experimental purpose**

[1423] The purpose of this study was to evaluate the anti-tumor activity and toxic side effects of the compounds of the present disclosure, 065M and 077B2, after 16 consecutive days of oral administration in a KURAMOCHI ovarian cancer xenograft model.

[1424] 2. Experimental materials

10 **[1425]** NOD SCID mice, female, SPF grade, purchased from Beijing Anikeepter Biotech Co., Ltd.

[1426] KURAMOCHI cells, purchased from JCRB.

[1427] 3. Experimental procedures

[1428] 3.1 Cell culture

15 **[1429]** KURAMOCHI tumor cells (purchased from JCBR) were cultured in RPMI 1640 medium containing 10% inactivated fetal bovine serum, 100 U/mL penicillin, and 100 µg/mL streptomycin in an incubator at 37°C with 5% CO₂. The culture medium was

changed weekly. The cells were passaged when they reached 80% to 90% confluence, limiting the number of passages to no more than 4 to 5 times. Tumor cells in the logarithmic growth phase were used for *in vivo* implantation.

[1430] 3.2 Cell inoculation

5 [1431] KURAMOCHI tumor cells (2×10^7 cells) resuspended in serum-free RPMI 1640 medium + Matrigel (1:1) were subcutaneously inoculated into the right flank of each experimental animal at a dose of 200 μ L. A total of 35 mice were inoculated: 35 mice for the efficacy study; 15 mice for the PK/PD study; 10 mice remaining after grouping. When the tumor volume reached approximately 150 to 200 mm³, the mice were grouped for dosing
10 to initiate the efficacy study. Specifically, they were divided into 7 groups, with 5 mice per group. The remaining animals were grouped for dosing when the tumor volume reached approximately 250 mm³.

[1432] 3.3 Tumor grouping, treatment, and measurements

[1433] a. Groups and dosing regimens are shown in Table 20.

15 [1434] Table 20: *In vivo* efficacy study design

Group	Number of animals	Treatment	Dose (mg/kg)*	Concentration (mg/mL)*	Route of administration	Regimen
G1	5	Vehicle control	-	-	PO	QD $\times$ 16 days
G2	5	Comparative	30	3	PO	QD $\times$ 16 days

		compound				
G3	5	065M	30	3	PO	QD × 16 days
G4	5	077B2	30	3	PO	BID × 16 days
G5	5	077B2	100	10	PO	QD × 16 days

[1435] Note: QD: once daily; BID: twice daily.

[1436] b. Treatment was initiated after grouping, with a dosing volume of 10 µL/g body weight via oral administration (PO). Animals were weighed daily before dosing and administered once daily for 21 consecutive days. Tumor diameters were measured twice weekly.

[1437] c. Tumor volume (TV) was measured twice weekly to monitor changes in tumor size and growth rate. Tumor volume was calculated as: $V = 1/2 \times a \times b^2$, where a and b represent tumor length and tumor width, respectively. The growth inhibitory effect of compounds on tumor tissue was evaluated using tumor growth inhibition (TGI (%)). $TGI (\%) = [1 - (\text{average tumor volume of a given treatment group} - \text{average tumor volume of the treatment group on the day of grouping}) / (\text{average tumor volume of the negative control group} - \text{average tumor volume of the negative control group on the day of grouping})] \times 100\%$. Data for both the treatment group and the negative control group were collected on the same day.

[1438] d. The mice were weighed during tumor measurements. The relationship between changes in body weight and time of treatment was recorded. The survival and health status of the mice, including general conditions such as activity level and food intake during the dosing period, were also observed. Treatment was discontinued if the body weight of a

single animal decreased by more than 15%. Treatment was resumed when the body weight recovered to within 10% of baseline. If treatment was discontinued for more than 48 hours and the animal was in good condition, treatment could be resumed even if the body weight had not recovered to within 10%. Nutritional gel supplementation was provided during
5 treatment discontinuation.

[1439] e. At the study endpoint, the mice were euthanized. Carcasses were frozen in a freezer and transferred to a qualified medical waste disposal unit for disposal.

[1440] 4. Experimental results

[1441] Table 21: Experimental data

Group	Dose (mg/kg)	Tumor volume ^a (mm ³)	TGI (%)
G1: Vehicle control	-	567 ± 66	-
G2: Comparative compound QD	30	90 ± 22	120
G3: 065M QD	30	62 ± 6	127
G4: 077B2 BID	30	61 ± 9	127
G5: 077B2 QD	100	57 ± 10	127

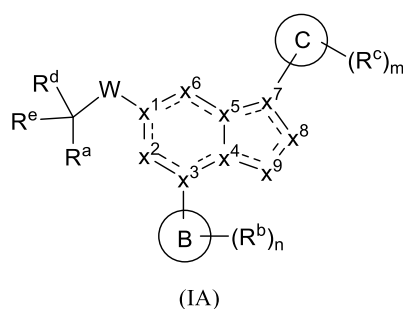
10 [1442] ^aMean ± SEM.

[1443] 5. Experimental conclusion

[1444] As shown in Table 21 above, both compound 065M and compound 077B2 significantly inhibited tumor growth. In addition, good tolerability was observed in mice.

CLAIMS

1. A compound of formula (IA), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof,



5

wherein

x^1 is selected from the group consisting of C, CR^{x1} , and N, wherein R^{x1} is selected from the group consisting of H, halogen, hydroxyl, $-NR^{n1}R^{n2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

x^2 is selected from the group consisting of CR^{x2} , N, $C(=O)$, and $C(=CR^{x2})$, wherein R^{x2} is selected from the group consisting of H, halogen, hydroxyl, amino, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-NR^{n1}R^{n2}$, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$, wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro,

15

hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd},
 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and
 5- to 10-membered heteroaryl;

x³ is selected from the group consisting of C, CR^{x3}, and N, wherein R^{x3} is selected from
 5 the group consisting of H, halogen, hydroxyl, -NRⁿ¹Rⁿ², C₁₋₄ alkyl, and -OC₁₋₄ alkyl;

x⁴ is selected from the group consisting of C, CR^{x4}, and N, wherein R^{x4} is selected from
 the group consisting of H, halogen, hydroxyl, -NRⁿ¹Rⁿ², C₁₋₄ alkyl, and -OC₁₋₄ alkyl;

x⁵ is selected from the group consisting of C, CR^{x5}, and N, wherein R^{x5} is selected from
 the group consisting of H, halogen, hydroxyl, -NRⁿ¹Rⁿ², C₁₋₄ alkyl, and -OC₁₋₄ alkyl;

10 x⁶ is selected from the group consisting of CR^{x6}, N, C(=O), and C(=CR^{x6}), wherein R^{x6}
 is selected from the group consisting of H, halogen, hydroxyl, cyano, C₂₋₆ alkenyl, C₂₋₆
 alkynyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -NRⁿ¹Rⁿ², -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to
 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-
 membered heteroaryl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd};
 15 wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to
 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to
 10-membered heteroaryl are optionally substituted by one or more substituents selected from
 the group consisting of halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl,
 C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro,
 20 hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd},
 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and

5- to 10-membered heteroaryl;

x^7 is selected from the group consisting of C, CR^{x7} , and N, wherein R^{x7} is selected from the group consisting of H, halogen, hydroxyl, $-NR^{n1}R^{n2}$, C_{1-4} alkyl, and $-OC_{1-4}$ alkyl;

x^8 is selected from the group consisting of N, O, CR^{x8} , $CR^{x8}R^{x8}$, NR^{x8} , $S(O)_p$, $C(=O)$,
 5 and $C(=CR^{x8})$, wherein R^{x8} , at each occurrence, is identical or different, and is independently selected from the group consisting of H, deuterium, halogen, hydroxyl, $-NR^{n1}R^{n2}$, cyano, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, $-OR^f$, $-C(O)R^{ba}$, $-S(O)_pR^{ba}$, $-N=S(O)R^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, and $-C(O)NR^{bc}R^{bd}$; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba1}$, $S(O)_pR^{ba1}$, $S(O)_pNR^{be1}R^{bf1}$, $-C(O)OR^{bb1}$, $-C(O)NR^{bc1}R^{bd1}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

alternatively, two R^{x8} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6}

deuteroalkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{bc}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

5 x⁹ is selected from the group consisting of CR^{x9}, N, O, NR^{x9}, S(O)_p, CR^{x9}R^{x9}, and C(=CR^{x8}), wherein R^{x9}, at each occurrence, is identical or different, and is independently selected from the group consisting of H, deuterium, halogen, hydroxyl, -NRⁿ¹Rⁿ², cyano, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, -OR^f, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{bc}R^{bf}, -C(O)OR^{bb}, and -C(O)NR^{bc}R^{bd}; wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{bc1}R^{bf1}, -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

alternatively, two R^{x9} attached to the same carbon atom together form a 3- to 8-membered cycloalkyl or 3- to 8-membered heterocyclyl ring; wherein the 3- to 8-membered cycloalkyl and 3- to 8-membered heterocyclyl are optionally substituted by one or more

substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, C₁₋₆ deuterioalkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

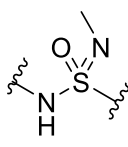
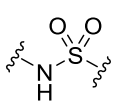
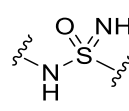
alternatively, R^{x8} and R^{x9}, together with the atom to which they are attached, form a 3- to 7-membered ring; wherein the 3- to 7-membered ring is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, C₁₋₆ deuterioalkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -OR^f, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, C₁₋₆ deuterioalkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NRⁿ¹Rⁿ², nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{bal}, S(O)_pR^{bal}, S(O)_pNR^{bel}R^{bfl}, -C(O)OR^{bb1}, -C(O)NR^{bcl}R^{bdl}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

$\diagup$ is a single bond or a double bond;

R^a , R^d , and R^e are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, halogen, C_{1-6} alkyl, cyano, $-NR^{n1}R^{n2}$, hydroxyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-C_{1-6}$ alkoxy- C_{1-6} alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba1}$, $S(O)_pR^{ba1}$, $S(O)_pNR^{be1}R^{bf1}$, $-C(O)OR^{bb1}$, $-C(O)NR^{bc1}R^{bd1}$, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

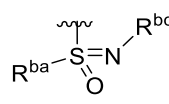
alternatively, any two of R^a , R^d , and R^e , together with the atom to which they are attached, form a 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, or 5- to 10-membered heteroaryl ring; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C_{1-6} alkyl, C_{1-6} deuterioalkyl, oxo, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, cyano, $-NR^{a1}R^{a2}$, nitro, hydroxyl, C_{1-6} hydroxyalkyl, $-C(O)R^{ba}$, $S(O)_pR^{ba}$, $S(O)_pNR^{be}R^{bf}$, $-C(O)OR^{bb}$,

-C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

W is selected from the group consisting of , , and ;

ring B is selected from the group consisting of 3- to 10-membered cycloalkyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, 5- to 7-membered monocyclic heterocyclyl, 7- to 12-membered spiro heterocyclyl, 6- to 10-membered bridged heterocyclyl, and 6- to 10-membered fused heterocyclyl;

each R^b is identical or different, and is independently selected from the group consisting of hydrogen, deuterium, halogen, C₁₋₆ alkyl, cyano, hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -NRⁿ¹Rⁿ², -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl,

, -OR^f, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, S(O)_pNR^{bc}R^{bf}, and S(O)_pR^{ba};

wherein the C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, -C₁₋₆ alkoxy-C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{be1}R^{bf1}, -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl,

3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, -

5 C(O)R^{ba2}, S(O)_pR^{ba2}, S(O)_pNR^{be2}R^{bf2}, -C(O)OR^{bb2}, -C(O)NR^{bc2}R^{bd2}, and C₁₋₆ hydroxyalkyl;

Rⁿ¹, Rⁿ², R^{a1}, and R^{a2} are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, C₁₋₆ alkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, -OR^f, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-

10 membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deutoalkoxy, C₁₋₆

15 deutoalkyl, cyano, amino, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are identical or different, and are each independently selected from the group consisting of hydrogen, deuterium, C₁₋₆ alkyl, C₁₋₆ haloalkoxy, C₁₋₆ hydroxyalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ deutoalkoxy, C₁₋₆ alkoxy, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6-

20 to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-

membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deutoalkoxy, C₁₋₆ deutoalkyl, -OR^f, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{be1}R^{bfl}, -C(O)OR^{bb1},
 5 -C(O)NR^{bc1}R^{bd1}, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

alternatively, Rⁿ¹ and Rⁿ², R^{a1} and R^{a2}, R^{bc} and R^{bd}, or R^{be} and R^{bf}, together with the nitrogen atom to which they are attached, form a 3- to 7-membered heterocyclyl ring; wherein the 3- to 7-membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, C₁₋₆ deutoalkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy,
 10 C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;

ring C is selected from the group consisting of 3- to 10-membered cycloalkyl, 3- to 10-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl;
 15

each R^c is identical or different, and is independently selected from the group consisting of hydrogen, deuterium, halogen, C₁₋₆ alkyl, cyano, -NRⁿ¹Rⁿ², hydroxyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, -C₁₋₆ alkoxy-C₁₋₆ alkyl, -C(O)R^{ba}, S(O)_pR^{ba}, S(O)_pNR^{be}R^{bf}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 3- to 8-membered cycloalkyl, 3- to 8-membered
 20 heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl,

and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, C₁₋₆ hydroxyalkyl, -C(O)R^{ba1}, S(O)_pR^{ba1}, S(O)_pNR^{be1}R^{bfl},
 5 -C(O)OR^{bb1}, -C(O)NR^{bc1}R^{bd1}, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl,
 10 C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, -C(O)R^{ba2}, S(O)_pR^{ba2}, S(O)_pNR^{be2}R^{bfl}, -C(O)OR^{bb2}, -C(O)NR^{bc2}R^{bd2}, and C₁₋₆ hydroxyalkyl;

R^{ba1}, R^{bb1}, R^{bc1}, R^{bd1}, R^{be1}, R^{bfl}, R^{ba2}, R^{bb2}, R^{bc2}, R^{bd2}, R^{be2}, and R^{bfl} are identical or different, and are each independently selected from the group consisting of hydrogen,
 15 deuterium, C₁₋₆ alkyl, C₁₋₆ haloalkoxy, C₁₋₆ alkoxy, C₁₋₆ hydroxyalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ deutoalkoxy, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or
 20 more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋

₆ haloalkoxy, C₁₋₆ deuteroalkoxy, C₁₋₆ deuteroalkyl, cyano, -NR^{a1}R^{a2}, -OR^f, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

R^f is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl; wherein the C₁₋₆ alkyl, 3- to 8-membered cycloalkyl, 3- to 8-membered heterocyclyl, 6- to 10-membered aryl, and 5- to 10-membered heteroaryl are optionally substituted by one or more substituents selected from the group consisting of deuterium, halogen, C₁₋₆ alkyl, oxo, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₆ haloalkenyl, C₂₋₆ haloalkynyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ deuteroalkyl, C₁₋₆ deuteroalkoxy, cyano, -NR^{a1}R^{a2}, nitro, hydroxyl, and C₁₋₆ hydroxyalkyl;

n is selected from the group consisting of 0, 1, 2, and 3;

m is selected from the group consisting of 0, 1, 2, and 3;

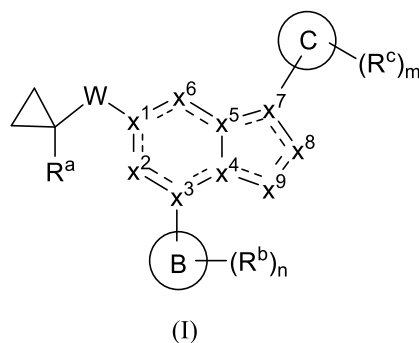
p is selected from the group consisting of 0, 1, and 2.

2. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to claim 1, wherein R^d and R^e, together with the atom to which they are attached, form a 3- to 6-membered cycloalkyl or 3- to 6-membered heterocyclyl ring.

3. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative

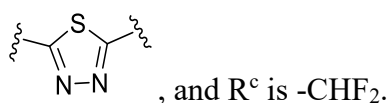
thereof according to claim 1 or 2, wherein R^d and R^e , together with the atom to which they are attached, form a cyclopropyl or oxetanyl ring.

4. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof,
 5 the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to 3, which is a compound of formula (I), a pharmaceutically acceptable salt thereof, or a stereoisomer thereof,

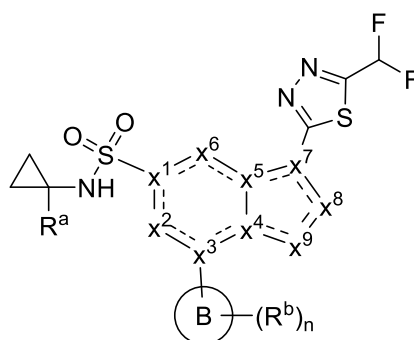


- wherein , ring B, ring C, R^b , R^a , R^c , m , n , W , and x^1 to x^9 are as defined in at least
 10 one of claims 1 to 3.

5. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof,
 the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to 4, wherein ring C is 5-membered heteroaryl;
 15 each R^c is identical or different, and is independently C_{1-6} haloalkyl; preferably, ring C is



6. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to 5, which is a compound of formula (II), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:



(II)

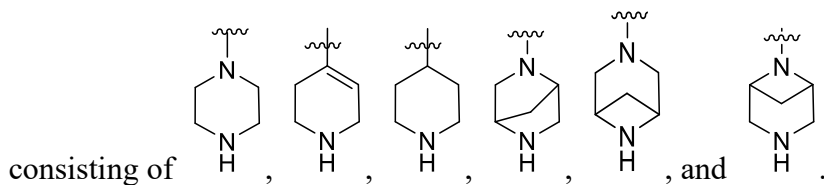
wherein Ra , x^1 , x^2 , x^3 , x^4 , x^5 , x^6 , x^7 , x^8 , x^9 , ring B, R^b , Ra , and n are as defined in at least one of claims 1 to 5.

7. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to 6, wherein R^a is selected from the group consisting of $-\text{CH}_3$, $-\text{CH}_2\text{F}$, $-\text{CN}$, $-\text{CH}_2=\text{CHF}$, $-\text{CHF}_2$, $-\text{CHF}_3$, and $-\text{CD}_3$; preferably, R^a is selected from the group consisting of $-\text{CH}_3$, $-\text{CH}_2\text{F}$, and $-\text{CN}$.

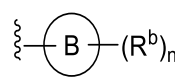
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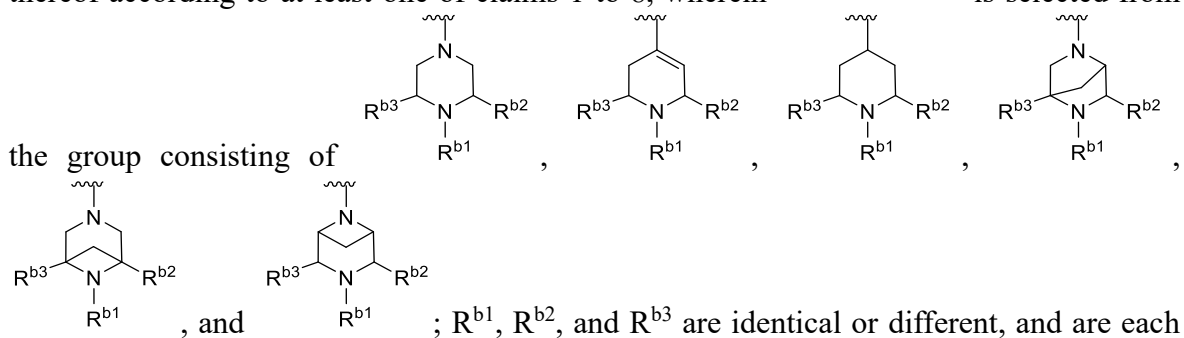
8. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof

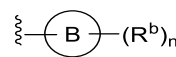
thereof according to at least one of claims 1 to 7, wherein ring B is selected from the group

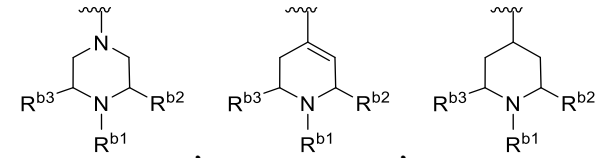
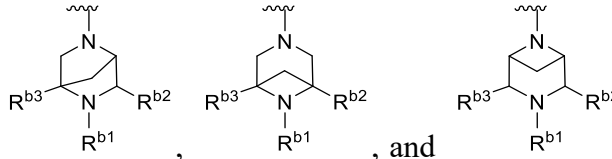


9. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof,
5 the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative

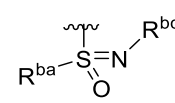
thereof according to at least one of claims 1 to 8, wherein  is selected from



independently R^b ; R^b is as defined in at least one of claims 1 to 8; preferably, 

- 10 is selected from the group consisting of ,
, and ; R^{b1} is selected from the group consisting

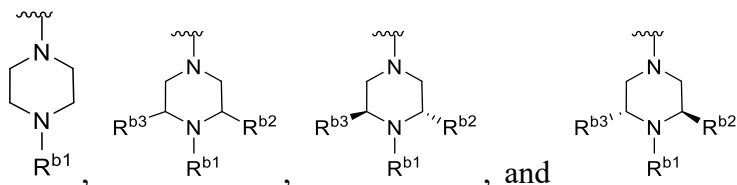
of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 5- to 6-membered heteroaryl optionally substituted by

C_{1-6} alkyl, , $S(O)_2NR^{be}R^{bf}$, and $-S(O)R^{ba}$; R^{b2} and R^{b3} are identical or different,

- 15 and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6}

alkenyl, and C₂₋₆ alkynyl; R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are as defined in at least one of

claims 1 to 8; more preferably, $\text{---}(\text{B})\text{---}(\text{R}^b)_n$ is selected from the group consisting of



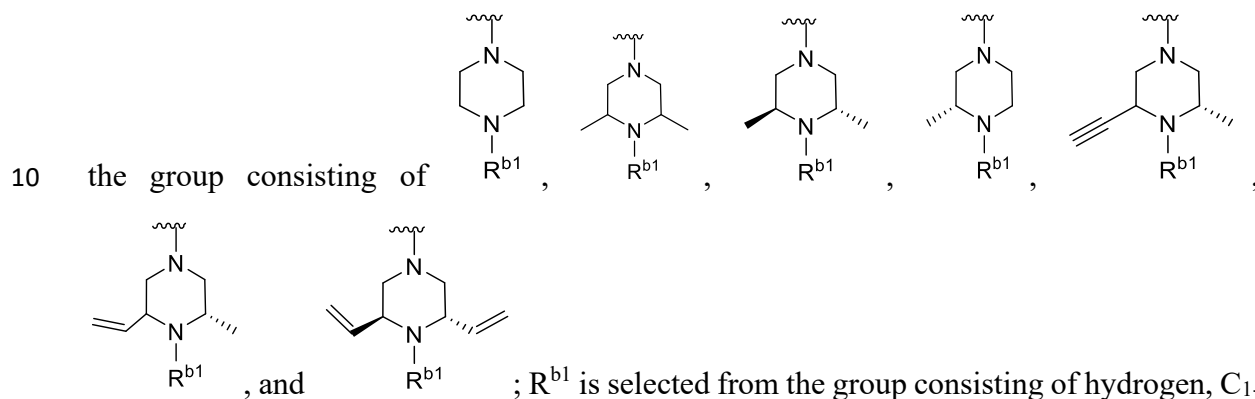
; R^{b1} is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered heterocyclyl, -

5 S(O)₂R^{ba}, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 5- to 6-membered heteroaryl optionally

substituted by C₁₋₆ alkyl, $\text{R}^{\text{ba}}\text{---}\text{S}(=\text{O})\text{---}\text{N}(\text{R}^{\text{bc}})\text{---}$, S(O)₂NR^{be}R^{bf}, and -S(O)R^{ba}; R^{b2} and R^{b3} are

identical or different, and are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, and C₂₋₆ alkynyl; R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are as

defined in at least one of claims 1 to 8; further preferably, $\text{---}(\text{B})\text{---}(\text{R}^b)_n$ is selected from

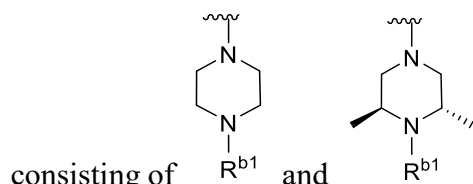


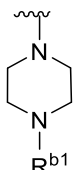
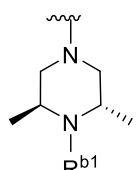
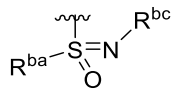
6 alkyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered heterocyclyl, -S(O)₂R^{ba}, -C(O)R^{ba}, -C(O)OR^{bb},

-C(O)NR^{bc}R^{bd}, 5- to 6-membered heteroaryl optionally substituted by C₁₋₆ alkyl,

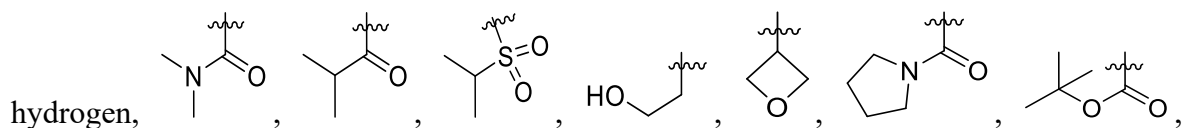
$\text{R}^{\text{ba}}\text{---}\text{S}(=\text{O})\text{---}\text{N}(\text{R}^{\text{bc}})\text{---}$, S(O)₂NR^{be}R^{bf}, and -S(O)R^{ba}; R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are as defined in

15 at least one of claims 1 to 8; most preferably, $\text{---}(\text{B})\text{---}(\text{R}^b)_n$ is selected from the group



consisting of  and ; R^{b1} is selected from the group consisting of hydrogen, C_{1-6} hydroxyalkyl, 3- to 8-membered heterocyclyl, $-S(O)_2R^{ba}$, $-C(O)R^{ba}$, $-C(O)OR^{bb}$, $-C(O)NR^{bc}R^{bd}$, 5- to 6-membered heteroaryl optionally substituted by C_{1-6} alkyl, , $S(O)_2NR^{be}R^{bf}$, and $-S(O)R^{ba}$; R^{ba} , R^{bb} , R^{bc} , R^{bd} , R^{be} , and R^{bf} are identical or
 5 different, and are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, 3- to 8-membered heterocyclyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} deuterioalkyl, 3- to 8-membered cycloalkyl, C_{1-6} alkoxy, C_{2-6} alkenyl, and 5- to 6-membered heteroaryl; wherein the C_{1-6} alkyl, 3- to 8-membered heterocyclyl, 3- to 8-membered cycloalkyl, and 5- to 6-membered heteroaryl are optionally substituted by one or more substituents selected
 10 from the group consisting of C_{1-6} alkyl, halogen, C_{1-6} deuterioalkyl, C_{1-6} haloalkyl, hydroxyl, C_{1-6} alkoxy, C_{1-6} deuterioalkoxy, $-C(O)OR^{bb1}$, and $-NR^{a1}R^{a2}$; R^{bb1} , R^{a1} , and R^{a2} are as defined in at least one of claims 1 to 8.

10. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to 9, wherein R^b and R^{b1} are each identical or different, and are each independently selected from the group consisting of



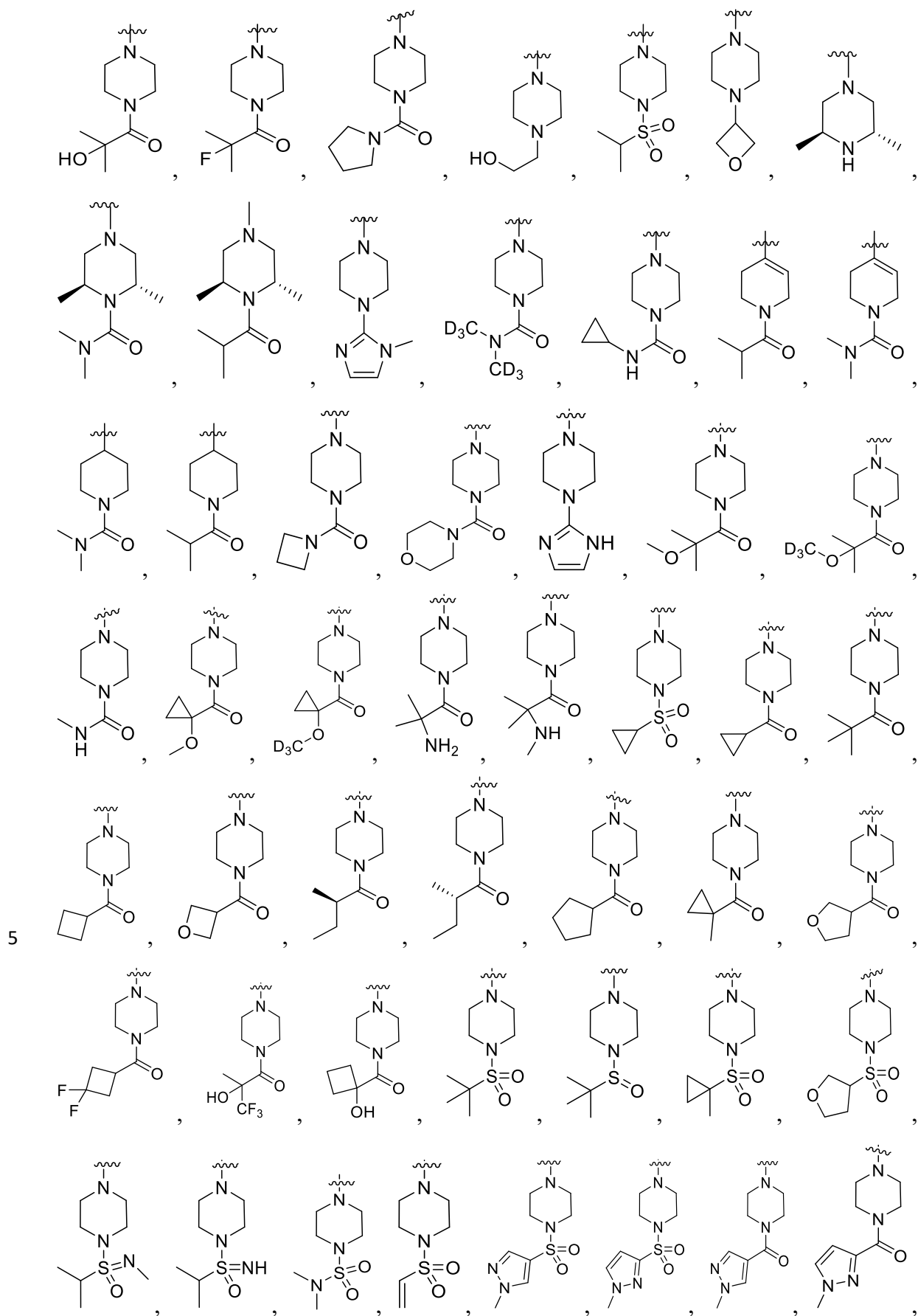
derivative thereof according to at least one of claims 1 to 10, wherein  is

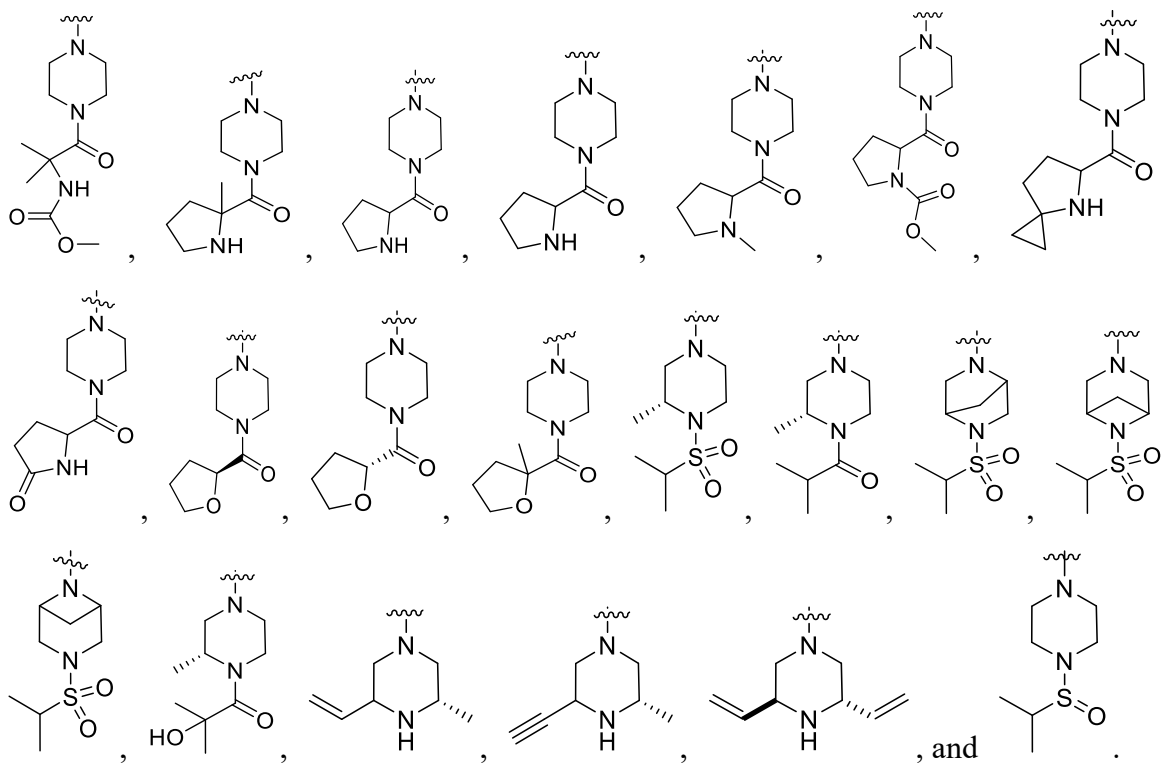
selected from the group consisting of



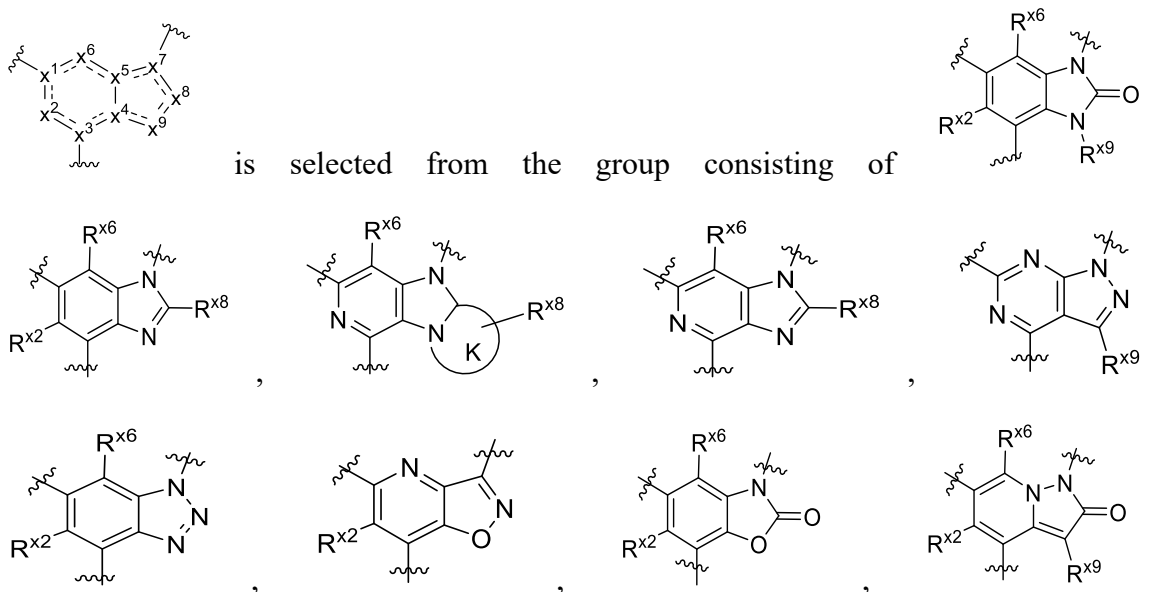


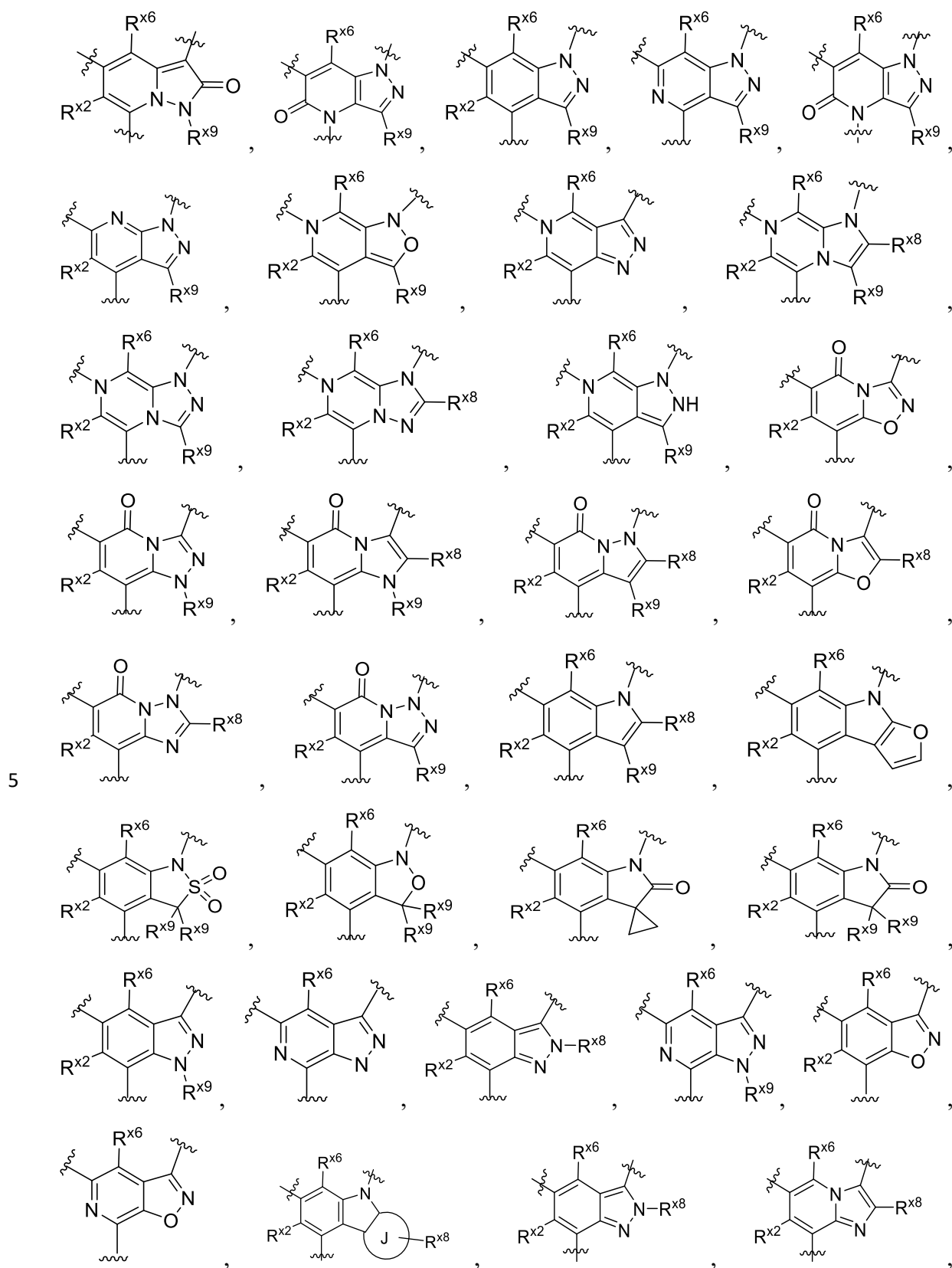


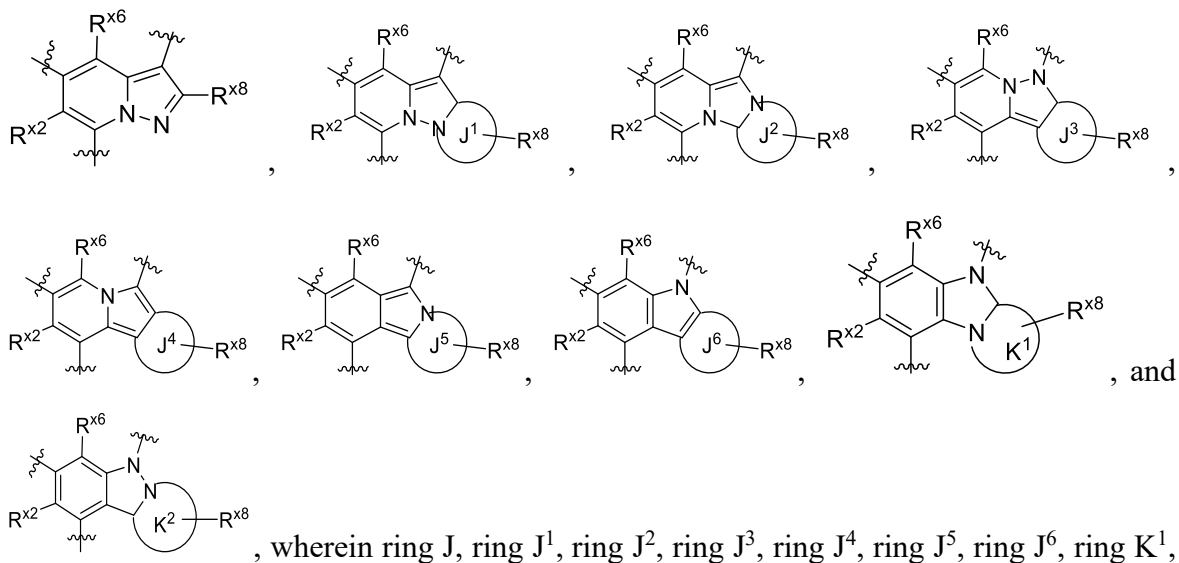




- 5 12. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to 11, wherein the structural moiety

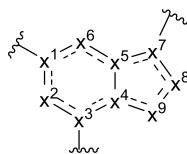






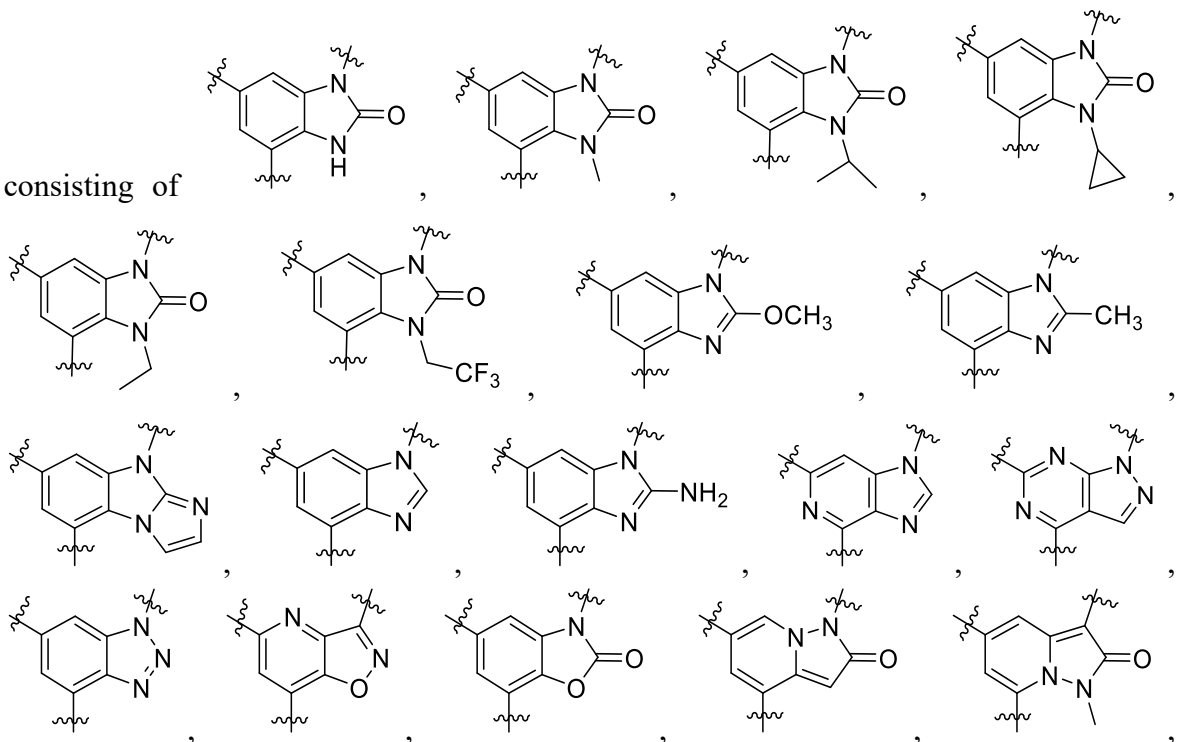
, wherein ring J, ring J^1 , ring J^2 , ring J^3 , ring J^4 , ring J^5 , ring J^6 , ring K^1 , ring K^2 , and ring K are identical or different, and are each independently an optionally
 5 substituted 3- to 7-membered ring; R^{x2} , R^{x6} , R^{x8} , and R^{x9} are as defined in at least one of

claims 1 to 14; preferably, the structural moiety

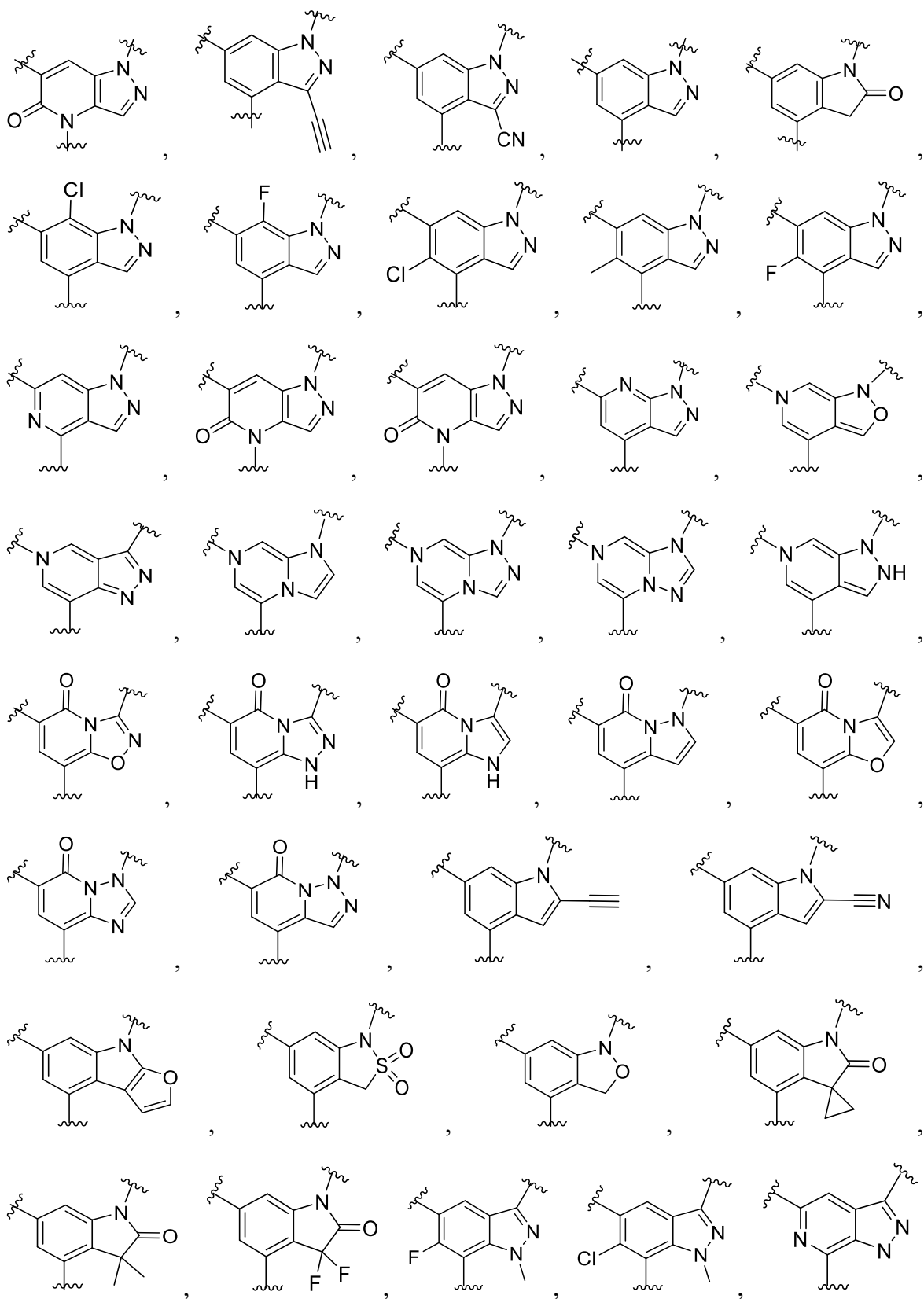


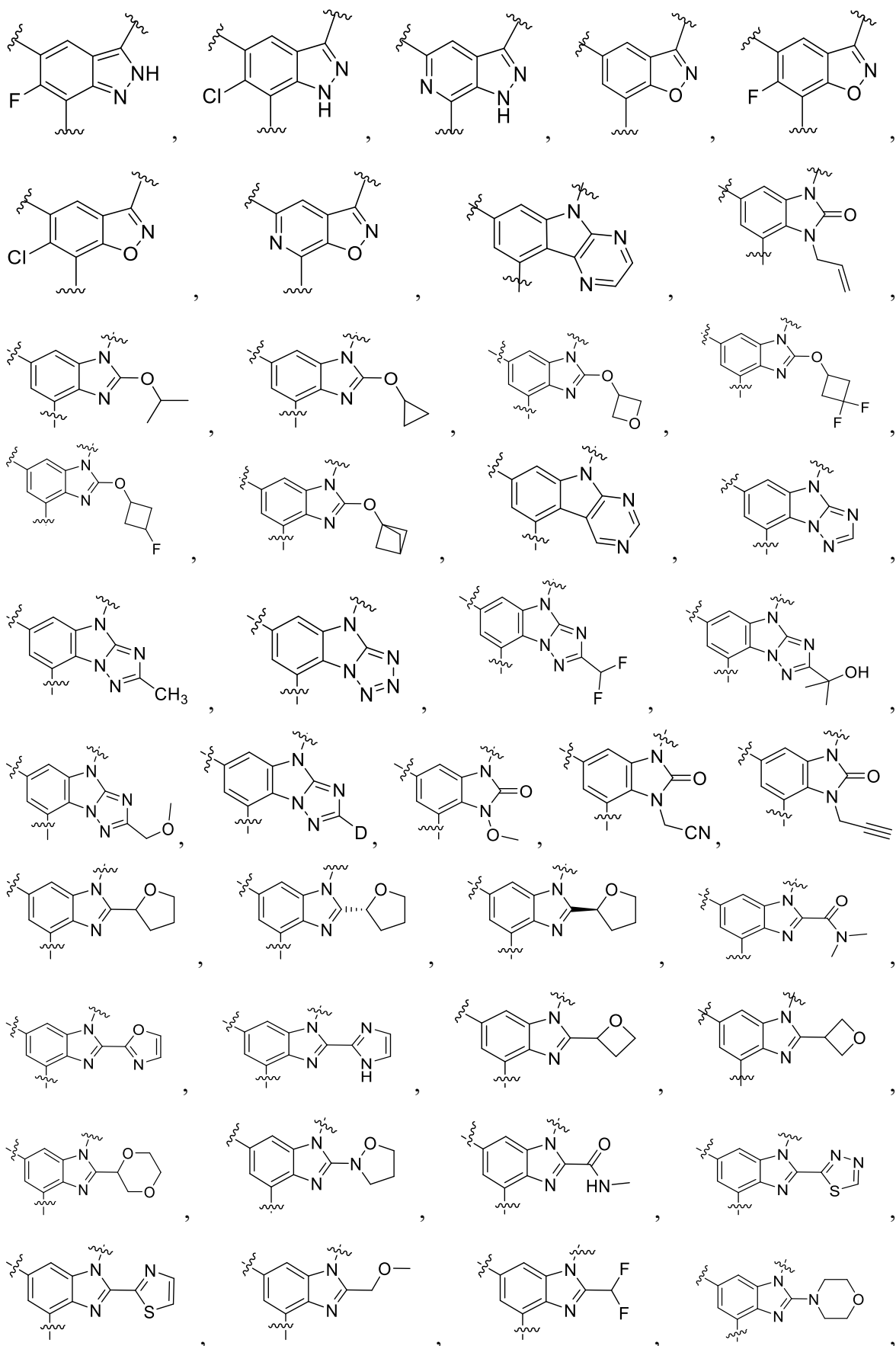
is selected from the group

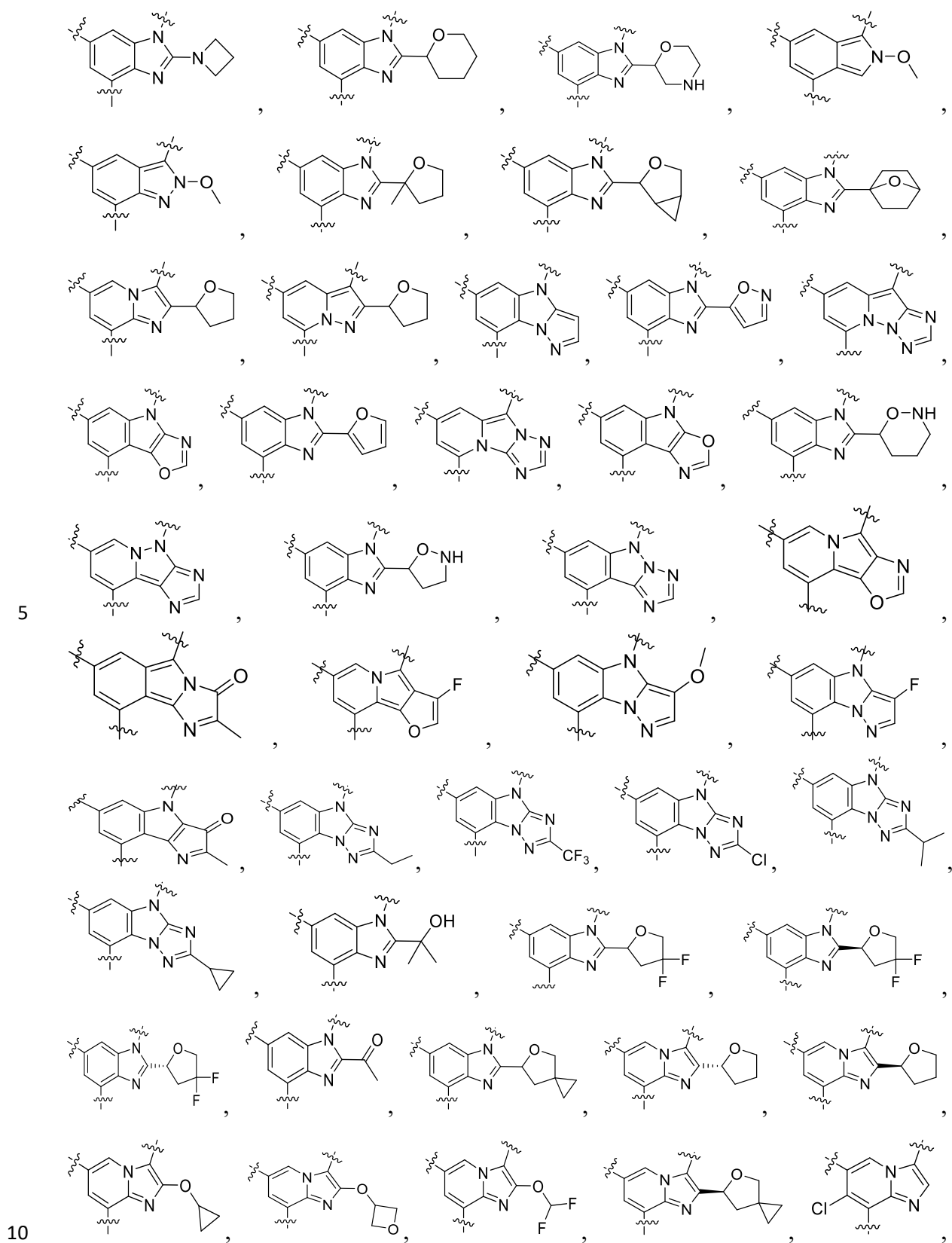
consisting of

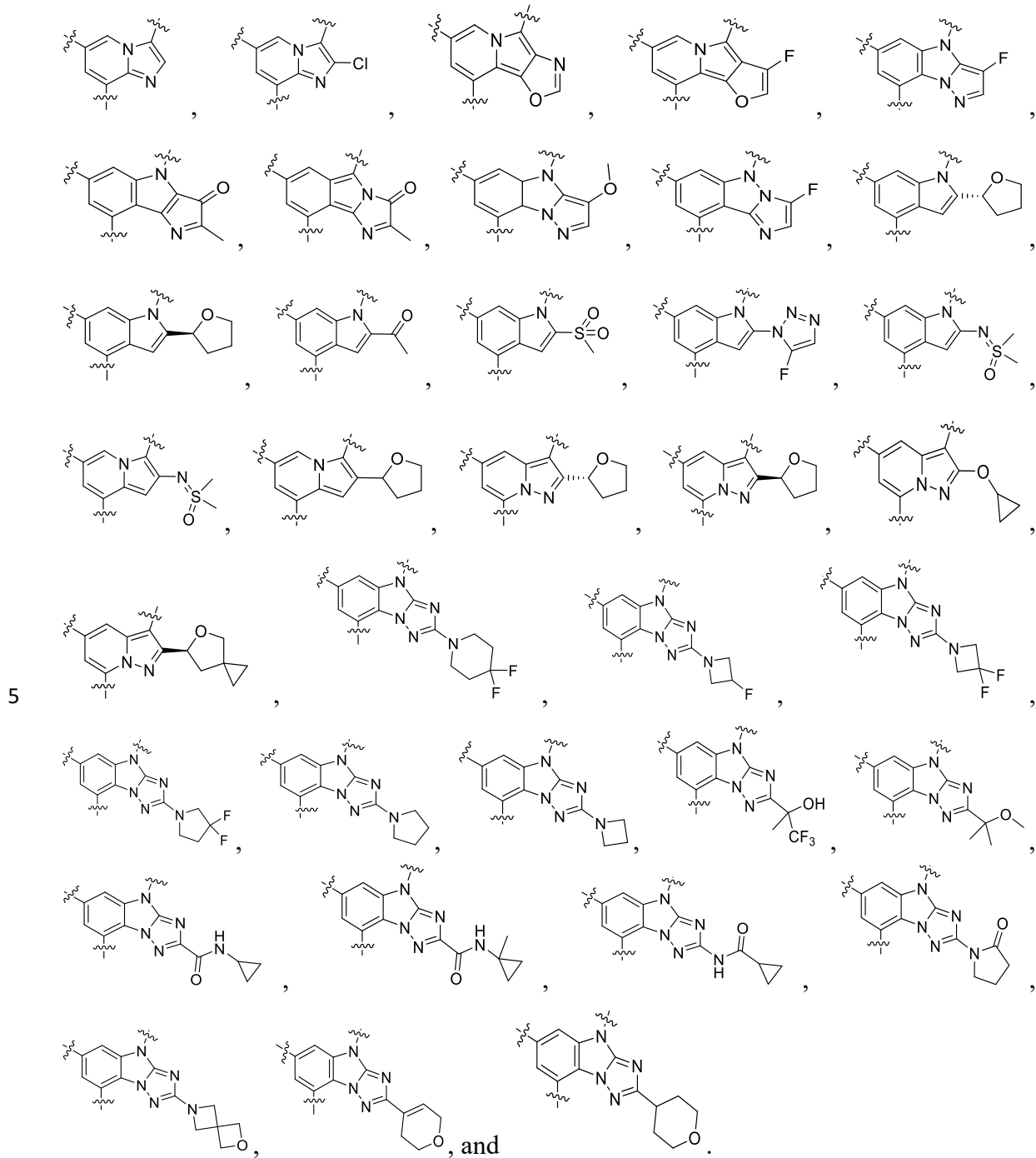


5



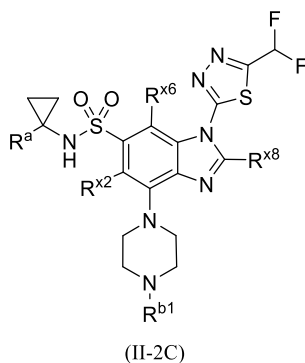
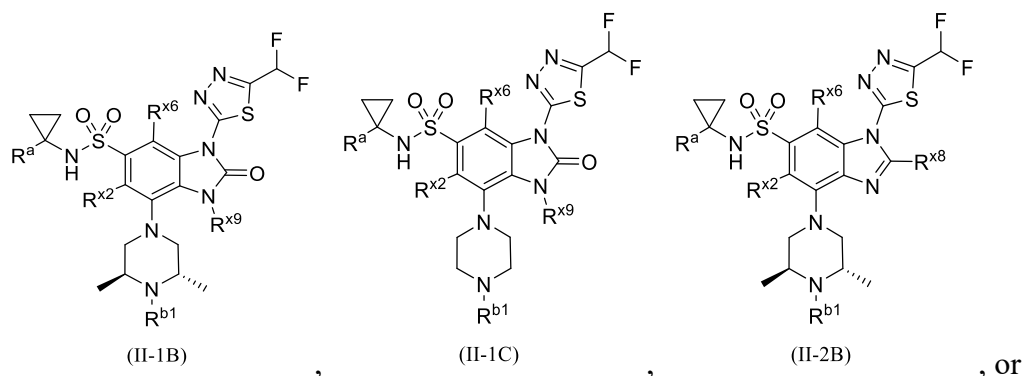






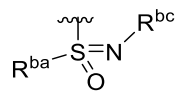
10 13. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to 12, which is a compound of formula

(II-1B), formula (II-1C), formula (II-2B), or formula (II-2C), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:



5

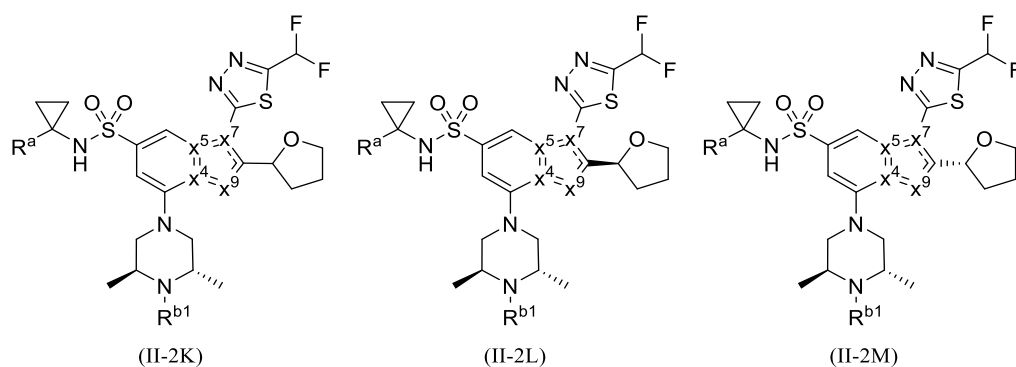
wherein R^{b1} is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, 3- to 8-membered heterocyclyl, -S(O)₂R^{ba}, -C(O)R^{ba}, -C(O)OR^{bb}, -C(O)NR^{bc}R^{bd}, 5- to 6-membered heteroaryl optionally substituted by C₁₋₆ alkyl,



10 R^{bf} are as defined in at least one of claims 1 to 12.

14. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic

derivative thereof according to at least one of claims 1 to 13, which is a compound of formula (II-2K), formula (II-2L), or formula (II-2M), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:



5

wherein

$\diagup$ is a single bond or a double bond;

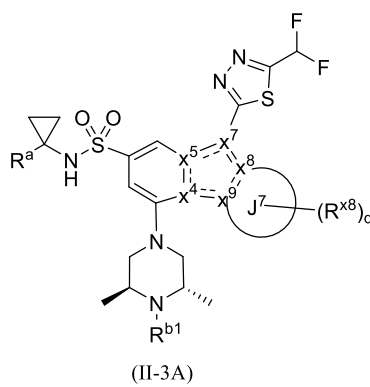
x^4 , x^5 , and x^7 are identical or different, and are each independently selected from the group consisting of N and C;

10 x^9 is selected from the group consisting of N and CH;

and the ring containing x^4 , x^5 , x^7 , and x^9 is an aromatic ring;

R^{b1} is R^b ; R^b and R^a are as defined in at least one of claims 1 to 13.

15 15. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to 14, which is a compound of formula (II-3A), a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof:



wherein

--- is a single bond or a double bond;

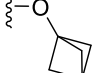
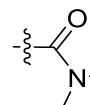
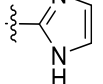
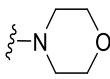
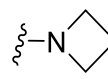
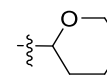
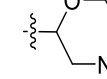
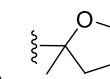
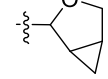
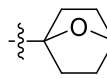
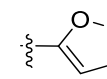
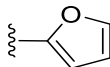
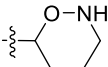
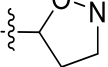
x^4 , x^5 , x^7 , x^8 , and x^9 are identical or different, and are each independently selected from
 5 the group consisting of N and C; and the ring containing x^4 , x^5 , x^7 , x^8 , and x^9 is an aromatic
 ring;

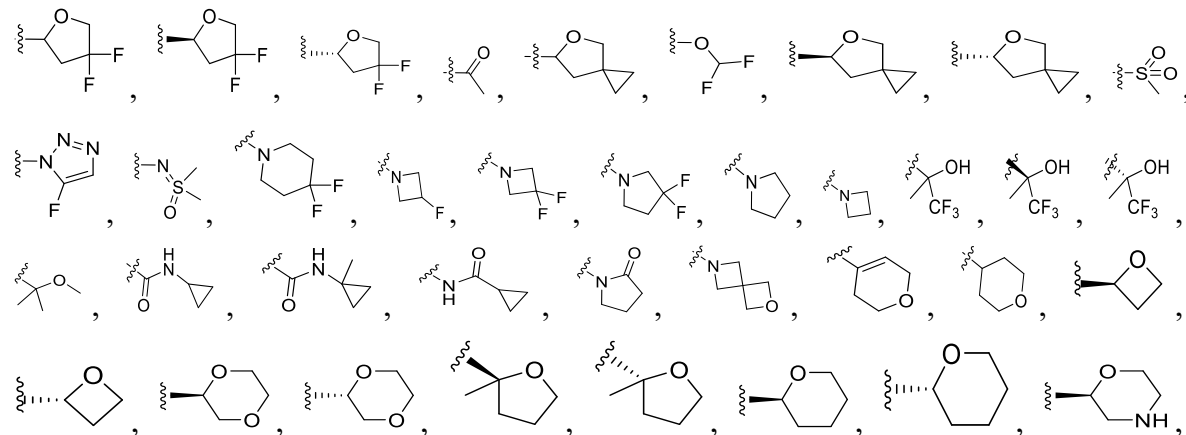
ring J^7 is selected from the group consisting of 5- to 10-membered heteroaryl and 3- to
 8-membered heterocyclyl;

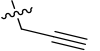
q is selected from the group consisting of 0, 1, and 2;

10 R^{b1} is R^b ; R^b , R^a , and R^{x8} are as defined in at least one of claims 1 to 14.

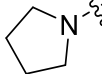
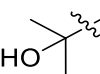
16. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer
 thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic
 derivative thereof according to at least one of claims 1 to 15, wherein ring J, ring J^1 , ring J^2 ,
 15 ring J^3 , ring J^4 , ring J^5 , ring J^6 , ring J^7 , ring K^1 , ring K^2 , and ring K are identical or different,
 and are each independently a 3- to 7-membered ring, preferably 5- to 10-membered
 heteroaryl or 3- to 8-membered heterocyclyl, more preferably 5- to 10-membered heteroaryl,

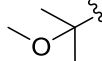
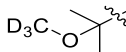
deuterium, methyl, amino, methoxy, , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , oxo, Cl, F, ethyl, trifluoromethyl, isopropyl, cyclopropyl,

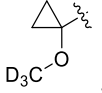
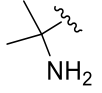
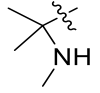
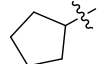
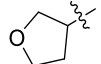


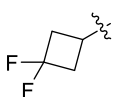
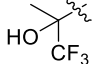
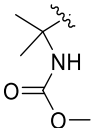
18. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to 17, wherein R^{x9} is selected from the group consisting of methyl, ethyl, isopropyl, cyclopropyl, -CH₂CF₃, , methoxy, , and .

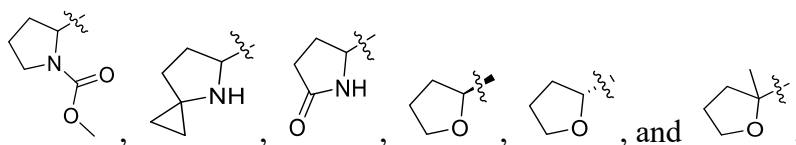
10 19. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to 18, wherein R^{ba}, R^{bb}, R^{bc}, R^{bd}, R^{be}, and R^{bf} are identical or different, and are each independently selected from the group

consisting of hydrogen, methyl, -CD₃, isopropyl, *tert*-butyl, , , ,

15 , methoxy, *tert*-butoxy, , , , , , ,

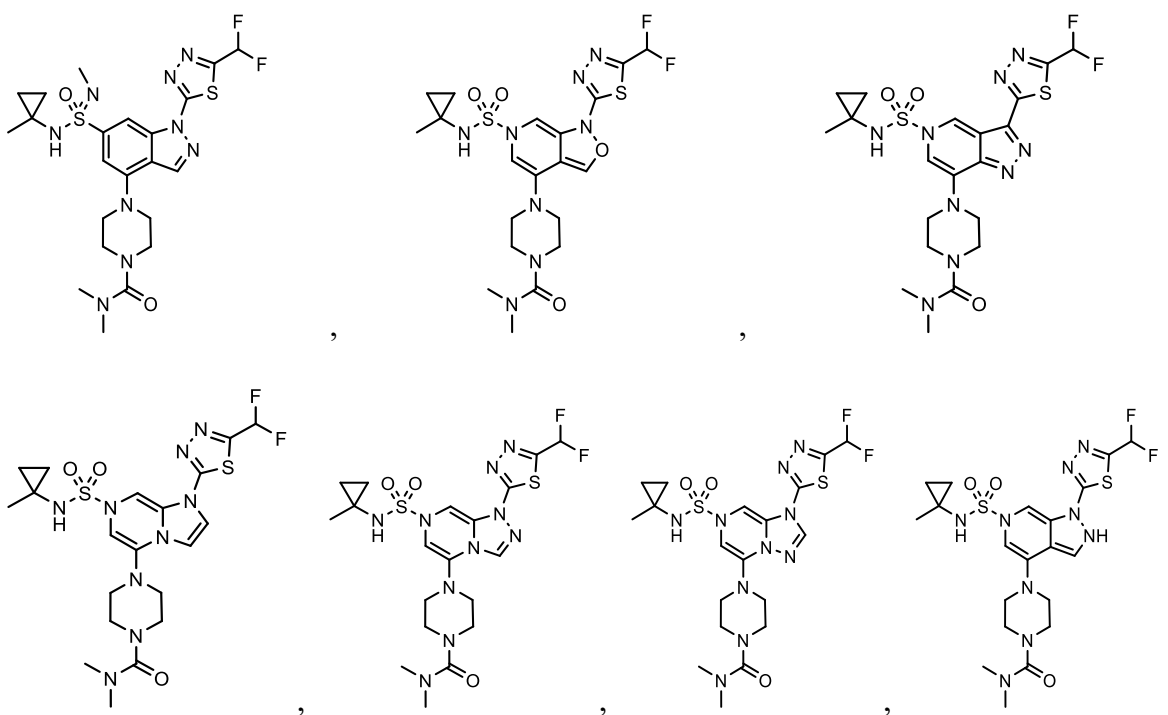
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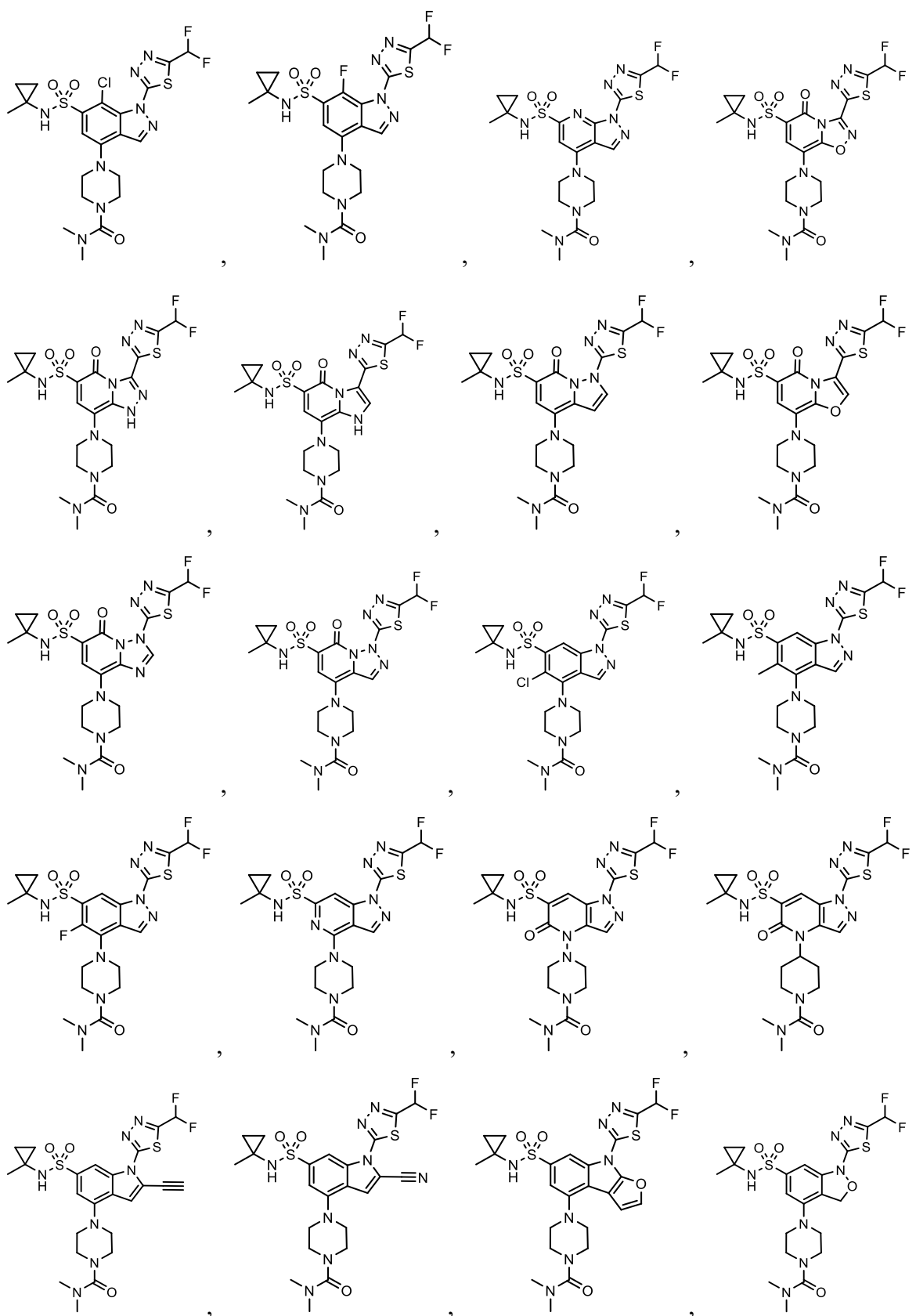
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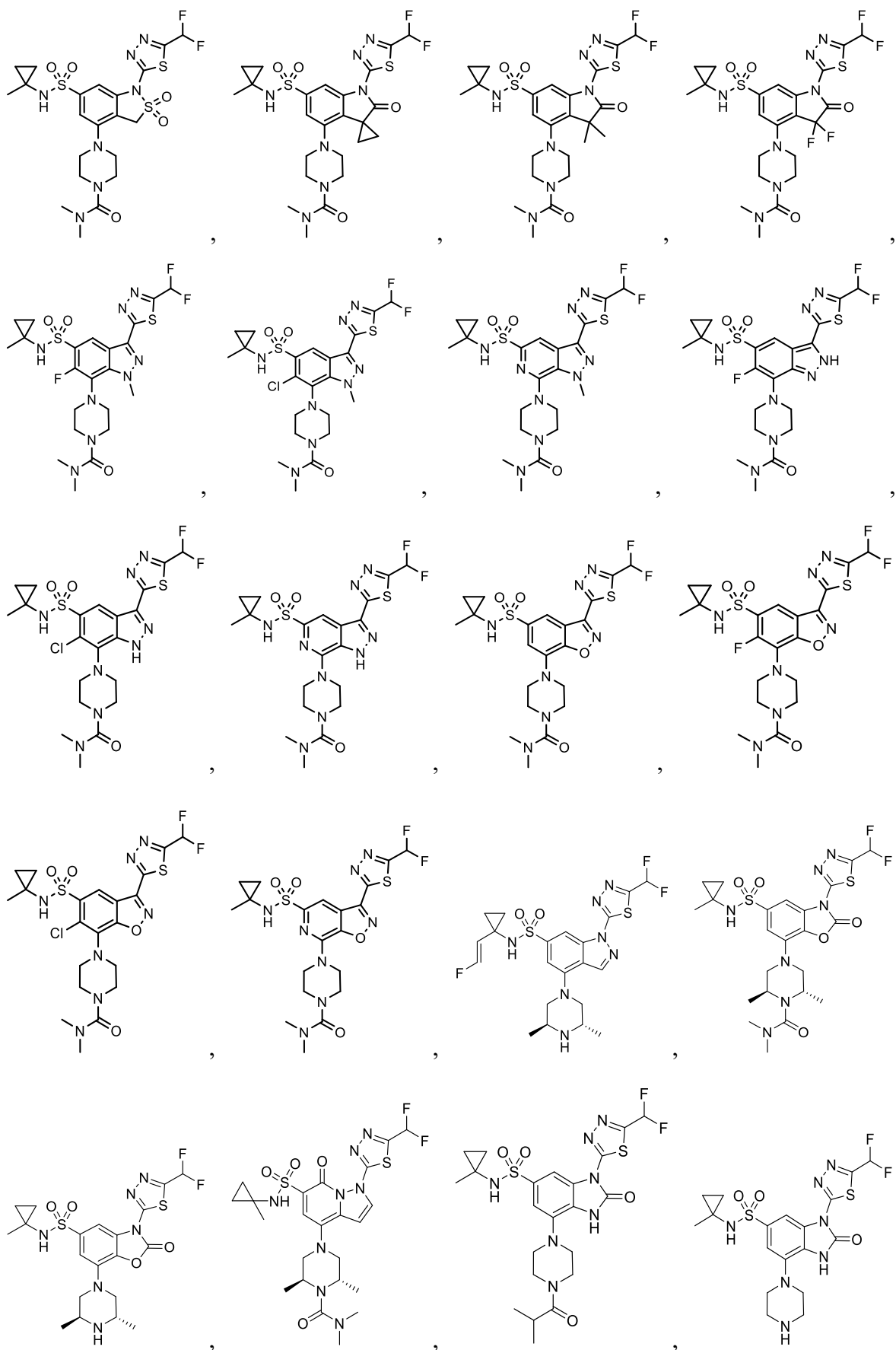


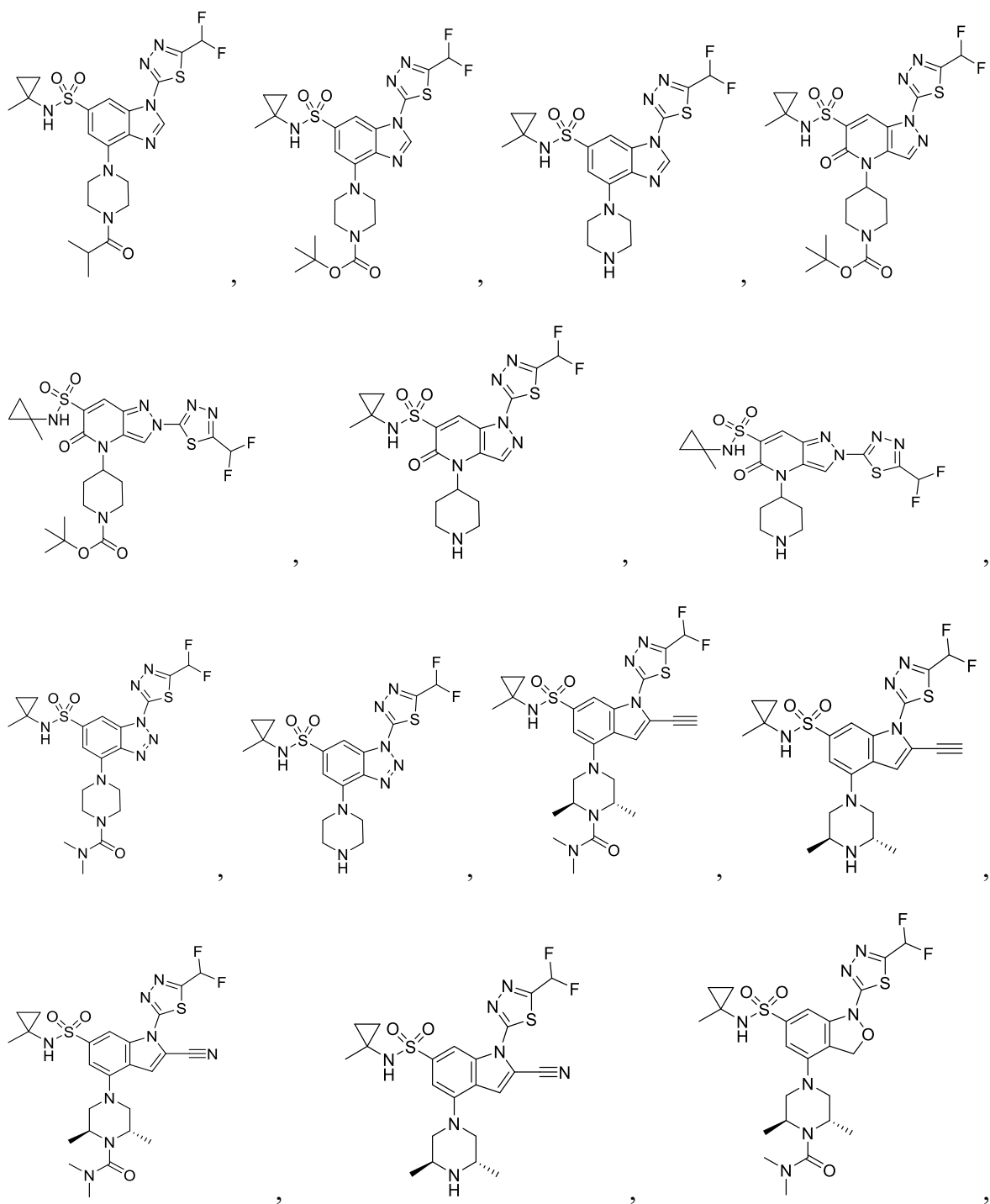
20. The compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to 19, wherein R^{b1} , at each occurrence, is identical or different, and is independently hydrogen.

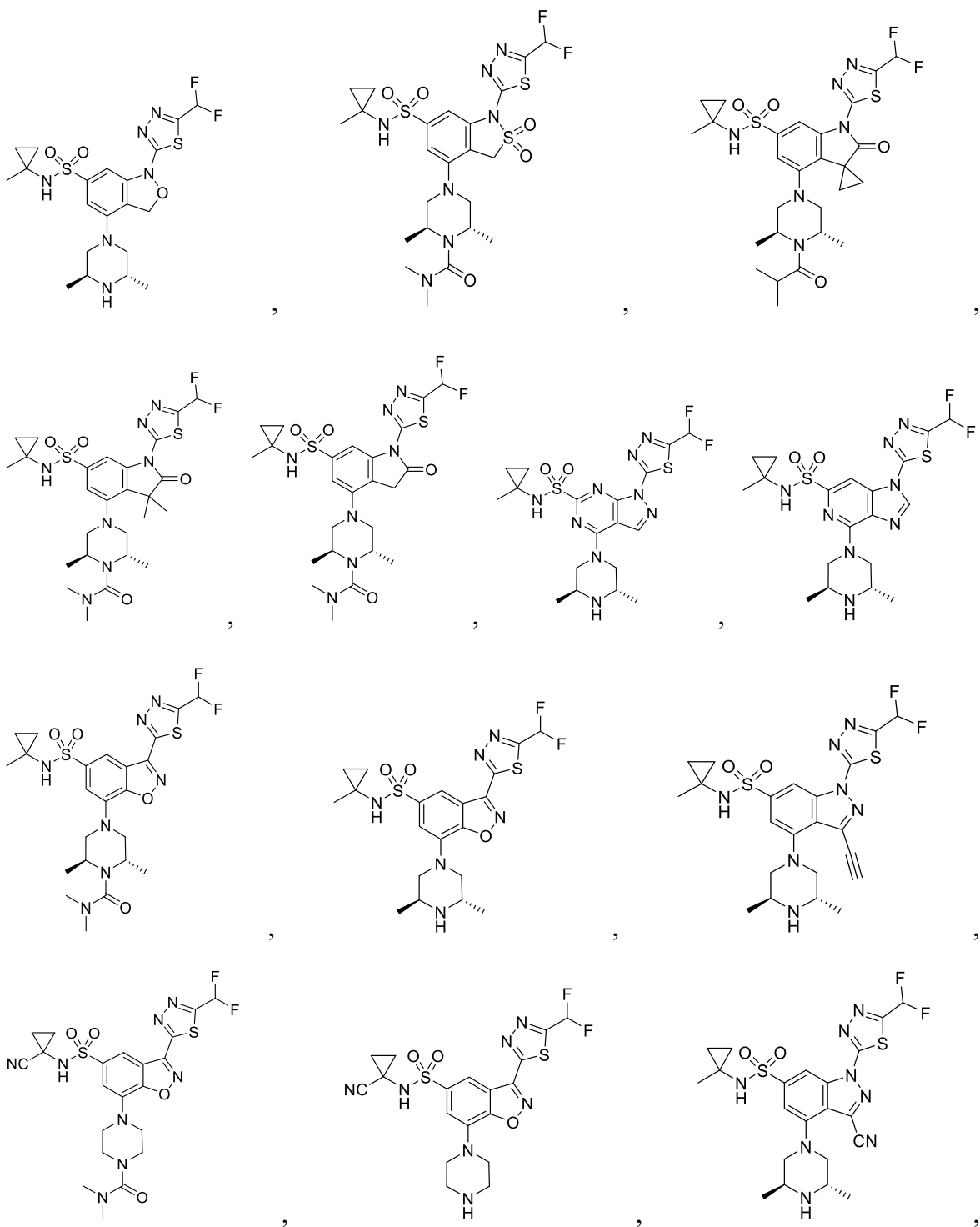
21. A compound, a pharmaceutically acceptable salt thereof, a stereoisomer thereof, a prodrug thereof, an N-oxide thereof, a solvate thereof, or an isotopic derivative thereof, wherein the compound is selected from the group consisting of any one of the following compounds:

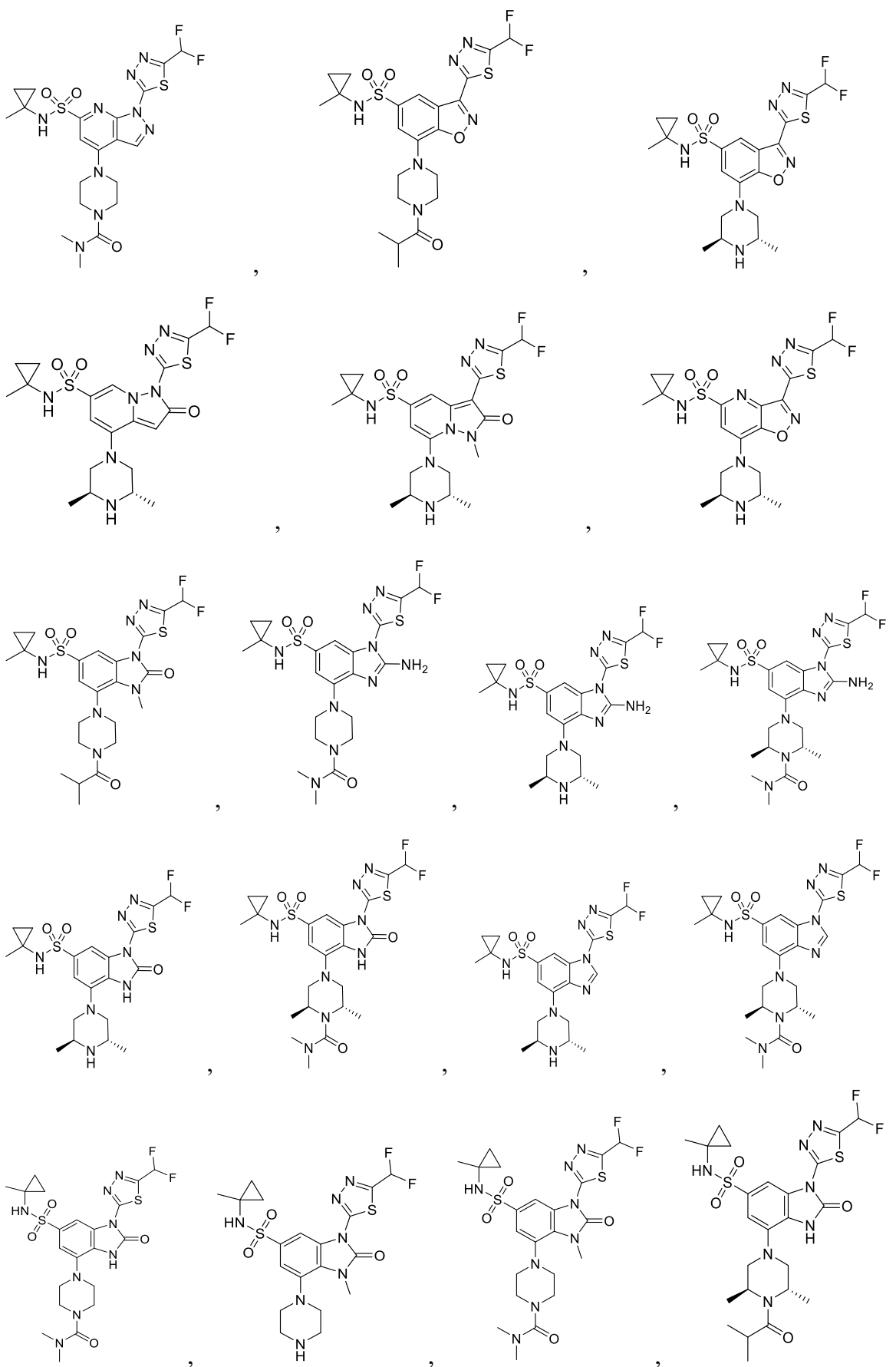


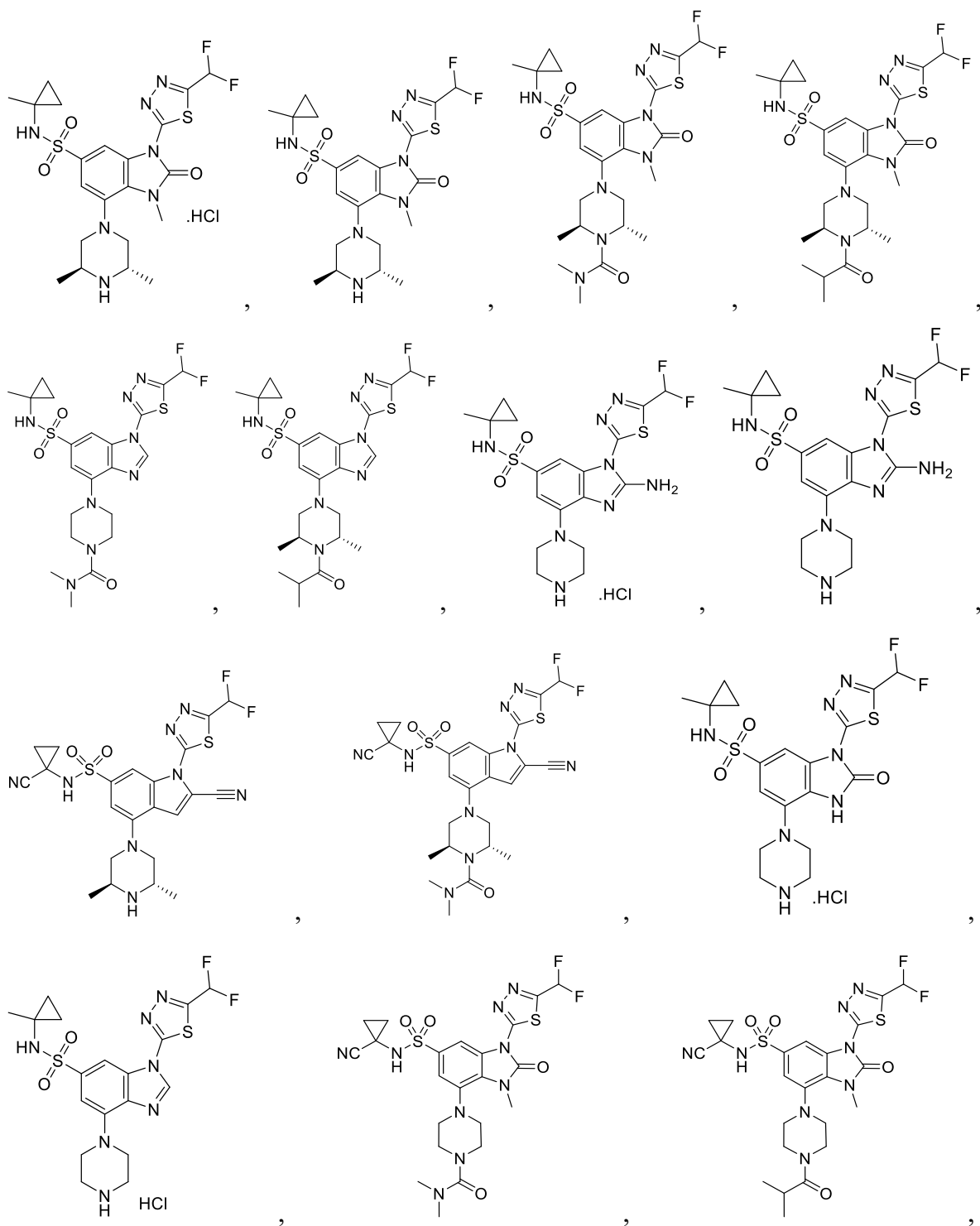


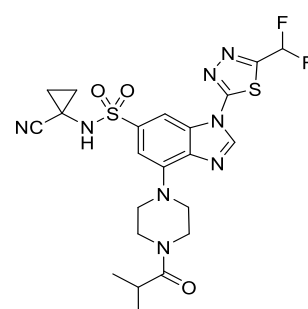
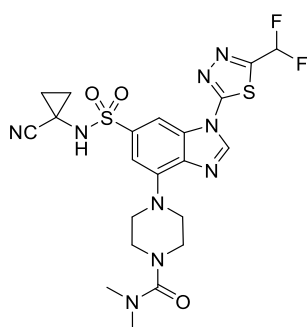
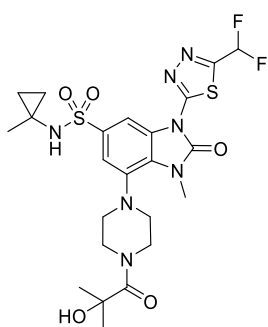
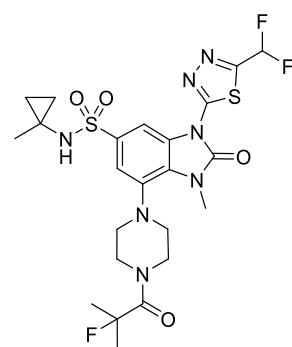
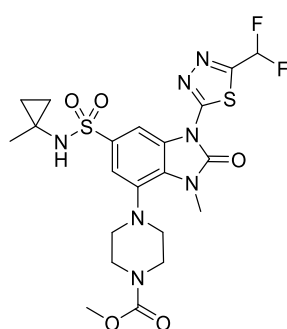
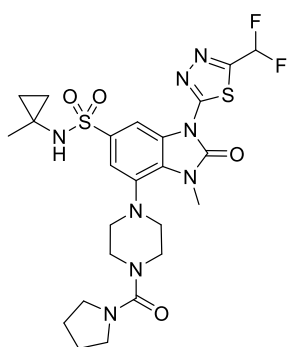
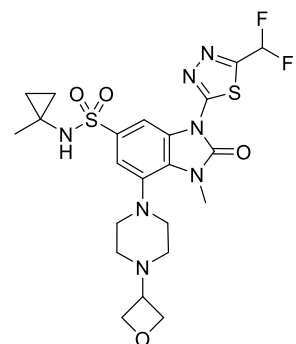
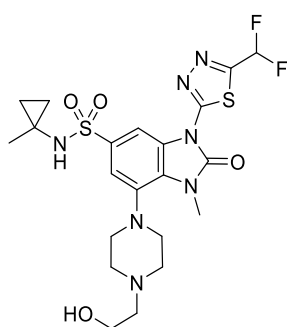
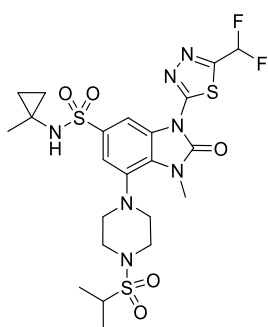
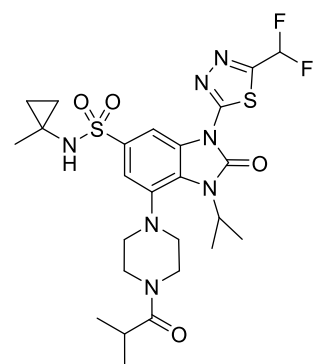
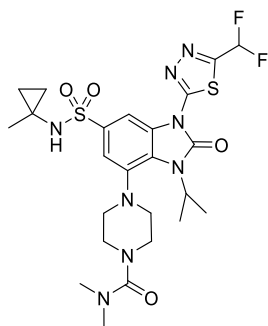
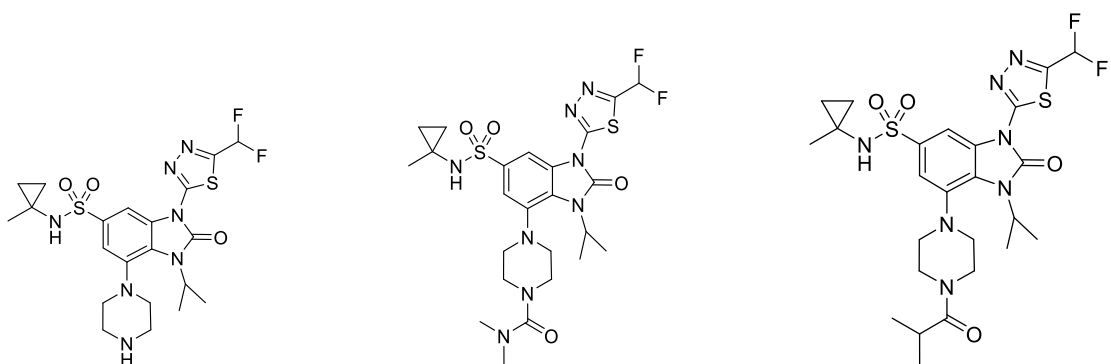


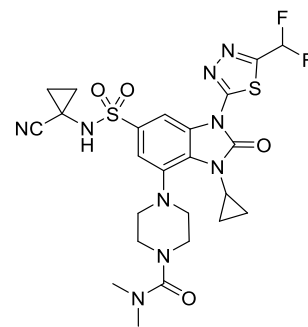
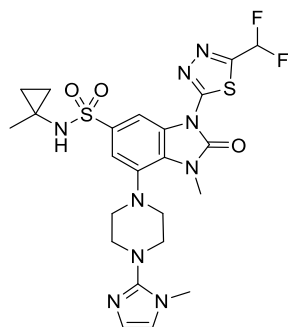
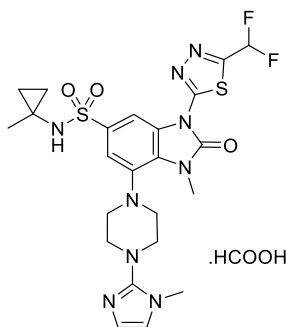
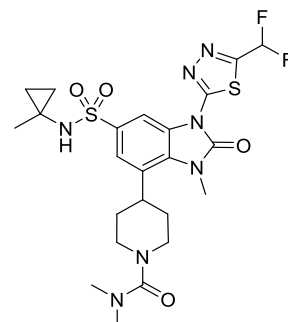
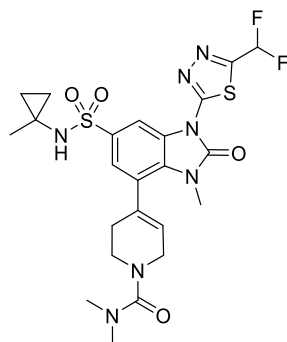
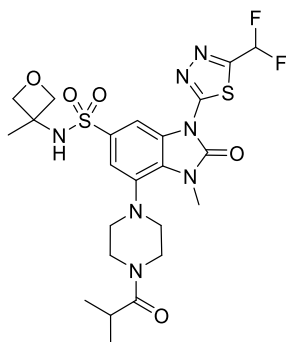
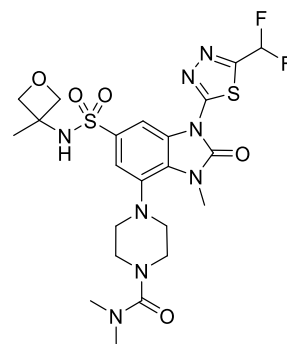
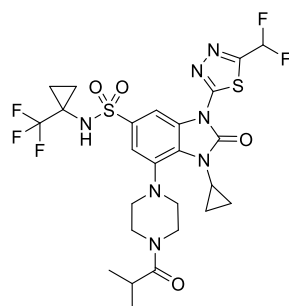
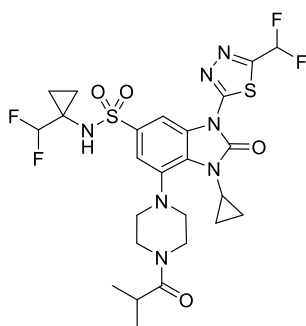
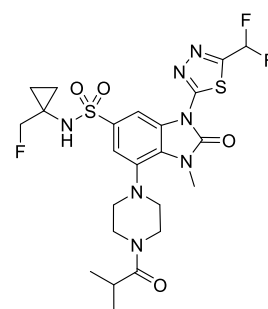
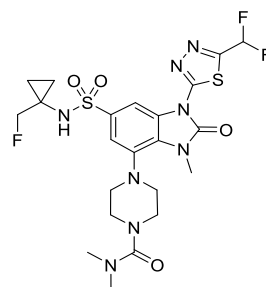
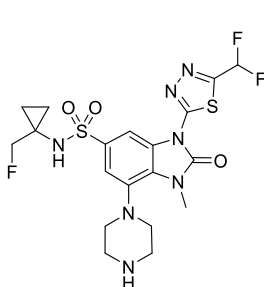
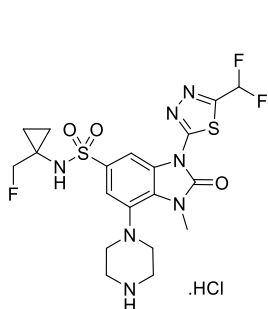
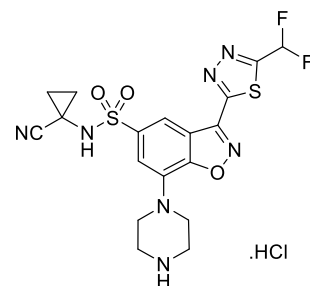
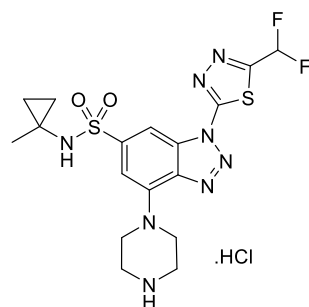
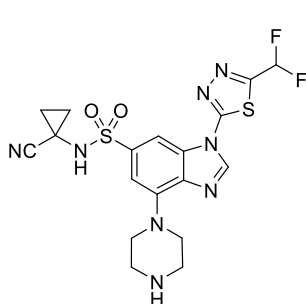


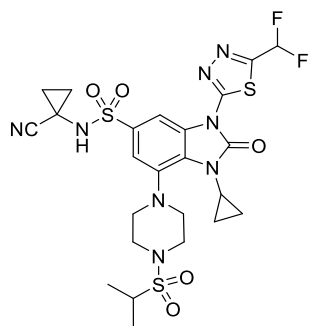
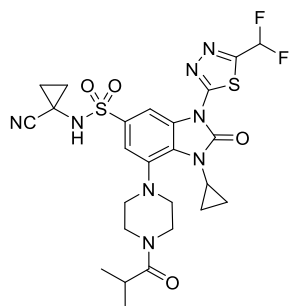
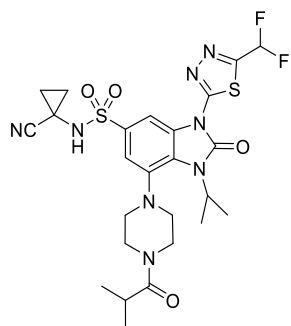
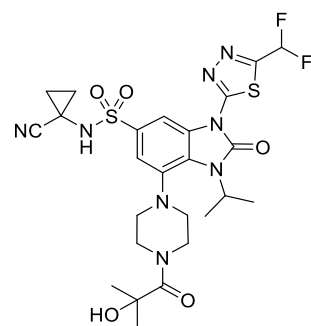
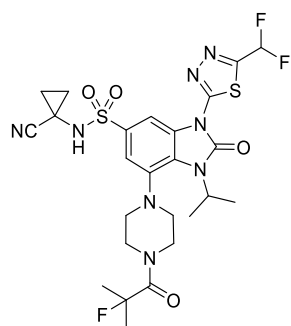
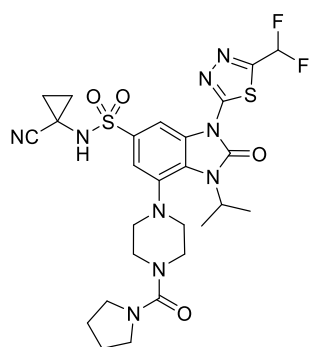
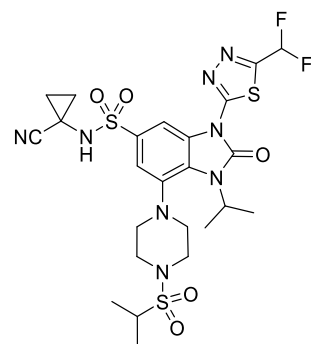
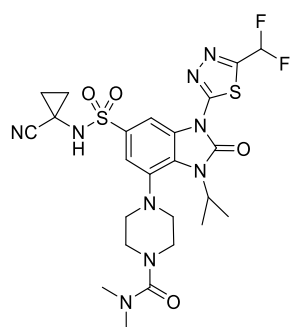
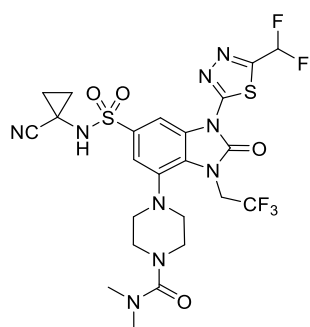
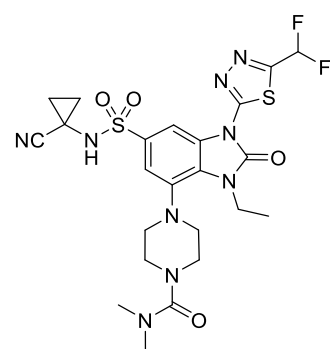
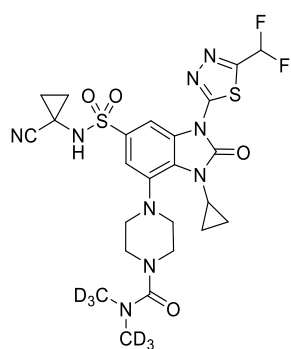
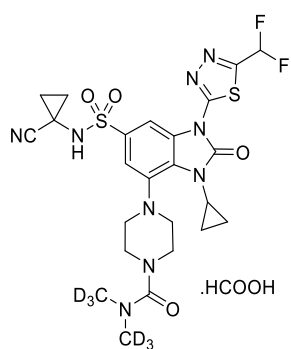


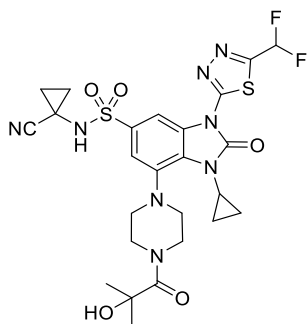




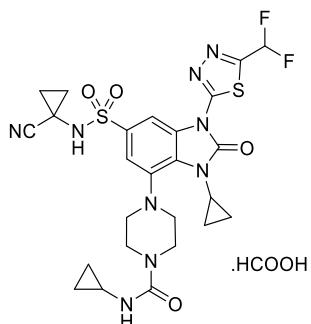




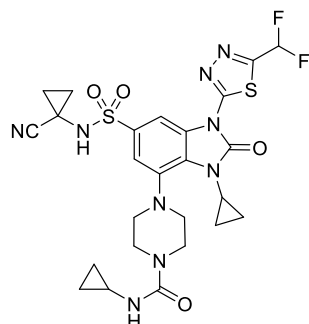




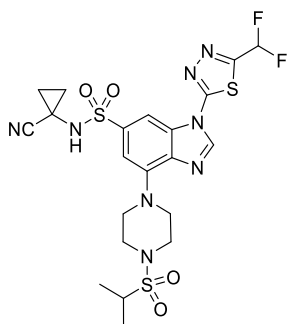
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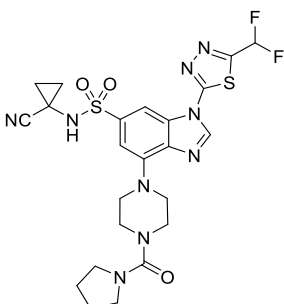
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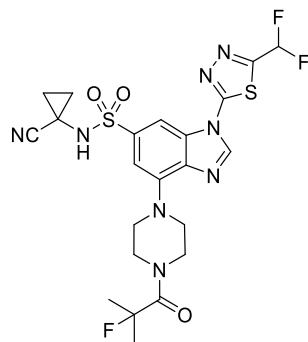
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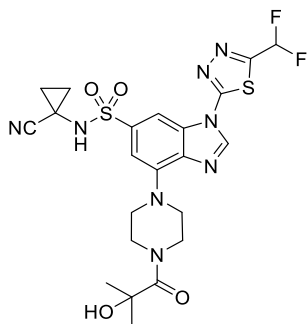
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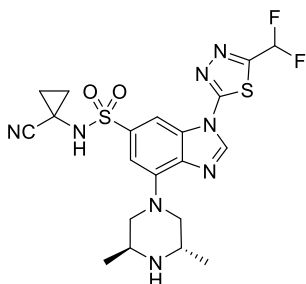
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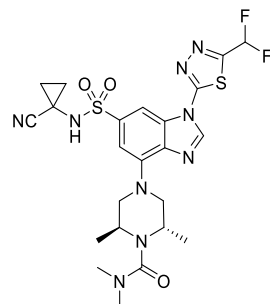
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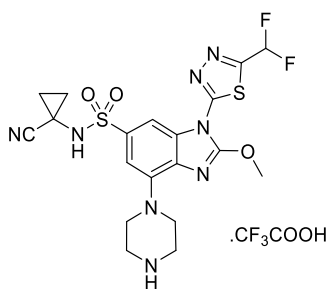
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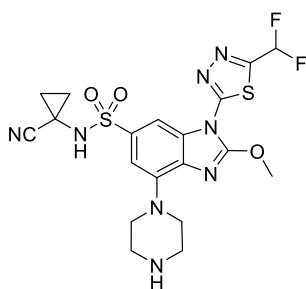
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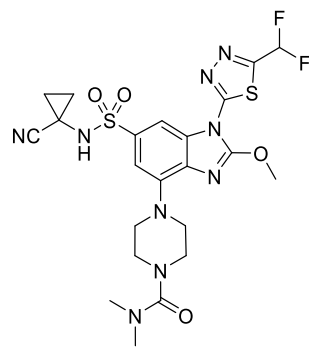
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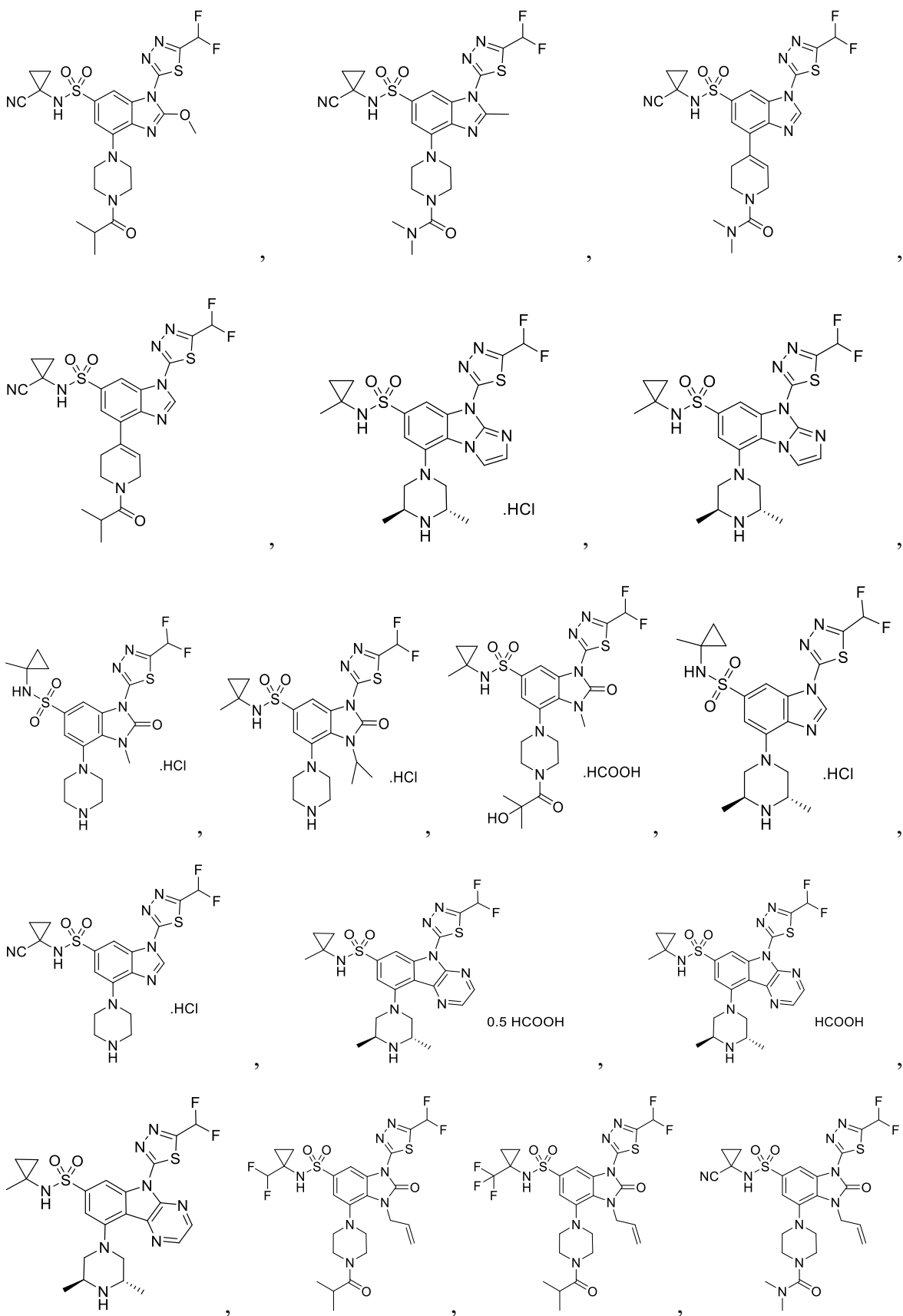
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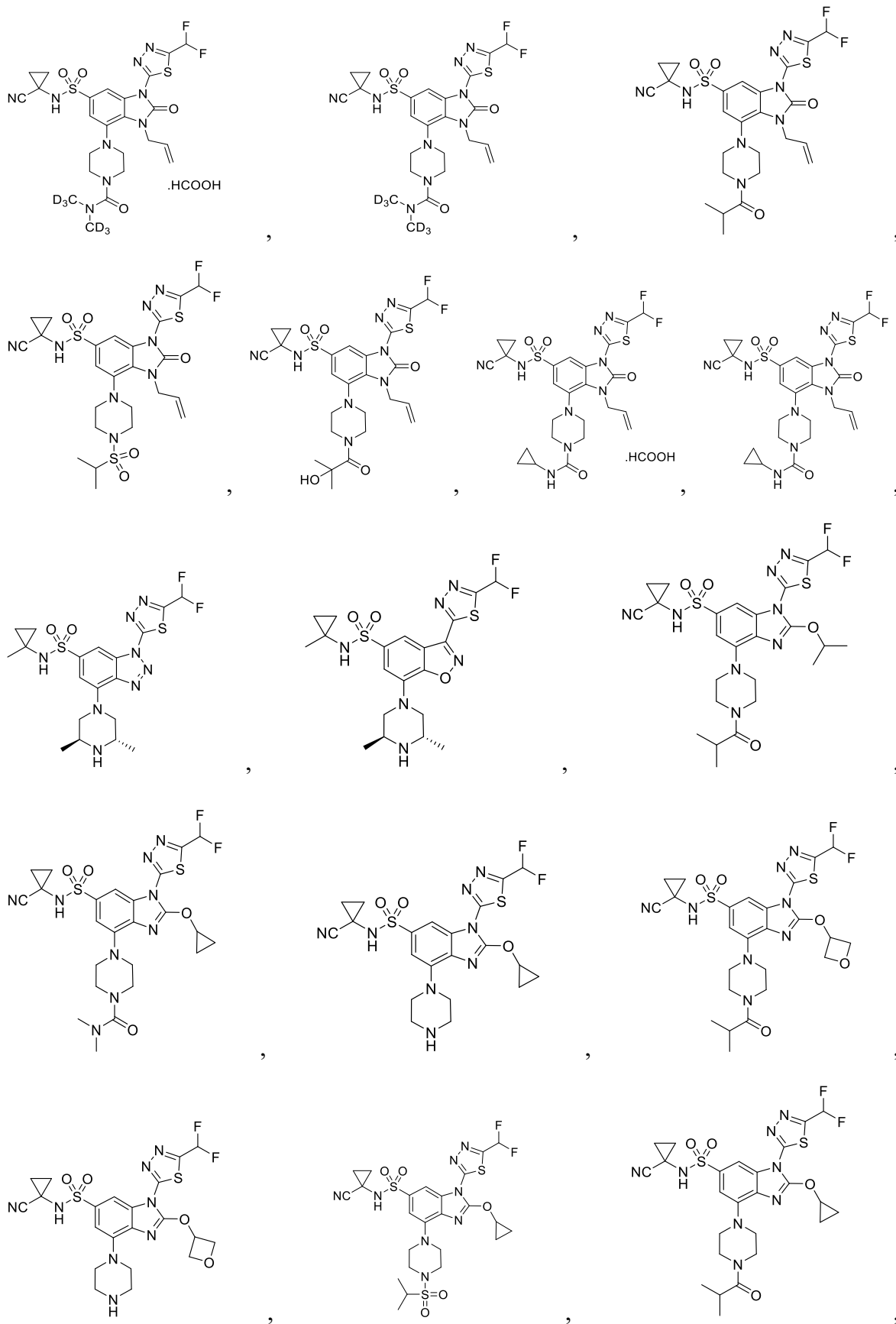


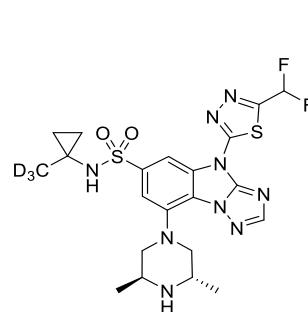
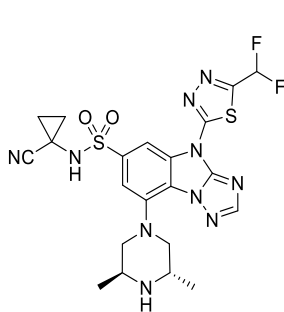
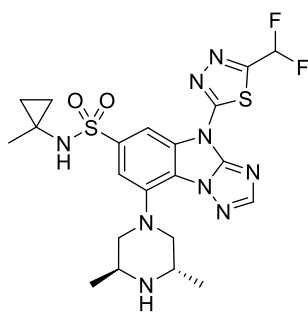
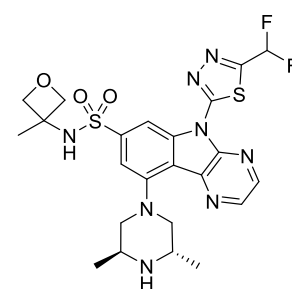
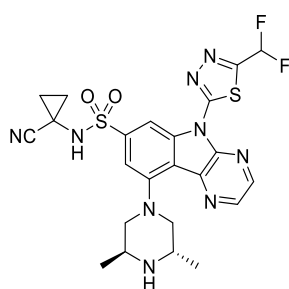
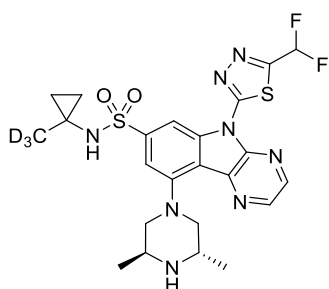
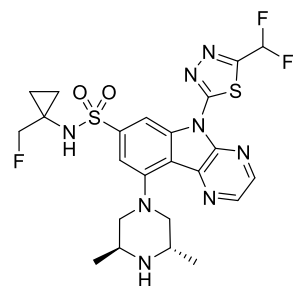
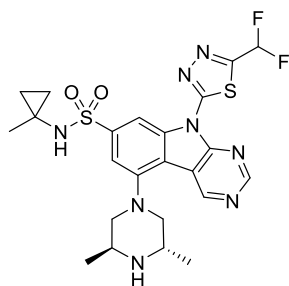
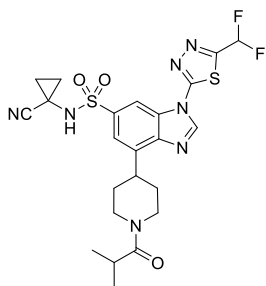
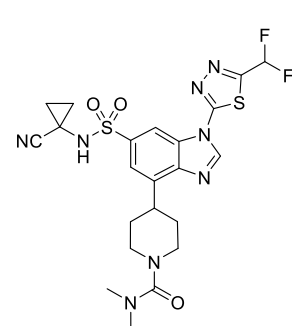
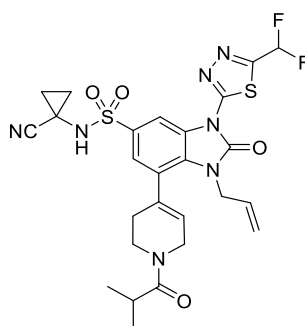
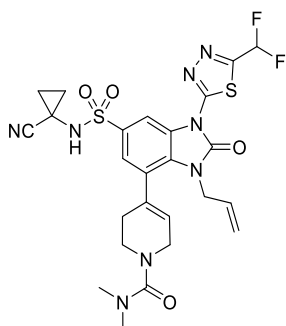
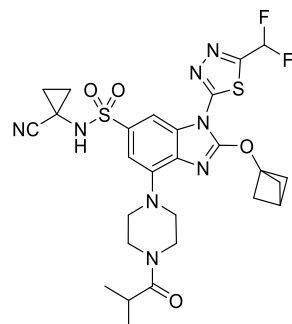
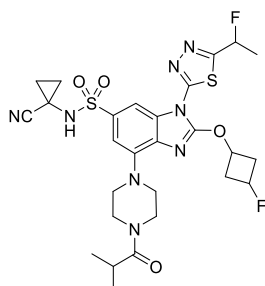
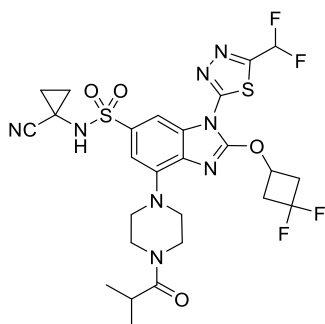
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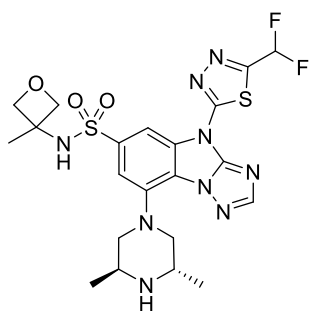


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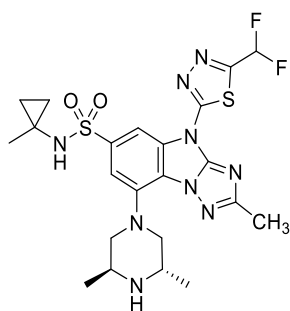




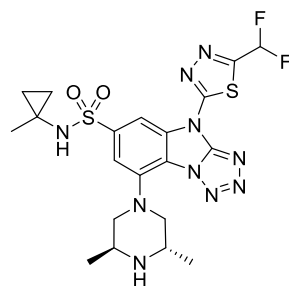




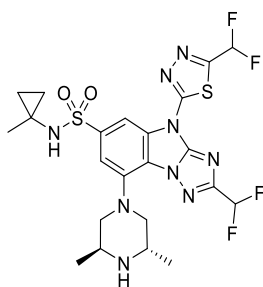
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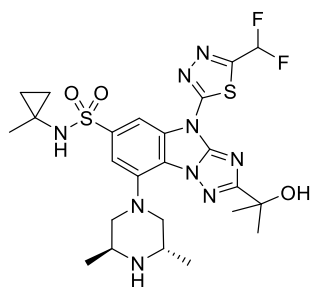
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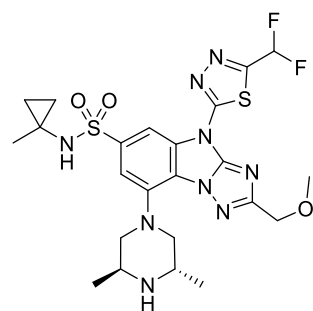
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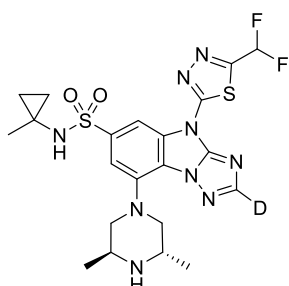
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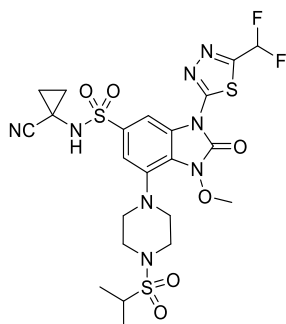
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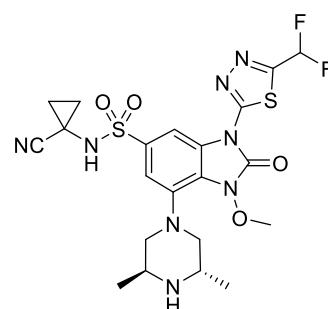
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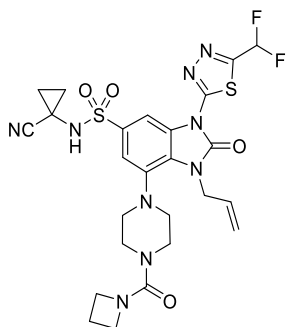
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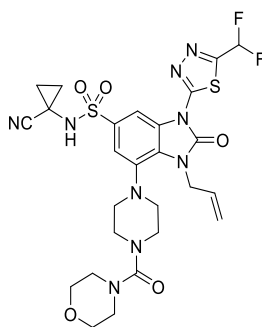
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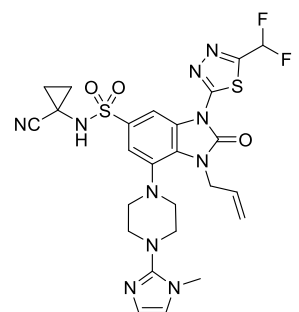
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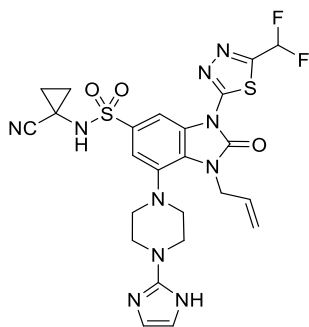
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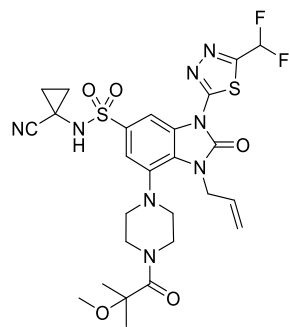
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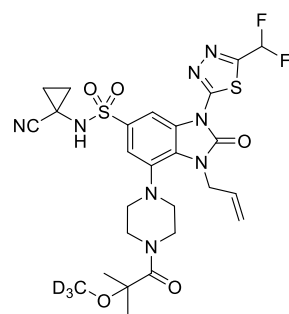
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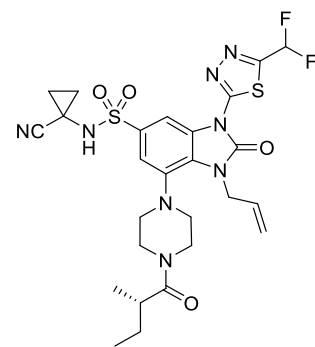
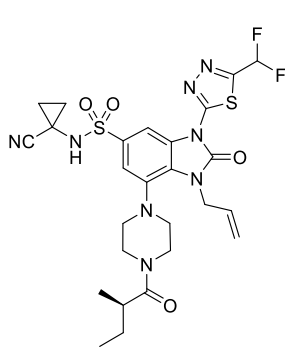
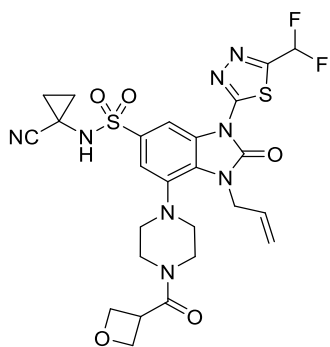
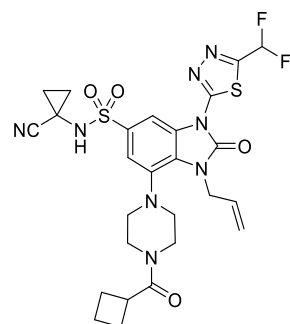
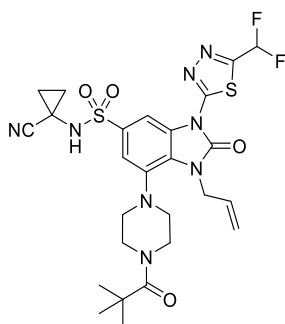
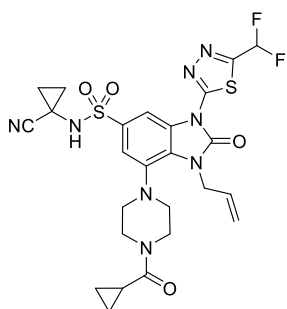
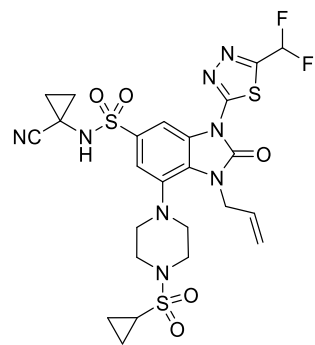
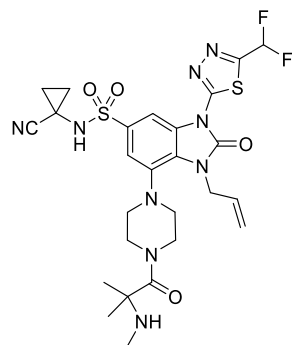
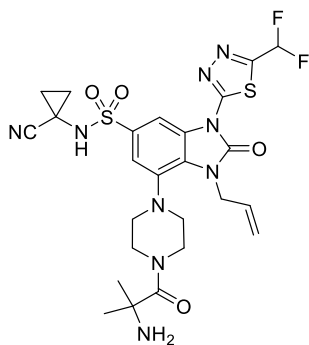
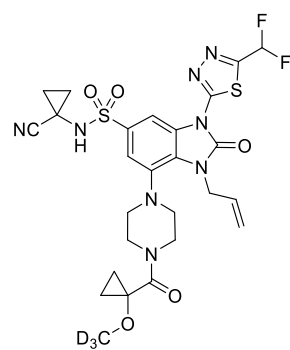
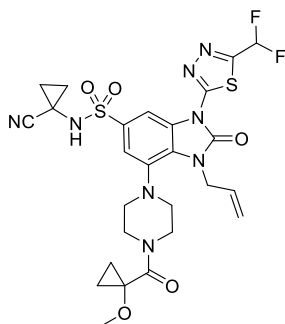
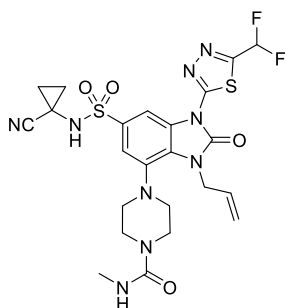
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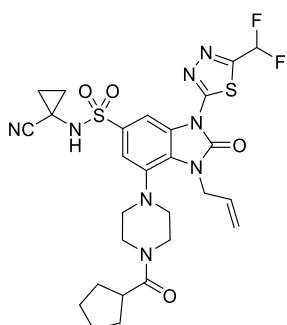


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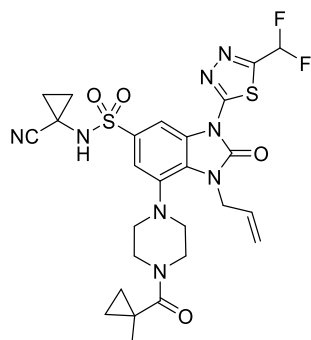


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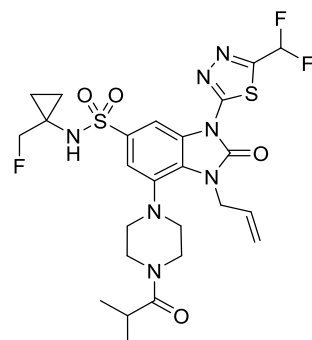




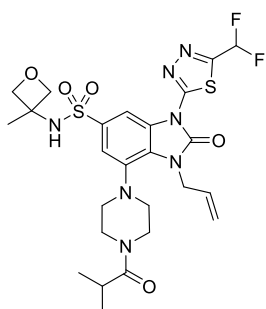
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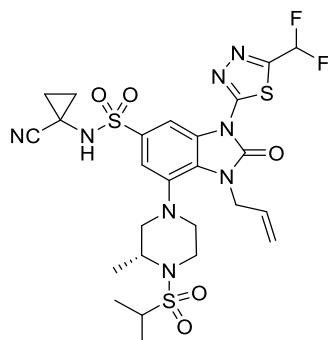
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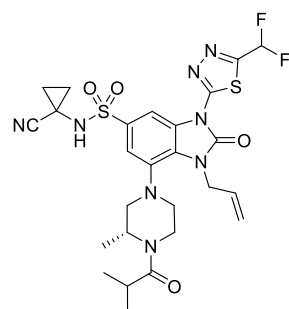
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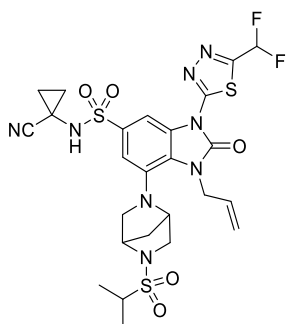
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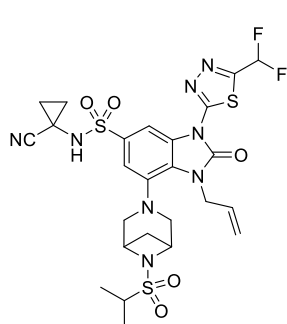
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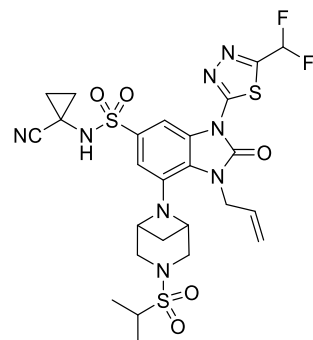
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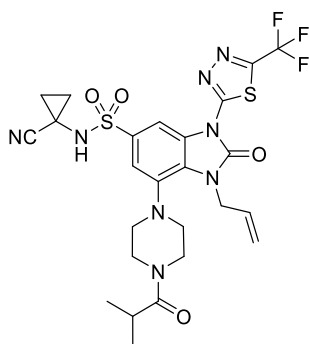
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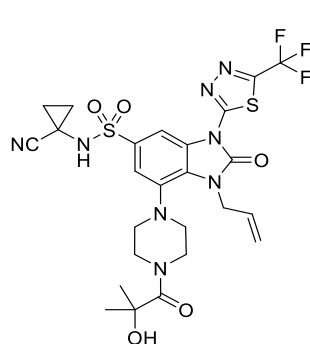
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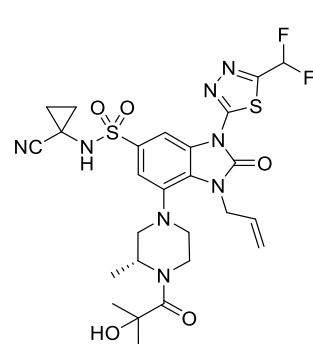
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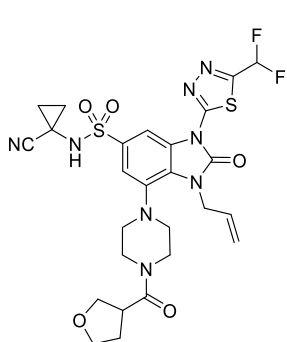
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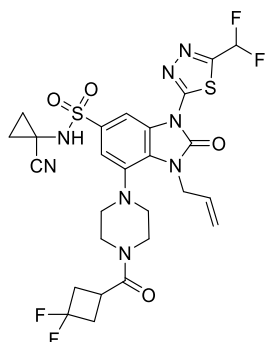
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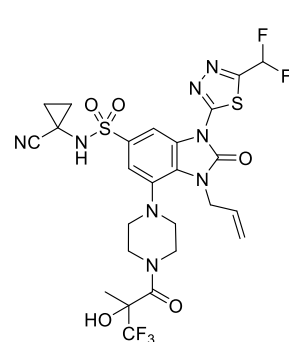
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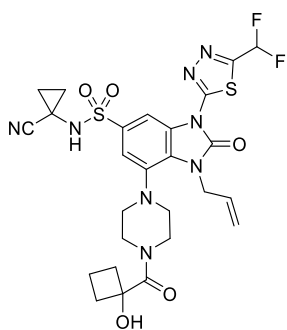
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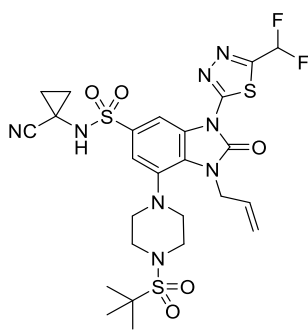
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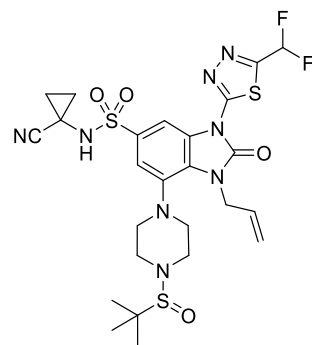
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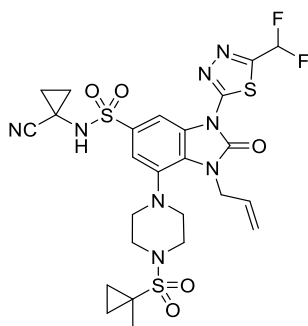
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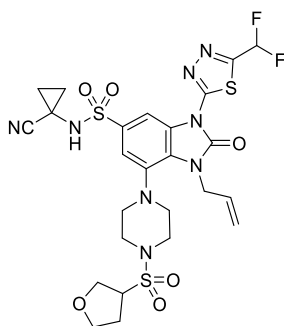
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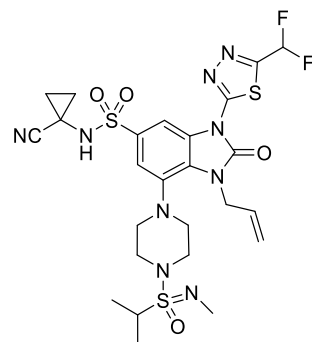
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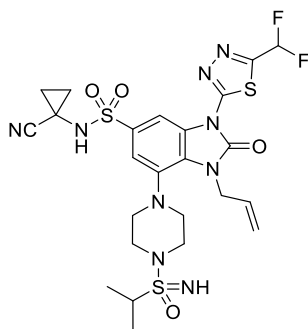
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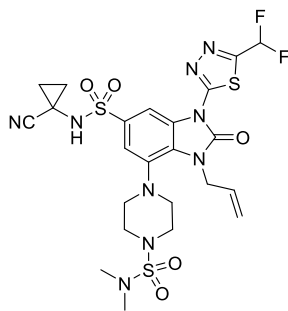
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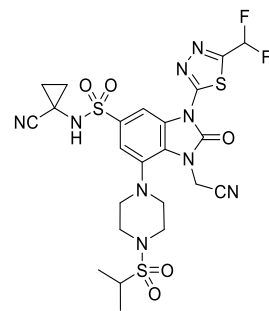
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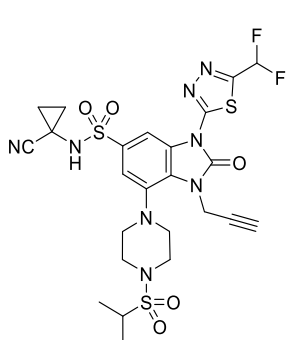
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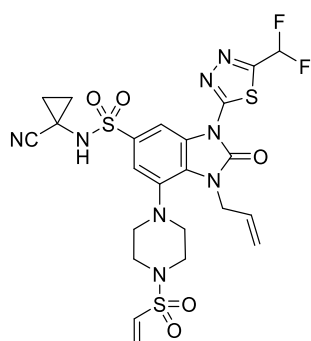
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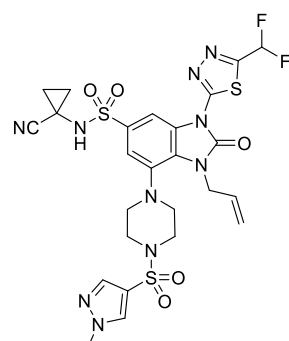
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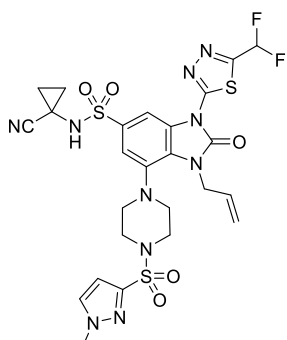
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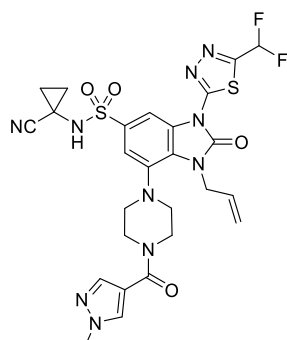
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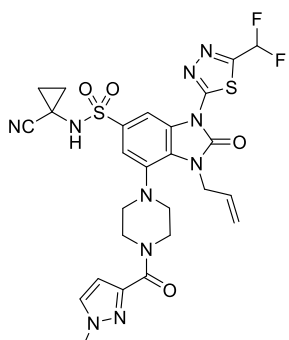
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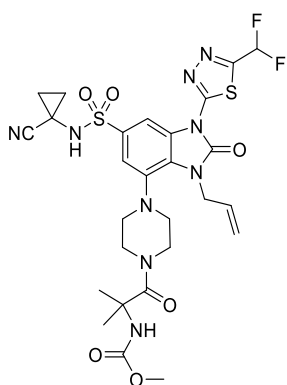
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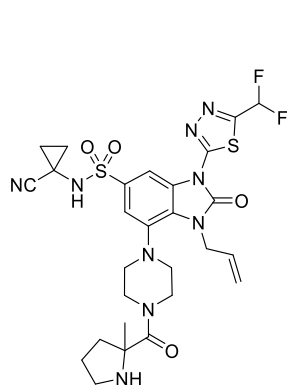
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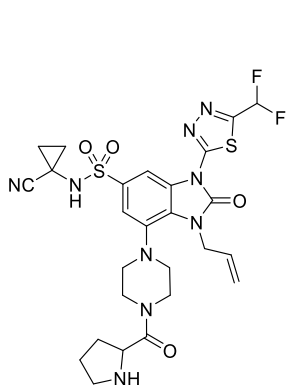
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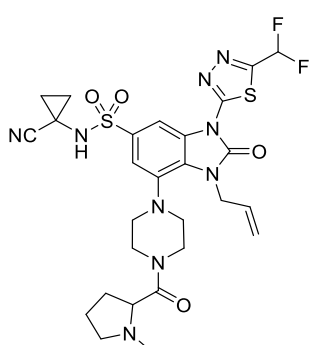
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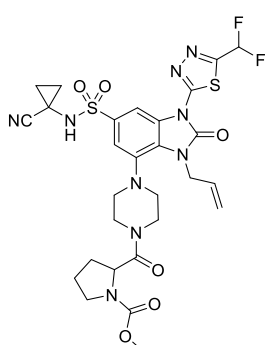
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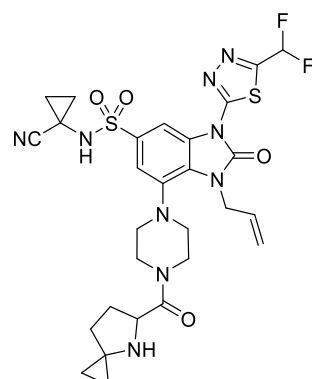
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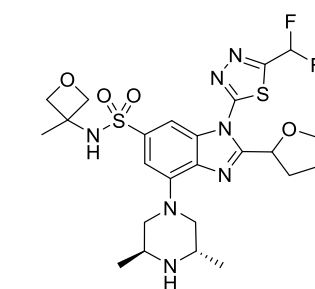
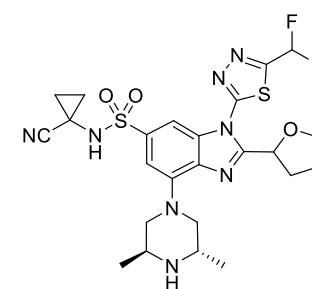
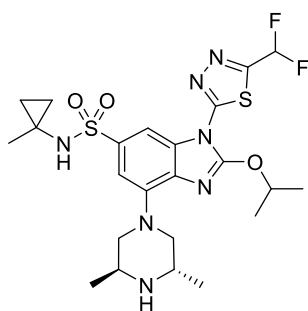
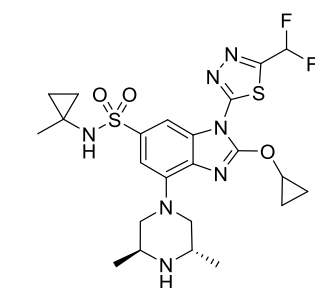
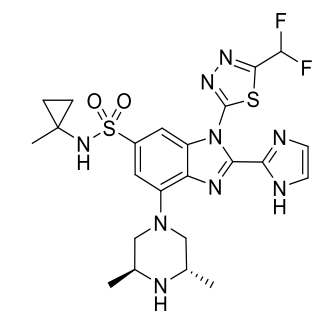
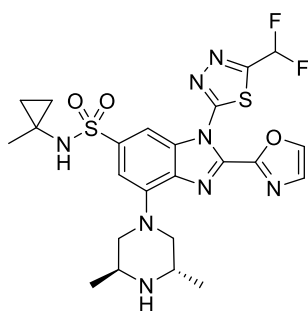
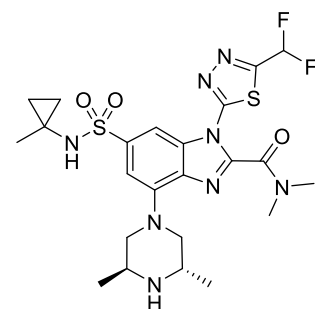
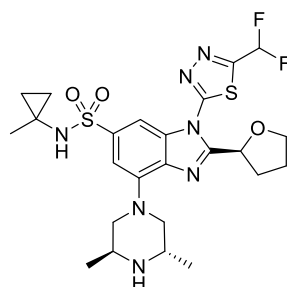
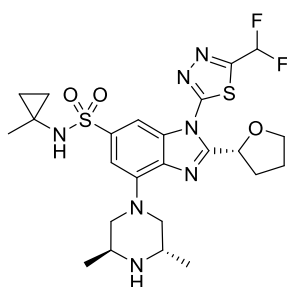
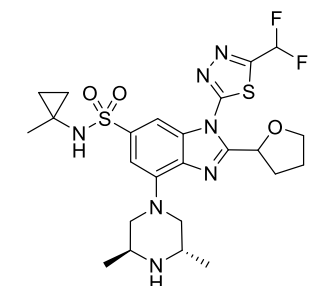
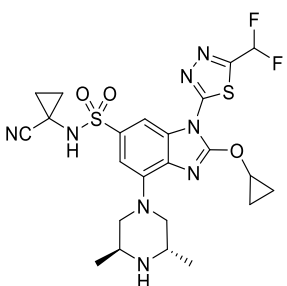
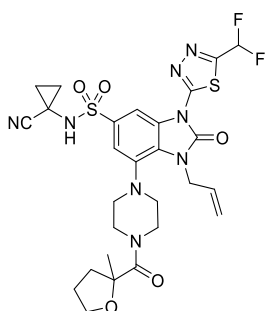
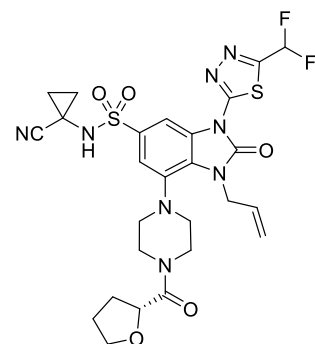
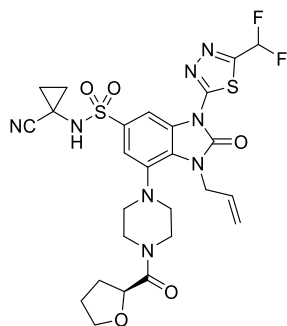
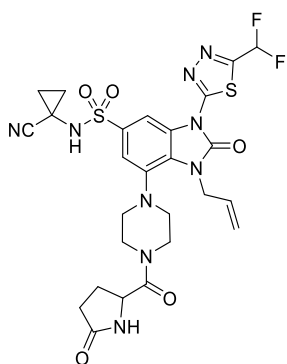
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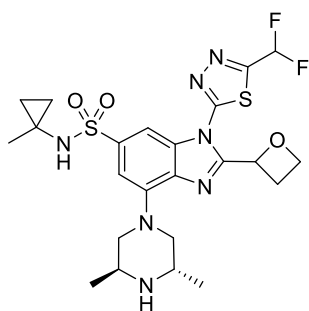


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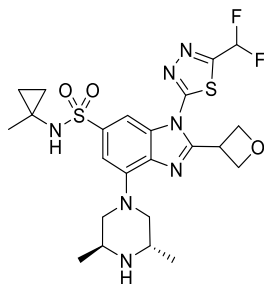


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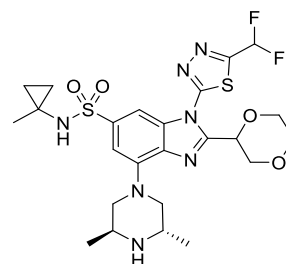




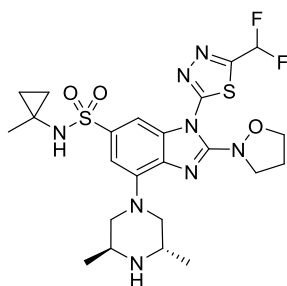
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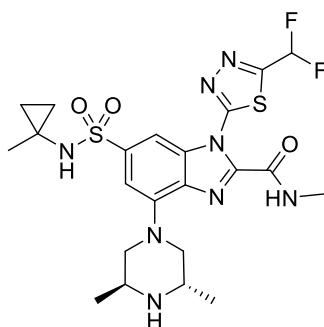
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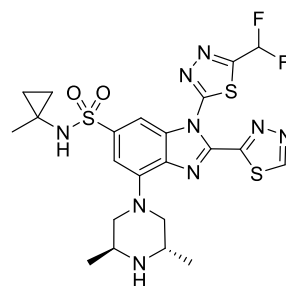
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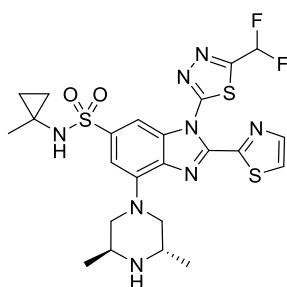
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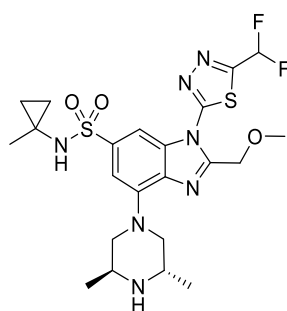
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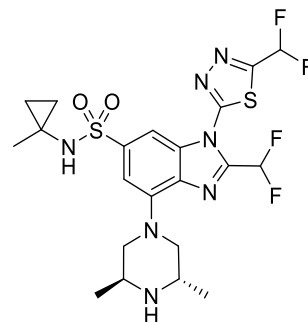
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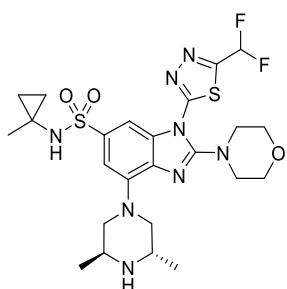
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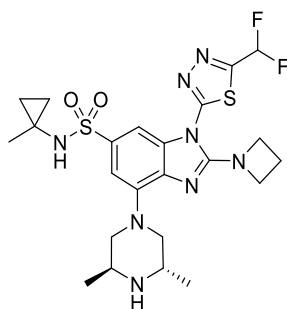
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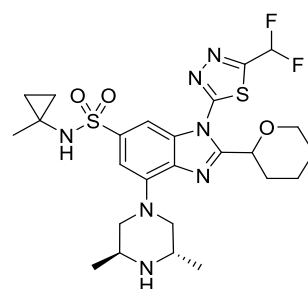
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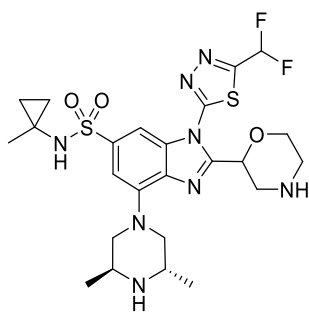
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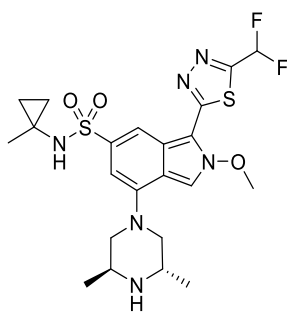
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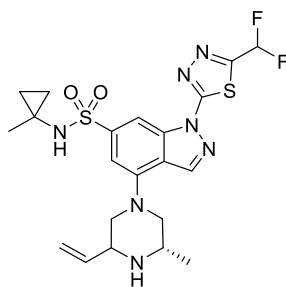
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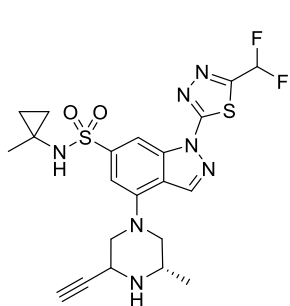
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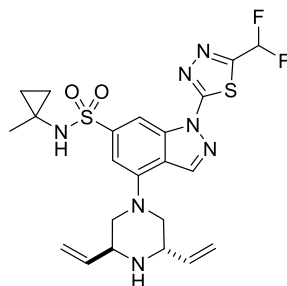
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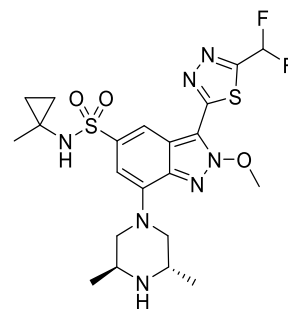
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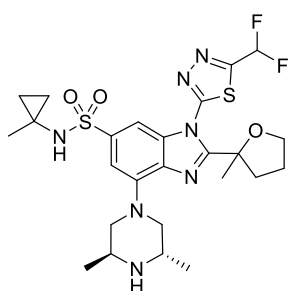
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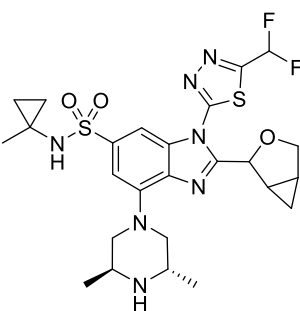
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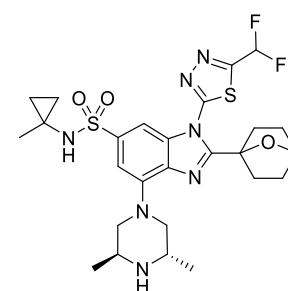
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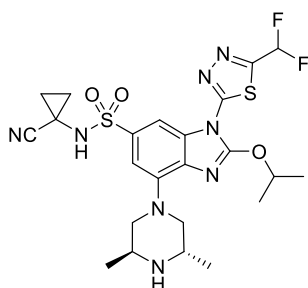
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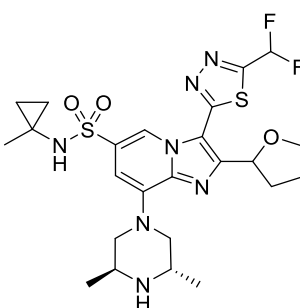
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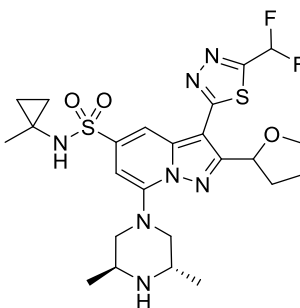
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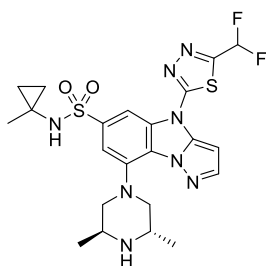
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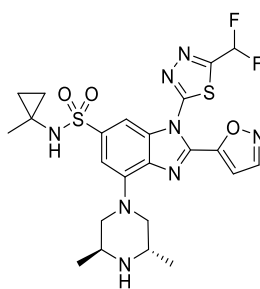
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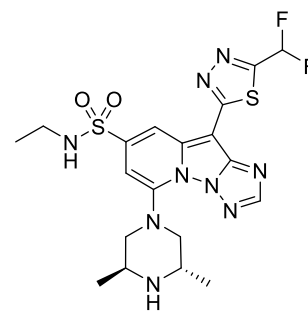
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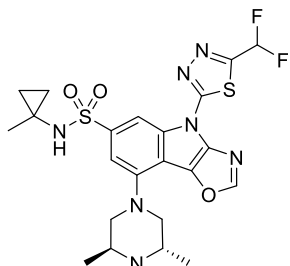
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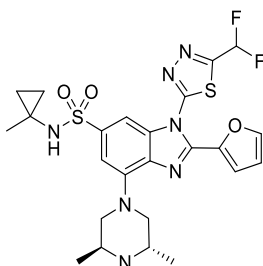
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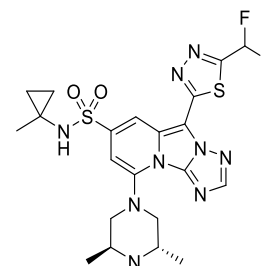
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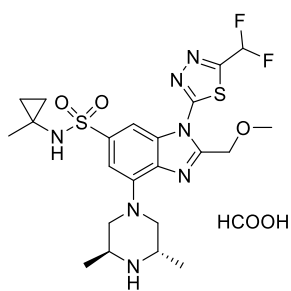
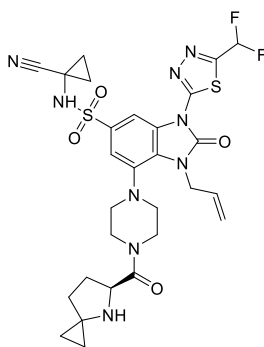
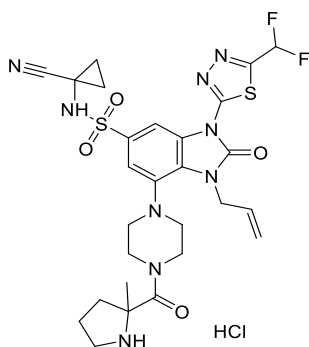
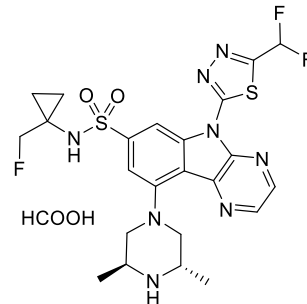
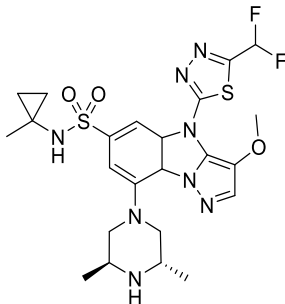
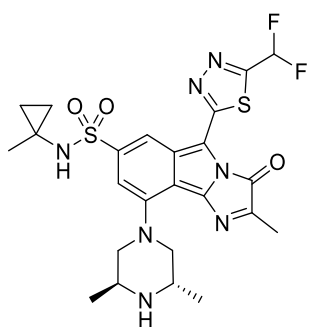
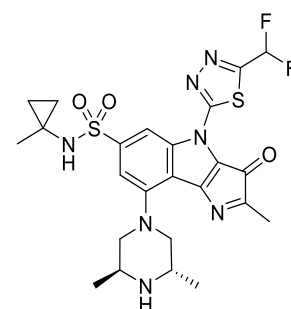
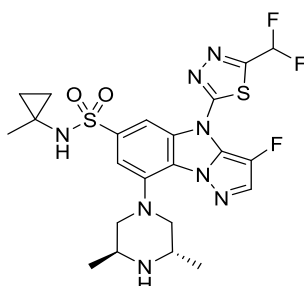
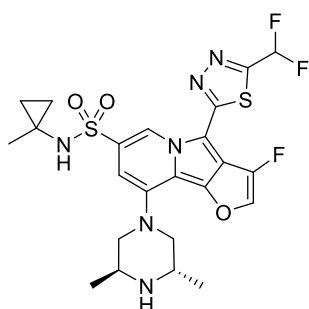
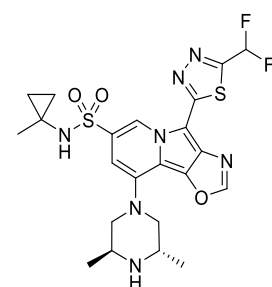
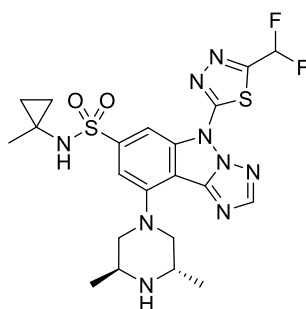
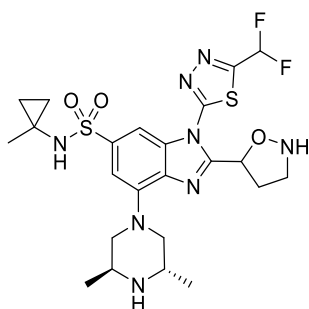
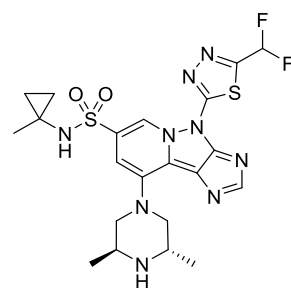
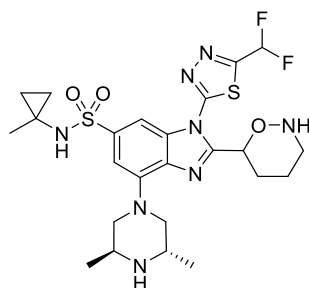
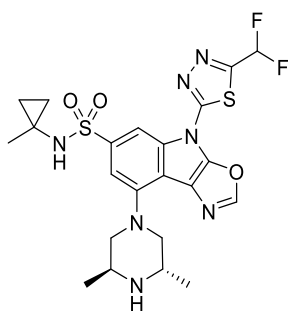
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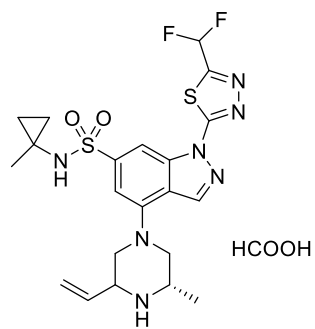
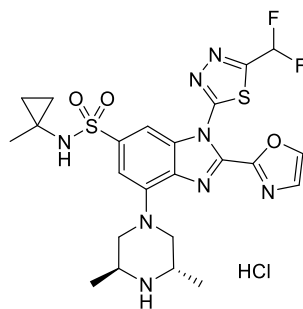
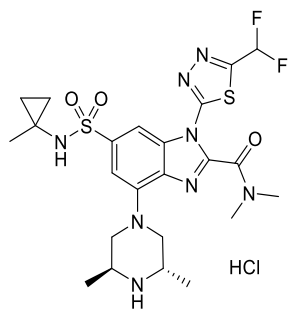
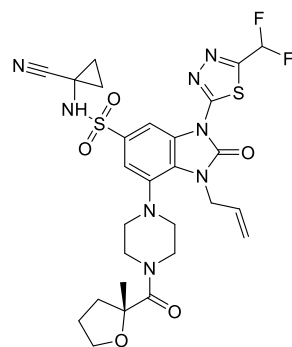
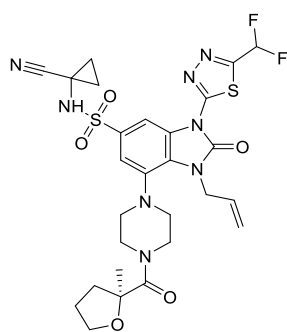
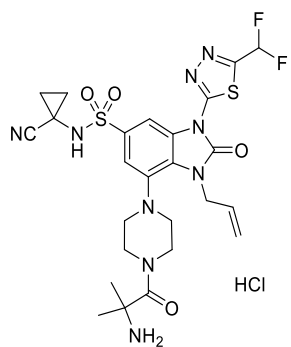
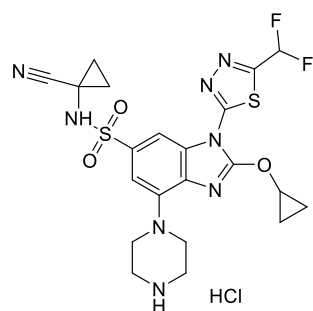
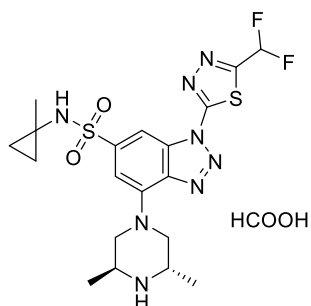
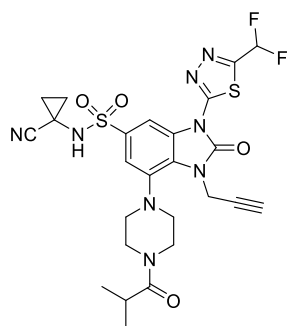
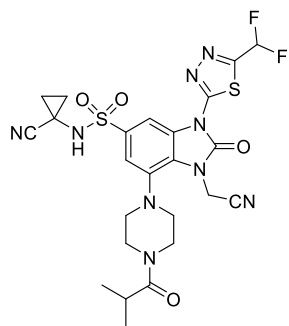
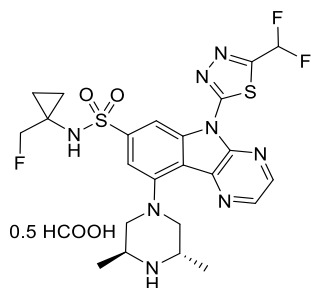
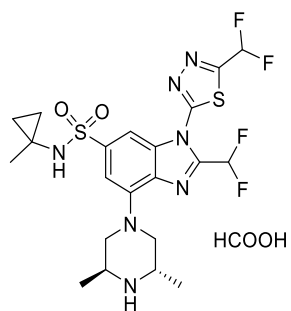


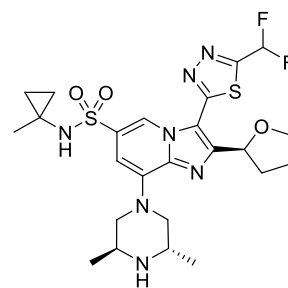
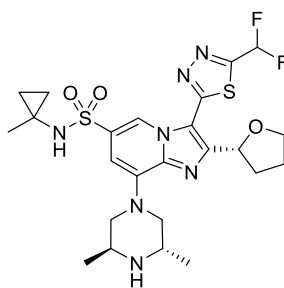
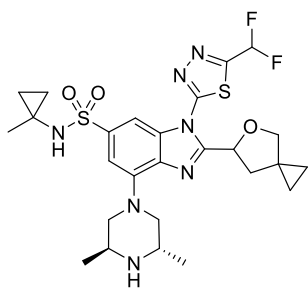
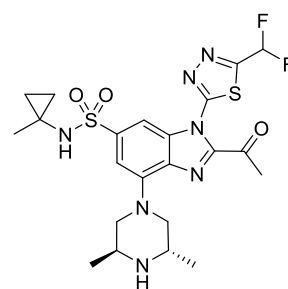
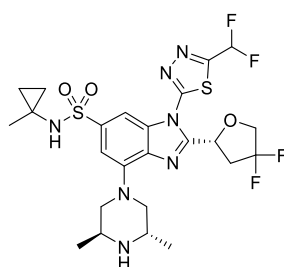
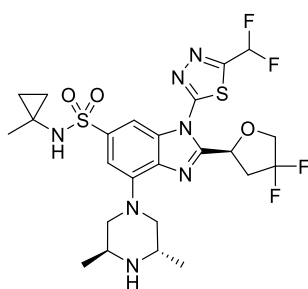
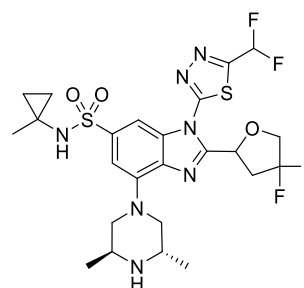
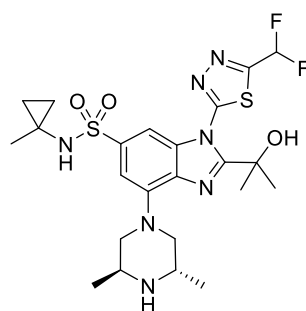
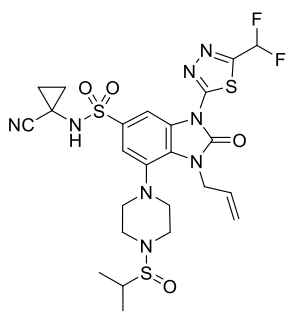
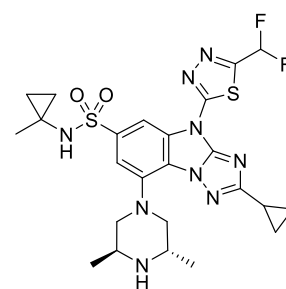
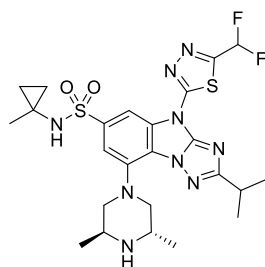
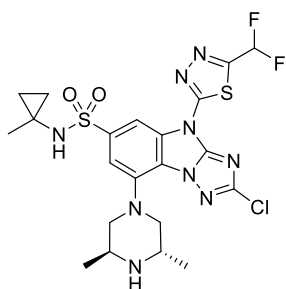
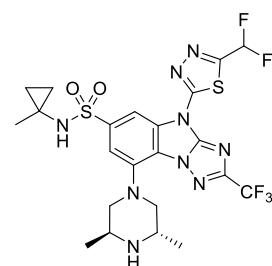
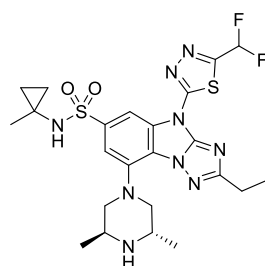
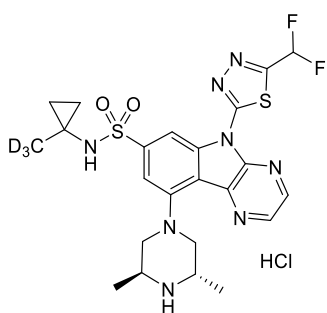
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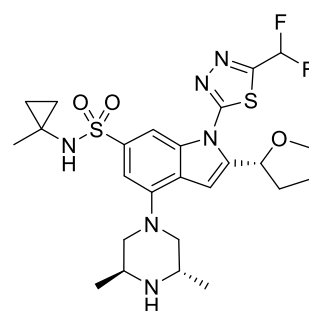
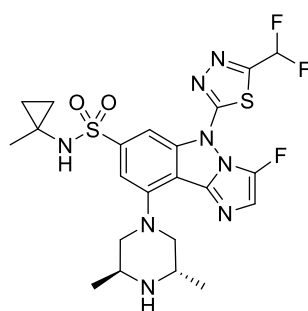
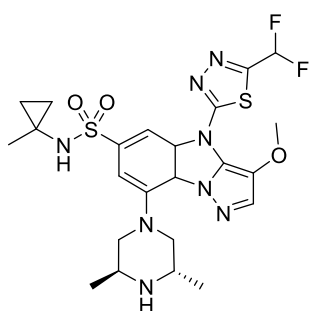
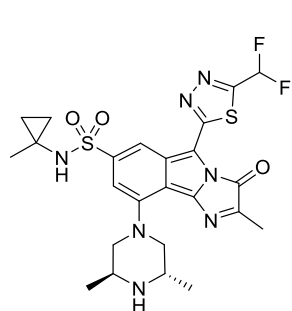
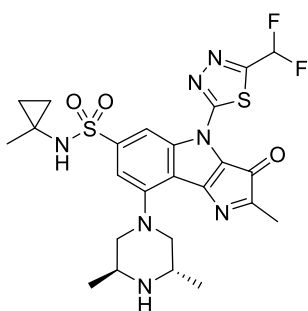
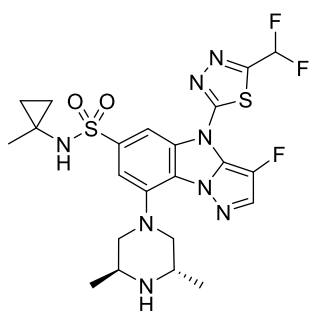
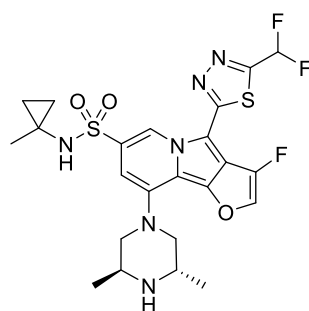
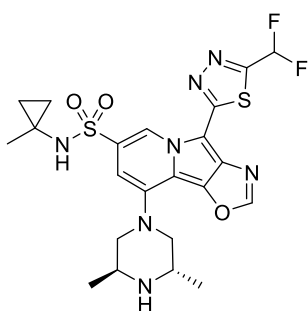
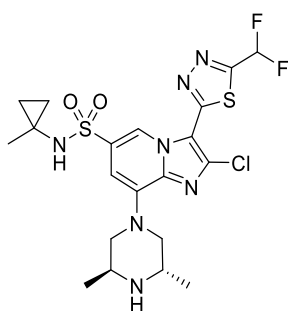
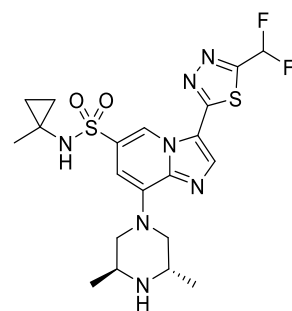
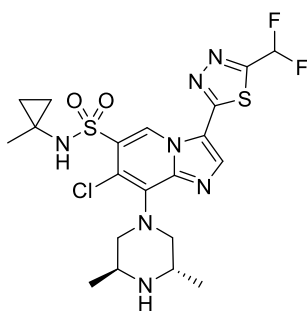
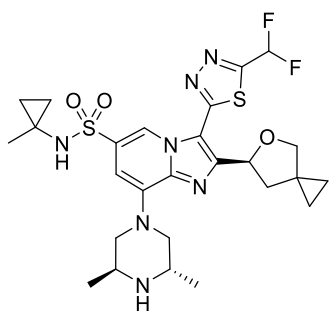
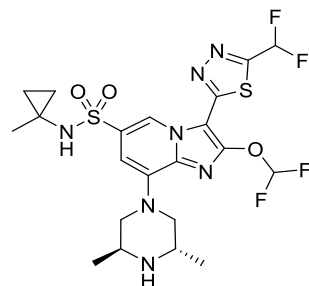
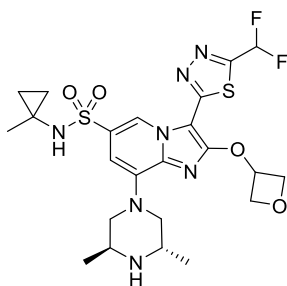
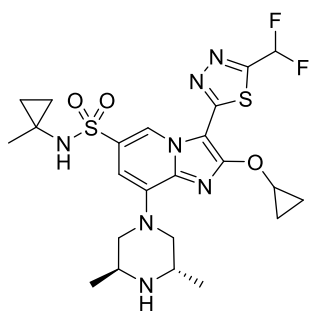


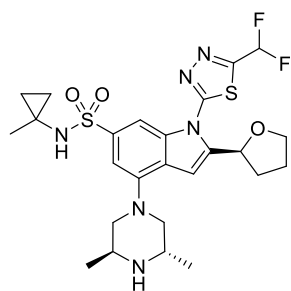
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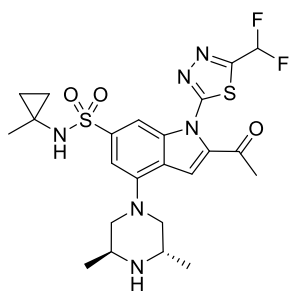




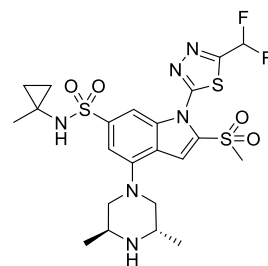




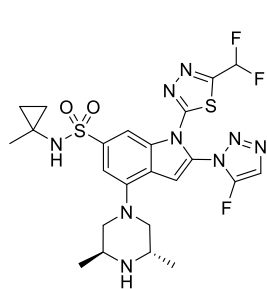
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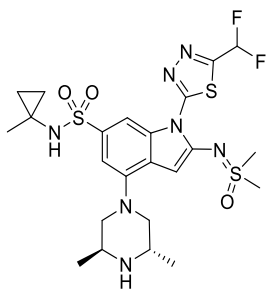
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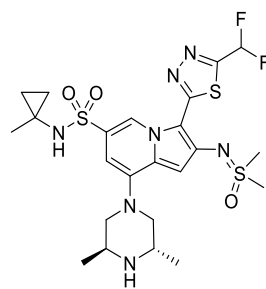
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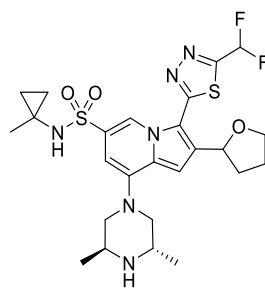
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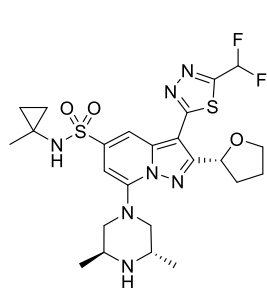
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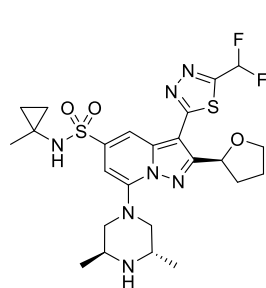
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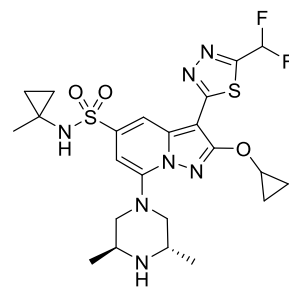
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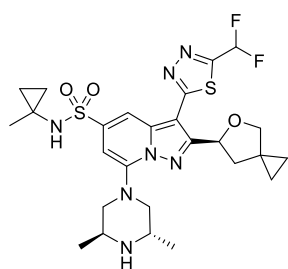
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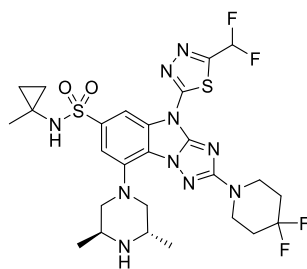
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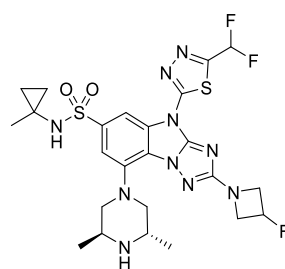
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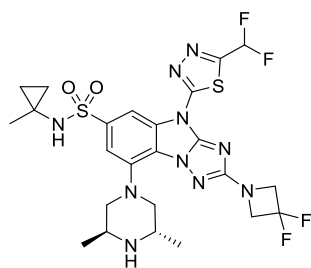
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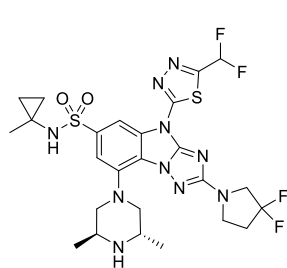
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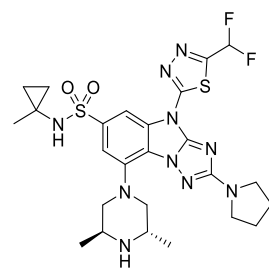
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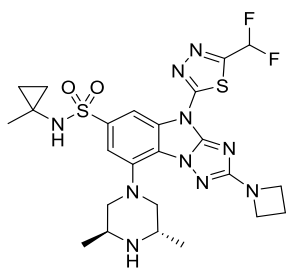
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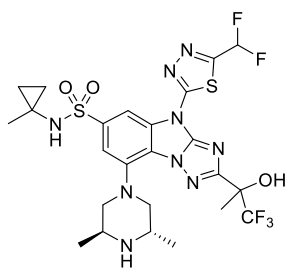
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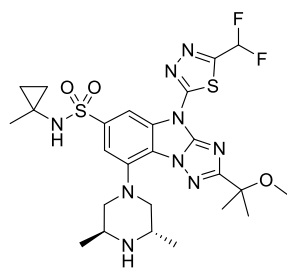
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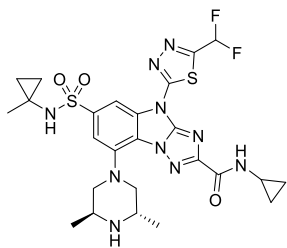
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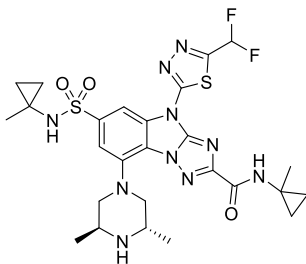
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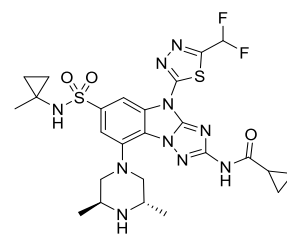
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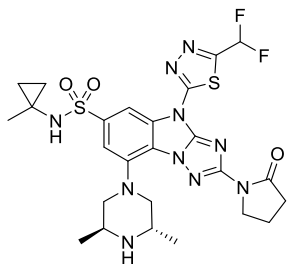
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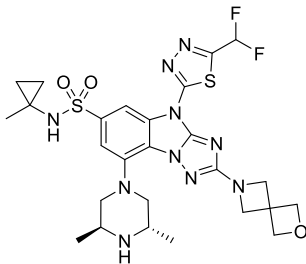
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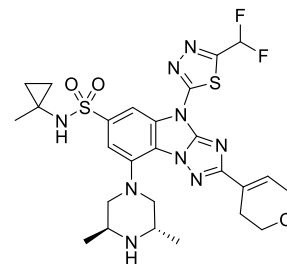
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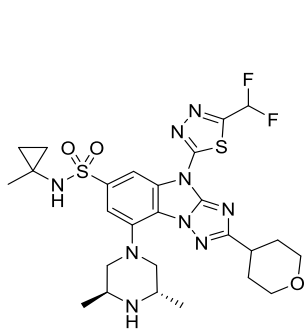
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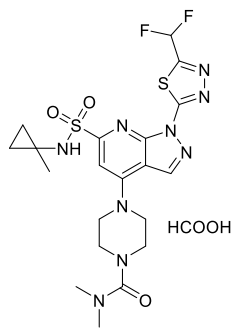
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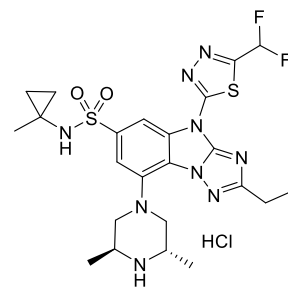
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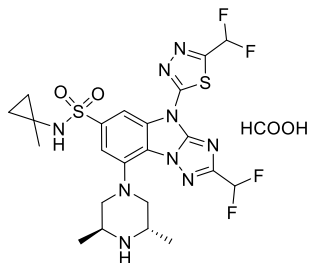
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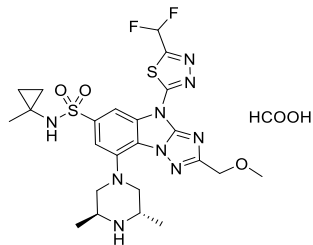
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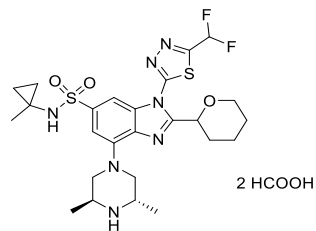
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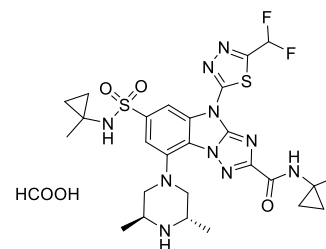
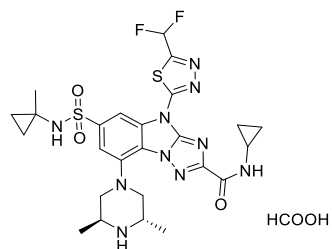
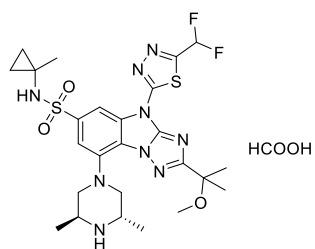
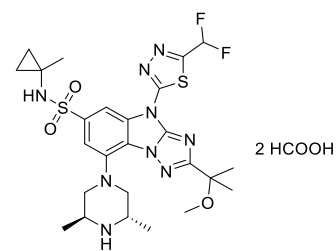
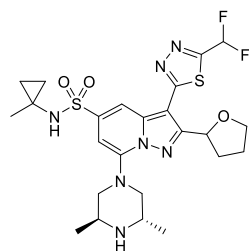
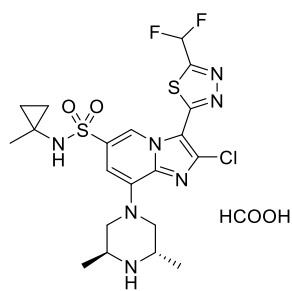
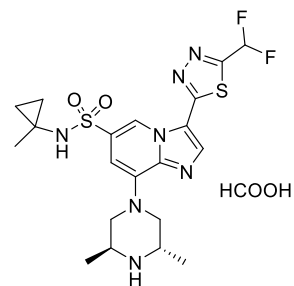
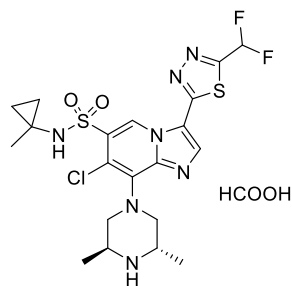
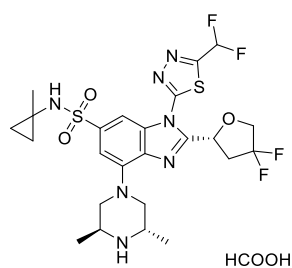
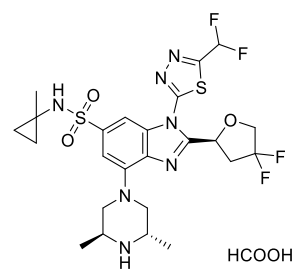
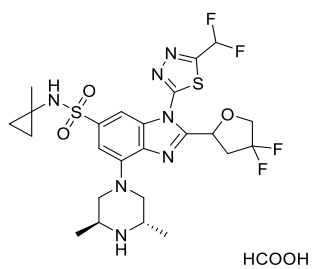
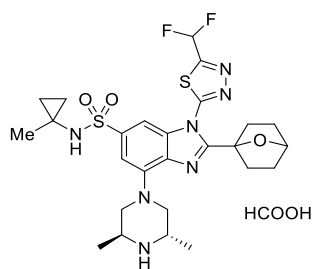
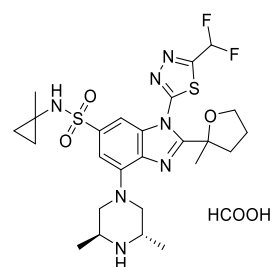
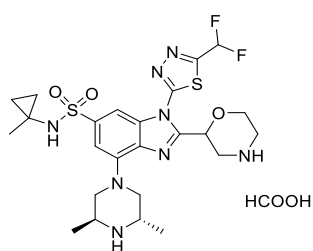
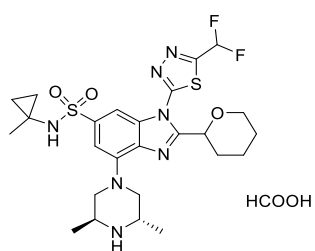
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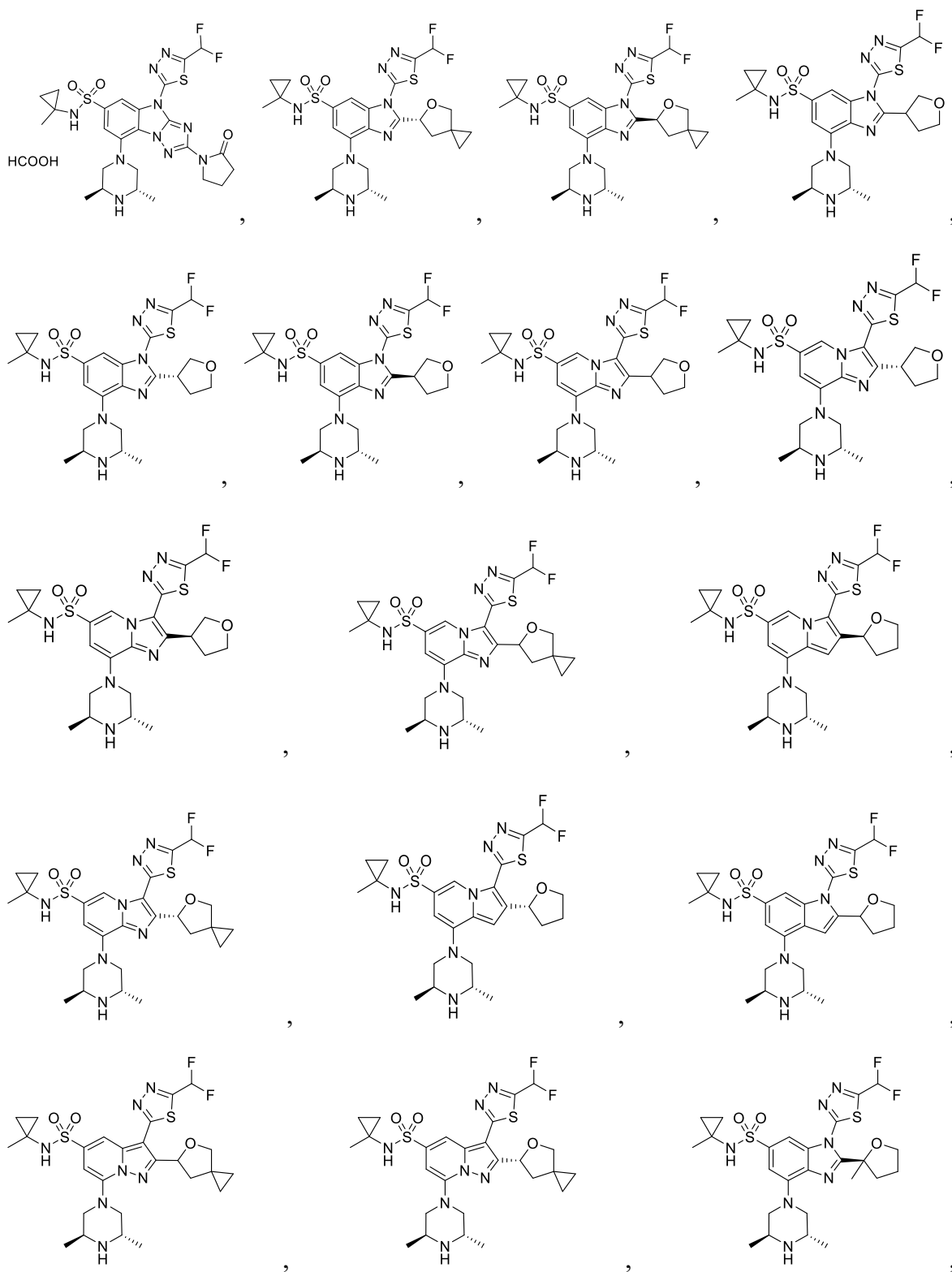


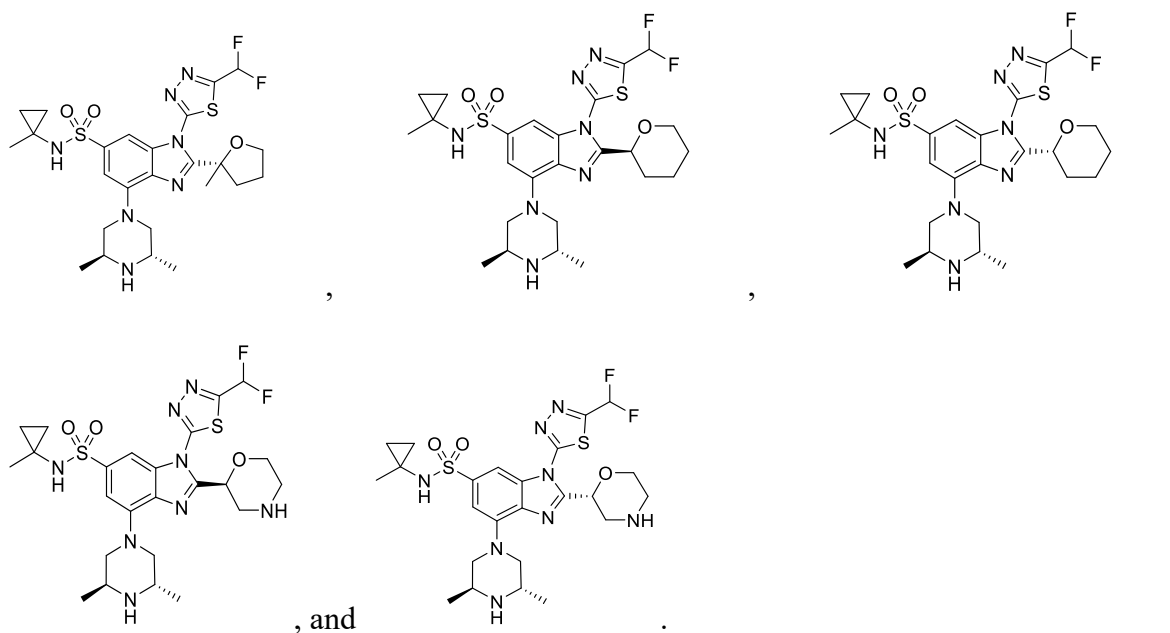
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22. A pharmaceutical composition comprising the compound, the pharmaceutically
 5 acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof,
 the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to
 21, and a pharmaceutically acceptable carrier.

23. Use of the compound, the pharmaceutically acceptable salt thereof, the stereoisomer
 10 thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic
 derivative thereof according to at least one of claims 1 to 21, or the pharmaceutical
 composition according to claim 22, in the manufacture of a medicament for the treatment of
 PARG-mediated cancer.

15 24. A method of treating PARG-mediated cancer, comprising administering to a patient

a therapeutically effective amount of the compound, the pharmaceutically acceptable salt thereof, the stereoisomer thereof, the prodrug thereof, the N-oxide thereof, the solvate thereof, or the isotopic derivative thereof according to at least one of claims 1 to 21, or the pharmaceutical composition according to claim 22.

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25. The use according to claim 23 or the method according to claim 24, wherein the cancer is selected from the group consisting of ovarian cancer, pancreatic cancer, breast cancer, and prostate cancer.