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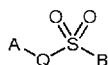
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(54) Title: INHIBITORS OF PARG

(57) Abstract: The present invention relates to sulfonamides of Formula (I) which are inhibitors of PARG and are useful in the treatment of cancer.



(I)



## INHIBITORS OF PARG

### CROSS-REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Application Nos. 63/518,738,  
5 filed August 10, 2023, and 63/658,747, filed June 11, 2024, the disclosures of which are  
incorporated herein by reference in their entirety.

### FIELD OF THE INVENTION

The present invention relates to sulfonamides and related compounds which are  
10 inhibitors of PARG and are useful in the treatment of cancer.

### BACKGROUND OF THE INVENTION

Cancer is a disease caused by abnormal and unregulated cell division. One of the  
hallmarks of cancer is the up or downregulation of cellular stress pathways which the cancer  
15 cells or tumor use for a proliferative advantage. These cellular stress pathways often include,  
but are not limited to, oxidative stress, DNA damage stress, DNA replicative stress,  
transcriptional stress, hypoxia, and others.

ADP-ribose, as well as the enzymes that generate ADP-ribose (Poly(ADP-ribose)  
polymerases or PARPs) and hydrolyze ADP-ribose (Poly(ADP-ribose) glycohydrolases or  
20 PARGs), play critical roles in regulating cellular stress responses. There are two forms of  
ADP-ribose in the cell, mono(ADP-ribose) (MAR) and Poly(ADP-ribose) (PAR). Both forms  
of ADP-ribose are generated by a family of 17 PARP proteins, whose key roles in the cell are  
to regulate cellular stress responses (Cohen MS, Chang P. Nat Chem Biol. 2018).

In humans, PARG exists as a single gene with 3 splicing isoforms. These isoforms  
25 function in and are localized to the nucleus, cytoplasm, and mitochondria. The best  
understood function for PARG is in DNA damage repair. However, PARG also regulates  
gene splicing, transcriptional and epigenetic pathways (Bock FJ, Todorova TT, Chang P. Mol  
Cell 2015) (Le May, Litis et al. Mol Cell. 2012) (Dahl, Maturi et al. Plos One, 2014)  
(Guastafierro, Catizone et al. Biochem J 2013) (Caiafa, Guastafierro et al. FASEB J 2009),  
30 cell division (Chang and Mitchison Nature 2004), the cytoplasmic stress response (Leung,  
Chang et al. Mol Cell 2011), and other cellular stresses.

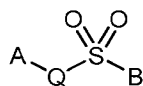
Modulation of both MAR and PAR levels have been shown to be effective treatments  
for multiple cancers. Inhibiting ADP-ribose synthesis through the use of PARP inhibitors can  
be used for the treatment of multiple cancer types. PARG inhibitors work by modulating

cellular stress responses such as the DNA damage response (DDR) and the replicative stress response. DDR and replicative stress are very important cellular stress responses for cancers because they are a consequence of all cellular stress responses, thus many cancers have them. Cancers accumulate DNA damage due to the upregulation of cellular stress pathways and subsequent errors in DNA replication. In cancers, single-strand breaks (SSBs) are the most common type of DNA damage lesion and PARG together with PARP1 play important roles in single strand break repair (SSBR) and another repair mechanism called base excision repair (BER). PARP1 recognizes the break, binds to it, and rapidly synthesizes PAR onto itself (automodification) and histone proteins. Multiple DNA repair proteins, including a master regulator XRCC1, bind to and are recruited to the newly synthesized PAR and then repair the break (Mortusewicz, Fouquerel et al. Nucleic Acid Res. 2011). Thus, the rapid increase in PAR acts as a key DNA repair signal. The signal initiated by PAR is transient as it becomes rapidly degraded by PARG. If PARG is absent or non-functional, PAR rapidly accumulates in the cancer cell and is toxic, resulting in cell death. When PARP1 is bound to or automodified by PAR, its catalytic activity is reduced and therefore PARG activity helps activate PARP1 and is an important regulator to keep the DNA damage repair signal “on” (Curtin and Szabo Mol Aspects Med. 2013).

PARG depletion by RNA interference (RNAi) has been shown to kill cancer cells and to result in tumor regression in multiple murine cancer models. Human and murine cells that are null or depleted for PARG display an increased sensitivity to DNA damaging agents demonstrating a general defect in DNA damage related stress responses upon inhibition or depletion of PARG. Other cancer relevant stress pathways have also been shown to be defective upon PARG knockdown, suggesting PARG is an attractive target for the treatment of multiple cancer types. In humans, PARG depletion kills lung, ovarian, breast, cervical, and pancreatic cancer cells *in vitro*. Xenograft models of these human cancers implanted into mice show tumor regression when PARG protein expression is knocked down. Together, these results demonstrate that PARG is an effective target for the treatment of multiple stress-dependent cancers, and potentially cancers where cellular stress responses are not obviously present. This invention seeks to provide cell permeable inhibitors of PARG.

## SUMMARY OF THE INVENTION

The present invention is directed to a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof, wherein constituent members are defined below.

5           The present invention is further directed to a pharmaceutical composition comprising a compound of Formula I, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

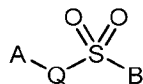
          The present invention is further directed to a method of inhibiting the activity of PARG comprising contacting a compound of Formula I, or a pharmaceutically acceptable salt  
10 thereof, with PARG.

          The present invention is further directed to a method of treating a disease or disorder in a patient in need of treatment, where the disease or disorder is characterized by overexpression or increased activity of PARG, comprising administering to the patient a therapeutically effective amount of a compound of Formula I, or a pharmaceutically  
15 acceptable salt thereof.

          The present invention is further directed to a method of treating cancer in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of an agent that inhibits PARG activity, such as a compound of Formula I, or a pharmaceutically acceptable salt thereof. The present disclosure also provides uses of the  
20 compounds described herein in the manufacture of a medicament for use in therapy. The present disclosure also provides the compounds described herein for use in therapy.

## DETAILED DESCRIPTION

The present invention is directed to a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

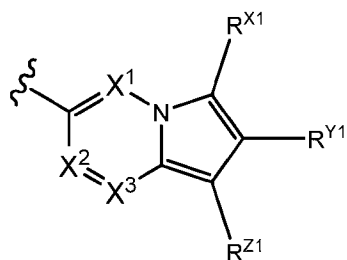
Q is NH or CH<sub>2</sub>;

A is C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, Cy, or Cy-C<sub>1-4</sub> alkyl-, wherein said C<sub>1-6</sub>  
30 alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of A are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub>

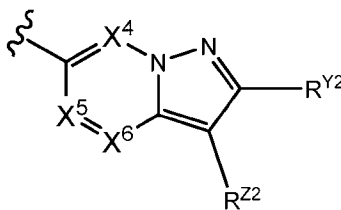


- haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a</sup>, SR<sup>a</sup>, C(O)R<sup>b</sup>, C(O)NR<sup>c</sup>R<sup>d</sup>, C(O)OR<sup>a</sup>, OC(O)R<sup>b</sup>, OC(O)NR<sup>c</sup>R<sup>d</sup>, C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(O)R<sup>b</sup>, NR<sup>c</sup>C(O)OR<sup>a</sup>, NR<sup>c</sup>C(O)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>S(O)R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>, S(O)R<sup>b</sup>, S(O)NR<sup>c</sup>R<sup>d</sup>, S(O)<sub>2</sub>R<sup>b</sup>, and S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>,

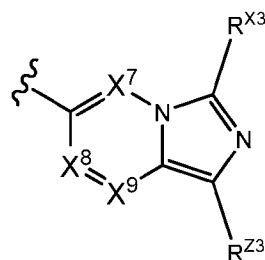
B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), formula (h), formula (i), formula (j), or formula (k):



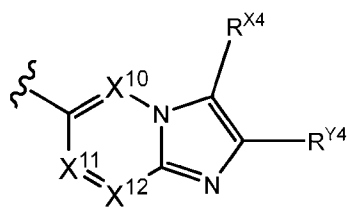
(a)



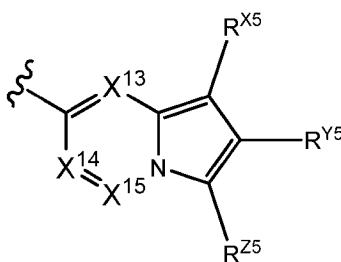
(b)



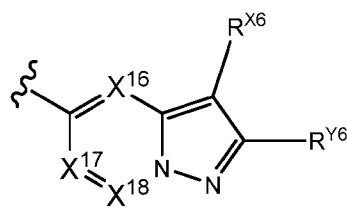
(c)



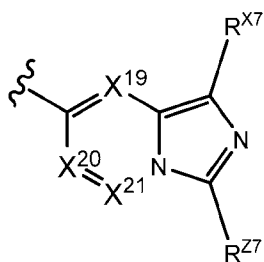
(d)



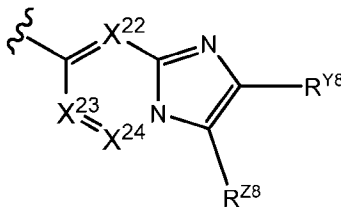
(e)



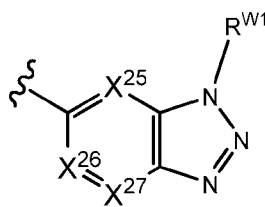
(f)



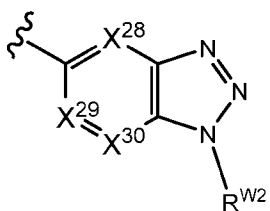
(g)



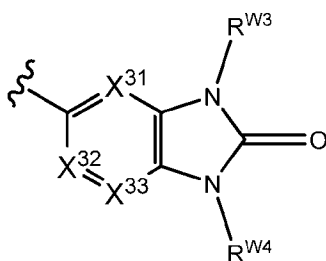
(h)



(i)



(j)



(k);

$X^1$  is N or  $CR^1$ ;

$X^2$  is N or  $CR^2$ ;

$X^3$  is N or  $CR^3$ ;

$X^4$  is N or  $CR^4$ ;

5  $X^5$  is N or  $CR^5$ ;

$X^6$  is N or  $CR^6$ ;

$X^7$  is N or  $CR^7$ ;

$X^8$  is N or  $CR^8$ ;

$X^9$  is N or  $CR^9$ ;

10  $X^{10}$  is N or  $CR^{10}$ ;

$X^{11}$  is N or  $CR^{11}$ ;

$X^{12}$  is N or  $CR^{12}$ ;

$X^{13}$  is N or  $CR^{13}$ ;

$X^{14}$  is N or  $CR^{14}$ ;

15  $X^{15}$  is N or  $CR^{15}$ ;

$X^{16}$  is N or  $CR^{16}$ ;

$X^{17}$  is N or  $CR^{17}$ ;

$X^{18}$  is N or  $CR^{18}$ ;

$X^{19}$  is N or  $CR^{19}$ ;

20  $X^{20}$  is N or  $CR^{20}$ ;

$X^{21}$  is N or  $CR^{21}$ ;

$X^{22}$  is N or  $CR^{22}$ ;

$X^{23}$  is N or  $CR^{23}$ ;

$X^{24}$  is N or  $CR^{24}$ ;

25  $X^{25}$  is N or  $CR^{25}$ ;

$X^{26}$  is N or  $CR^{26}$ ;

$X^{27}$  is N or  $CR^{27}$ ;

- $X^{28}$  is N or  $CR^{28}$ ;  
 $X^{29}$  is N or  $CR^{29}$ ;  
 $X^{30}$  is N or  $CR^{30}$ ;  
 $X^{31}$  is N or  $CR^{31}$ ;  
5  $X^{32}$  is N or  $CR^{32}$ ;  
 $X^{33}$  is N or  $CR^{33}$ ;  
 wherein no more than two of  $X^1$ ,  $X^2$ , and  $X^3$  are simultaneously N;  
 wherein no more than two of  $X^4$ ,  $X^5$ , and  $X^6$  are simultaneously N;  
 wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;  
 10 wherein no more than two of  $X^{10}$ ,  $X^{11}$ , and  $X^{12}$  are simultaneously N;  
 wherein no more than two of  $X^{13}$ ,  $X^{14}$ , and  $X^{15}$  are simultaneously N;  
 wherein no more than two of  $X^{16}$ ,  $X^{17}$ , and  $X^{18}$  are simultaneously N;  
 wherein no more than two of  $X^{19}$ ,  $X^{20}$ , and  $X^{21}$  are simultaneously N;  
 wherein no more than two of  $X^{22}$ ,  $X^{23}$ , and  $X^{24}$  are simultaneously N;  
 15 wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;  
 wherein no more than two of  $X^{28}$ ,  $X^{29}$ , and  $X^{30}$  are simultaneously N;  
 wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;  
 each Cy is independently selected from C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered  
 heteroaryl, and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4,  
 20 or 5 substituents independently selected from  $R^{Cy}$ ;  
 each  $R^{Cy}$  is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub>  
 haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub>  
 alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>,  
 C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>,  
 25 NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>,  
 NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and  
 S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub>  
 cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered  
 heterocycloalkyl-C<sub>1-4</sub> alkyl of  $R^{Cy}$  is optionally substituted by 1, 2, or 3 substituents  
 30 independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>,  
 OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>,  
 NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>,  
 NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>.

$R^1, R^2, R^4, R^5, R^7, R^8, R^{10}, R^{11}, R^{13}, R^{14}, R^{16}, R^{17}, R^{19}, R^{20}, R^{22}, R^{23}, R^{25}, R^{26}, R^{28}, R^{29}, R^{31}$ , and  $R^{32}$  are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;

$R^3, R^6, R^9, R^{12}, R^{15}, R^{18}, R^{21}, R^{24}, R^{27}, R^{30}$ , and  $R^{33}$  are each independently selected from H, halo, OR<sup>a2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $R^3, R^6, R^9, R^{12}, R^{15}, R^{18}, R^{21}, R^{24}, R^{27}, R^{30}$ , and  $R^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>q</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>,

$R^{X1}, R^{X3}, R^{X4}, R^{X5}, R^{X6}, R^{X7}, R^{Y1}, R^{Y2}, R^{Y4}, R^{Y5}, R^{Y6}, R^{Y8}, R^{Z1}, R^{Z2}, R^{Z3}, R^{Z5}, R^{Z7}$ , and  $R^{Z8}$  are each independently selected from H, halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl of  $R^{X1}, R^{X3}, R^{X4}, R^{X5}, R^{X6}, R^{X7}, R^{Y1}, R^{Y2}, R^{Y4}, R^{Y5}, R^{Y6}, R^{Y8}, R^{Z1}, R^{Z2}, R^{Z3}, R^{Z5}, R^{Z7}$ , and  $R^{Z8}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>,

$R^{W1}, R^{W2}, R^{W3}$ , and  $R^{W4}$  are each independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4 R<sup>'</sup>;

each R<sup>'</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>,

- $\text{NR}^{\text{c}3}\text{S}(\text{O})\text{R}^{\text{b}3}$ ,  $\text{NR}^{\text{c}3}\text{S}(\text{O})_2\text{R}^{\text{b}3}$ ,  $\text{NR}^{\text{c}3}\text{S}(\text{O})_2\text{NR}^{\text{c}3}\text{R}^{\text{d}3}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}3}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}3}\text{R}^{\text{d}3}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}3}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c}3}\text{R}^{\text{d}3}$ , wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>c</sup> is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>c3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>c3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>;
- 10 each R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>a1</sup>, R<sup>b1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>b3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>a1</sup>, R<sup>b1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>b3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>c4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>c4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>;
- 15 or R<sup>c</sup> and R<sup>d</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>c4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>c4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>;
- 20 or R<sup>c1</sup> and R<sup>d1</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>c4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>c4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>;
- 30

or  $R^{c2}$  and  $R^{d2}$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  
 5  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ,

or  $R^{c3}$  and  $R^{d3}$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  
 10  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ,

or  $R^{c4}$  and  $R^{d4}$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  
 15  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ,

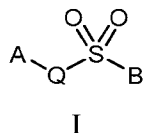
each  $R^{a4}$ ,  $R^{b4}$ ,  $R^{c4}$ , and  $R^{d4}$  is independently selected from H,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, wherein said  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl are each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino,  $NHC_{1-4}$  alkyl,  $N(C_{1-4}$  alkyl)<sub>2</sub>, halo,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy,  $C_{1-6}$  haloalkyl, and  $C_{1-6}$  haloalkoxy;  
 20  
 25

each  $R^e$ ,  $R^{e1}$ ,  $R^{e2}$ ,  $R^{e3}$ , and  $R^{e4}$  is independently selected from H,  $C_{1-4}$  alkyl, and CN;  
 30 and

q is an integer selected from 1, 2, 3, 4, 5, and 6;

wherein when B is formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

The present invention is also directed to a compound of Formula I:

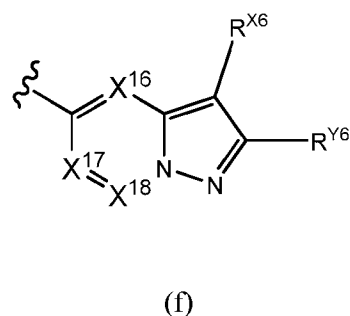
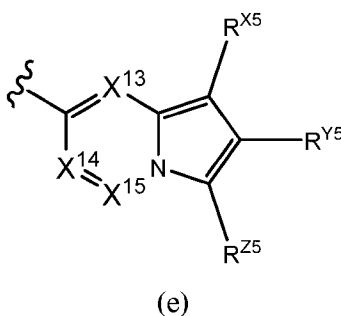
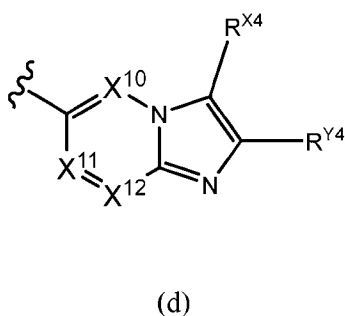
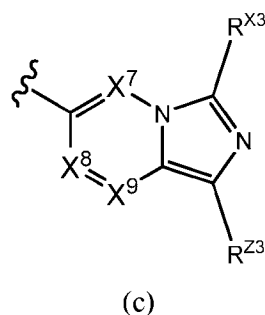
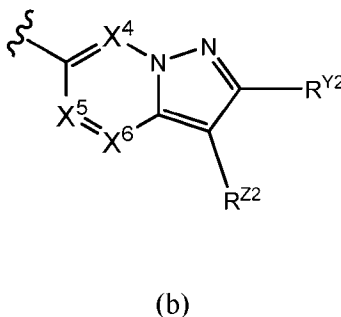
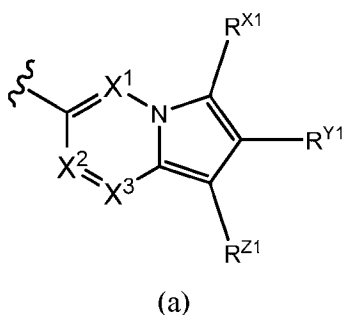


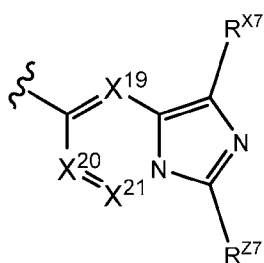
or a pharmaceutically acceptable salt thereof, wherein:

5 Q is NH or CH<sub>2</sub>;

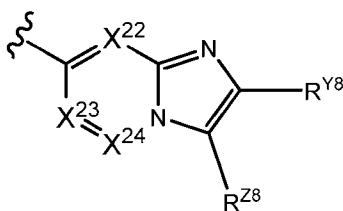
A is C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, Cy, or Cy-C<sub>1-4</sub> alkyl-, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of A are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a</sup>, SR<sup>a</sup>, C(O)R<sup>b</sup>, C(O)NR<sup>c</sup>R<sup>d</sup>, C(O)OR<sup>a</sup>, OC(O)R<sup>b</sup>, OC(O)NR<sup>c</sup>R<sup>d</sup>, C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(O)R<sup>b</sup>, NR<sup>c</sup>C(O)OR<sup>a</sup>, NR<sup>c</sup>C(O)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>S(O)R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>, S(O)R<sup>b</sup>, S(O)NR<sup>c</sup>R<sup>d</sup>, S(O)<sub>2</sub>R<sup>b</sup>, and S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>,

15 B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), formula (h), formula (i), formula (j), or formula (k):

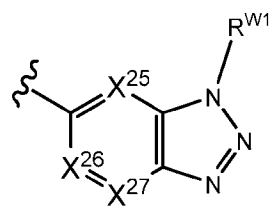




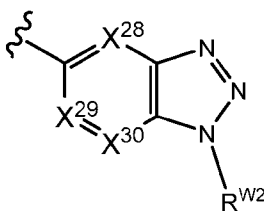
(g)



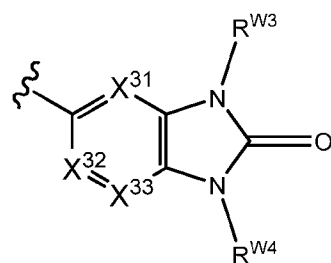
(h)



(i)



(j)



(k);

$X^1$  is N or CR<sup>1</sup>;

$X^2$  is N or CR<sup>2</sup>;

$X^3$  is N or CR<sup>3</sup>;

$X^4$  is N or CR<sup>4</sup>;

5  $X^5$  is N or CR<sup>5</sup>;

$X^6$  is N or CR<sup>6</sup>;

$X^7$  is N or CR<sup>7</sup>;

$X^8$  is N or CR<sup>8</sup>;

$X^9$  is N or CR<sup>9</sup>;

10  $X^{10}$  is N or CR<sup>10</sup>;

$X^{11}$  is N or CR<sup>11</sup>;

$X^{12}$  is N or CR<sup>12</sup>;

$X^{13}$  is N or CR<sup>13</sup>;

$X^{14}$  is N or CR<sup>14</sup>;

15  $X^{15}$  is N or CR<sup>15</sup>;

$X^{16}$  is N or CR<sup>16</sup>;

$X^{17}$  is N or CR<sup>17</sup>;

$X^{18}$  is N or CR<sup>18</sup>;

$X^{19}$  is N or CR<sup>19</sup>;



- $X^{20}$  is N or  $CR^{20}$ ;  
 $X^{21}$  is N or  $CR^{21}$ ;  
 $X^{22}$  is N or  $CR^{22}$ ;  
 $X^{23}$  is N or  $CR^{23}$ ;  
5  $X^{24}$  is N or  $CR^{24}$ ;  
 $X^{25}$  is N or  $CR^{25}$ ;  
 $X^{26}$  is N or  $CR^{26}$ ;  
 $X^{27}$  is N or  $CR^{27}$ ;  
 $X^{28}$  is N or  $CR^{28}$ ;  
10  $X^{29}$  is N or  $CR^{29}$ ;  
 $X^{30}$  is N or  $CR^{30}$ ;  
 $X^{31}$  is N or  $CR^{31}$ ;  
 $X^{32}$  is N or  $CR^{32}$ ;  
 $X^{33}$  is N or  $CR^{33}$ ;  
15 wherein no more than two of  $X^1$ ,  $X^2$ , and  $X^3$  are simultaneously N;  
wherein no more than two of  $X^4$ ,  $X^5$ , and  $X^6$  are simultaneously N;  
wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;  
wherein no more than two of  $X^{10}$ ,  $X^{11}$ , and  $X^{12}$  are simultaneously N;  
wherein no more than two of  $X^{13}$ ,  $X^{14}$ , and  $X^{15}$  are simultaneously N;  
20 wherein no more than two of  $X^{16}$ ,  $X^{17}$ , and  $X^{18}$  are simultaneously N;  
wherein no more than two of  $X^{19}$ ,  $X^{20}$ , and  $X^{21}$  are simultaneously N;  
wherein no more than two of  $X^{22}$ ,  $X^{23}$ , and  $X^{24}$  are simultaneously N;  
wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;  
wherein no more than two of  $X^{28}$ ,  $X^{29}$ , and  $X^{30}$  are simultaneously N;  
25 wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;  
each Cy is independently selected from C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from  $R^{Cy}$ ;  
each  $R^{Cy}$  is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl, C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and

- S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>Cy</sup> is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>,  
R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>13</sup>, R<sup>14</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>19</sup>, R<sup>20</sup>, R<sup>22</sup>, R<sup>23</sup>, R<sup>25</sup>, R<sup>26</sup>, R<sup>28</sup>, R<sup>29</sup>, R<sup>31</sup>, and R<sup>32</sup> are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;  
R<sup>3</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>12</sup>, R<sup>15</sup>, R<sup>18</sup>, R<sup>21</sup>, R<sup>24</sup>, R<sup>27</sup>, R<sup>30</sup>, and R<sup>33</sup> are each independently selected from H, halo, OR<sup>a2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of R<sup>3</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>12</sup>, R<sup>15</sup>, R<sup>18</sup>, R<sup>21</sup>, R<sup>24</sup>, R<sup>27</sup>, R<sup>30</sup>, and R<sup>33</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>q</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>,  
R<sup>X1</sup>, R<sup>X3</sup>, R<sup>X4</sup>, R<sup>X5</sup>, R<sup>X6</sup>, R<sup>X7</sup>, R<sup>Y1</sup>, R<sup>Y2</sup>, R<sup>Y4</sup>, R<sup>Y5</sup>, R<sup>Y6</sup>, R<sup>Y8</sup>, R<sup>Z1</sup>, R<sup>Z2</sup>, R<sup>Z3</sup>, R<sup>Z5</sup>, R<sup>Z7</sup>, and R<sup>Z8</sup> are each independently selected from H, halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl of R<sup>X1</sup>, R<sup>X3</sup>, R<sup>X4</sup>, R<sup>X5</sup>, R<sup>X6</sup>, R<sup>X7</sup>, R<sup>Y1</sup>, R<sup>Y2</sup>, R<sup>Y4</sup>, R<sup>Y5</sup>, R<sup>Y6</sup>, R<sup>Y8</sup>, R<sup>Z1</sup>, R<sup>Z2</sup>, R<sup>Z3</sup>, R<sup>Z5</sup>, R<sup>Z7</sup>, and R<sup>Z8</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

$R^{W1}$ ,  $R^{W2}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4  $R'$ ;

each  $R'$  is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of  $R'$  is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>;

each  $R^a$ ,  $R^b$ ,  $R^c$ ,  $R^d$ ,  $R^{a1}$ ,  $R^{b1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{b3}$ ,  $R^{c3}$ , and  $R^{d3}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of  $R^a$ ,  $R^b$ ,  $R^c$ ,  $R^d$ ,  $R^{a1}$ ,  $R^{b1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{b3}$ ,  $R^{c3}$ , and  $R^{d3}$  is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>;

or  $R^c$  and  $R^d$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>,

$C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  
 $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  
 $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ;

- or  $R^{c1}$  and  $R^{d1}$ , together with the N atom to which they are attached, form a 4-7  
 5 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents  
 independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  
 $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  
 $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  
 $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ,  
 10 or  $R^{c2}$  and  $R^{d2}$ , together with the N atom to which they are attached, form a 4-7  
 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents  
 independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  
 $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  
 $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  
 15  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ;

- or  $R^{c3}$  and  $R^{d3}$ , together with the N atom to which they are attached, form a 4-7  
 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents  
 independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  
 $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  
 20  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  
 $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ;

- or  $R^{c4}$  and  $R^{d4}$ , together with the N atom to which they are attached, form a 4-7  
 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents  
 independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  
 25  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  
 $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  
 $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ;

- each  $R^{a4}$ ,  $R^{b4}$ ,  $R^{c4}$ , and  $R^{d4}$  is independently selected from H,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  
 $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10  
 30 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered  
 heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, wherein said  $C_{1-6}$  alkyl,  
 $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered  
 heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl,  
 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl are

each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkyl, and C<sub>1-6</sub> haloalkoxy;

each R<sup>e</sup>, R<sup>e1</sup>, R<sup>e2</sup>, R<sup>e3</sup>, and R<sup>e4</sup> is independently selected from H, C<sub>1-4</sub> alkyl, and CN;

and

5 q is an integer selected from 1, 2, 3, 4, 5, and 6;

wherein when B is formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

The present invention is also directed to a compound of Formula I:

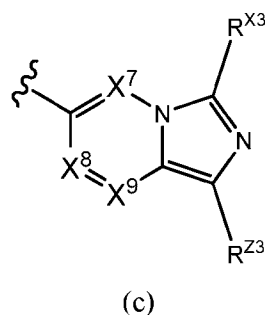
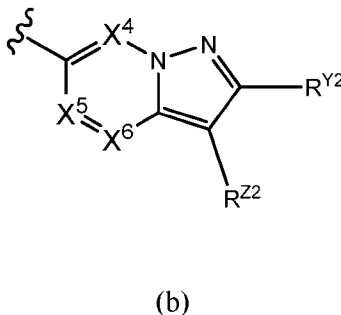
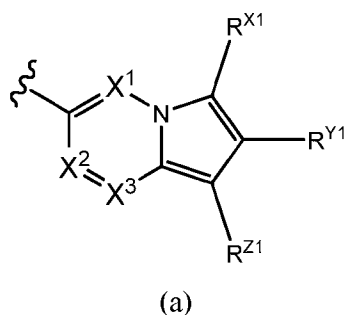


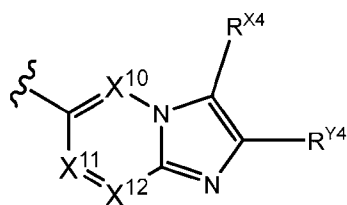
or a pharmaceutically acceptable salt thereof, wherein:

Q is NH or CH<sub>2</sub>;

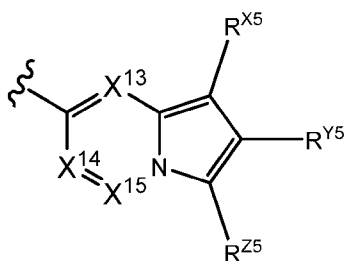
A is C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, Cy, or Cy-C<sub>1-4</sub> alkyl-, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of A are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a</sup>, SR<sup>a</sup>, C(O)R<sup>b</sup>, C(O)NR<sup>c</sup>R<sup>d</sup>, C(O)OR<sup>a</sup>, OC(O)R<sup>b</sup>, OC(O)NR<sup>c</sup>R<sup>d</sup>, C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(O)R<sup>b</sup>, NR<sup>c</sup>C(O)OR<sup>a</sup>, NR<sup>c</sup>C(O)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>S(O)R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>, S(O)R<sup>b</sup>, S(O)NR<sup>c</sup>R<sup>d</sup>, S(O)<sub>2</sub>R<sup>b</sup>, and S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>,

B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), formula (h), formula (i), formula (j), or formula (k):

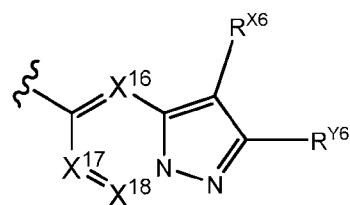




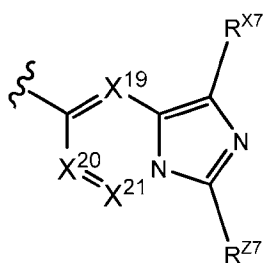
(d)



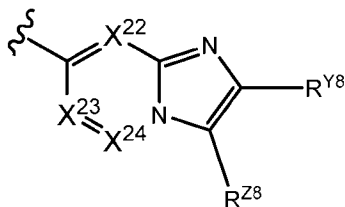
(e)



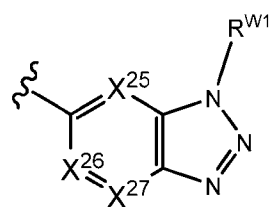
(f)



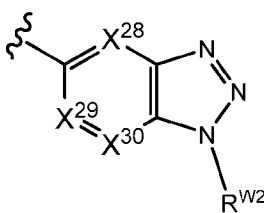
(g)



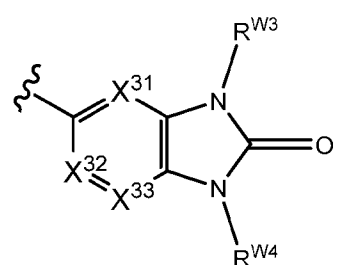
(h)



(i)



(j)



(k);

$X^1$  is N or  $CR^1$ ;

$X^2$  is N or  $CR^2$ ;

$X^3$  is N or  $CR^3$ ;

$X^4$  is N or  $CR^4$ ;

5  $X^5$  is N or  $CR^5$ ;

$X^6$  is N or  $CR^6$ ;

$X^7$  is N or  $CR^7$ ;

$X^8$  is N or  $CR^8$ ;

$X^9$  is N or  $CR^9$ ;

10  $X^{10}$  is N or  $CR^{10}$ ;

$X^{11}$  is N or  $CR^{11}$ ;

$X^{12}$  is N or  $CR^{12}$ ;

- $X^{13}$  is N or  $CR^{13}$ ;  
 $X^{14}$  is N or  $CR^{14}$ ;  
 $X^{15}$  is N or  $CR^{15}$ ;  
 $X^{16}$  is N or  $CR^{16}$ ;  
5  $X^{17}$  is N or  $CR^{17}$ ;  
 $X^{18}$  is N or  $CR^{18}$ ;  
 $X^{19}$  is N or  $CR^{19}$ ;  
 $X^{20}$  is N or  $CR^{20}$ ;  
 $X^{21}$  is N or  $CR^{21}$ ;  
10  $X^{22}$  is N or  $CR^{22}$ ;  
 $X^{23}$  is N or  $CR^{23}$ ;  
 $X^{24}$  is N or  $CR^{24}$ ;  
 $X^{25}$  is N or  $CR^{25}$ ;  
 $X^{26}$  is N or  $CR^{26}$ ;  
15  $X^{27}$  is N or  $CR^{27}$ ;  
 $X^{28}$  is N or  $CR^{28}$ ;  
 $X^{29}$  is N or  $CR^{29}$ ;  
 $X^{30}$  is N or  $CR^{30}$ ;  
 $X^{31}$  is N or  $CR^{31}$ ;  
20  $X^{32}$  is N or  $CR^{32}$ ;  
 $X^{33}$  is N or  $CR^{33}$ ;  
wherein no more than two of  $X^1$ ,  $X^2$ , and  $X^3$  are simultaneously N;  
wherein no more than two of  $X^4$ ,  $X^5$ , and  $X^6$  are simultaneously N;  
wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;  
25 wherein no more than two of  $X^{10}$ ,  $X^{11}$ , and  $X^{12}$  are simultaneously N;  
wherein no more than two of  $X^{13}$ ,  $X^{14}$ , and  $X^{15}$  are simultaneously N;  
wherein no more than two of  $X^{16}$ ,  $X^{17}$ , and  $X^{18}$  are simultaneously N;  
wherein no more than two of  $X^{19}$ ,  $X^{20}$ , and  $X^{21}$  are simultaneously N;  
wherein no more than two of  $X^{22}$ ,  $X^{23}$ , and  $X^{24}$  are simultaneously N;  
30 wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;  
wherein no more than two of  $X^{28}$ ,  $X^{29}$ , and  $X^{30}$  are simultaneously N;  
wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each Cy is independently selected from C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>;

each R<sup>Cy</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>Cy</sup> is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>;

R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>13</sup>, R<sup>14</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>19</sup>, R<sup>20</sup>, R<sup>22</sup>, R<sup>23</sup>, R<sup>25</sup>, R<sup>26</sup>, R<sup>28</sup>, R<sup>29</sup>, R<sup>31</sup>, and R<sup>32</sup> are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;

R<sup>3</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>12</sup>, R<sup>15</sup>, R<sup>18</sup>, R<sup>21</sup>, R<sup>24</sup>, R<sup>27</sup>, R<sup>30</sup>, and R<sup>33</sup> are each independently selected from H, halo, OR<sup>a2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of R<sup>3</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>12</sup>, R<sup>15</sup>, R<sup>18</sup>, R<sup>21</sup>, R<sup>24</sup>, R<sup>27</sup>, R<sup>30</sup>, and R<sup>33</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>;

R<sup>X1</sup>, R<sup>X3</sup>, R<sup>X4</sup>, R<sup>X5</sup>, R<sup>X6</sup>, R<sup>X7</sup>, R<sup>Y1</sup>, R<sup>Y2</sup>, R<sup>Y4</sup>, R<sup>Y5</sup>, R<sup>Y6</sup>, R<sup>Y8</sup>, R<sup>Z1</sup>, R<sup>Z2</sup>, R<sup>Z3</sup>, R<sup>Z5</sup>, R<sup>Z7</sup>, and R<sup>Z8</sup> are each independently selected from H, halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl of R<sup>X1</sup>, R<sup>X3</sup>, R<sup>X4</sup>, R<sup>X5</sup>, R<sup>X6</sup>, R<sup>X7</sup>, R<sup>Y1</sup>, R<sup>Y2</sup>, R<sup>Y4</sup>, R<sup>Y5</sup>, R<sup>Y6</sup>, R<sup>Y8</sup>, R<sup>Z1</sup>, R<sup>Z2</sup>, R<sup>Z3</sup>, R<sup>Z5</sup>, R<sup>Z7</sup>, and R<sup>Z8</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from



- halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>,  
5 C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>,  
R<sup>W1</sup>, R<sup>W2</sup>, R<sup>W3</sup>, and R<sup>W4</sup> are each independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4 R<sup>ˆ</sup>;  
10 each R<sup>ˆ</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>,  
15 NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>ˆ</sup> is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>,  
20 each R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>a1</sup>, R<sup>b1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>b3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>a1</sup>, R<sup>b1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>b3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, CN, OR<sup>a4</sup>,  
25

$SR^{a4}$ ,  $C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ .

or  $R^c$  and  $R^d$ , together with the N atom to which they are attached, form a 4-7

5 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ,

10 or  $R^{c1}$  and  $R^{d1}$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,   
15  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ,

or  $R^{c2}$  and  $R^{d2}$ , together with the N atom to which they are attached, form a 4-7

membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,   
20  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ,

or  $R^{c3}$  and  $R^{d3}$ , together with the N atom to which they are attached, form a 4-7

membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,   
25  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ,

or  $R^{c4}$  and  $R^{d4}$ , together with the N atom to which they are attached, form a 4-7

membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,   
30  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ,

each  $R^{a4}$ ,  $R^{b4}$ ,  $R^{c4}$ , and  $R^{d4}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl are each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkyl, and C<sub>1-6</sub> haloalkoxy; and

each  $R^e$ ,  $R^{e1}$ ,  $R^{e2}$ ,  $R^{e3}$ , and  $R^{e4}$  is independently selected from H, C<sub>1-4</sub> alkyl, and CN; wherein when B is formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

In some embodiments, Q is NH. In some embodiments, Q is CH<sub>2</sub>.

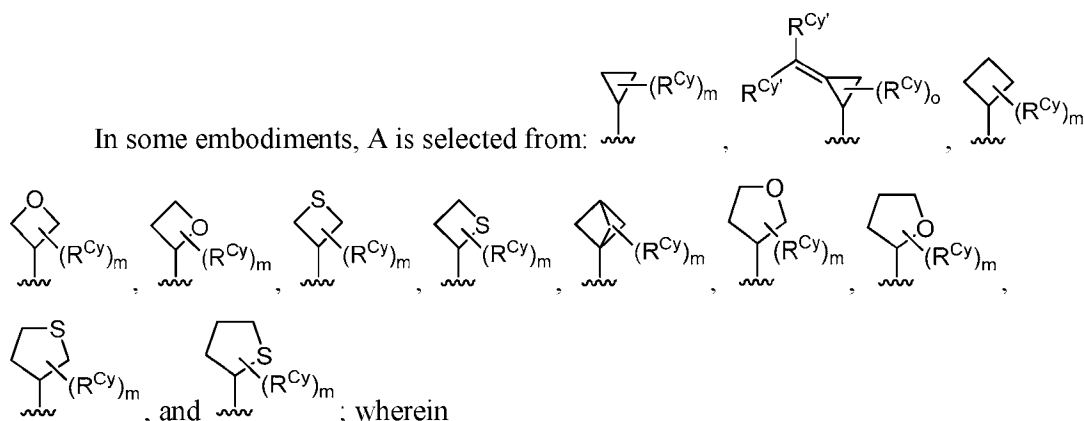
In some embodiments, A is C<sub>1-6</sub> alkyl. In some embodiments, A is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a</sup>, SR<sup>a</sup>, C(O)R<sup>b</sup>, C(O)NR<sup>c</sup>R<sup>d</sup>, C(O)OR<sup>a</sup>, OC(O)R<sup>b</sup>, OC(O)NR<sup>c</sup>R<sup>d</sup>, C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(O)R<sup>b</sup>, NR<sup>c</sup>C(O)OR<sup>a</sup>, NR<sup>c</sup>C(O)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>S(O)R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>, S(O)R<sup>b</sup>, S(O)NR<sup>c</sup>R<sup>d</sup>, S(O)<sub>2</sub>R<sup>b</sup>, and S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>. In some embodiments, A is C<sub>2-6</sub> alkenyl. In some embodiments, A is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a</sup>, SR<sup>a</sup>, C(O)R<sup>b</sup>, C(O)NR<sup>c</sup>R<sup>d</sup>, C(O)OR<sup>a</sup>, OC(O)R<sup>b</sup>, OC(O)NR<sup>c</sup>R<sup>d</sup>, C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(O)R<sup>b</sup>, NR<sup>c</sup>C(O)OR<sup>a</sup>, NR<sup>c</sup>C(O)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>S(O)R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>, S(O)R<sup>b</sup>, S(O)NR<sup>c</sup>R<sup>d</sup>, S(O)<sub>2</sub>R<sup>b</sup>, and S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>. In some embodiments, A is C<sub>2-6</sub> alkynyl. In some embodiments, A is C<sub>2-6</sub> alkynyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a</sup>, SR<sup>a</sup>, C(O)R<sup>b</sup>, C(O)NR<sup>c</sup>R<sup>d</sup>, C(O)OR<sup>a</sup>, OC(O)R<sup>b</sup>, OC(O)NR<sup>c</sup>R<sup>d</sup>, C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(O)R<sup>b</sup>, NR<sup>c</sup>C(O)OR<sup>a</sup>, NR<sup>c</sup>C(O)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>S(O)R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>, S(O)R<sup>b</sup>, S(O)NR<sup>c</sup>R<sup>d</sup>, S(O)<sub>2</sub>R<sup>b</sup>, and S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>.

membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a</sup>, SR<sup>a</sup>, C(O)R<sup>b</sup>, C(O)NR<sup>c</sup>R<sup>d</sup>, C(O)OR<sup>a</sup>, OC(O)R<sup>b</sup>, OC(O)NR<sup>c</sup>R<sup>d</sup>, C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(O)R<sup>b</sup>, NR<sup>c</sup>C(O)OR<sup>a</sup>, NR<sup>c</sup>C(O)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>S(O)R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>, S(O)R<sup>b</sup>, S(O)NR<sup>c</sup>R<sup>d</sup>, S(O)<sub>2</sub>R<sup>b</sup>, and S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>. In some  
 5 embodiments, A is Cy. In some embodiments, A is Cy-C<sub>1-4</sub> alkyl.

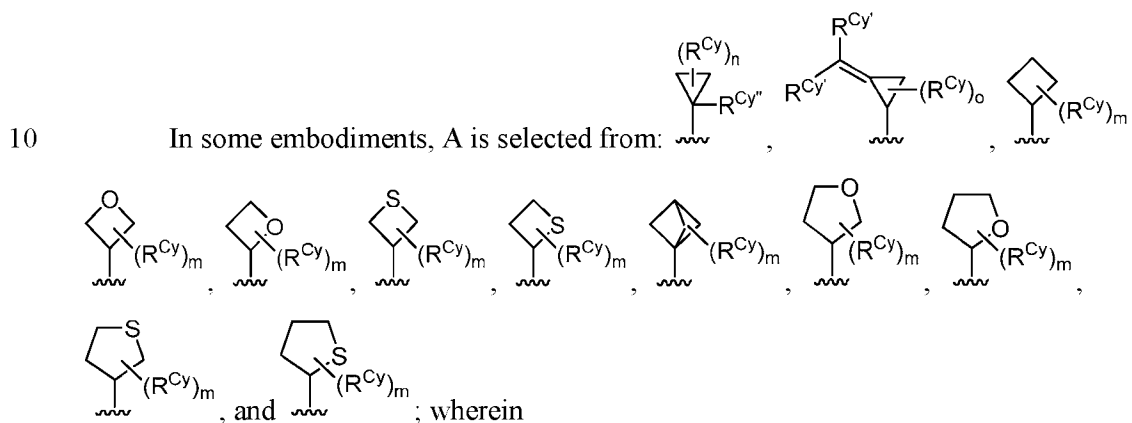
In some embodiments, A is selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>. In some embodiments, A is C<sub>3-7</sub> cycloalkyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>. In some embodiments, A is  
 10 cyclopropyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>, wherein at least one R<sup>Cy</sup> is C<sub>1-6</sub> alkyl. In some embodiments, A is cyclopropyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>, wherein at least one R<sup>Cy</sup> is methyl. In some embodiments, A is cyclopropyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>, wherein at least  
 15 one R<sup>Cy</sup> is CN. In some embodiments, A is cyclopropyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>, wherein the cyclopropyl is substituted with methyl and CN.

In some embodiments, A is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>. In some embodiments, A is  
 20 oxetanyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>. In some embodiments, A is oxetanyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>,

In some embodiments, A is oxetanyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>, wherein at least one R<sup>Cy</sup> is C<sub>1-6</sub> alkyl, C<sub>1-6</sub>  
 25 haloalkyl, or CN. In some embodiments, A is oxetanyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>, wherein at least one R<sup>Cy</sup> is methyl, fluoromethyl, or CN.



- each  $R^{Cy'}$  is selected from from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>,  
 5 C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>,  
 NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>,  
 NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>;  
 m is an integer selected from 0, 1, 2, 3, 4, and 5; and  
 o is an integer selected from 0, 1, 2, and 3.



- each  $R^{Cy'}$  is selected from from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>,  
 C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>,  
 15 NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>,  
 NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>;

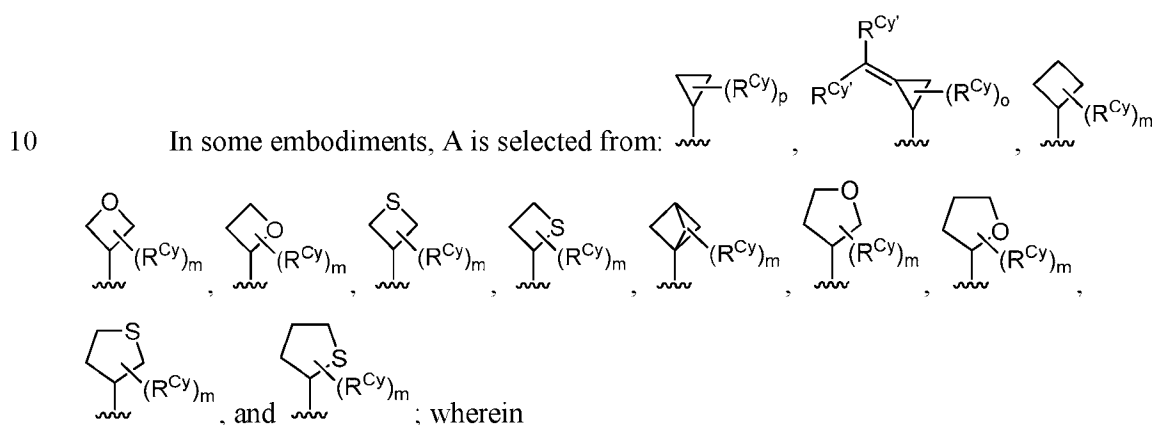
- $R^{Cy''}$  is selected from halo, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub>  
 cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-  
 C<sub>1-4</sub> alkyl, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>,  
 20 C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>,  
 NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>,  
 S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub>

alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>Cy</sup> is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>,  
 5 NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>;

m is an integer selected from 0, 1, 2, 3, 4, and 5;

n is an integer selected from 0, 1, 2, 3, and 4; and

o is an integer selected from 0, 1, 2, and 3.

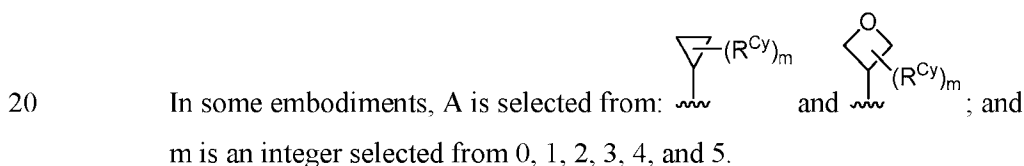


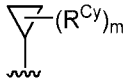
each R<sup>Cy'</sup> is selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>,  
 15 NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>;

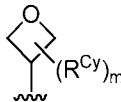
m is an integer selected from 0, 1, 2, 3, 4, and 5;

o is an integer selected from 0, 1, 2, and 3; and

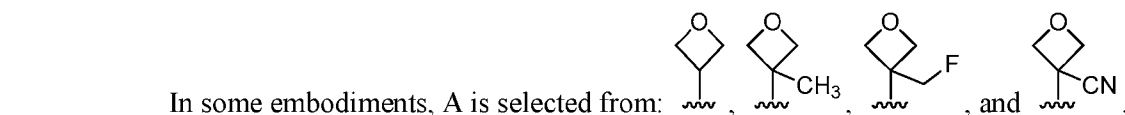
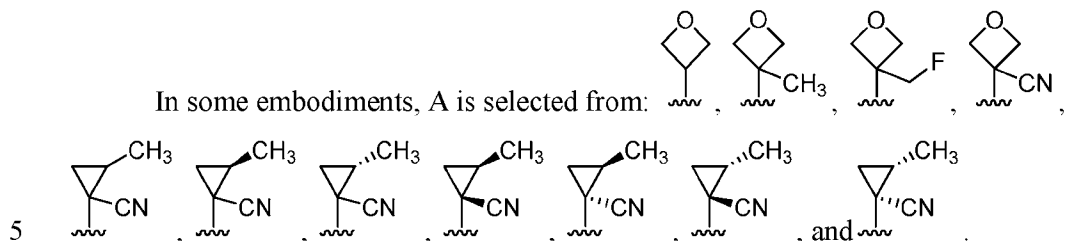
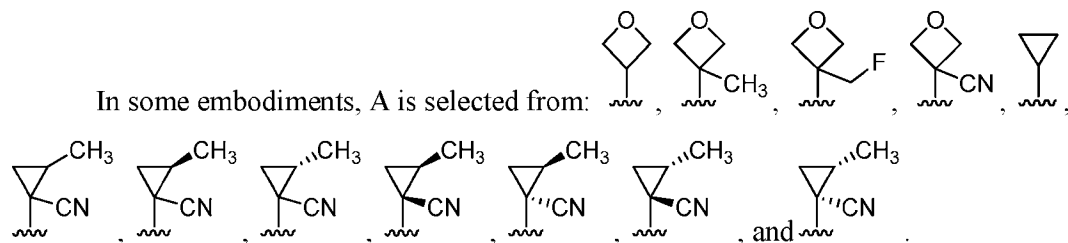
p is an integer selected from 0, 2, 3, 4, and 5.



In some embodiments, A is: ; and m is an integer selected from 0, 1, 2, 3, 4, and 5.

In some embodiments, A is selected from: ; and

m is an integer selected from 0, 1, 2, 3, 4, and 5.

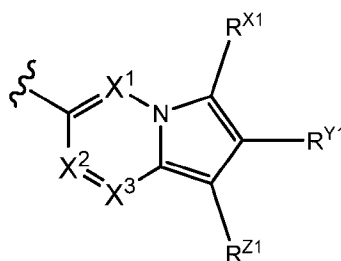


In some embodiments, each  $R^{Cy}$  is independently selected from halo, C<sub>2-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>2-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of  $R^{Cy}$  is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>.

In some embodiments, each  $R^{Cy}$  is independently selected from halo, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered

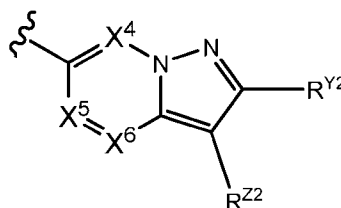
heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>Cy</sup> is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>.

In some embodiments, B is of formula (a):



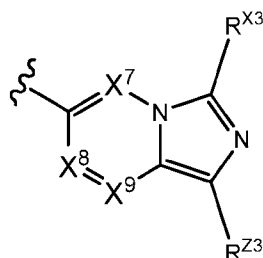
(a).

In some embodiments, B is of formula (b):



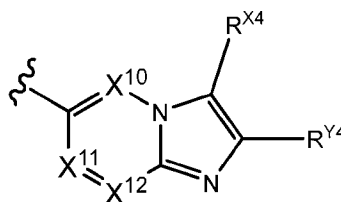
(b).

In some embodiments, B is of formula (c):



(c).

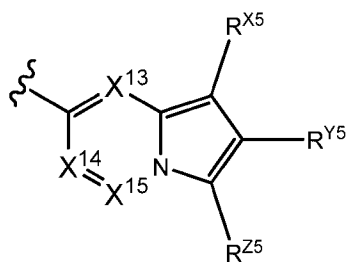
In some embodiments, B is of formula (d):





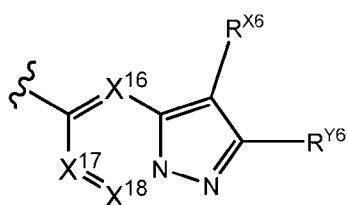
(d).

In some embodiments, B is of formula (e):



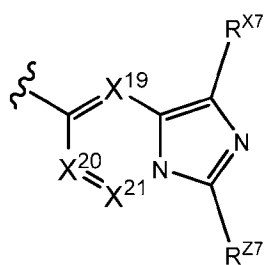
(e).

In some embodiments, B is of formula (f):



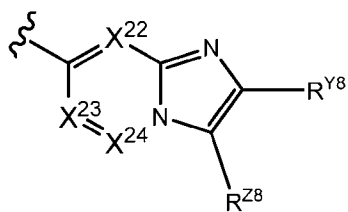
(f).

In some embodiments, B is of formula (g):



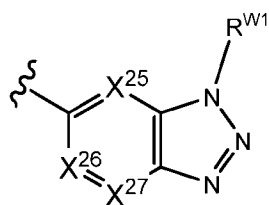
(g).

In some embodiments, B is of formula (h):



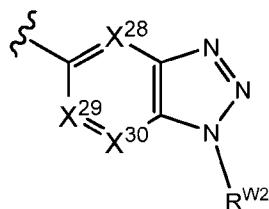
(h).

5 In some embodiments, B is of formula (i):



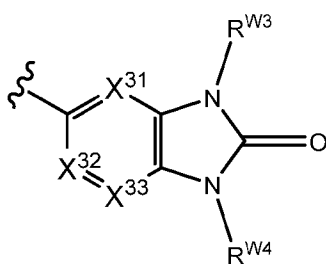
(i).

In some embodiments, B is of formula (j):



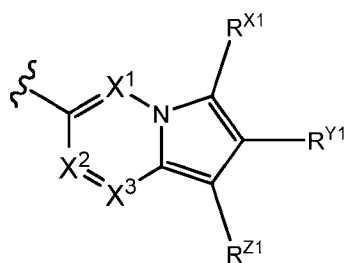
(j).

In some embodiments, B is of formula (k):

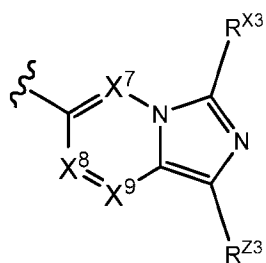


(k).

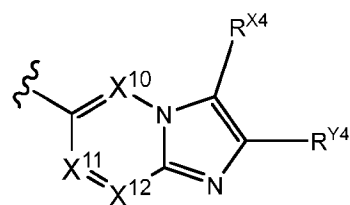
In some embodiments, B is of formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), formula (i), or formula (k):



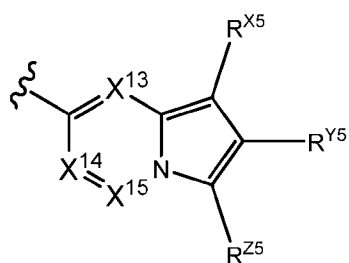
(a)



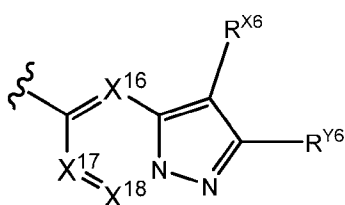
(c)



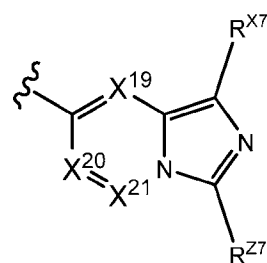
(d)



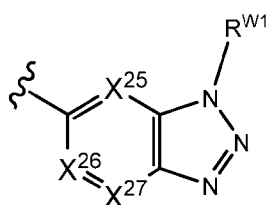
(e)



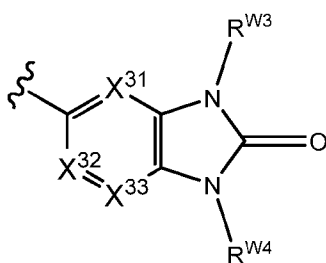
(f)



(g)

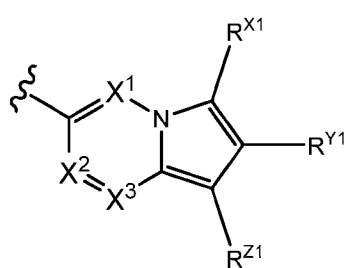


(i)

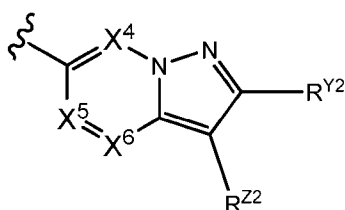


(k)

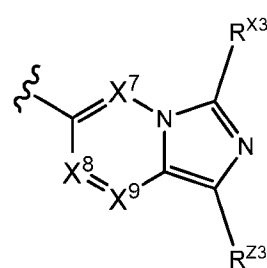
In some embodiments, B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (h):



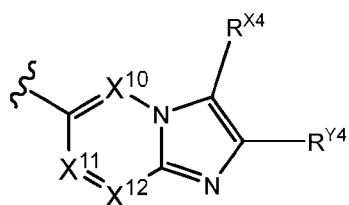
(a)



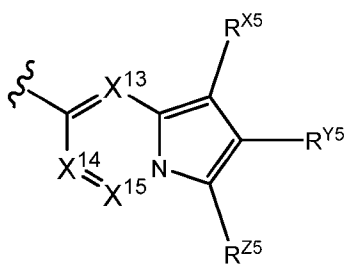
(b)



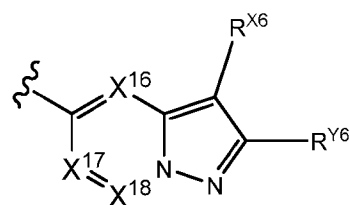
(c)



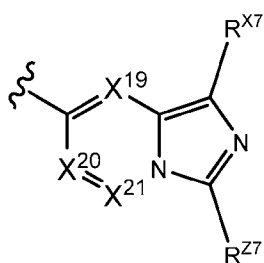
(d)



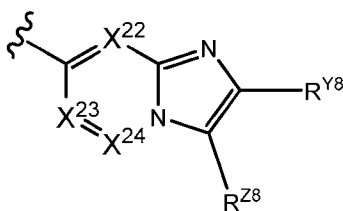
(e)



(f)

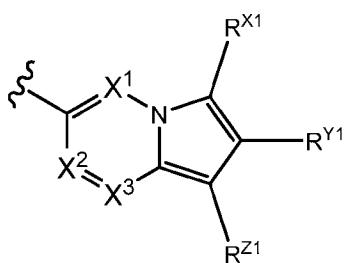


(g)

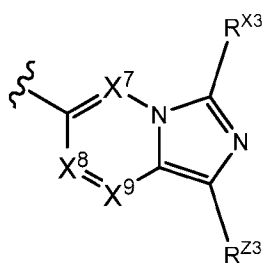


(h).

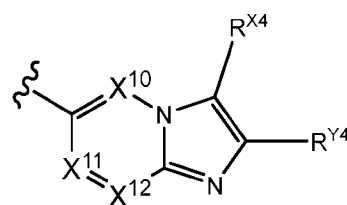
In some embodiments, B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (h):



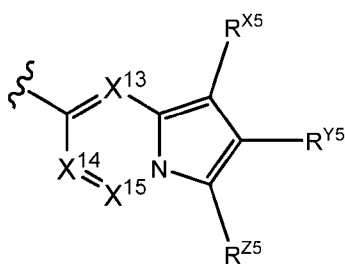
(a)



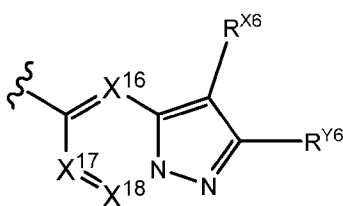
(c)



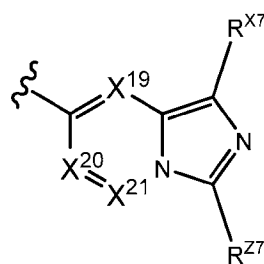
(d)



(e)

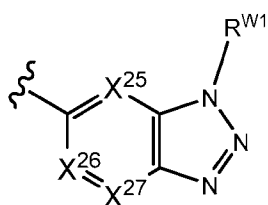


(f)

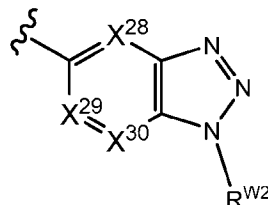


(g).

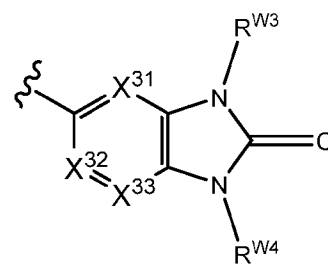
In some embodiments, B is of formula (i), formula (j), or formula (k):



(i)

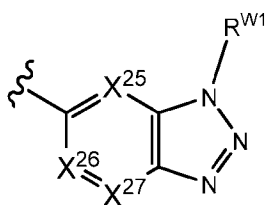


(j)

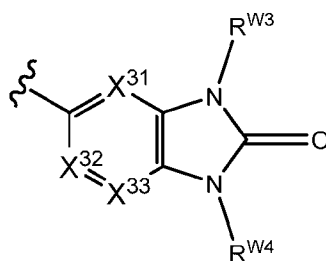


(k).

In some embodiments, B is of formula (i) or formula (k):

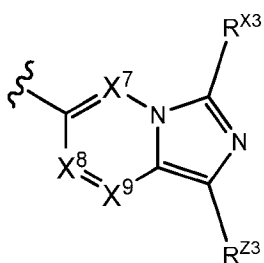


(i)

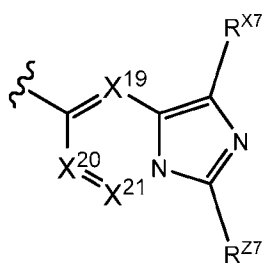


(k).

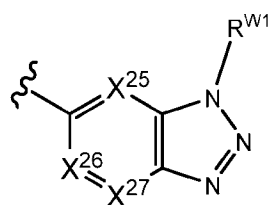
In some embodiments, B is of formula (c), formula (g), formula (i), formula (j), or formula (k):



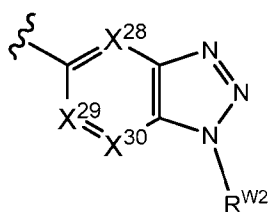
(c)



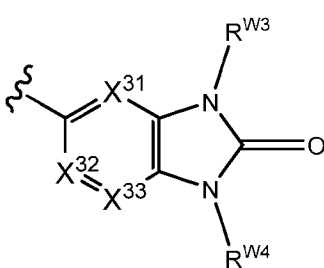
(g)



(i)

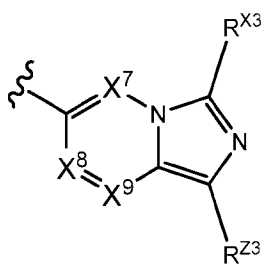


(j)

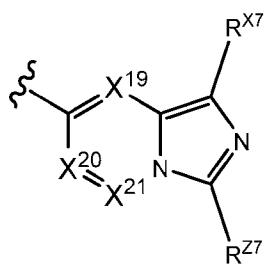


(k).

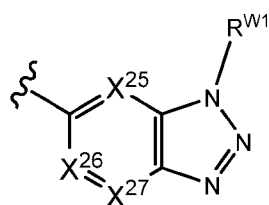
In some embodiments, B is of formula (c), formula (g), formula (i), or formula (k):



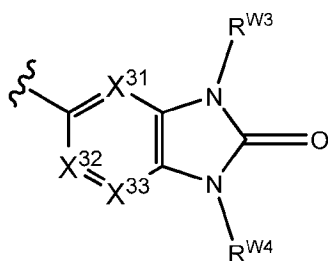
(c)



(g)

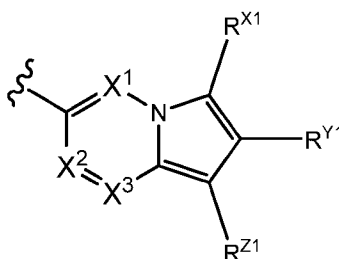


(i)



(k).

In some embodiments, B is of formula (a):



(a).

In some embodiments,  $X^1$  is N. In some embodiments,  $X^1$  is  $CR^1$ .

In some embodiments,  $X^2$  is N. In some embodiments,  $X^2$  is  $CR^2$ .

In some embodiments,  $X^3$  is N. In some embodiments,  $X^3$  is  $CR^3$ .

5 In some embodiments,  $X^1$  is  $CR^1$ ;  $X^2$  is  $CR^2$ ; and  $X^3$  is  $CR^3$ .

In some embodiments,  $R^1$  is H. In some embodiments,  $R^1$  is halo. In some embodiments,  $R^1$  is  $C_{1-4}$  alkyl.

In some embodiments,  $R^2$  is H. In some embodiments,  $R^2$  is halo. In some embodiments,  $R^2$  is  $C_{1-4}$  alkyl.

10 In some embodiments,  $R^3$  is H. In some embodiments,  $R^3$  is halo. In some embodiments,  $R^3$  is  $OR^{a2}$ . In some embodiments,  $R^3$  is  $NR^{c2}R^{d2}$ . In some embodiments,  $R^3$  is  $C_{6-10}$  aryl. In some embodiments,  $R^3$  is  $C_{6-10}$  aryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ ,  $NR^cS(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^3$  is  $C_{3-7}$  cycloalkyl. In some embodiments,  $R^3$  is  $C_{3-7}$  cycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from

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halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>3</sup> is 5-10 membered heteroaryl. In some embodiments, R<sup>3</sup> is 5-10 membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>3</sup> is 4-10 membered heterocycloalkyl. In some embodiments, R<sup>3</sup> is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments, R<sup>X1</sup> is H. In some embodiments, R<sup>X1</sup> is halo. In some embodiments, R<sup>X1</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>X1</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>X1</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>X1</sup> is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10

membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>X1</sup> is 5-membered heteroaryl. In some embodiments, R<sup>X1</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments, R<sup>Y1</sup> is H. In some embodiments, R<sup>Y1</sup> is halo. In some embodiments, R<sup>Y1</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>Y1</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>Y1</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>Y1</sup> is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>Y1</sup> is 5-membered heteroaryl. In some embodiments, R<sup>Y1</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4

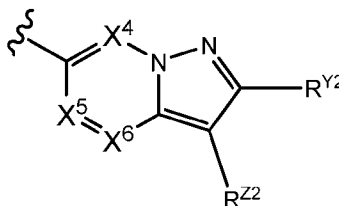


substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>,  
 5 C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments, R<sup>Z1</sup> is H. In some embodiments, R<sup>Z1</sup> is halo. In some  
 10 embodiments, R<sup>Z1</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>Z1</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>,  
 15 C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>Z1</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>Z1</sup> is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  
 20 C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>,  
 25 NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>Z1</sup> is 5-membered heteroaryl. In some embodiments, R<sup>Z1</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>,  
 30 C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

$\text{NR}^{\text{c}2}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ .

In some embodiments, B is of formula (b):



(b).

In some embodiments,  $\text{X}^4$  is N. In some embodiments,  $\text{X}^4$  is  $\text{CR}^4$ .

5 In some embodiments,  $\text{X}^5$  is N. In some embodiments,  $\text{X}^5$  is  $\text{CR}^5$ .

In some embodiments,  $\text{X}^6$  is N. In some embodiments,  $\text{X}^6$  is  $\text{CR}^6$ .

In some embodiments,  $\text{X}^4$  is  $\text{CR}^4$ ,  $\text{X}^5$  is  $\text{CR}^5$ , and  $\text{X}^6$  is  $\text{CR}^6$ .

In some embodiments,  $\text{R}^4$  is H. In some embodiments,  $\text{R}^4$  is halo. In some embodiments,  $\text{R}^4$  is  $\text{C}_{1-4}$  alkyl.

10 In some embodiments,  $\text{R}^5$  is H. In some embodiments,  $\text{R}^5$  is halo. In some embodiments,  $\text{R}^5$  is  $\text{C}_{1-4}$  alkyl.

In some embodiments,  $\text{R}^6$  is H. In some embodiments,  $\text{R}^6$  is halo. In some embodiments,  $\text{R}^6$  is  $\text{OR}^{\text{a}2}$ . In some embodiments,  $\text{R}^6$  is  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ . In some embodiments,  $\text{R}^6$  is  $\text{C}_{6-10}$  aryl. In some embodiments,  $\text{R}^6$  is  $\text{C}_{6-10}$  aryl optionally substituted with 1, 2, 3, or 4

15 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$  haloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{\text{a}2}$ ,  $\text{SR}^{\text{a}2}$ ,  $\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(=\text{NR}^{\text{e}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,

$\text{NR}^{\text{c}2}\text{C}(=\text{NR}^{\text{e}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,

20  $\text{NR}^{\text{c}2}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ . In some embodiments,  $\text{R}^6$  is  $\text{C}_{3-7}$  cycloalkyl. In some embodiments,  $\text{R}^6$  is  $\text{C}_{3-7}$  cycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$  haloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl,

25 CN,  $\text{NO}_2$ ,  $\text{OR}^{\text{a}2}$ ,  $\text{SR}^{\text{a}2}$ ,  $\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(=\text{NR}^{\text{e}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(=\text{NR}^{\text{e}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ . In some embodiments,  $\text{R}^6$  is 5-10 membered heteroaryl. In

some embodiments,  $R^6$  is 5-10 membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ ,  $NR^cS(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^6$  is 4-10 membered heterocycloalkyl. In some

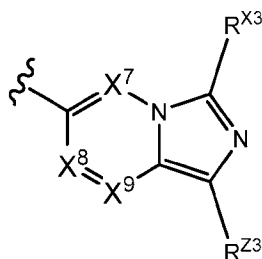
embodiments,  $R^6$  is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ ,  $NR^cS(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ .

In some embodiments,  $R^{X2}$  is H. In some embodiments,  $R^{X2}$  is halo. In some embodiments,  $R^{X2}$  is  $C_{1-6}$  alkyl. In some embodiments,  $R^{X2}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{X2}$  is  $C_{2-6}$  alkenyl. In some embodiments,  $R^{X1}$  is  $C_{2-6}$  alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{X2}$  is 5-membered heteroaryl. In some

- embodiments,  $R^{X2}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ .
- 10 In some embodiments,  $R^{Y2}$  is H. In some embodiments,  $R^{Y2}$  is halo. In some embodiments,  $R^{Y2}$  is  $C_{1-6}$  alkyl. In some embodiments,  $R^{Y2}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{Y2}$  is  $C_{2-6}$  alkenyl. In some embodiments,  $R^{Y2}$  is  $C_{2-6}$  alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{Y2}$  is 5-membered heteroaryl. In some embodiments,  $R^{Y2}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ .

$\text{NR}^{\text{c}2}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ .

In some embodiments, B is of formula (c):



(c).

In some embodiments,  $\text{X}^7$  is N. In some embodiments,  $\text{X}^7$  is  $\text{CR}^7$ .

5 In some embodiments,  $\text{X}^8$  is N. In some embodiments,  $\text{X}^8$  is  $\text{CR}^8$ .

In some embodiments,  $\text{X}^9$  is N. In some embodiments,  $\text{X}^9$  is  $\text{CR}^9$ .

In some embodiments,  $\text{X}^7$  is  $\text{CR}^7$ ;  $\text{X}^8$  is  $\text{CR}^8$ ; and  $\text{X}^9$  is  $\text{CR}^9$ .

In some embodiments,  $\text{R}^7$  is H. In some embodiments,  $\text{R}^7$  is halo. In some embodiments,  $\text{R}^7$  is  $\text{C}_{1-4}$  alkyl.

10 In some embodiments,  $\text{R}^8$  is H. In some embodiments,  $\text{R}^8$  is halo. In some embodiments,  $\text{R}^8$  is  $\text{C}_{1-4}$  alkyl. In some embodiments,  $\text{R}^8$  is selected from H, fluoro, and bromo.

In some embodiments,  $\text{R}^9$  is H. In some embodiments,  $\text{R}^9$  is halo. In some embodiments,  $\text{R}^9$  is  $\text{OR}^{\text{a}2}$ . In some embodiments,  $\text{R}^9$  is  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ . In some embodiments,  $\text{R}^9$  is

15  $\text{C}_{6-10}$  aryl. In some embodiments,  $\text{R}^9$  is  $\text{C}_{6-10}$  aryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$  haloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{\text{a}2}$ ,  $\text{SR}^{\text{a}2}$ ,  $\text{C}(\text{O})\text{R}^{\text{b}2}$ ,

$\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(=\text{NR}^{\text{c}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,

20  $\text{NR}^{\text{c}2}\text{C}(=\text{NR}^{\text{c}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,

$\text{NR}^{\text{c}2}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and

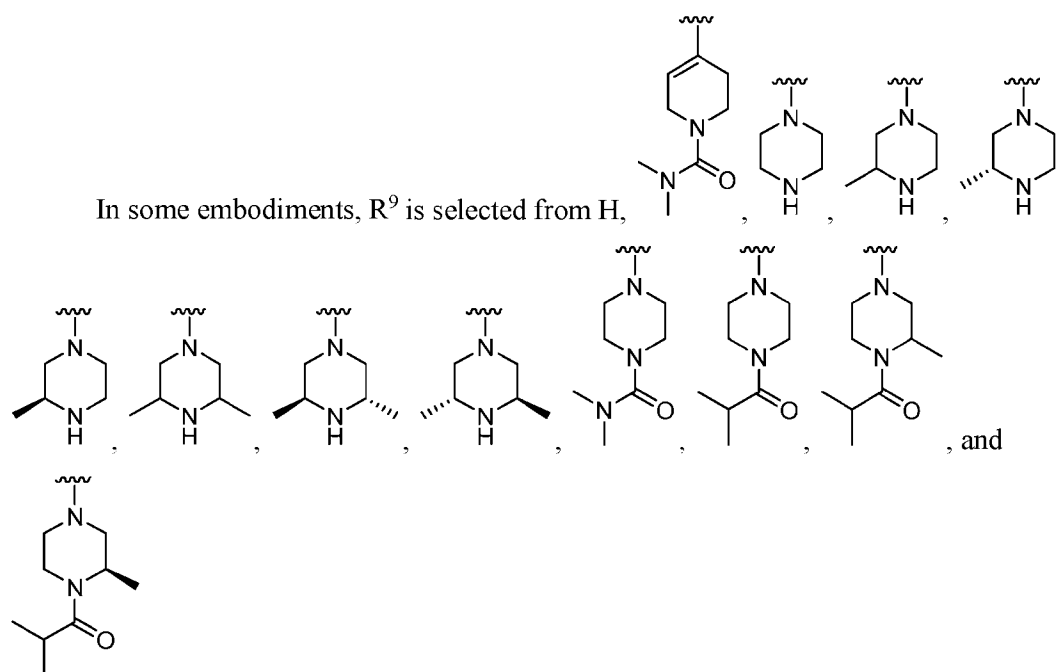
$\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ . In some embodiments,  $\text{R}^9$  is  $\text{C}_{3-7}$  cycloalkyl. In some embodiments,  $\text{R}^9$  is  $\text{C}_{3-7}$  cycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from

25  $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{\text{a}2}$ ,  $\text{SR}^{\text{a}2}$ ,  $\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,

$\text{C}(=\text{NR}^{\text{c}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(=\text{NR}^{\text{c}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,

$\text{NR}^c\text{C}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{NR}^c\text{S}(\text{O})\text{R}^{b2}$ ,  $\text{NR}^{c2}\text{S}(\text{O})_2\text{R}^{b2}$ ,  $\text{NR}^{c2}\text{S}(\text{O})_2\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{S}(\text{O})\text{R}^{b2}$ ,  $\text{S}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  
 $\text{S}(\text{O})_2\text{R}^{b2}$ , and  $\text{S}(\text{O})_2\text{NR}^{c2}\text{R}^{d2}$ . In some embodiments,  $\text{R}^9$  is 5-10 membered heteroaryl. In  
 some embodiments,  $\text{R}^9$  is 5-10 membered heteroaryl optionally substituted with 1, 2, 3, or 4  
 5 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$   
 haloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$   
 alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{a2}$ ,  $\text{SR}^{a2}$ ,  $\text{C}(\text{O})\text{R}^{b2}$ ,  
 $\text{C}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{C}(\text{O})\text{OR}^{a2}$ ,  $\text{OC}(\text{O})\text{R}^{b2}$ ,  $\text{OC}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{C}(=\text{NR}^{e2})\text{NR}^{c2}\text{R}^{d2}$ ,  
 $\text{NR}^{c2}\text{C}(=\text{NR}^{e2})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{NR}^{c2}\text{C}(\text{O})\text{R}^{b2}$ ,  $\text{NR}^c\text{C}(\text{O})\text{OR}^{a2}$ ,  $\text{NR}^c\text{C}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  
 $\text{NR}^c\text{S}(\text{O})\text{R}^{b2}$ ,  $\text{NR}^{c2}\text{S}(\text{O})_2\text{R}^{b2}$ ,  $\text{NR}^{c2}\text{S}(\text{O})_2\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{S}(\text{O})\text{R}^{b2}$ ,  $\text{S}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{S}(\text{O})_2\text{R}^{b2}$ , and  
 10  $\text{S}(\text{O})_2\text{NR}^{c2}\text{R}^{d2}$ . In some embodiments,  $\text{R}^9$  is 4-10 membered heterocycloalkyl. In some  
 embodiments,  $\text{R}^9$  is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4  
 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$   
 haloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$   
 alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{a2}$ ,  $\text{SR}^{a2}$ ,  $\text{C}(\text{O})\text{R}^{b2}$ ,  
 15  $\text{C}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{C}(\text{O})\text{OR}^{a2}$ ,  $\text{OC}(\text{O})\text{R}^{b2}$ ,  $\text{OC}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{C}(=\text{NR}^{e2})\text{NR}^{c2}\text{R}^{d2}$ ,  
 $\text{NR}^{c2}\text{C}(=\text{NR}^{e2})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{NR}^{c2}\text{C}(\text{O})\text{R}^{b2}$ ,  $\text{NR}^c\text{C}(\text{O})\text{OR}^{a2}$ ,  $\text{NR}^c\text{C}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  
 $\text{NR}^c\text{S}(\text{O})\text{R}^{b2}$ ,  $\text{NR}^{c2}\text{S}(\text{O})_2\text{R}^{b2}$ ,  $\text{NR}^{c2}\text{S}(\text{O})_2\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{S}(\text{O})\text{R}^{b2}$ ,  $\text{S}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{S}(\text{O})_2\text{R}^{b2}$ , and  
 $\text{S}(\text{O})_2\text{NR}^{c2}\text{R}^{d2}$ .

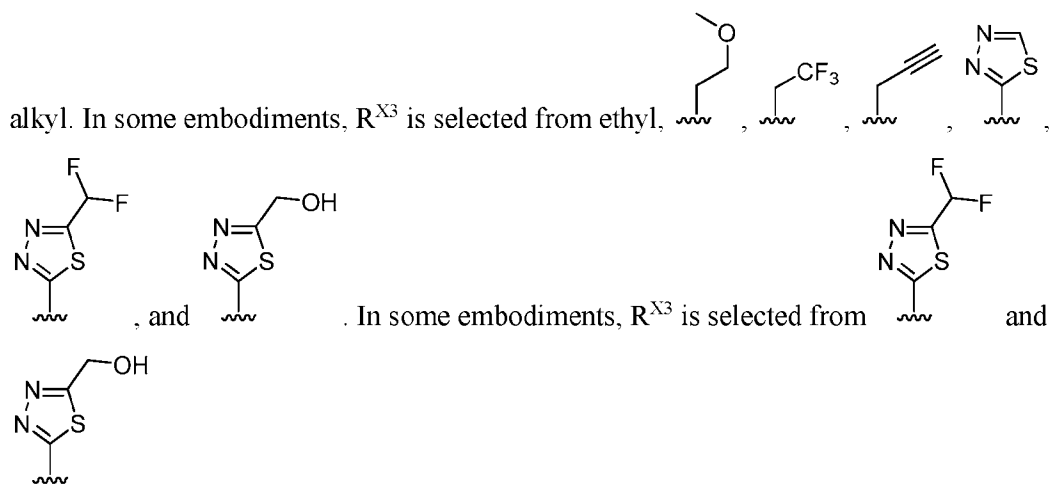
In some embodiments,  $\text{R}^9$  is selected from H and 4-10 membered heterocycloalkyl,  
 20 wherein said 4-10 membered heterocycloalkyl is optionally substituted with 1, 2, 3, or 4  
 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$   
 haloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$   
 alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{a2}$ ,  $\text{SR}^{a2}$ ,  $\text{C}(\text{O})\text{R}^{b2}$ ,  
 $\text{C}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{C}(\text{O})\text{OR}^{a2}$ ,  $\text{OC}(\text{O})\text{R}^{b2}$ ,  $\text{OC}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{C}(=\text{NR}^{e2})\text{NR}^{c2}\text{R}^{d2}$ ,  
 25  $\text{NR}^{c2}\text{C}(=\text{NR}^{e2})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{NR}^{c2}\text{C}(\text{O})\text{R}^{b2}$ ,  $\text{NR}^c\text{C}(\text{O})\text{OR}^{a2}$ ,  $\text{NR}^c\text{C}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  
 $\text{NR}^c\text{S}(\text{O})\text{R}^{b2}$ ,  $\text{NR}^{c2}\text{S}(\text{O})_2\text{R}^{b2}$ ,  $\text{NR}^{c2}\text{S}(\text{O})_2\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{S}(\text{O})\text{R}^{b2}$ ,  $\text{S}(\text{O})\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{S}(\text{O})_2\text{R}^{b2}$ , and  
 $\text{S}(\text{O})_2\text{NR}^{c2}\text{R}^{d2}$ .



- In some embodiments,  $R^{X3}$  is H. In some embodiments,  $R^{X3}$  is halo. In some
- 5 embodiments,  $R^{X3}$  is  $C_{1-6}$  alkyl. In some embodiments,  $R^{X3}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,
- 10  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{X3}$  is  $C_{2-6}$  alkenyl. In some embodiments,  $R^{X3}$  is  $C_{2-6}$  alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,
- 15  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,
- 20  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{X3}$  is 5-membered heteroaryl. In some embodiments,  $R^{X3}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$

haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>,  
 5 NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments, R<sup>X3</sup> is selected from C<sub>1-6</sub> alkyl and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4 R<sup>7</sup>. In some embodiments, R<sup>X3</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 R<sup>7</sup>, selected from halo, OR<sup>a3</sup>, and CN. In some  
 10 embodiments, R<sup>X3</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 C<sub>1-6</sub>

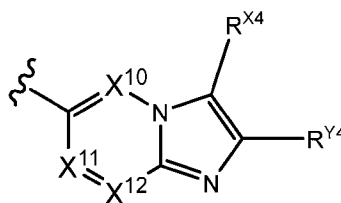


15 In some embodiments, R<sup>Z3</sup> is H. In some embodiments, R<sup>Z3</sup> is halo. In some embodiments, R<sup>Z3</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>Z3</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>Z3</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>Z3</sup> is C<sub>2-6</sub>  
 20 alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-



- C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>Z3</sup> is 5-membered heteroaryl. In some embodiments, R<sup>Z3</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.
- In some embodiments, R<sup>Z3</sup> is selected from H and halo. In some embodiments, R<sup>Z3</sup> is selected from H and chloro.

In some embodiments, B is of formula (d):



(d).

- In some embodiments, X<sup>10</sup> is N. In some embodiments, X<sup>10</sup> is CR<sup>10</sup>.  
 In some embodiments, X<sup>11</sup> is N. In some embodiments, X<sup>11</sup> is CR<sup>11</sup>.  
 In some embodiments, X<sup>12</sup> is N. In some embodiments, X<sup>12</sup> is CR<sup>12</sup>.  
 In some embodiments, X<sup>10</sup> is CR<sup>10</sup>, X<sup>11</sup> is CR<sup>11</sup>, and X<sup>12</sup> is CR<sup>12</sup>.  
 In some embodiments, R<sup>10</sup> is H. In some embodiments, R<sup>10</sup> is halo. In some embodiments, R<sup>10</sup> is C<sub>1-4</sub> alkyl.  
 In some embodiments, R<sup>11</sup> is H. In some embodiments, R<sup>11</sup> is halo. In some embodiments, R<sup>11</sup> is C<sub>1-4</sub> alkyl.  
 In some embodiments, R<sup>12</sup> is H. In some embodiments, R<sup>12</sup> is halo. In some embodiments, R<sup>12</sup> is OR<sup>a2</sup>. In some embodiments, R<sup>12</sup> is NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>12</sup> is C<sub>6-10</sub> aryl. In some embodiments, R<sup>12</sup> is C<sub>6-10</sub> aryl optionally substituted with 1, 2, 3, or 4

substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>12</sup> is C<sub>3-7</sub> cycloalkyl. In some embodiments, R<sup>12</sup> is C<sub>3-7</sub> cycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>12</sup> is 5-10 membered heteroaryl. In some embodiments, R<sup>12</sup> is 5-10 membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>12</sup> is 4-10 membered heterocycloalkyl. In some embodiments, R<sup>12</sup> is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

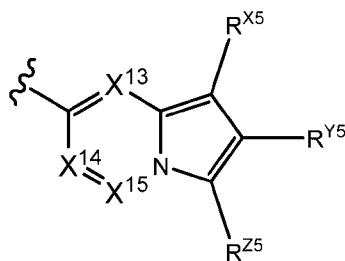
In some embodiments, R<sup>X4</sup> is H. In some embodiments, R<sup>X4</sup> is halo. In some embodiments, R<sup>X4</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>X4</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered

heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>X4</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>X4</sup> is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>X4</sup> is 5-membered heteroaryl. In some embodiments, R<sup>X4</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments, R<sup>Y4</sup> is H. In some embodiments, R<sup>Y4</sup> is halo. In some embodiments, R<sup>Y4</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>Y4</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>Y4</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>Y4</sup> is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,

- C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>,  
 5 C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>Y4</sup> is 5-membered heteroaryl. In some embodiments, R<sup>Y4</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub>  
 10 haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>,  
 15 NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments, B is of formula (e):



(e).

- In some embodiments, X<sup>13</sup> is N. In some embodiments, X<sup>13</sup> is CR<sup>13</sup>.  
 In some embodiments, X<sup>14</sup> is N. In some embodiments, X<sup>14</sup> is CR<sup>14</sup>.  
 20 In some embodiments, X<sup>15</sup> is N. In some embodiments, X<sup>15</sup> is CR<sup>15</sup>.  
 In some embodiments, X<sup>13</sup> is CR<sup>13</sup>; X<sup>14</sup> is CR<sup>14</sup>; and X<sup>15</sup> is CR<sup>15</sup>.  
 In some embodiments, R<sup>13</sup> is H. In some embodiments, R<sup>13</sup> is halo. In some embodiments, R<sup>13</sup> is C<sub>1-4</sub> alkyl.  
 In some embodiments, R<sup>14</sup> is H. In some embodiments, R<sup>14</sup> is halo. In some  
 25 embodiments, R<sup>14</sup> is C<sub>1-4</sub> alkyl.  
 In some embodiments, R<sup>15</sup> is H. In some embodiments, R<sup>15</sup> is halo. In some  
 embodiments, R<sup>15</sup> is OR<sup>a2</sup>. In some embodiments, R<sup>15</sup> is NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>15</sup>

is C<sub>6-10</sub> aryl. In some embodiments, R<sup>15</sup> is C<sub>6-10</sub> aryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>,  
5 C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>15</sup> is C<sub>3-7</sub> cycloalkyl. In some embodiments, R<sup>15</sup> is C<sub>3-7</sub> cycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from  
10 halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>,  
15 S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>15</sup> is 5-10 membered heteroaryl. In some embodiments, R<sup>15</sup> is 5-10 membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>,  
20 C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>15</sup> is 4-10 membered heterocycloalkyl. In some  
25 embodiments, R<sup>15</sup> is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>,  
C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and  
30 S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments, R<sup>X5</sup> is H. In some embodiments, R<sup>X5</sup> is halo. In some embodiments, R<sup>X5</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>X5</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub>

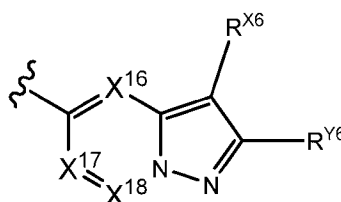
- alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>X5</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>X5</sup> is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>X5</sup> is 5-membered heteroaryl. In some embodiments, R<sup>X5</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.
- 25 In some embodiments, R<sup>Y5</sup> is H. In some embodiments, R<sup>Y5</sup> is halo. In some embodiments, R<sup>Y5</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>Y5</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>Y5</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>Y5</sup> is C<sub>2-6</sub>

alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2R<sup>d2</sup></sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2R<sup>d2</sup></sup>, C(=NR<sup>e2</sup>)NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2R<sup>d2</sup></sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2R<sup>d2</sup></sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2R<sup>d2</sup></sup>. In some embodiments, R<sup>Y5</sup> is 5-membered heteroaryl. In some embodiments, R<sup>Y5</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2R<sup>d2</sup></sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2R<sup>d2</sup></sup>, C(=NR<sup>e2</sup>)NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2R<sup>d2</sup></sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2R<sup>d2</sup></sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2R<sup>d2</sup></sup>.

In some embodiments, R<sup>Z5</sup> is H. In some embodiments, R<sup>Z5</sup> is halo. In some embodiments, R<sup>Z5</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>Z5</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2R<sup>d2</sup></sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2R<sup>d2</sup></sup>, C(=NR<sup>e2</sup>)NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2R<sup>d2</sup></sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2R<sup>d2</sup></sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2R<sup>d2</sup></sup>. In some embodiments, R<sup>Z5</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>Z5</sup> is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2R<sup>d2</sup></sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2R<sup>d2</sup></sup>, C(=NR<sup>e2</sup>)NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2R<sup>d2</sup></sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2R<sup>d2</sup></sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2R<sup>d2</sup></sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2R<sup>d2</sup></sup>.

S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>Z5</sup> is 5-membered heteroaryl. In some embodiments, R<sup>Z5</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments, B is of formula (f):



(f).

In some embodiments, X<sup>16</sup> is N. In some embodiments, X<sup>16</sup> is CR<sup>16</sup>.  
 In some embodiments, X<sup>17</sup> is N. In some embodiments, X<sup>17</sup> is CR<sup>17</sup>.  
 In some embodiments, X<sup>18</sup> is N. In some embodiments, X<sup>18</sup> is CR<sup>18</sup>.  
 In some embodiments, X<sup>16</sup> is CR<sup>16</sup>, X<sup>17</sup> is CR<sup>17</sup>; and X<sup>18</sup> is CR<sup>18</sup>.  
 In some embodiments, R<sup>16</sup> is H. In some embodiments, R<sup>16</sup> is halo. In some embodiments, R<sup>16</sup> is C<sub>1-4</sub> alkyl.  
 In some embodiments, R<sup>17</sup> is H. In some embodiments, R<sup>17</sup> is halo. In some embodiments, R<sup>17</sup> is C<sub>1-4</sub> alkyl.  
 In some embodiments, R<sup>18</sup> is H. In some embodiments, R<sup>18</sup> is halo. In some embodiments, R<sup>18</sup> is OR<sup>a2</sup>. In some embodiments, R<sup>18</sup> is NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>18</sup> is C<sub>6-10</sub> aryl. In some embodiments, R<sup>18</sup> is C<sub>6-10</sub> aryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and



$S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{18}$  is  $C_{3-7}$  cycloalkyl. In some embodiments,  $R^{18}$  is  $C_{3-7}$  cycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl,

5  $CN$ ,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ ,  $NR^cS(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{18}$  is 5-10 membered heteroaryl. In some embodiments,  $R^{18}$  is 5-10 membered heteroaryl optionally substituted with 1, 2, 3, or 4

10 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl,  $CN$ ,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ ,

15  $NR^cS(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{15}$  is 4-10 membered heterocycloalkyl. In some embodiments,  $R^{15}$  is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$

20 alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl,  $CN$ ,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ ,  $NR^cS(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ .

25 In some embodiments,  $R^{X6}$  is H. In some embodiments,  $R^{X6}$  is halo. In some embodiments,  $R^{X6}$  is  $C_{1-6}$  alkyl. In some embodiments,  $R^{X6}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl-

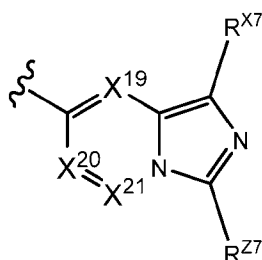
30  $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl,  $CN$ ,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{X6}$  is  $C_{2-6}$  alkenyl. In some embodiments,  $R^{X6}$  is  $C_{2-6}$

alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>X6</sup> is 5-membered heteroaryl. In some embodiments, R<sup>X6</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments, R<sup>Y6</sup> is H. In some embodiments, R<sup>Y6</sup> is halo. In some embodiments, R<sup>Y6</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>Y6</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>Y6</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>Y6</sup> is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

$S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{Y6}$  is 5-membered heteroaryl. In some  
embodiments,  $R^{Y6}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  
substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$   
haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered  
5 heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl-  
 $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  
 $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  
 $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  
 $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  
10  $S(O)_2NR^{c2}R^{d2}$ .

In some embodiments, B is of formula (g):



(g).

In some embodiments,  $X^{19}$  is N. In some embodiments,  $X^{19}$  is  $CR^{19}$ .  
In some embodiments,  $X^{20}$  is N. In some embodiments,  $X^{20}$  is  $CR^{20}$ .  
In some embodiments,  $X^{21}$  is N. In some embodiments,  $X^{21}$  is  $CR^{21}$ .  
15 In some embodiments,  $X^{19}$  is  $CR^{19}$ ,  $X^{20}$  is  $CR^{20}$ , and  $X^{21}$  is  $CR^{21}$ .  
In some embodiments,  $R^{19}$  is H. In some embodiments,  $R^{19}$  is halo. In some  
embodiments,  $R^{19}$  is  $C_{1-4}$  alkyl.

In some embodiments,  $R^{20}$  is H. In some embodiments,  $R^{20}$  is halo. In some  
embodiments,  $R^{20}$  is  $C_{1-4}$  alkyl.  
20 In some embodiments,  $R^{21}$  is H. In some embodiments,  $R^{21}$  is halo. In some  
embodiments,  $R^{21}$  is  $OR^{a2}$ . In some embodiments,  $R^{21}$  is  $NR^{c2}R^{d2}$ . In some embodiments,  $R^{21}$   
is  $C_{6-10}$  aryl. In some embodiments,  $R^{21}$  is  $C_{6-10}$  aryl optionally substituted with 1, 2, 3, or 4  
substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$   
haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$   
alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  
25  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  
 $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,

$\text{NR}^c\text{S(O)}\text{R}^{b2}$ ,  $\text{NR}^{c2}\text{S(O)}_2\text{R}^{b2}$ ,  $\text{NR}^{c2}\text{S(O)}_2\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{S(O)}\text{R}^{b2}$ ,  $\text{S(O)}\text{NR}^{c2}\text{R}^{d2}$ ,  $\text{S(O)}_2\text{R}^{b2}$ , and  $\text{S(O)}_2\text{NR}^{c2}\text{R}^{d2}$ . In some embodiments,  $\text{R}^{21}$  is C<sub>3-7</sub> cycloalkyl. In some embodiments,  $\text{R}^{21}$  is C<sub>3-7</sub> cycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments,  $\text{R}^{21}$  is 5-10 membered heteroaryl. In some embodiments,  $\text{R}^{21}$  is 5-10 membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments,  $\text{R}^{21}$  is 4-10 membered heterocycloalkyl. In some embodiments,  $\text{R}^{21}$  is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments,  $\text{R}^{X7}$  is H. In some embodiments,  $\text{R}^{X7}$  is halo. In some embodiments,  $\text{R}^{X7}$  is C<sub>1-6</sub> alkyl. In some embodiments,  $\text{R}^{X7}$  is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

$S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{X7}$  is  $C_{2-6}$  alkenyl. In some embodiments,  $R^{X7}$  is  $C_{2-6}$  alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{X7}$  is 5-membered heteroaryl. In some

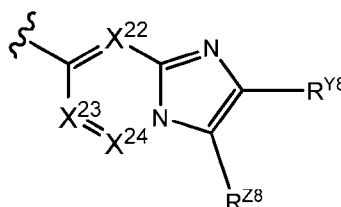
embodiments,  $R^{X7}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ .

In some embodiments,  $R^{Z7}$  is H. In some embodiments,  $R^{Z7}$  is halo. In some

embodiments,  $R^{Z7}$  is  $C_{1-6}$  alkyl. In some embodiments,  $R^{Z7}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{Z7}$  is  $C_{2-6}$  alkenyl. In some embodiments,  $R^{Z7}$  is  $C_{2-6}$  alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,

$\text{NR}^{\text{c}2}\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  
 $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ . In some embodiments,  $\text{R}^{\text{Z}7}$  is 5-membered heteroaryl. In some  
 5 embodiments,  $\text{R}^{\text{Z}7}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  
 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$   
 haloalkyl,  $\text{C}_{6-10}$  aryl,  $\text{C}_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered  
 heterocycloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl-  
 $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{\text{a}2}$ ,  $\text{SR}^{\text{a}2}$ ,  $\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  
 $\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(=\text{NR}^{\text{e}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  
 $\text{NR}^{\text{c}2}\text{C}(=\text{NR}^{\text{e}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  
 10  $\text{NR}^{\text{c}2}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  
 $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ .

In some embodiments, B is of formula (h):



(h).

In some embodiments,  $\text{X}^{\text{Z}2}$  is N. In some embodiments,  $\text{X}^{\text{Z}2}$  is  $\text{CR}^{\text{Z}2}$ .  
 In some embodiments,  $\text{X}^{\text{Z}3}$  is N. In some embodiments,  $\text{X}^{\text{Z}3}$  is  $\text{CR}^{\text{Z}3}$ .  
 15 In some embodiments,  $\text{X}^{\text{Z}4}$  is N. In some embodiments,  $\text{X}^{\text{Z}4}$  is  $\text{CR}^{\text{Z}4}$ .  
 In some embodiments,  $\text{X}^{\text{Z}2}$  is  $\text{CR}^{\text{Z}2}$ ,  $\text{X}^{\text{Z}3}$  is  $\text{CR}^{\text{Z}3}$ ; and  $\text{X}^{\text{Z}4}$  is  $\text{CR}^{\text{Z}4}$ .  
 In some embodiments,  $\text{R}^{\text{Z}2}$  is H. In some embodiments,  $\text{R}^{\text{Z}2}$  is halo. In some  
 embodiments,  $\text{R}^{\text{Z}2}$  is  $\text{C}_{1-4}$  alkyl.  
 In some embodiments,  $\text{R}^{\text{Z}3}$  is H. In some embodiments,  $\text{R}^{\text{Z}3}$  is halo. In some  
 20 embodiments,  $\text{R}^{\text{Z}3}$  is  $\text{C}_{1-4}$  alkyl.

In some embodiments,  $\text{R}^{\text{Z}4}$  is H. In some embodiments,  $\text{R}^{\text{Z}4}$  is halo. In some  
 embodiments,  $\text{R}^{\text{Z}4}$  is  $\text{OR}^{\text{a}2}$ . In some embodiments,  $\text{R}^{\text{Z}4}$  is  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ . In some embodiments,  $\text{R}^{\text{Z}4}$   
 is  $\text{C}_{6-10}$  aryl. In some embodiments,  $\text{R}^{\text{Z}4}$  is  $\text{C}_{6-10}$  aryl optionally substituted with 1, 2, 3, or 4  
 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$   
 25 haloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$   
 alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{\text{a}2}$ ,  $\text{SR}^{\text{a}2}$ ,  $\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  
 $\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(=\text{NR}^{\text{e}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  
 $\text{NR}^{\text{c}2}\text{C}(=\text{NR}^{\text{e}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,

$\text{NR}^{\text{c}}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ . In some embodiments,  $\text{R}^{24}$  is C<sub>3-7</sub> cycloalkyl. In some embodiments,  $\text{R}^{24}$  is C<sub>3-7</sub> cycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments,  $\text{R}^{24}$  is 5-10 membered heteroaryl. In some embodiments,  $\text{R}^{24}$  is 5-10 membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments,  $\text{R}^{24}$  is 4-10 membered heterocycloalkyl. In some embodiments,  $\text{R}^{24}$  is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments,  $\text{R}^{\text{X}8}$  is H. In some embodiments,  $\text{R}^{\text{X}8}$  is halo. In some embodiments,  $\text{R}^{\text{X}8}$  is C<sub>1-6</sub> alkyl. In some embodiments,  $\text{R}^{\text{X}8}$  is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>X8</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>X8</sup> is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>X8</sup> is 5-membered heteroaryl. In some

embodiments, R<sup>X8</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

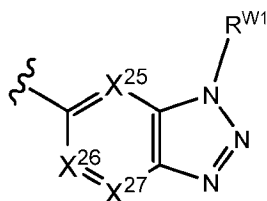
In some embodiments, R<sup>Y8</sup> is H. In some embodiments, R<sup>Y8</sup> is halo. In some

embodiments, R<sup>Y8</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>Y8</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>Y8</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>Y8</sup> is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.



$\text{NR}^{\text{c}2}\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  
 $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ . In some embodiments,  $\text{R}^{\text{Y}8}$  is 5-membered heteroaryl. In some  
 5 embodiments,  $\text{R}^{\text{Y}8}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  
 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$   
 haloalkyl,  $\text{C}_{6-10}$  aryl,  $\text{C}_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered  
 heterocycloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl-  
 $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{\text{a}2}$ ,  $\text{SR}^{\text{a}2}$ ,  $\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  
 $\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(=\text{NR}^{\text{e}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  
 $\text{NR}^{\text{c}2}\text{C}(=\text{NR}^{\text{e}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  
 10  $\text{NR}^{\text{c}2}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  
 $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ .

In some embodiments, B is of formula (i):



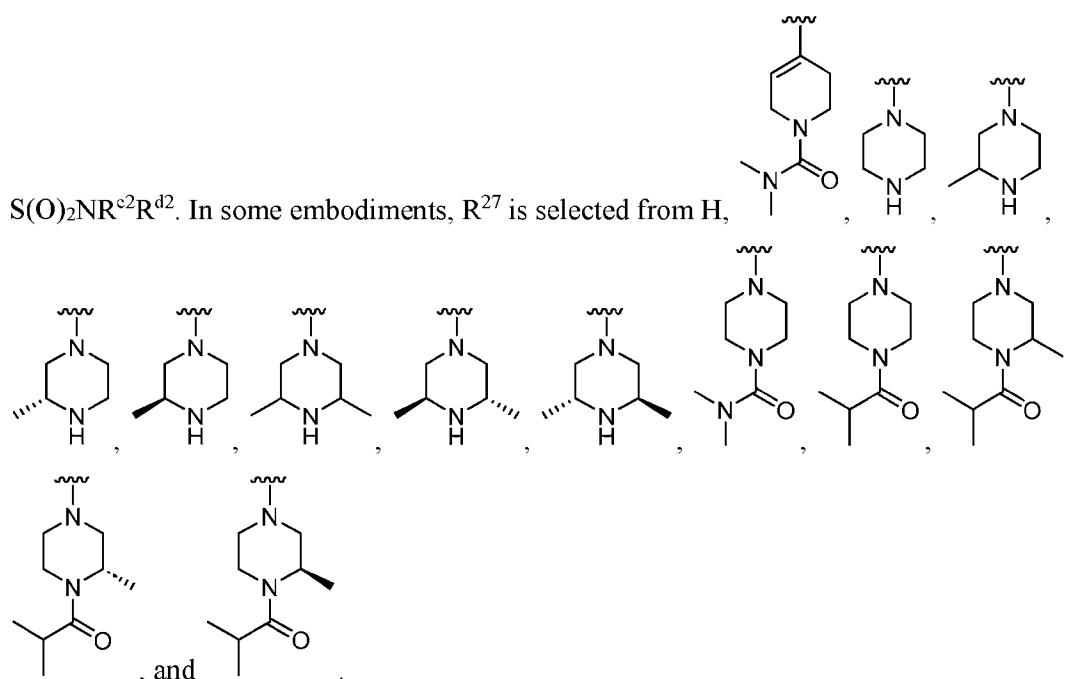
(i).

In some embodiments,  $\text{X}^{25}$  is N. In some embodiments,  $\text{X}^{25}$  is  $\text{CR}^{25}$ .  
 In some embodiments,  $\text{X}^{26}$  is N. In some embodiments,  $\text{X}^{26}$  is  $\text{CR}^{26}$ .  
 15 In some embodiments,  $\text{X}^{27}$  is N. In some embodiments,  $\text{X}^{27}$  is  $\text{CR}^{27}$ .  
 In some embodiments,  $\text{X}^{25}$  is  $\text{CR}^{25}$ ;  $\text{X}^{26}$  is  $\text{CR}^{26}$ ; and  $\text{X}^{27}$  is  $\text{CR}^{27}$ .  
 In some embodiments,  $\text{R}^{25}$  is H. In some embodiments,  $\text{R}^{25}$  is halo. In some  
 embodiments,  $\text{R}^{25}$  is  $\text{C}_{1-4}$  alkyl.  
 In some embodiments,  $\text{R}^{26}$  is H. In some embodiments,  $\text{R}^{26}$  is halo. In some  
 20 embodiments,  $\text{R}^{26}$  is  $\text{C}_{1-4}$  alkyl. In some embodiments,  $\text{R}^{26}$  is selected from H, fluoro, and  
 bromo.  
 In some embodiments,  $\text{R}^{27}$  is H. In some embodiments,  $\text{R}^{27}$  is halo. In some  
 embodiments,  $\text{R}^{27}$  is  $\text{OR}^{\text{a}2}$ . In some embodiments,  $\text{R}^{27}$  is  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ . In some embodiments,  $\text{R}^{27}$   
 is  $\text{C}_{6-10}$  aryl. In some embodiments,  $\text{R}^{27}$  is  $\text{C}_{6-10}$  aryl optionally substituted with 1, 2, 3, or 4  
 25 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$   
 haloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$   
 alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{\text{a}2}$ ,  $\text{SR}^{\text{a}2}$ ,  $\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  
 $\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(=\text{NR}^{\text{e}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,

NR<sup>c</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>,  
NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and  
S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>27</sup> is C<sub>3-7</sub> cycloalkyl. In some embodiments, R<sup>27</sup> is C<sub>3-7</sub>  
cycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from  
halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub>  
alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl,  
CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>,  
C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>,  
NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>,  
S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>27</sup> is 5-10 membered heteroaryl. In  
some embodiments, R<sup>27</sup> is 5-10 membered heteroaryl optionally substituted with 1, 2, 3, or 4  
substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub>  
haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub>  
alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>,  
C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>,  
NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>,  
NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and  
S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>27</sup> is 4-10 membered heterocycloalkyl. In some  
embodiments, R<sup>27</sup> is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4  
substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub>  
haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub>  
alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>,  
C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>,  
NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>,  
NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and  
S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments, R<sup>27</sup> is selected from H and 4-10 membered heterocycloalkyl, wherein said 4-10 membered heterocycloalkyl is optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and

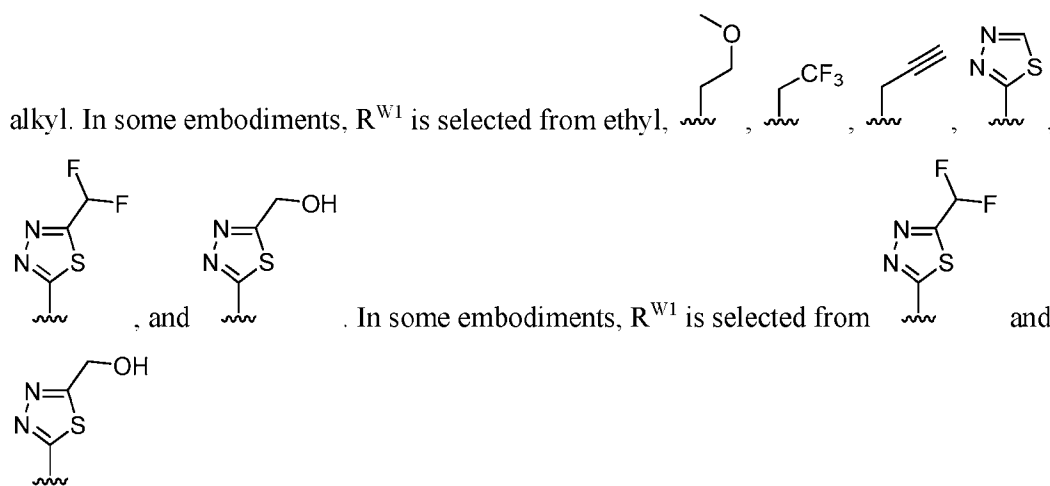
$\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ . In some embodiments,  $\text{R}^{27}$  is selected from H,



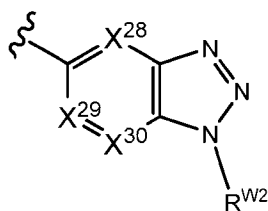
In some embodiments, R<sup>W1</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>W1</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 R'. In some embodiments, R<sup>W1</sup> is C<sub>2-6</sub> alkenyl. In some embodiments, R<sup>W1</sup> is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 R'. In some embodiments, R<sup>W1</sup> is 5-membered heteroaryl. In some embodiments, R<sup>W1</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 R'.

In some embodiments, R<sup>W1</sup> is selected from C<sub>1-6</sub> alkyl and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4 R<sup>•</sup>. In some embodiments, R<sup>W1</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 R<sup>•</sup>, selected from halo, OR<sup>a3</sup>, and CN. In some embodiments, R<sup>W1</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 C<sub>1-6</sub>

alkyl. In some embodiments, R<sup>w1</sup> is selected from ethyl,



In some embodiments, B is of formula (j):



(j).

In some embodiments,  $X^{28}$  is N. In some embodiments,  $X^{28}$  is  $CR^{28}$ .

In some embodiments,  $X^{29}$  is N. In some embodiments,  $X^{29}$  is  $CR^{29}$ .

In some embodiments,  $X^{30}$  is N. In some embodiments,  $X^{30}$  is  $CR^{30}$ .

In some embodiments,  $X^{28}$  is  $CR^{28}$ ;  $X^{29}$  is  $CR^{29}$ ; and  $X^{30}$  is  $CR^{30}$ .

5 In some embodiments,  $R^{28}$  is H. In some embodiments,  $R^{28}$  is halo. In some embodiments,  $R^{28}$  is  $C_{1-4}$  alkyl.

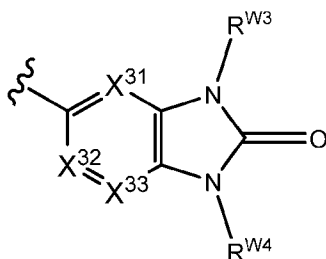
In some embodiments,  $R^{29}$  is H. In some embodiments,  $R^{29}$  is halo. In some embodiments,  $R^{29}$  is  $C_{1-4}$  alkyl.

In some embodiments,  $R^{30}$  is H. In some embodiments,  $R^{30}$  is halo. In some  
 10 embodiments,  $R^{30}$  is  $OR^{a2}$ . In some embodiments,  $R^{30}$  is  $NR^{c2}R^{d2}$ . In some embodiments,  $R^{30}$   
 is  $C_{6-10}$  aryl. In some embodiments,  $R^{30}$  is  $C_{6-10}$  aryl optionally substituted with 1, 2, 3, or 4  
 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$   
 haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$   
 alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  
 15  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  
 $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  
 $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  
 $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{30}$  is  $C_{3-7}$  cycloalkyl. In some embodiments,  $R^{30}$  is  $C_{3-}$   
 $C_{7}$  cycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from  
 20 halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl-  
 $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl,  
 CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  
 $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  
 $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  
 25  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{30}$  is 5-10 membered heteroaryl. In  
 some embodiments,  $R^{30}$  is 5-10 membered heteroaryl optionally substituted with 1, 2, 3, or 4  
 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$   
 haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$

alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>,  
 C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>,  
 NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>,  
 NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and  
 5 S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, R<sup>30</sup> is 4-10 membered heterocycloalkyl. In some  
 embodiments, R<sup>30</sup> is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4  
 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub>  
 haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub>  
 alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>,  
 10 C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>,  
 NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>,  
 NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and  
 S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments, R<sup>W2</sup> is C<sub>1-6</sub> alkyl. In some embodiments, R<sup>W2</sup> is C<sub>1-6</sub> alkyl  
 15 optionally substituted with 1, 2, 3, or 4 R<sup>1</sup>. In some embodiments, R<sup>W2</sup> is C<sub>2-6</sub> alkenyl. In  
 some embodiments, R<sup>W2</sup> is C<sub>2-6</sub> alkenyl optionally substituted with 1, 2, 3, or 4 R<sup>1</sup>. In some  
 embodiments, R<sup>W2</sup> is 5-membered heteroaryl. In some embodiments, R<sup>W2</sup> is 5-membered  
 heteroaryl optionally substituted with 1, 2, 3, or 4 R<sup>1</sup>.

In some embodiments, B is of formula (k):



(k).

20 In some embodiments, X<sup>31</sup> is N. In some embodiments, X<sup>31</sup> is CR<sup>31</sup>.

In some embodiments, X<sup>32</sup> is N. In some embodiments, X<sup>32</sup> is CR<sup>32</sup>.

In some embodiments, X<sup>33</sup> is N. In some embodiments, X<sup>33</sup> is CR<sup>33</sup>.

In some embodiments, X<sup>31</sup> is CR<sup>31</sup>, X<sup>32</sup> is CR<sup>32</sup>, and X<sup>33</sup> is CR<sup>33</sup>.

In some embodiments, R<sup>31</sup> is H. In some embodiments, R<sup>31</sup> is halo. In some  
 25 embodiments, R<sup>31</sup> is C<sub>1-4</sub> alkyl.

In some embodiments,  $R^{32}$  is H. In some embodiments,  $R^{32}$  is halo. In some embodiments,  $R^{32}$  is  $C_{1-4}$  alkyl. In some embodiments,  $R^{32}$  is selected from H, fluoro, and bromo.

In some embodiments,  $R^{33}$  is H. In some embodiments,  $R^{33}$  is halo. In some  
 5 embodiments,  $R^{33}$  is  $OR^{a2}$ . In some embodiments,  $R^{33}$  is  $NR^{c2}R^{d2}$ . In some embodiments,  $R^{33}$   
 is  $C_{6-10}$  aryl. In some embodiments,  $R^{33}$  is  $C_{6-10}$  aryl optionally substituted with 1, 2, 3, or 4  
 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$   
 haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$   
 alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $(CH_2)_mOR^{a2}$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  
 10  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  
 $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  
 $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  
 $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{33}$  is  $C_{3-7}$  cycloalkyl. In some embodiments,  $R^{33}$  is  $C_{3-}$   
 7 cycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from  
 15 halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl-  
 $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl,  
 CN,  $NO_2$ ,  $(CH_2)_mOR^{a2}$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  
 $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  
 $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  
 20  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{33}$  is 5-10 membered  
 heteroaryl. In some embodiments,  $R^{33}$  is 5-10 membered heteroaryl optionally substituted  
 with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$   
 alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered  
 heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $(CH_2)_mOR^{a2}$ ,  
 25  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  
 $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  
 $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  
 $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{33}$  is 4-10 membered heterocycloalkyl.  
 In some embodiments,  $R^{33}$  is 4-10 membered heterocycloalkyl optionally substituted with 1,  
 30 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  
 $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$   
 alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $(CH_2)_mOR^{a2}$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  
 $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  
 $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,

$$\text{NR}^c\text{S}(\text{O})\text{R}^{b2}, \text{NR}^{c2}\text{S}(\text{O})_2\text{R}^{b2}, \text{NR}^{c2}\text{S}(\text{O})_2\text{NR}^{c2}\text{R}^{d2}, \text{S}(\text{O})\text{R}^{b2}, \text{S}(\text{O})\text{NR}^{c2}\text{R}^{d2}, \text{S}(\text{O})_2\text{R}^{b2}, \text{and} \\ \text{S}(\text{O})_2\text{NR}^{c2}\text{R}^{d2}.$$

In some embodiments,  $R^{33}$  is H. In some embodiments,  $R^{33}$  is halo. In some embodiments,  $R^{33}$  is  $OR^{a2}$ . In some embodiments,  $R^{33}$  is  $NR^{c2}R^{d2}$ . In some embodiments,  $R^{33}$  is  $C_{6-10}$  aryl. In some embodiments,  $R^{33}$  is  $C_{6-10}$  aryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ ,  $NR^cS(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{33}$  is  $C_{3-7}$  cycloalkyl. In some embodiments,  $R^{33}$  is  $C_{3-7}$  cycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ ,  $NR^cS(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{33}$  is 5-10 membered heteroaryl. In some embodiments,  $R^{33}$  is 5-10 membered heteroaryl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ ,  $NR^cS(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments,  $R^{33}$  is 4-10 membered heterocycloalkyl. In some embodiments,  $R^{33}$  is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ .

$\text{NR}^{\text{c}}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ .

In some embodiments,  $\text{R}^{33}$  is selected from H, halo,  $\text{OR}^{\text{a}2}$ ,  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}_{6-10}$  aryl,  $\text{C}_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said

5  $\text{C}_{6-10}$  aryl,  $\text{C}_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $\text{R}^3$ ,  $\text{R}^6$ ,  $\text{R}^9$ ,  $\text{R}^{12}$ ,  $\text{R}^{15}$ ,  $\text{R}^{18}$ ,  $\text{R}^{21}$ ,  $\text{R}^{24}$ ,  $\text{R}^{27}$ ,  $\text{R}^{30}$ , and  $\text{R}^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$  haloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $(\text{CH}_2)_m\text{OR}^{\text{a}2}$ ,  $\text{OR}^{\text{a}2}$ ,  $\text{SR}^{\text{a}2}$ ,

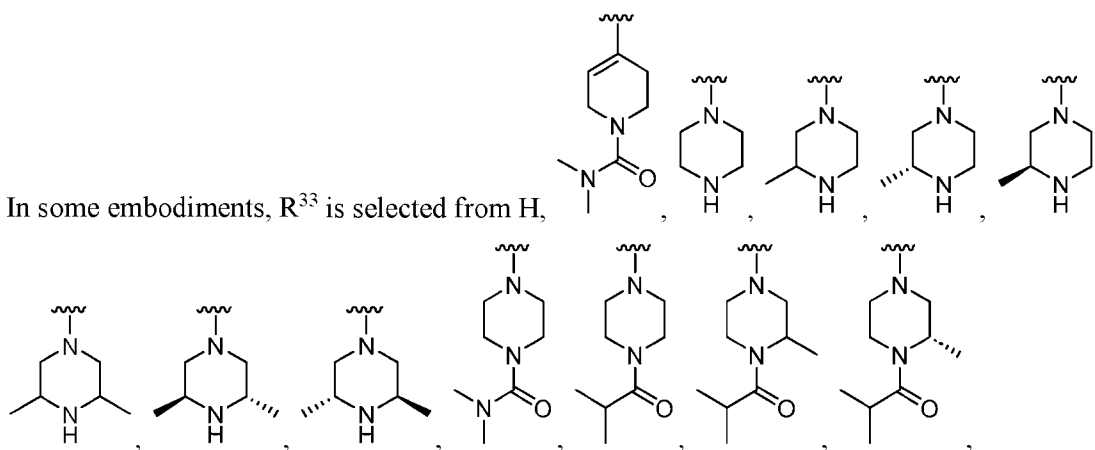
10  $\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(=\text{NR}^{\text{c}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(=\text{NR}^{\text{c}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ .

In some embodiments,  $\text{R}^{33}$  is selected from H and 4-10 membered heterocycloalkyl,

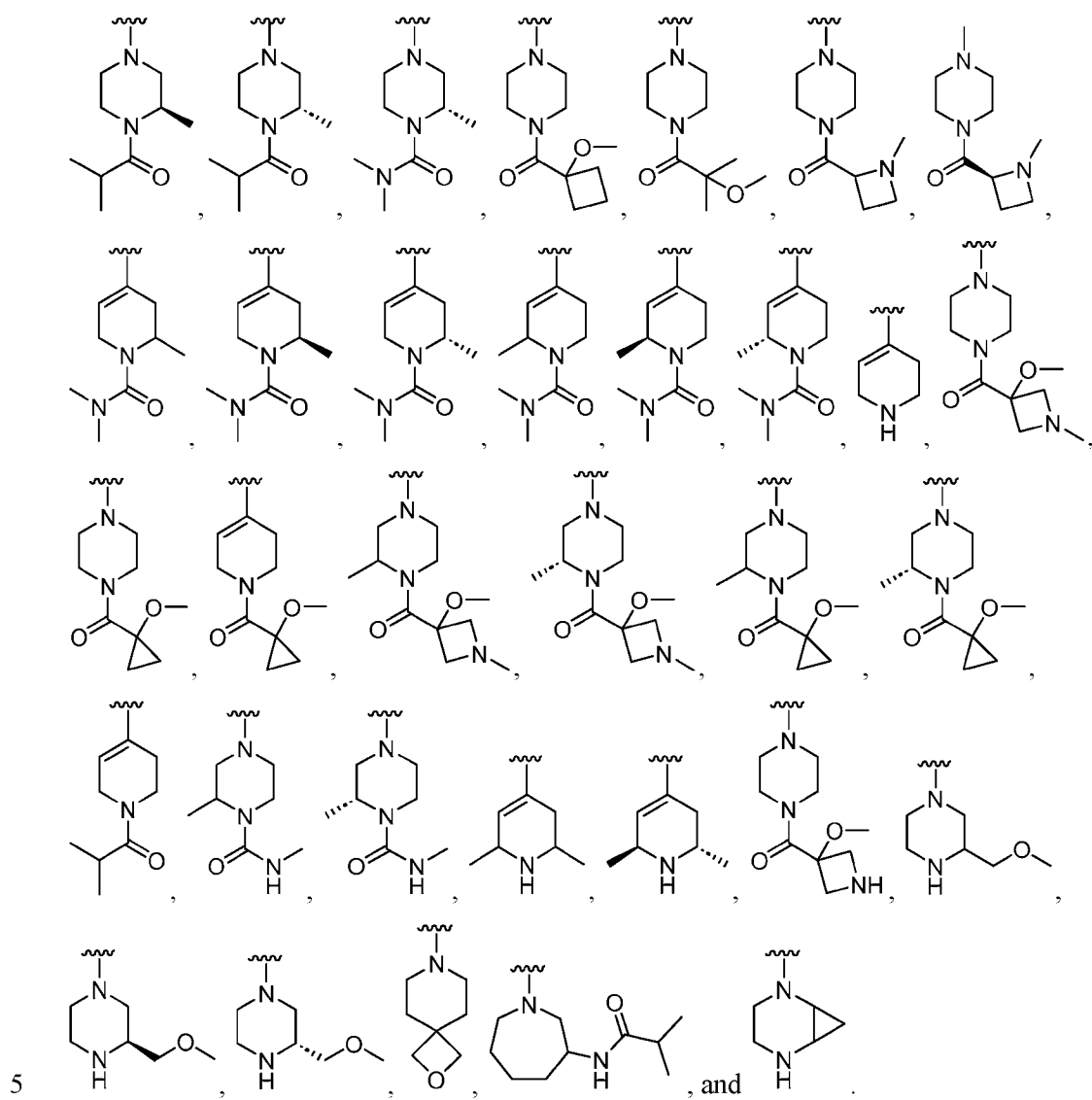
15 wherein said 4-10 membered heterocycloalkyl is optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$  haloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{\text{a}2}$ ,  $\text{SR}^{\text{a}2}$ ,  $\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(=\text{NR}^{\text{c}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,

20  $\text{NR}^{\text{c}2}\text{C}(=\text{NR}^{\text{c}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ .

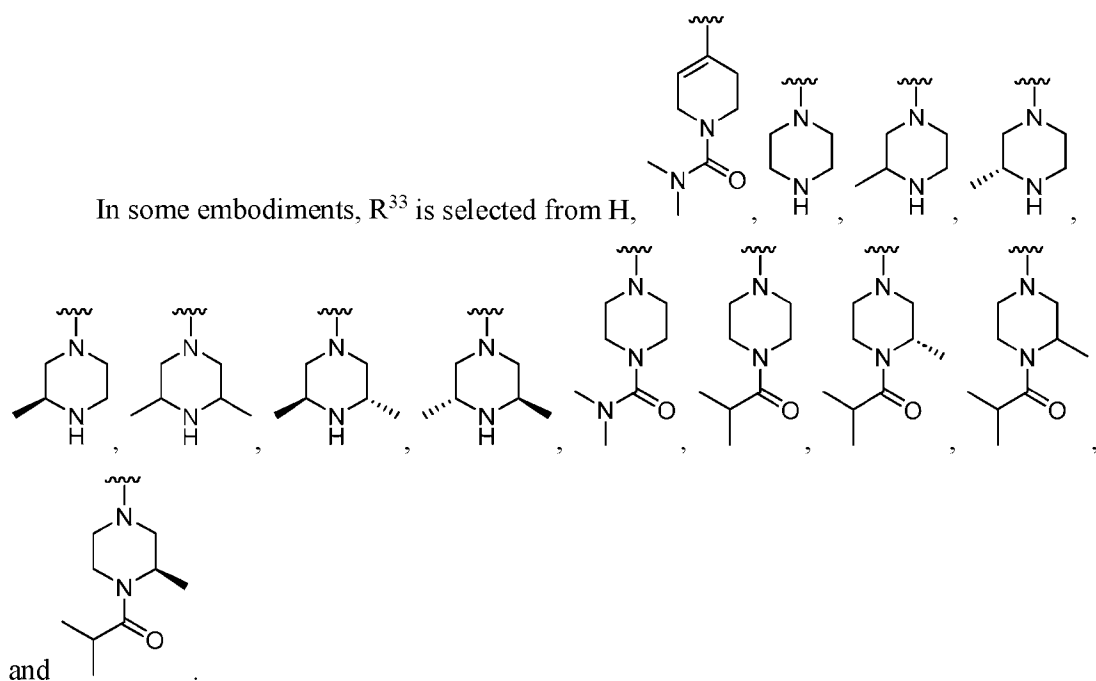
In some embodiments,  $\text{R}^{33}$  is selected from H,



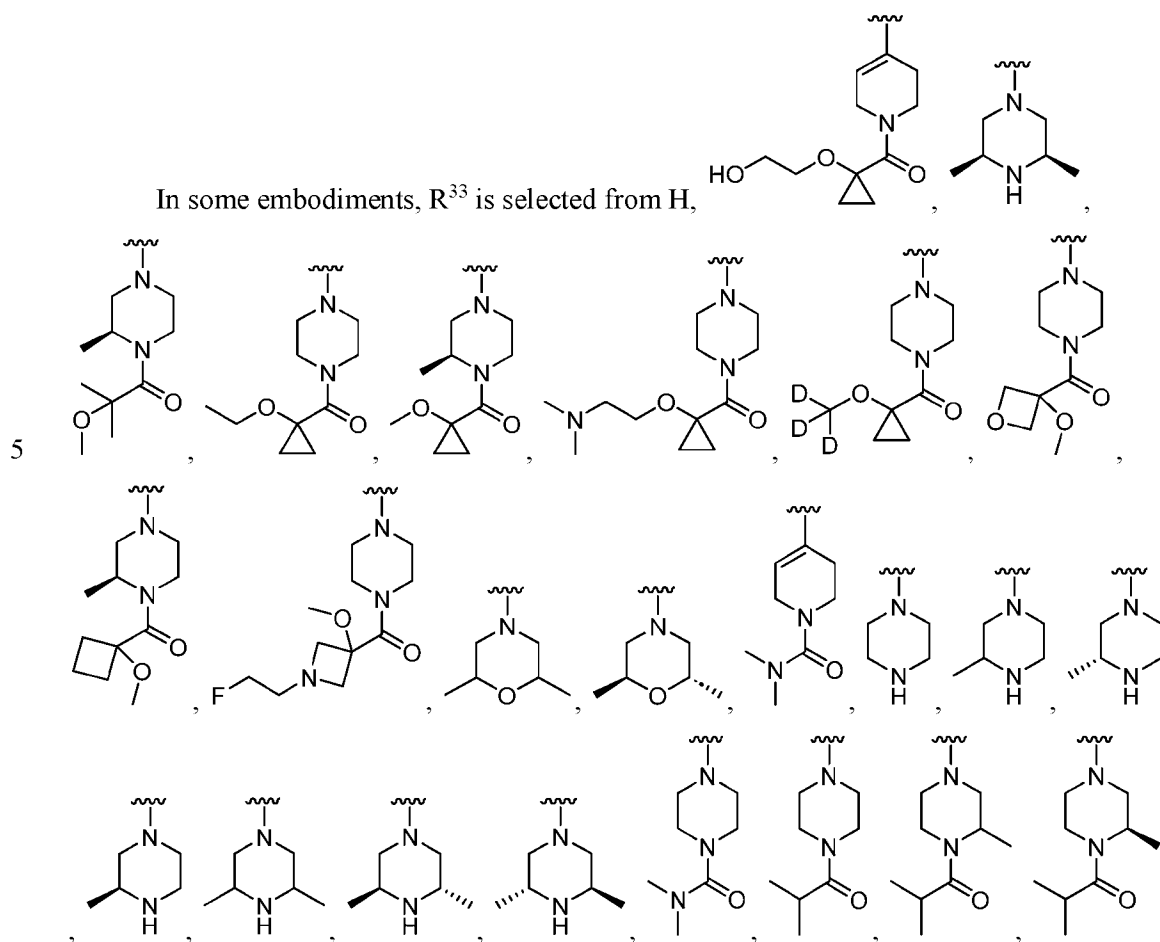


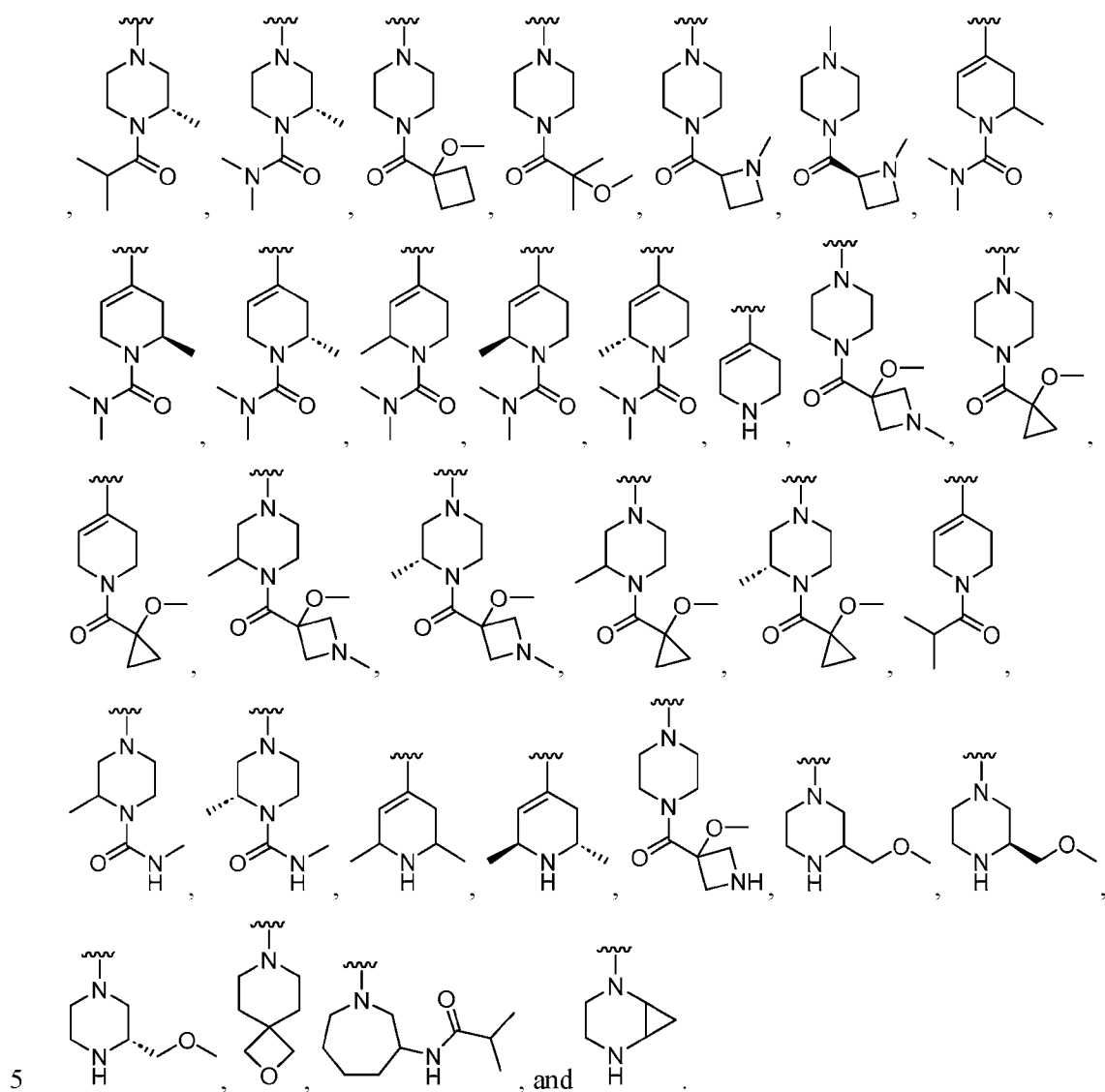


In some embodiments,  $R^{33}$  is selected from H,

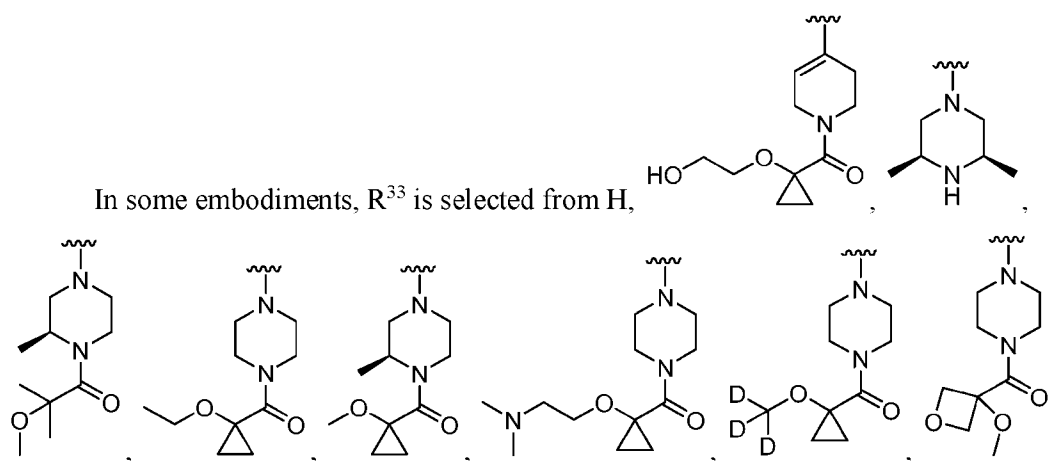


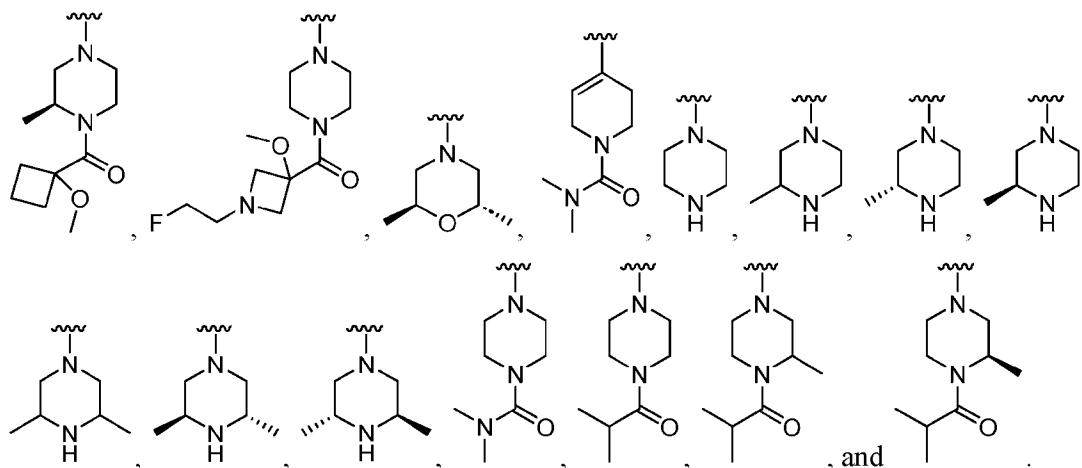
In some embodiments,  $R^{33}$  is selected from H,





In some embodiments,  $R^{33}$  is selected from H,

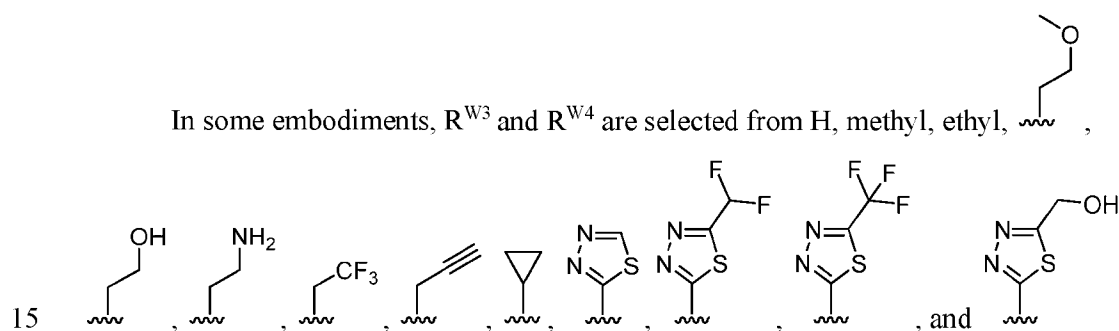


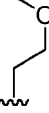


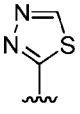
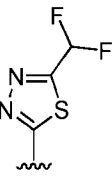
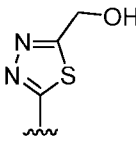
In some embodiments,  $R^{W3}$  and  $R^{W4}$  are selected from H,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{3-7}$  cycloalkyl, and 5-membered heteroaryl, wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{3-7}$  cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4  $R'$ .

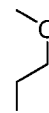
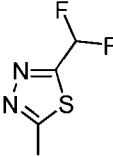
In some embodiments,  $R^{W3}$  and  $R^{W4}$  are selected from  $C_{1-6}$  alkyl and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4  $R'$ . In some embodiments,  $R^{W3}$  and  $R^{W4}$  are  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4  $R'$ , selected from halo,  $OR^{a3}$ , and CN. In some embodiments,  $R^{W3}$  and  $R^{W4}$  are 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  $C_{1-6}$  alkyl.

In some embodiments, at least one of  $R^{W3}$  and  $R^{W4}$  is 1,3,4-thiadiazolyl optionally substituted with 1  $R'$ . In some embodiments, at least one of  $R^{W3}$  and  $R^{W4}$  is 1,3,4-thiadiazolyl optionally substituted with difluoromethyl, trifluoromethyl, or methanol.



In some embodiments,  $R^{W3}$  and  $R^{W4}$  are selected from ethyl, , , ,

, , and . In some embodiments,  $R^{W3}$  and  $R^{W4}$  are selected from

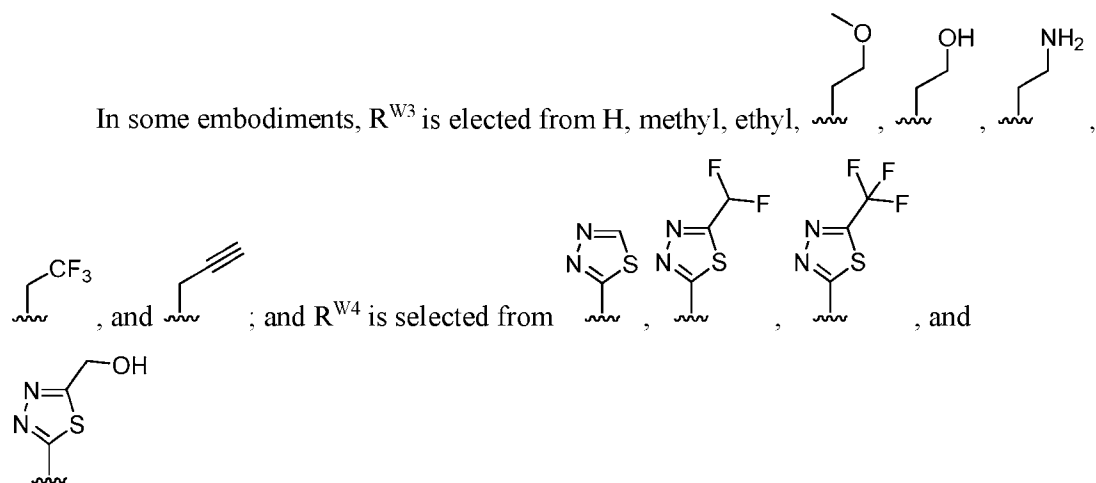
ethyl, , , , and .

In some embodiments,  $R^{W3}$  is selected from H,  $C_{1-6}$  alkyl, and  $C_{3-7}$  cycloalkyl, wherein  
 5 the  $C_{1-6}$  alkyl and  $C_{3-7}$  cycloalkyl are optionally substituted with 1, 2, 3, or 4  $R'$ ; and  
 $R^{W4}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  $R'$ .

In some embodiments,  $R^{W3}$  is H. In some embodiments,  $R^{W3}$  is  $C_{1-6}$  alkyl. In some  
 embodiments,  $R^{W3}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4  $R'$ . In some  
 embodiments,  $R^{W3}$  is  $C_{2-6}$  alkenyl. In some embodiments,  $R^{W3}$  is  $C_{2-6}$  alkenyl optionally  
 10 substituted with 1, 2, 3, or 4  $R'$ . In some embodiments,  $R^{W3}$  is 5-membered heteroaryl. In  
 some embodiments,  $R^{W2}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  
 $R'$ .

In some embodiments,  $R^{W3}$  is  $C_{1-6}$  alkyl. In some embodiments,  $R^{W3}$  is  $C_{1-6}$  alkyl  
 optionally substituted with 1, 2, 3, or 4  $R'$ . In some embodiments,  $R^{W3}$  is  $C_{2-6}$  alkenyl. In  
 15 some embodiments,  $R^{W3}$  is  $C_{2-6}$  alkenyl optionally substituted with 1, 2, 3, or 4  $R'$ . In some  
 embodiments,  $R^{W3}$  is 5-membered heteroaryl. In some embodiments,  $R^{W2}$  is 5-membered  
 heteroaryl optionally substituted with 1, 2, 3, or 4  $R'$ .

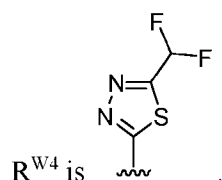
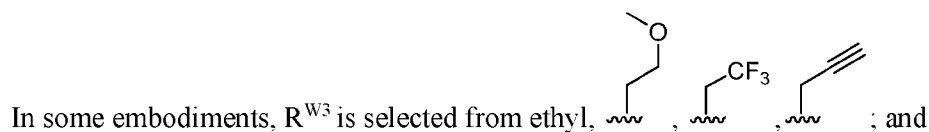
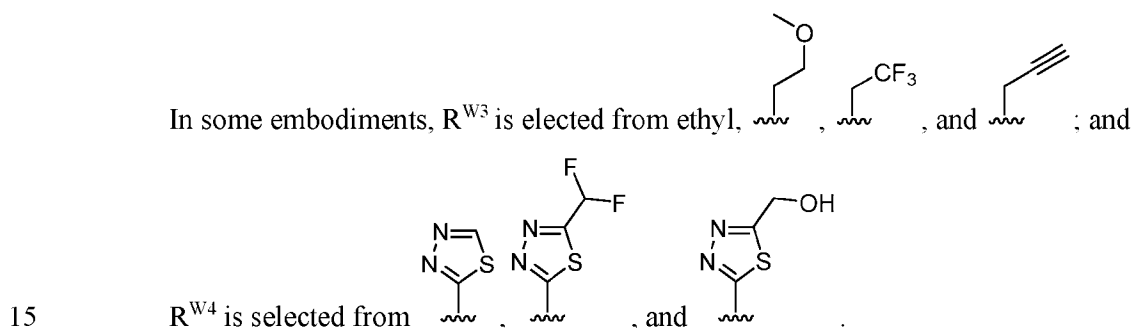
$R^{W3}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4  $R'$ , selected from halo,  $OR^{a3}$ ,  
 $NR^{c3}R^{d3}$ , and CN.



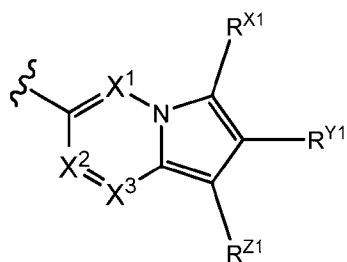
In some embodiments,  $R^{W3}$  is  $C_{1-6}$  alkyl and  $R^{W4}$  is 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4  $R'$ . In some embodiments,  $R^{W3}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4  $R'$ , selected from halo,  $OR^{a3}$ , and CN.

In some embodiments,  $R^{W4}$  is  $C_{1-6}$  alkyl. In some embodiments,  $R^{W4}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4  $R'$ . In some embodiments,  $R^{W4}$  is  $C_{2-6}$  alkenyl. In some embodiments,  $R^{W4}$  is  $C_{2-6}$  alkenyl optionally substituted with 1, 2, 3, or 4  $R'$ . In some  
10      embodiments,  $R^{W4}$  is 5-membered heteroaryl. In some embodiments,  $R^{W4}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  $R'$ .

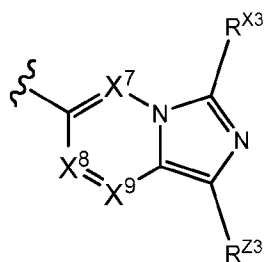
In some embodiments,  $R^{W4}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  $C_{1-6}$  alkyl.



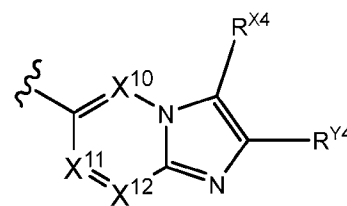
In some embodiments, B is of formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), formula (i), or formula (k):



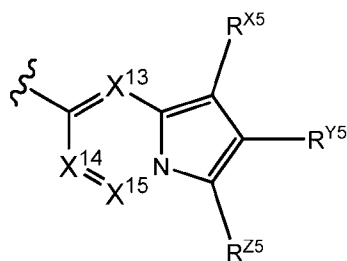
(a)



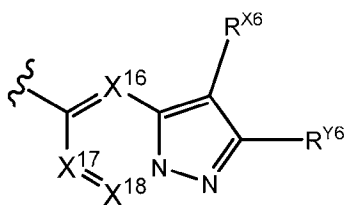
(c)



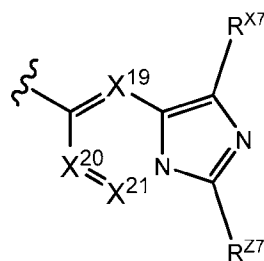
(d)



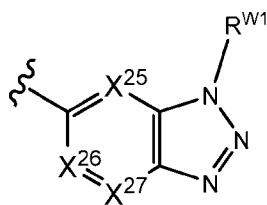
(e)



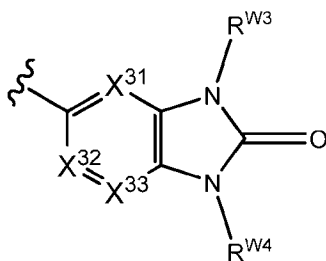
(f)



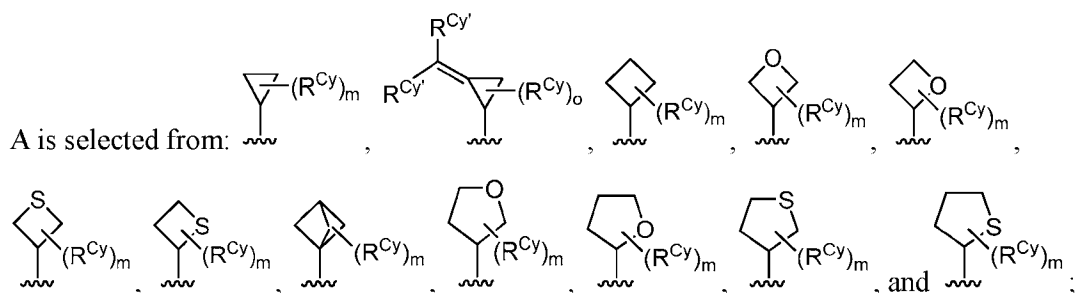
(g)



(i)



(k);



5 wherein

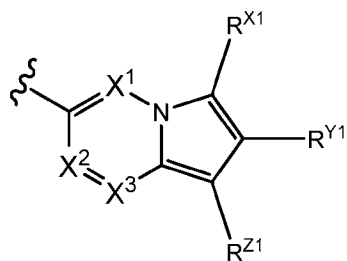
each  $R^{Cy'}$  is selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>,

$\text{NR}^{\text{c1}}\text{C}(\text{O})\text{R}^{\text{b1}}$ ,  $\text{NR}^{\text{c1}}\text{C}(\text{O})\text{OR}^{\text{a1}}$ ,  $\text{NR}^{\text{c1}}\text{C}(\text{O})\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{NR}^{\text{c1}}\text{S}(\text{O})\text{R}^{\text{b1}}$ ,  $\text{NR}^{\text{c1}}\text{S}(\text{O})_2\text{R}^{\text{b1}}$ ,  
 $\text{NR}^{\text{c1}}\text{S}(\text{O})_2\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{S}(\text{O})\text{R}^{\text{b1}}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b1}}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ;

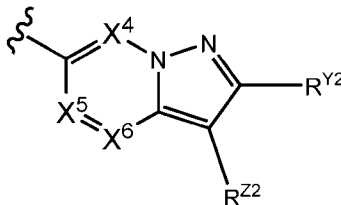
m is an integer selected from 0, 1, 2, 3, 4, and 5; and

o is an integer selected from 0, 1, 2, and 3.

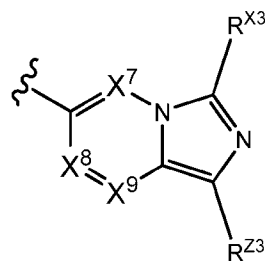
- 5 In some embodiments, B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (h):



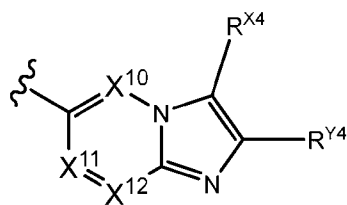
(a)



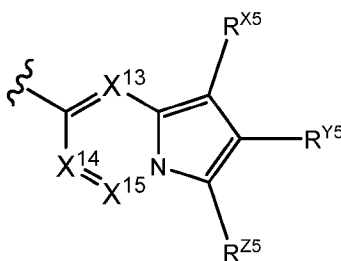
(b)



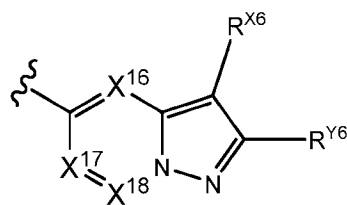
(c)



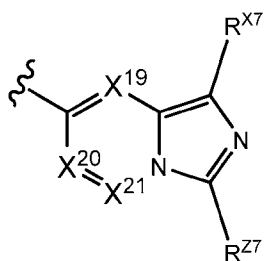
(d)



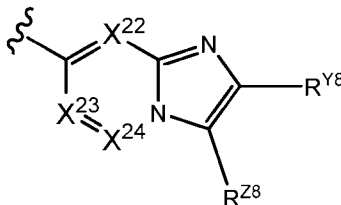
(e)



(f)

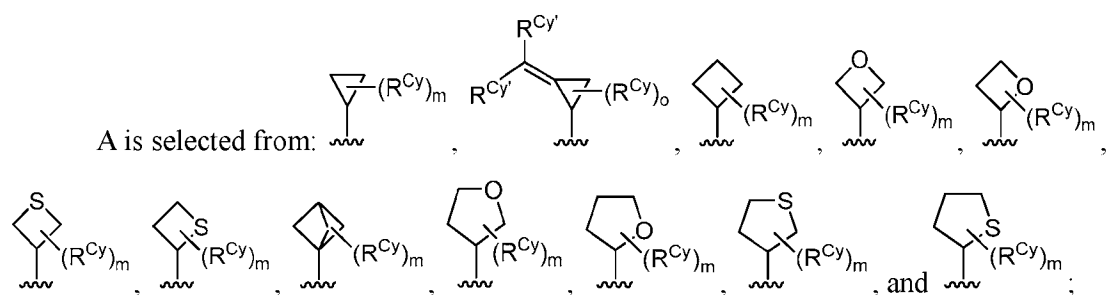


(g)



(h);



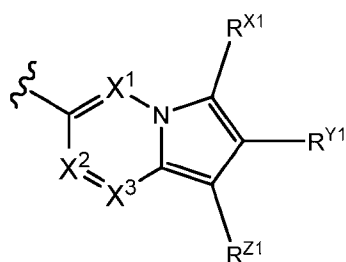


- each  $R^{Cy'}$  is selected from from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  
 5  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  
 $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  
 $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

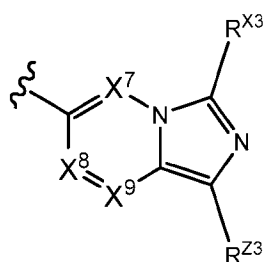
$m$  is an integer selected from 0, 1, 2, 3, 4, and 5; and

$o$  is an integer selected from 0, 1, 2, and 3.

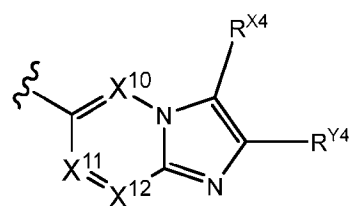
- 10 In some embodiments, B is of formula (a), formula (b), formula (c), formula (d),  
 formula (e), formula (f), formula (g), or formula (h):



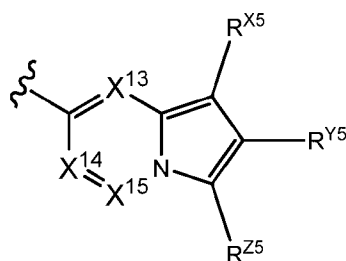
(a)



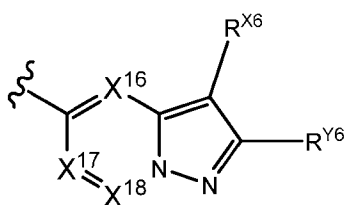
(c)



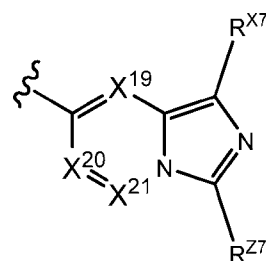
(d)



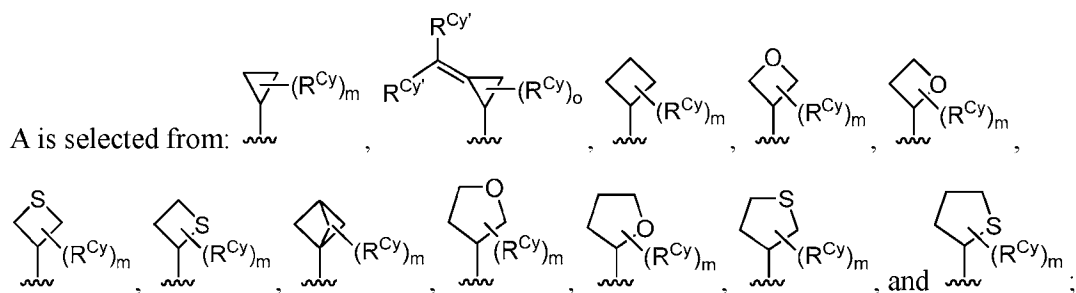
(e)



(f)



(g);



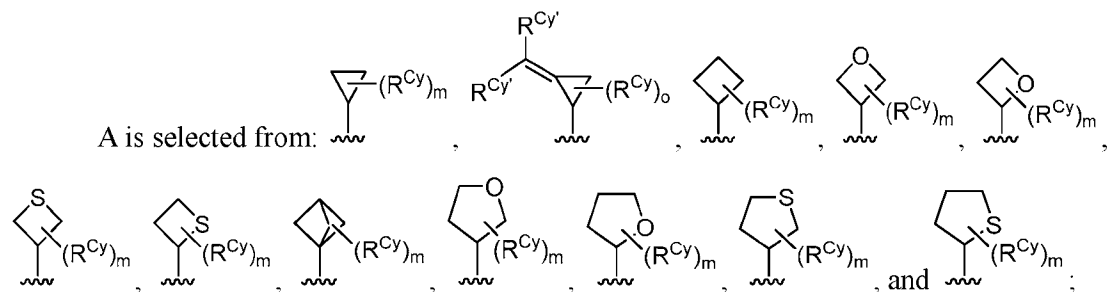
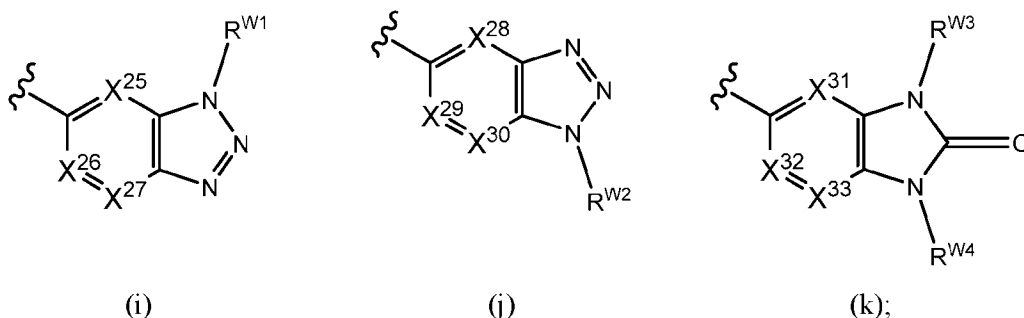
wherein

- each  $R^{Cy'}$  is selected from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  
 5  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  
 $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  
 $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

$m$  is an integer selected from 0, 1, 2, 3, 4, and 5; and

$o$  is an integer selected from 0, 1, 2, and 3.

- 10 In some embodiments, B is of formula (i), formula (j), or formula (k):



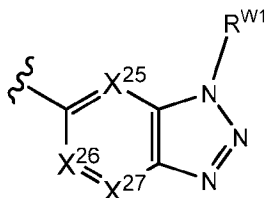
wherein

- each  $R^{Cy'}$  is selected from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  
 15  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  
 $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  
 $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

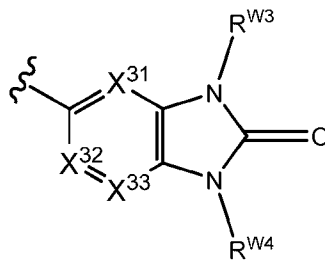
$m$  is an integer selected from 0, 1, 2, 3, 4, and 5; and

$o$  is an integer selected from 0, 1, 2, and 3.

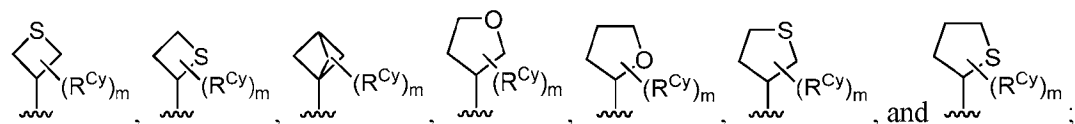
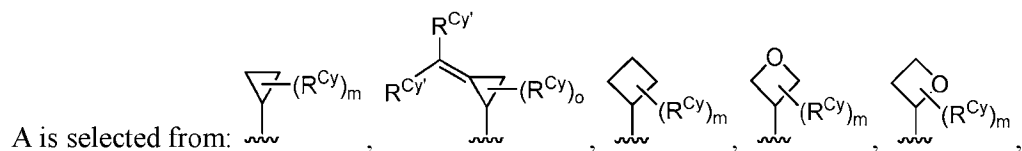
In some embodiments, B is of formula (i) or formula (k):



(i)



(k):



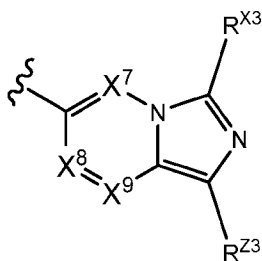
wherein

- 5 each  $R^{Cy'}$  is selected from from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

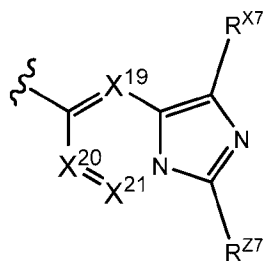
$m$  is an integer selected from 0, 1, 2, 3, 4, and 5; and

- 10  $o$  is an integer selected from 0, 1, 2, and 3.

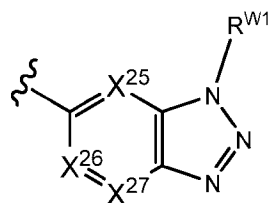
In some embodiments, B is of formula (c), formula (g), formula (i), formula (j), or formula (k):



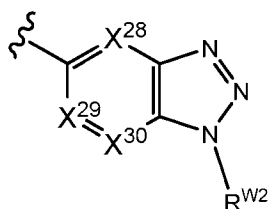
(c)



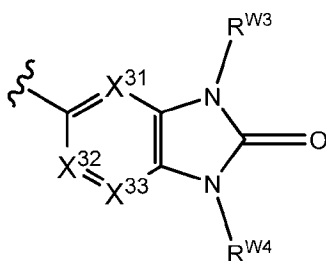
(g)



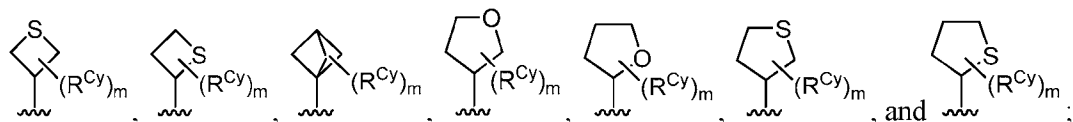
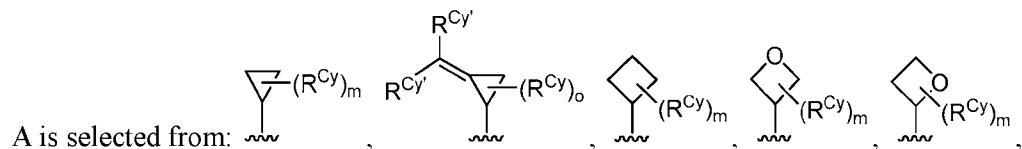
(i)



(j)



(k);



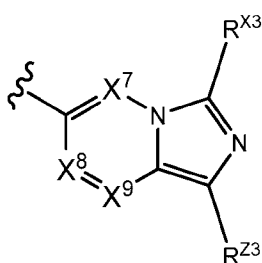
wherein

- each  $R^{Cy'}$  is selected from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  
 5  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  
 $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  
 $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

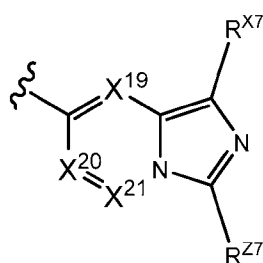
$m$  is an integer selected from 0, 1, 2, 3, 4, and 5; and

$o$  is an integer selected from 0, 1, 2, and 3.

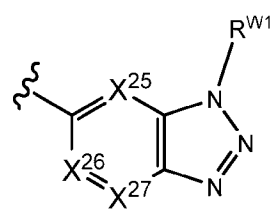
- 10 In some embodiments, B is of formula (c), formula (g), formula (i), formula (j), or formula (k):



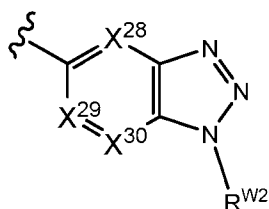
(c)



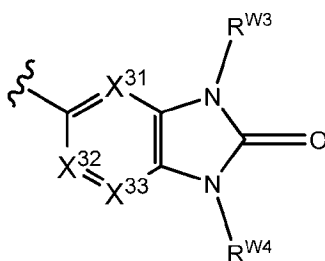
(g)



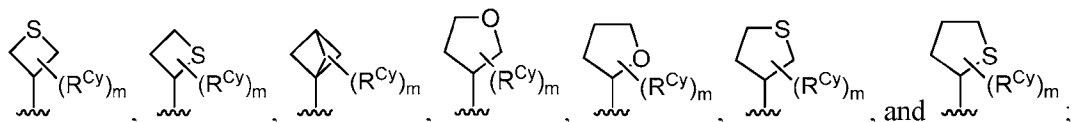
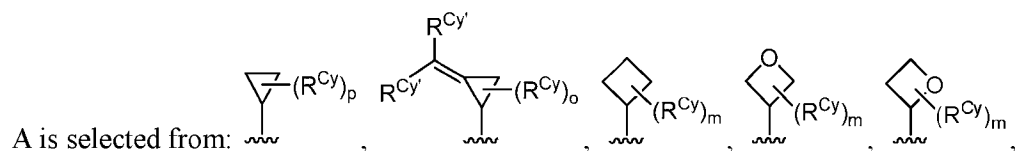
(i)



(j)



(k);



wherein

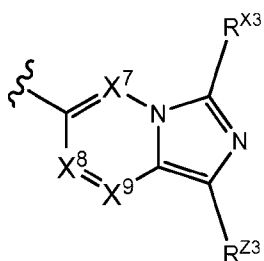
- each  $R^{Cy'}$  is selected from from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  
 5  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  
 $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  
 $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

$m$  is an integer selected from 0, 1, 2, 3, 4, and 5;

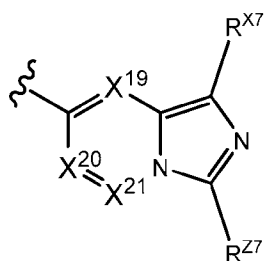
$o$  is an integer selected from 0, 1, 2, and 3; and

- 10  $p$  is an integer selected from 0, 2, 3, 4, and 5.

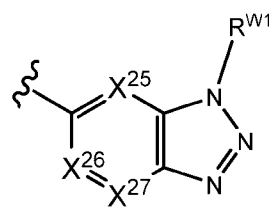
In some embodiments, B is of formula (c), formula (g), formula (i), or formula (k):



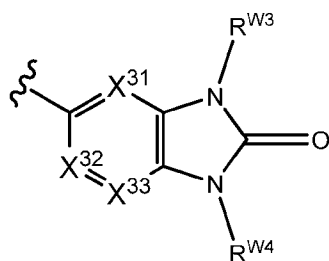
(c)



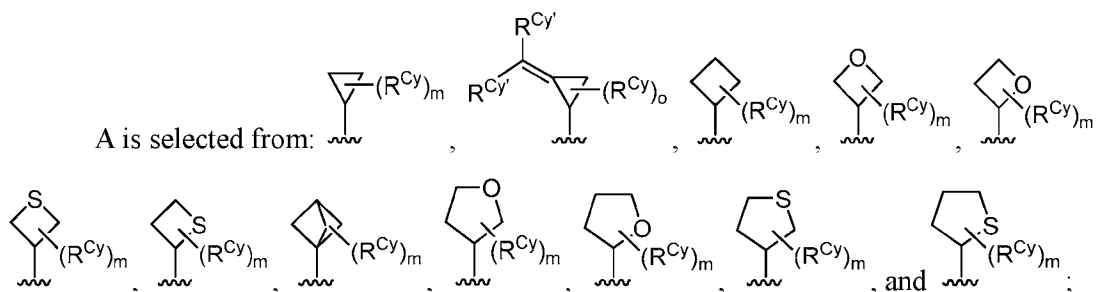
(g)



(i)



(k);



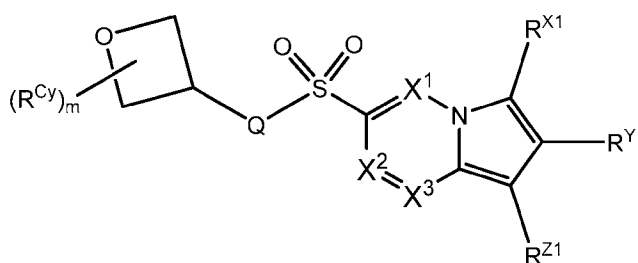
wherein

- each  $R^{Cy'}$  is selected from from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  
 5  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  
 $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  
 $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

$m$  is an integer selected from 0, 1, 2, 3, 4, and 5; and

$o$  is an integer selected from 0, 1, 2, and 3.

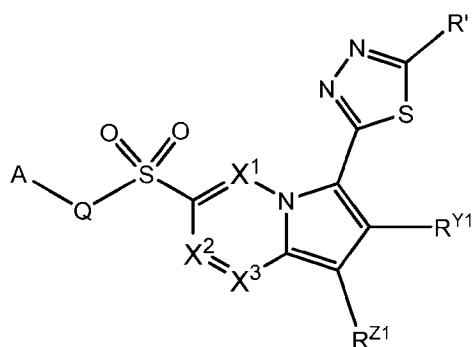
- 10 In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula II-A:



II-A

or a pharmaceutically acceptable salt thereof.

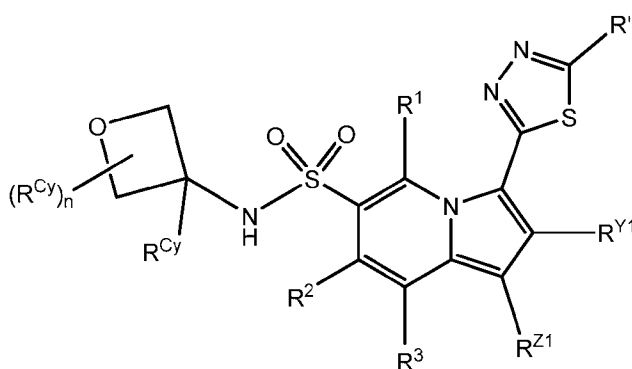
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula II-B:



II-B

or a pharmaceutically acceptable salt thereof.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula II-1:

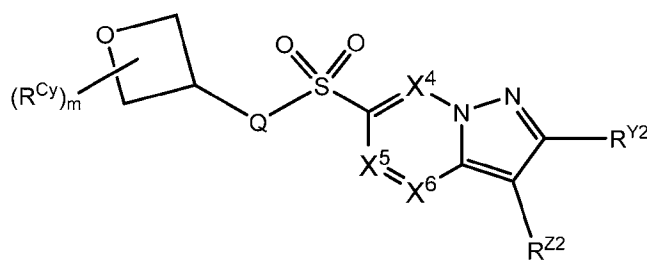


II-1

or a pharmaceutically acceptable salt thereof; wherein n is an integer selected from 0, 1, 2, 3,

5 and 4.

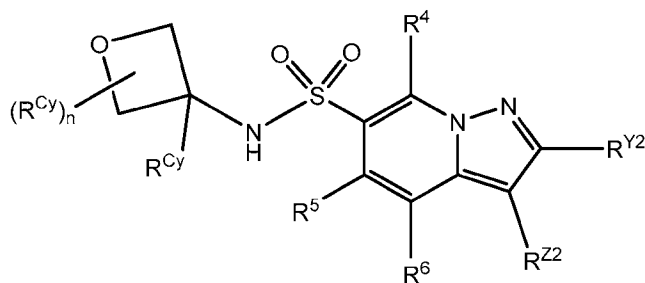
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula III-A:



III-A

or a pharmaceutically acceptable salt thereof.

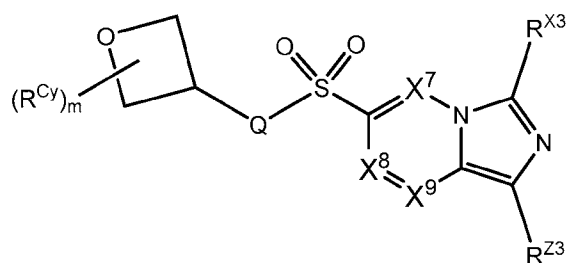
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula III-B:



III-1

or a pharmaceutically acceptable salt thereof; wherein n is an integer selected from 0, 1, 2, 3, and 4.

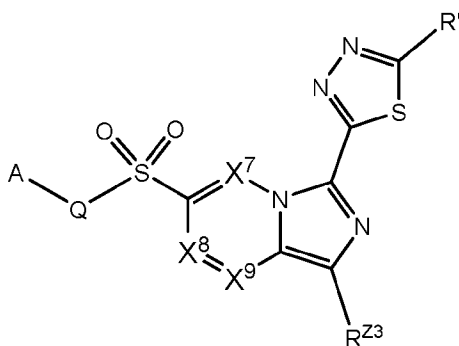
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula IV-A:



IV-A

5 or a pharmaceutically acceptable salt thereof.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula IV-B:



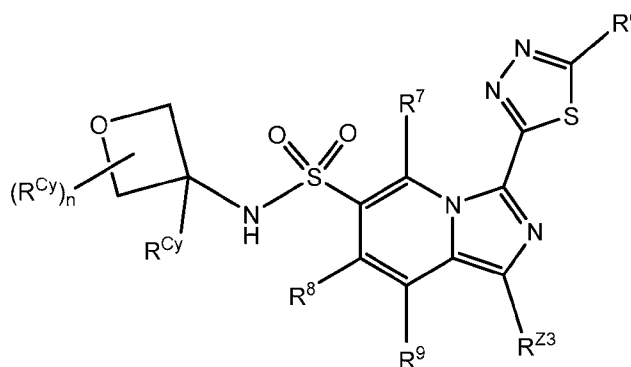
IV-B

or a pharmaceutically acceptable salt thereof.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula IV-1:

10

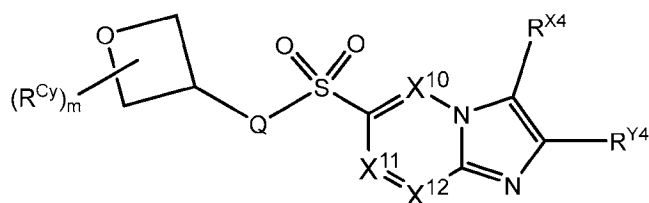




IV-1

or a pharmaceutically acceptable salt thereof, wherein n is an integer selected from 0, 1, 2, 3, and 4.

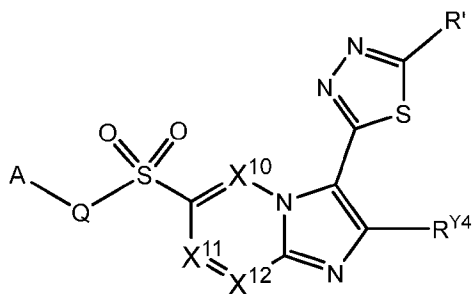
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula V-A:



V-A

5 or a pharmaceutically acceptable salt thereof.

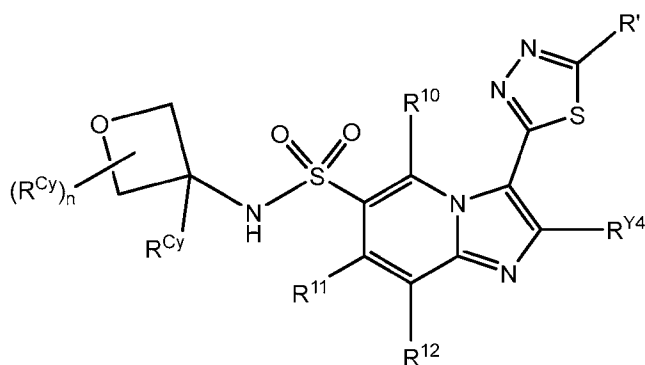
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula V-B:



V-B

or a pharmaceutically acceptable salt thereof.

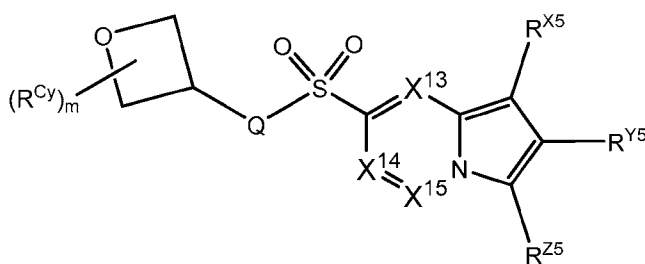
10 In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula V-1:



V-1

or a pharmaceutically acceptable salt thereof; wherein  $n$  is an integer selected from 0, 1, 2, 3, and 4.

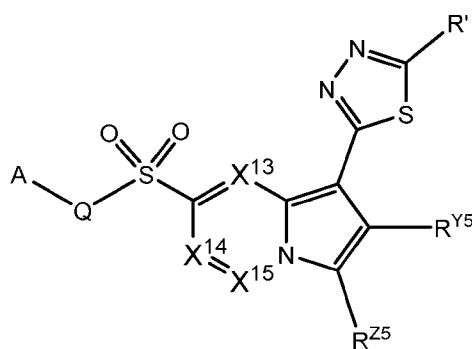
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula VI-A:



VI-A

5 or a pharmaceutically acceptable salt thereof.

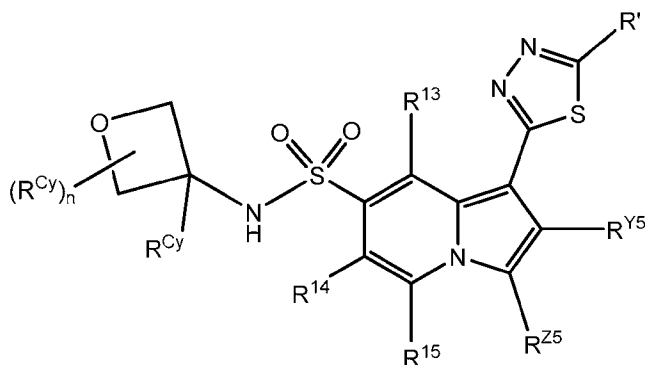
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula VI-B:



VI-B

or a pharmaceutically acceptable salt thereof.

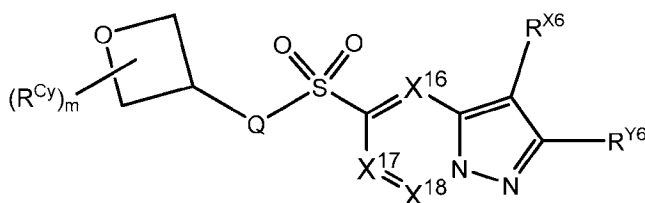
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula VI-1:



VI-1

or a pharmaceutically acceptable salt thereof, wherein n is an integer selected from 0, 1, 2, 3, and 4.

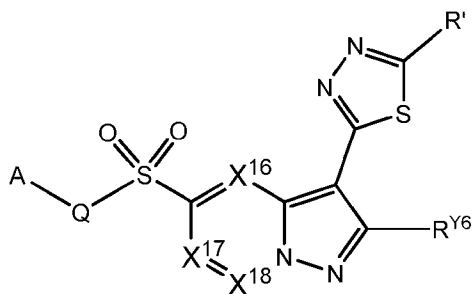
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula VII-A:



VII-A

5 or a pharmaceutically acceptable salt thereof.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula VII-B:

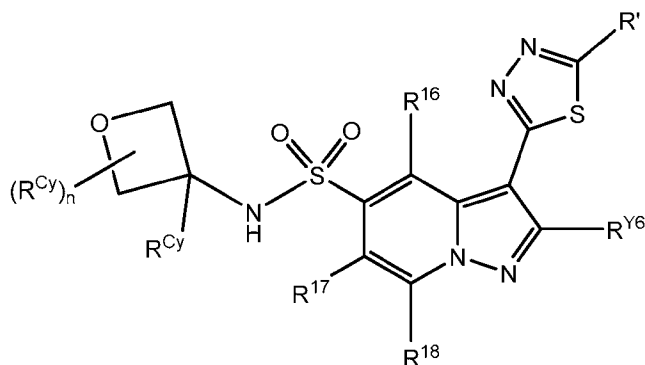


VII-B

or a pharmaceutically acceptable salt thereof.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula VII-1:

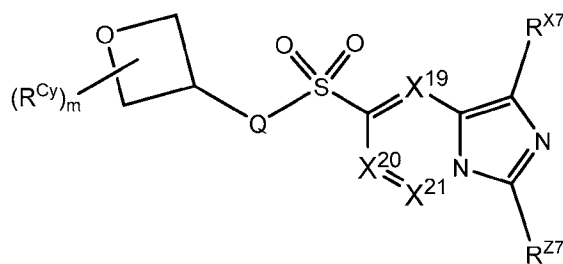
10



VII-1

or a pharmaceutically acceptable salt thereof, wherein n is an integer selected from 0, 1, 2, 3, and 4.

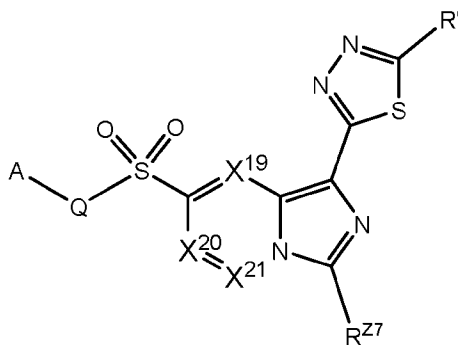
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula VIII-A:



VIII-A

5 or a pharmaceutically acceptable salt thereof.

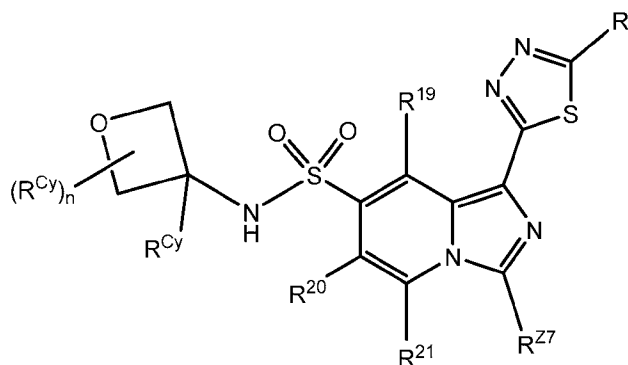
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula VIII-B:



VIII-B

or a pharmaceutically acceptable salt thereof.

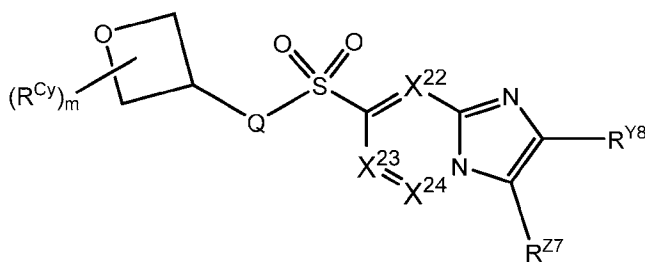
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula VIII-1:



VIII-1

or a pharmaceutically acceptable salt thereof; wherein n is an integer selected from 0, 1, 2, 3, and 4.

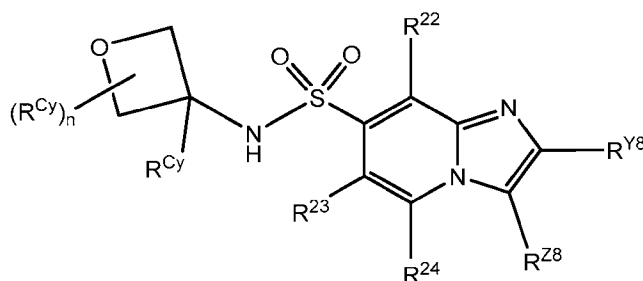
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula IX-A:



IX-A

5 or a pharmaceutically acceptable salt thereof.

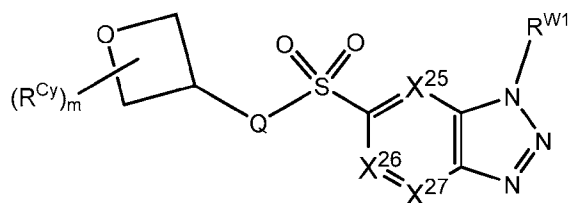
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula IX-1:



IX-1

or a pharmaceutically acceptable salt thereof; wherein n is an integer selected from 0, 1, 2, 3, and 4.

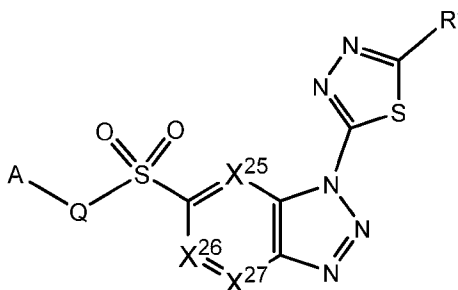
10 In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula X-A:



X-A

or a pharmaceutically acceptable salt thereof.

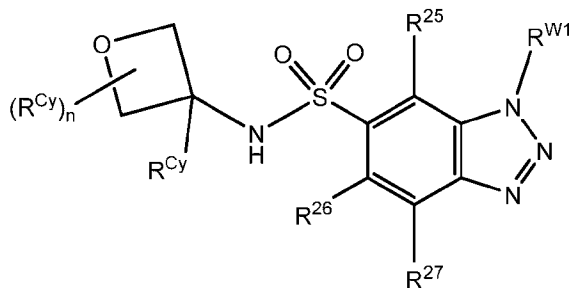
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula X-B:



X-B

or a pharmaceutically acceptable salt thereof.

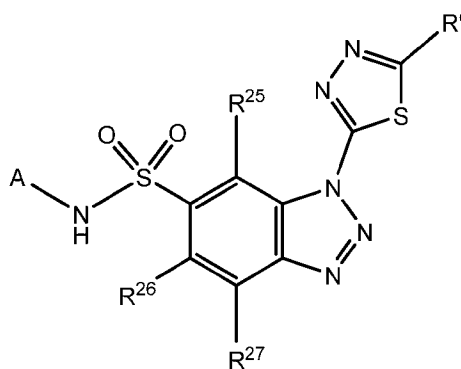
5 In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula X-1:



X-1

or a pharmaceutically acceptable salt thereof, wherein n is an integer selected from 0, 1, 2, 3, and 4.

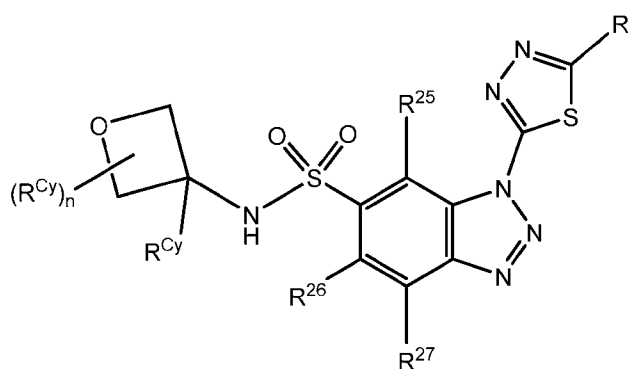
10 In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula X-2:



X-2

or a pharmaceutically acceptable salt thereof, wherein n is an integer selected from 0, 1, 2, 3, and 4.

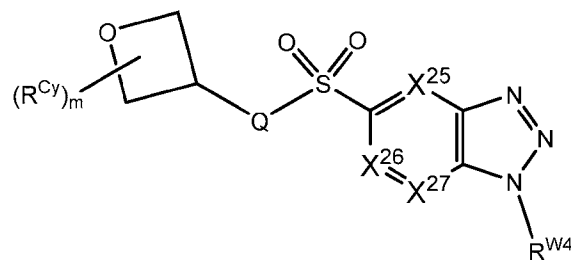
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula X-3:



X-3

- 5 or a pharmaceutically acceptable salt thereof, wherein n is an integer selected from 0, 1, 2, 3, and 4.

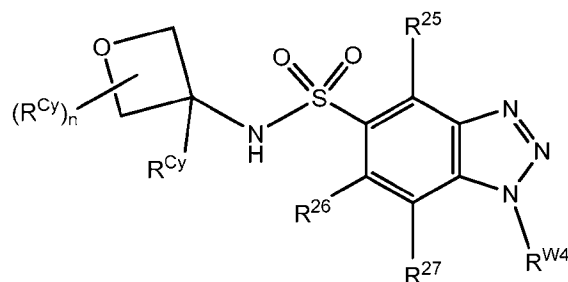
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula XI-A:



XI-A

or a pharmaceutically acceptable salt thereof.

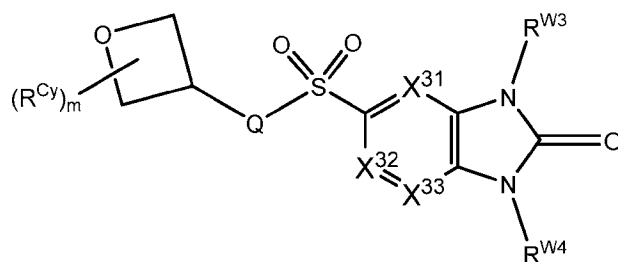
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula XI-1:



XI-1

or a pharmaceutically acceptable salt thereof; wherein n is an integer selected from 0, 1, 2, 3, and 4.

- 5 In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula XII-A:



XII-A

or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound is of Formula XII-A and Q is NH.

- In some embodiments, the compound is of Formula XII-A and  $R^{Cy}$  is selected from  
 10  $C_{1-6}$  alkyl and  $C_{1-6}$  haloalkyl. In some embodiments, the compound is of Formula XII-A and  $R^{Cy}$  is  $C_{1-6}$  alkyl. In some embodiments, the compound is of Formula XII-A and  $R^{Cy}$  is  $C_{1-6}$  haloalkyl. In some embodiments, the compound is of Formula XII-A and  $R^{Cy}$  is methyl. In some embodiments, the compound is of Formula XII-A and  $R^{Cy}$  is fluoromethyl.

In some embodiments, the compound is of Formula XII-A and m is 1.

- 15 In some embodiments, the compound is of Formula XII-A and  $X^{31}$  is  $CR^{31}$ .  
 In some embodiments, the compound is of Formula XII-A and  $X^{31}$  is CH.  
 In some embodiments, the compound is of Formula XII-A and  $X^{32}$  is  $CR^{32}$ .  
 In some embodiments, the compound is of Formula XII-A and  $X^{32}$  is CH.  
 In some embodiments, the compound is of Formula XII-A and  $X^{33}$  is  $CR^{33}$ .



In some embodiments, the compound is of Formula XII-A and CR<sup>33</sup> is 4-10 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-A and CR<sup>33</sup> is 6-9 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-A and CR<sup>33</sup> is 6 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-A and CR<sup>33</sup> is 7 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-A and CR<sup>33</sup> is 9 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-A and CR<sup>33</sup> is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>m</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, the compound is of Formula XII-A and CR<sup>33</sup> is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>m</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, the compound is of Formula XII-A and CR<sup>33</sup> is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> alkyl, (CH<sub>2</sub>)<sub>m</sub>OR<sup>a2</sup>, C(O)R<sup>b2</sup>, and C(O)NR<sup>c2</sup>R<sup>d2</sup>.

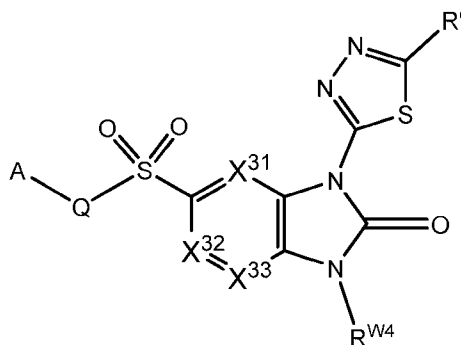
In some embodiments, the compound is of Formula XII-A and R<sup>W3</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 R', selected from halo, OR<sup>a3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, and CN.

In some embodiments, the compound is of Formula XII-A and R<sup>W4</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 C<sub>1-6</sub> alkyl.

In some embodiments, the compound is of Formula XII-A and R<sup>W3</sup> and R<sup>W4</sup> are each independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4 R'.

In some embodiments, the compound is of Formula XII-A and R<sup>W3</sup> is selected from H, C<sub>1-6</sub> alkyl, and C<sub>3-7</sub> cycloalkyl, wherein the C<sub>1-6</sub> alkyl and C<sub>3-7</sub> cycloalkyl are optionally substituted with 1, 2, 3, or 4 R'; and R<sup>W4</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 R'.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula XII-B:



XII-B

or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound is of Formula XII-B and Q is NH.

5 In some embodiments, the compound is of Formula XII-B and R<sup>Cy</sup> is selected from C<sub>1-6</sub> alkyl and C<sub>1-6</sub> haloalkyl. In some embodiments, the compound is of Formula XII-B and R<sup>Cy</sup> is C<sub>1-6</sub> alkyl. In some embodiments, the compound is of Formula XII-B and R<sup>Cy</sup> is C<sub>1-6</sub> haloalkyl. In some embodiments, the compound is of Formula XII-B and R<sup>Cy</sup> is methyl. In some embodiments, the compound is of Formula XII-B and R<sup>Cy</sup> is fluoromethyl.

10 In some embodiments, the compound is of Formula XII-B and m is 1.

In some embodiments, the compound is of Formula XII-B and X<sup>31</sup> is CR<sup>31</sup>.

In some embodiments, the compound is of Formula XII-B and X<sup>31</sup> is CH.

In some embodiments, the compound is of Formula XII-B and X<sup>32</sup> is CR<sup>32</sup>.

In some embodiments, the compound is of Formula XII-B and X<sup>32</sup> is CH.

15 In some embodiments, the compound is of Formula XII-B and X<sup>33</sup> is CR<sup>33</sup>.

In some embodiments, the compound is of Formula XII-B and CR<sup>33</sup> is 4-10 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-B and CR<sup>33</sup> is 6-9 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-B and CR<sup>33</sup> is 6 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-B and CR<sup>33</sup> is 7 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-B and CR<sup>33</sup> is 9 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-B and CR<sup>33</sup> is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-

20

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C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>m</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, the compound is of

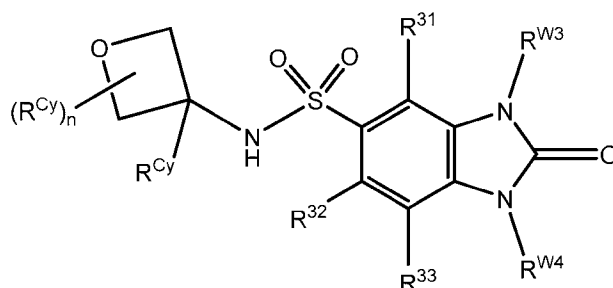
- 5 Formula XII-B and CR<sup>33</sup> is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>m</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>. In some embodiments, the compound is of Formula XII-B and
- 10 CR<sup>33</sup> is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> alkyl, (CH<sub>2</sub>)<sub>m</sub>OR<sup>a2</sup>, C(O)R<sup>b2</sup>, and C(O)NR<sup>c2</sup>R<sup>d2</sup>.

In some embodiments, the compound is of Formula XII-B and R<sup>W3</sup> is C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 R', selected from halo, OR<sup>a3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, and CN.

- 15 In some embodiments, the compound is of Formula XII-B and R' is C<sub>1-6</sub> haloalkyl.

In some embodiments, the compound is of Formula XII-B and R<sup>W3</sup> is selected from H, C<sub>1-6</sub> alkyl, and C<sub>3-7</sub> cycloalkyl, wherein the C<sub>1-6</sub> alkyl and C<sub>3-7</sub> cycloalkyl are optionally substituted with 1, 2, 3, or 4 R'; and R' is C<sub>1-6</sub> haloalkyl.

- In some embodiments, provided herein is a compound of Formula (I), or a
- 20 pharmaceutically acceptable salt thereof, having Formula XII-1:



XII-1

or a pharmaceutically acceptable salt thereof; wherein n is an integer selected from 0, 1, 2, 3, and 4.

- In some embodiments, the compound is of Formula XII-C and R<sup>Cy</sup> is selected from C<sub>1-6</sub> alkyl and C<sub>1-6</sub> haloalkyl. In some embodiments, the compound is of Formula XII-A and
- 25 R<sup>Cy</sup> is C<sub>1-6</sub> alkyl. In some embodiments, the compound is of Formula XII-C and R<sup>Cy</sup> is C<sub>1-6</sub>

haloalkyl. In some embodiments, the compound is of Formula XII-C and  $R^{Cy}$  is methyl. In some embodiments, the compound is of Formula XII-C and  $R^{Cy}$  is fluoromethyl.

In some embodiments, the compound is of Formula XII-C and  $n$  is 0.

In some embodiments, the compound is of Formula XII-C and  $R^{31}$  is H.

5 In some embodiments, the compound is of Formula XII-C and  $R^{32}$  is H.

In some embodiments, the compound is of Formula XII-C and  $R^{33}$  is 4-10 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-C and  $R^{33}$  is 6-9 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-C and  $R^{33}$  is 6 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-C and  $R^{33}$  is 7 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-C and  $R^{33}$  is 9 membered heterocycloalkyl. In some embodiments, the compound is of Formula XII-C and  $R^{33}$  is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $(CH_2)_mOR^{a2}$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments, the compound is of Formula XII-C and  $R^{33}$  is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl, CN,  $NO_2$ ,  $(CH_2)_mOR^{a2}$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ . In some embodiments, the compound is of Formula XII-C and  $R^{33}$  is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, or 4 substituents independently selected from  $C_{1-6}$  alkyl,  $(CH_2)_mOR^{a2}$ ,  $C(O)R^{b2}$ , and  $C(O)NR^{c2}R^{d2}$ .

In some embodiments, the compound is of Formula XII-C and  $R^{W3}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4  $R^7$ , selected from halo,  $OR^{a3}$ ,  $NR^{c3}R^{d3}$ , and CN.

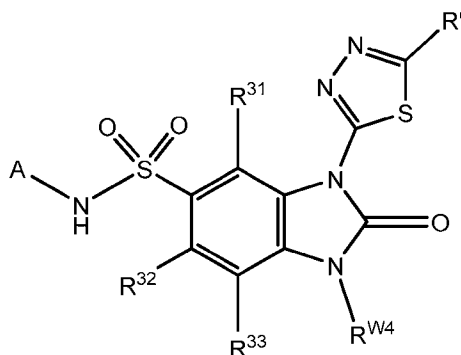
30 In some embodiments, the compound is of Formula XII-C and  $R^{W4}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  $C_{1-6}$  alkyl.

In some embodiments, the compound is of Formula XII-C and  $R^{W3}$  and  $R^{W4}$  are each independently selected from H,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{3-7}$  cycloalkyl, and 5-membered

heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4 R<sup>'</sup>.

In some embodiments, the compound is of Formula XII-C and R<sup>W3</sup> is selected from H, C<sub>1-6</sub> alkyl, and C<sub>3-7</sub> cycloalkyl, wherein the C<sub>1-6</sub> alkyl and C<sub>3-7</sub> cycloalkyl are optionally substituted with 1, 2, 3, or 4 R<sup>'</sup>; and R<sup>W4</sup> is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 R<sup>'</sup>.

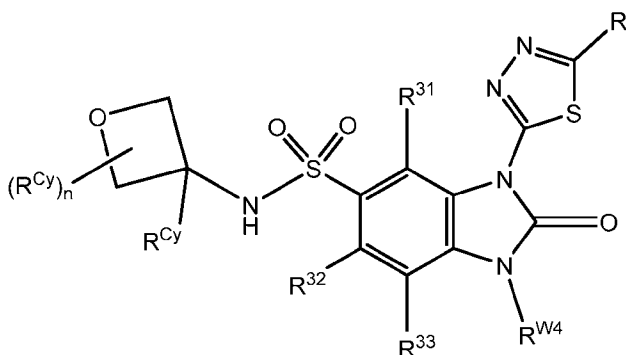
In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula XII-2:



XII-2

or a pharmaceutically acceptable salt thereof; wherein n is an integer selected from 0, 1, 2, 3, and 4.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, having Formula XII-3:



XII-3

or a pharmaceutically acceptable salt thereof; wherein n is an integer selected from 0, 1, 2, 3, and 4.

In some embodiments, m is 0. In some embodiments, m is 1. In some embodiments, m is 2. In some embodiments, m is 3. In some embodiments, m is 4. In some embodiments, m is 5. In some embodiments, m is an integer selected from 0, 2, 3, 4, and 5.

In some embodiments, n is 0. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4.

In some embodiments, o is 0. In some embodiments, o is 1. In some embodiments, o is 2. In some embodiments, o is 3.

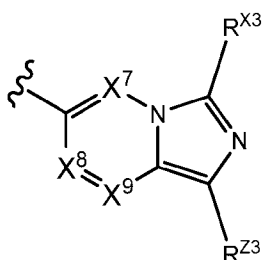
5 In some embodiments, p is 0. In some embodiments, p is 2. In some embodiments, p is 3. In some embodiments, p is 4. In some embodiments, p is 5.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, wherein:

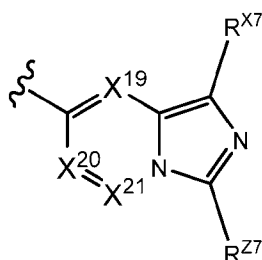
Q is NH or CH<sub>2</sub>;

10 A is Cy or Cy-C<sub>1-4</sub> alkyl-;

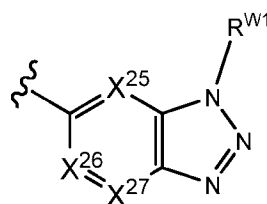
B is of formula (c), formula (g), formula (i), formula (j), or formula (k):



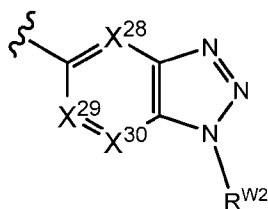
(c)



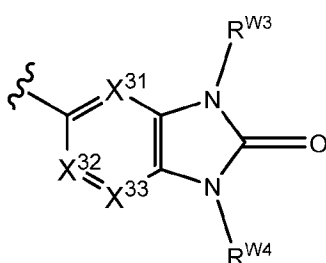
(g)



(i)



(j)



(k);

X<sup>7</sup> is N or CR<sup>7</sup>;

X<sup>8</sup> is N or CR<sup>8</sup>;

X<sup>9</sup> is N or CR<sup>9</sup>;

15 X<sup>19</sup> is N or CR<sup>19</sup>;

X<sup>20</sup> is N or CR<sup>20</sup>;

X<sup>21</sup> is N or CR<sup>21</sup>;

X<sup>25</sup> is N or CR<sup>25</sup>;

X<sup>26</sup> is N or CR<sup>26</sup>;

$X^{27}$  is N or  $CR^{27}$ ;

$X^{28}$  is N or  $CR^{28}$ ;

$X^{29}$  is N or  $CR^{29}$ ;

$X^{30}$  is N or  $CR^{30}$ ;

5  $X^{31}$  is N or  $CR^{31}$ ;

$X^{32}$  is N or  $CR^{32}$ ;

$X^{33}$  is N or  $CR^{33}$ ;

wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;

wherein no more than two of  $X^{19}$ ,  $X^{20}$ , and  $X^{21}$  are simultaneously N;

10 wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

wherein no more than two of  $X^{28}$ ,  $X^{29}$ , and  $X^{30}$  are simultaneously N;

wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each Cy is independently selected from  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, 15 or 5 substituents independently selected from  $R^{Cy}$ ;

each  $R^{Cy}$  is independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ , wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl of  $R^{Cy}$  is optionally substituted by 1, 2, or 3 substituents 25 independently selected from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

30  $R^7$ ,  $R^8$ ,  $R^{19}$ ,  $R^{20}$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{28}$ ,  $R^{29}$ ,  $R^{31}$ , and  $R^{32}$  are each independently selected from H, halo, and  $C_{1-4}$  alkyl;

$R^9$ ,  $R^{21}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each independently selected from H, halo,  $OR^{a2}$ ,  $NR^{c2}R^{d2}$ ,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $R^9$ ,  $R^{21}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each optionally substituted

with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>q</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>,  
 5 C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>;

R<sup>X3</sup>, R<sup>X7</sup>, R<sup>Z3</sup>, and R<sup>Z7</sup> are each independently selected from H, halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered  
 10 heteroaryl of R<sup>X3</sup>, R<sup>X7</sup>, R<sup>Z3</sup>, and R<sup>Z7</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>,  
 15 C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>;

R<sup>W1</sup>, R<sup>W2</sup>, R<sup>W3</sup>, and R<sup>W4</sup> are each independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or  
 20 4 R<sup>\*</sup>;

each R<sup>\*</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered  
 25 heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and  
 30 S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>\*</sup> is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>,



OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>c3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>c3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>;

each R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>a1</sup>, R<sup>b1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>b3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is

- 5 independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>a1</sup>, R<sup>b1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>b3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>;
- 10

- or R<sup>c</sup> and R<sup>d</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>;
- 20

- or R<sup>c1</sup> and R<sup>d1</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>;
- 25

- or R<sup>c2</sup> and R<sup>d2</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>;
- 30

or  $R^{c3}$  and  $R^{d3}$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  
 5  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ,

or  $R^{c4}$  and  $R^{d4}$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  
 10  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ .

each  $R^{a4}$ ,  $R^{b4}$ ,  $R^{c4}$ , and  $R^{d4}$  is independently selected from H,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10  
 15 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, wherein said  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl are  
 20 each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino,  $NHC_{1-4}$  alkyl,  $N(C_{1-4}$  alkyl)<sub>2</sub>, halo,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy,  $C_{1-6}$  haloalkyl, and  $C_{1-6}$  haloalkoxy;

each  $R^e$ ,  $R^{e1}$ ,  $R^{e2}$ ,  $R^{e3}$ , and  $R^{e4}$  is independently selected from H,  $C_{1-4}$  alkyl, and CN;  
 and

25 q is an integer selected from 1, 2, 3, 4, 5, and 6;

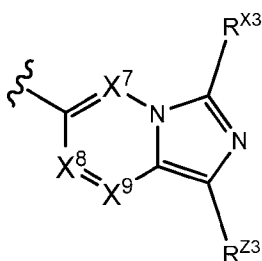
wherein when B is formula (c), formula (g), or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, wherein:

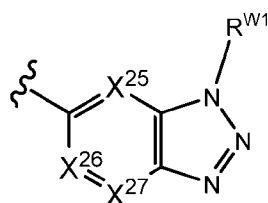
30 Q is NH or  $CH_2$ ;

A is Cy or Cy- $C_{1-4}$  alkyl-;

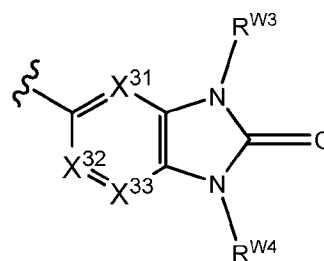
B is of formula (c), formula (i), or formula (k):



(c)



(i)



(k);

$X^7$  is N or CR<sup>7</sup>;

$X^8$  is N or CR<sup>8</sup>;

$X^9$  is N or CR<sup>9</sup>;

$X^{25}$  is N or CR<sup>25</sup>;

5  $X^{26}$  is N or CR<sup>26</sup>;

$X^{27}$  is N or CR<sup>27</sup>;

$X^{31}$  is N or CR<sup>31</sup>;

$X^{32}$  is N or CR<sup>32</sup>;

$X^{33}$  is N or CR<sup>33</sup>;

10 wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;

wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each Cy is independently selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered

heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently

15 selected from R<sup>Cy</sup>;

each R<sup>Cy</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, and NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of R<sup>Cy</sup> is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, and NR<sup>c1</sup>R<sup>d1</sup>;

20  $R^7$ ,  $R^8$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{31}$ , and  $R^{32}$  are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;

$R^9$ ,  $R^{27}$ , and  $R^{33}$  are each independently selected from H, halo, OR<sup>a2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $R^9$ ,  $R^{27}$ , and  $R^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>q</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, and C(O)OR<sup>a2</sup>;

$R^{X3}$  and  $R^{Z3}$  are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of  $R^{X3}$  and  $R^{Z3}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>,  
 5 C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>;

$R^{W1}$ ,  $R^{W2}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or  
 10 4 R<sup>7</sup>;

each R<sup>7</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, and NR<sup>c3</sup>R<sup>d3</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, and C<sub>6-10</sub> aryl of R<sup>7</sup> is optionally substituted with 1, 2, or 3 groups independently  
 15 selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, and NR<sup>c3</sup>R<sup>d3</sup>;

each R<sup>a1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>3-7</sub> cycloalkyl, and 4-10 membered heterocycloalkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, and 4-10 membered heterocycloalkyl of R<sup>a1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>c3</sup>,  
 20 and R<sup>d3</sup> is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-6</sub> haloalkyl, CN, and OR<sup>a4</sup>;

each R<sup>a4</sup> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, amino, NHC<sub>1-4</sub> alkyl, and N(C<sub>1-4</sub> alkyl)<sub>2</sub>;

q is an integer selected from 1, 2, 3, 4, 5, and 6;

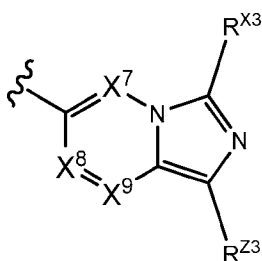
25 wherein when B is formula (c) or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, wherein:

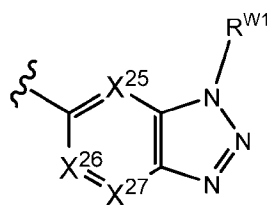
Q is NH;

30 A is Cy;

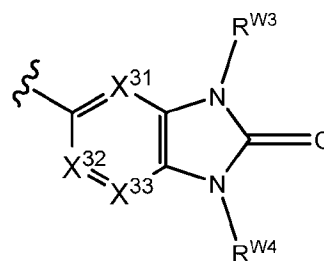
B is of formula (c), formula (i), or formula (k):



(c)



(i)



(k);

$X^7$  is  $CR^7$ ;

$X^8$  is  $CR^8$ ;

$X^9$  is  $CR^9$ ;

$X^{25}$  is  $CR^{25}$ ;

5  $X^{26}$  is  $CR^{26}$ ;

$X^{27}$  is  $CR^{27}$ ;

$X^{31}$  is  $CR^{31}$ ;

$X^{32}$  is  $CR^{32}$ ;

$X^{33}$  is  $CR^{33}$ ;

10 each Cy is independently selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>;

each R<sup>Cy</sup> is independently selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, and CN;

R<sup>7</sup>, R<sup>8</sup>, R<sup>25</sup>, R<sup>26</sup>, R<sup>31</sup>, and R<sup>32</sup> are each independently selected from H and halo;

15 R<sup>9</sup>, R<sup>27</sup>, and R<sup>33</sup> are each independently selected from H, halo, and 4-10 membered heterocycloalkyl, wherein 4-10 membered heterocycloalkyl of R<sup>9</sup>, R<sup>27</sup>, and R<sup>33</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> alkyl, (CH<sub>2</sub>)<sub>q</sub>OR<sup>a2</sup>, C(O)R<sup>b2</sup>, and C(O)NR<sup>c2</sup>R<sup>d2</sup>;

20 R<sup>X3</sup> and R<sup>Z3</sup> are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of R<sup>X3</sup> and R<sup>Z3</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> haloalkyl;

R<sup>W1</sup>, R<sup>W2</sup>, R<sup>W3</sup>, and R<sup>W4</sup> are each independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkynyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkynyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4 R<sup>\*</sup>;

25 each R<sup>\*</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkynyl, and C<sub>1-6</sub> haloalkyl, wherein the C<sub>1-6</sub> alkyl of R<sup>\*</sup> is optionally substituted with 1, 2, or 3 groups independently selected from OR<sup>a3</sup>;

each  $R^{a1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{c3}$ , and  $R^{d3}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>3-7</sub> cycloalkyl, and 4-10 membered heterocycloalkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>3-7</sub> cycloalkyl, and 4-10 membered heterocycloalkyl of  $R^{a1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{c3}$ , and  $R^{d3}$  is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from C<sub>1-6</sub> haloalkyl and  $OR^{a4}$ ;

each  $R^{a4}$  is independently selected from H, C<sub>1-6</sub> alkyl, and  $N(C_{1-4} \text{ alkyl})_2$ ;

q is 1;

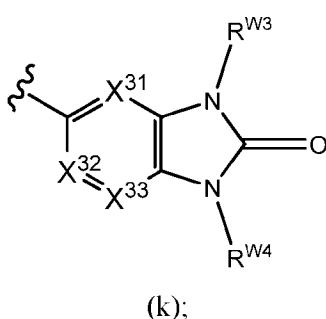
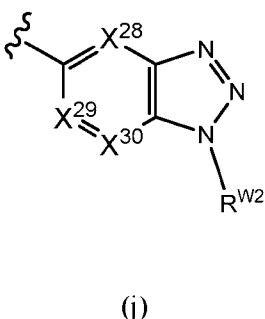
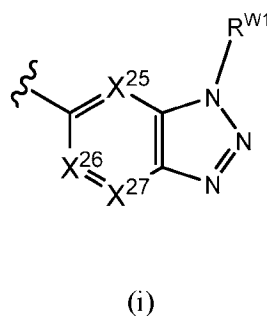
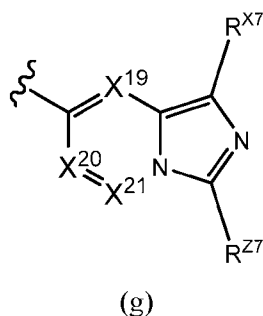
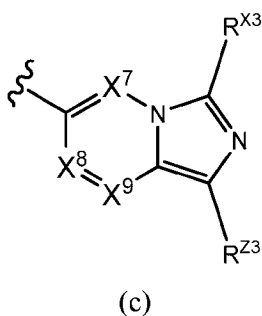
wherein when B is formula (c) or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, wherein:

Q is NH;

A is Cy or Cy-C<sub>1-4</sub> alkyl-;

B is of formula (c), formula (g), formula (i), formula (j), or formula (k):



$X^7$  is N or  $CR^7$ ;

$X^8$  is N or  $CR^8$ ;

$X^9$  is N or  $CR^9$ ;

$X^{19}$  is N or  $CR^{19}$ ;

$X^{20}$  is N or  $CR^{20}$ ;

$X^{21}$  is N or  $CR^{21}$ ;

$X^{25}$  is N or  $CR^{25}$ ;

$X^{26}$  is N or  $CR^{26}$ ;

$X^{27}$  is N or  $CR^{27}$ ;

5  $X^{28}$  is N or  $CR^{28}$ ;

$X^{29}$  is N or  $CR^{29}$ ;

$X^{30}$  is N or  $CR^{30}$ ;

$X^{31}$  is N or  $CR^{31}$ ;

$X^{32}$  is N or  $CR^{32}$ ;

10  $X^{33}$  is N or  $CR^{33}$ ;

wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;

wherein no more than two of  $X^{19}$ ,  $X^{20}$ , and  $X^{21}$  are simultaneously N;

wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

wherein no more than two of  $X^{28}$ ,  $X^{29}$ , and  $X^{30}$  are simultaneously N;

15 wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each  $Cy$  is independently selected from  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from  $R^{Cy}$ ;

each  $R^{Cy}$  is independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl, CN,  $NO_2$ ,  $OR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ , wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl of  $R^{Cy}$  is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

30  $R^7$ ,  $R^8$ ,  $R^{19}$ ,  $R^{20}$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{28}$ ,  $R^{29}$ ,  $R^{31}$ , and  $R^{32}$  are each independently selected from H, halo, and  $C_{1-4}$  alkyl;

$R^9$ ,  $R^{21}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each independently selected from H, halo,  $OR^{a2}$ ,  $NR^{c2}R^{d2}$ ,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-

10 membered heterocycloalkyl of  $R^9$ ,  $R^{21}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl, CN,  $NO_2$ ,  $(CH_2)_mOR^{a2}$ ,  $OR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  
 5  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ ,  
 $R^{X3}$ ,  $R^{X7}$ ,  $R^{Z3}$ , and  $R^{Z7}$  are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of  $R^{X3}$ ,  $R^{X7}$ ,  $R^{Z3}$ , and  $R^{Z7}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$   
 10 alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  
 15  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ ;

$R^{W1}$ ,  $R^{W2}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from H,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{3-7}$  cycloalkyl, and 5-membered heteroaryl, wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{3-7}$  cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4  $R^7$ ;  
 20 each  $R^7$  is independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl, CN,  $NO_2$ ,  $OR^{a3}$ ,  $SR^{a3}$ ,  $C(O)R^{b3}$ ,  $C(O)NR^{c3}R^{d3}$ ,  $C(O)OR^{a3}$ ,  $OC(O)R^{b3}$ ,  $OC(O)NR^{c3}R^{d3}$ ,  $C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}R^{d3}$ ,  $NR^{c3}C(O)R^{b3}$ ,  $NR^{c3}C(O)OR^{a3}$ ,  $NR^{c3}C(O)NR^{c3}R^{d3}$ ,  $NR^{c3}S(O)R^{b3}$ ,  $NR^{c3}S(O)_2R^{b3}$ ,  $NR^{c3}S(O)_2NR^{c3}R^{d3}$ ,  $S(O)R^{b3}$ ,  $S(O)NR^{c3}R^{d3}$ ,  $S(O)_2R^{b3}$ , and  $S(O)_2NR^{c3}R^{d3}$ , wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$   
 25 alkynyl,  $C_{1-6}$  haloalkyl, and  $C_{6-10}$  aryl of  $R^7$  is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN,  $NO_2$ ,  $OR^{a3}$ ,  $SR^{a3}$ ,  $C(O)R^{b3}$ ,  $C(O)NR^{c3}R^{d3}$ ,  $C(O)OR^{a3}$ ,  $OC(O)R^{b3}$ ,  $OC(O)NR^{c3}R^{d3}$ ,  $C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}R^{d3}$ ,  $NR^{c3}C(O)R^{b3}$ ,  $NR^{c3}C(O)OR^{a3}$ ,  $NR^{c3}C(O)NR^{c3}R^{d3}$ ,  $NR^{c3}S(O)R^{b3}$ ,  $NR^{c3}S(O)_2R^{b3}$ ,  $NR^{c3}S(O)_2NR^{c3}R^{d3}$ ,  $S(O)R^{b3}$ ,  $S(O)NR^{c3}R^{d3}$ ,  $S(O)_2R^{b3}$ , and  $S(O)_2NR^{c3}R^{d3}$ ;

30 each  $R^{a1}$ ,  $R^{b1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{b3}$ ,  $R^{c3}$ , and  $R^{d3}$  is independently selected from H,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, , wherein said  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl, and  $C_{2-6}$  alkynyl of  $R^{a1}$ ,  $R^{b1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{b3}$ ,  $R^{c3}$ , and  $R^{d3}$  is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl,  $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,



$C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  
 $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  
 $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ;

each  $R^{a4}$ ,  $R^{b4}$ ,  $R^{c4}$ , and  $R^{d4}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl,

- 5 C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl, wherein said C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl are each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkyl, and C<sub>1-6</sub> haloalkoxy; and

each  $R^e$ ,  $R^{e1}$ ,  $R^{e2}$ ,  $R^{e3}$ , and  $R^{e4}$  is independently selected from H, C<sub>1-4</sub> alkyl, and CN;

and

- 10 q is an integer selected from 1, 2, 3, 4, 5, and 6;

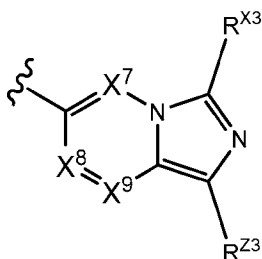
wherein when B is formula (c), formula (g), or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, wherein:

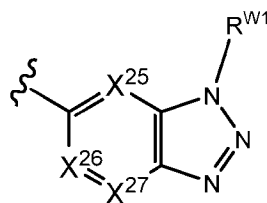
- 15 Q is NH;

A is Cy or Cy-C<sub>1-4</sub> alkyl-;

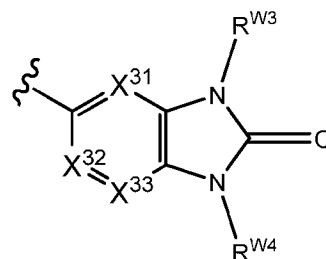
B is a group of formula (c), formula (i) or formula (k):



(c)



(i)



(k);

$X^7$  is N or CR<sup>7</sup>;

$X^8$  is N or CR<sup>8</sup>;

- 20  $X^9$  is N or CR<sup>9</sup>;

$X^{25}$  is N or CR<sup>25</sup>;

$X^{26}$  is N or CR<sup>26</sup>;

$X^{27}$  is N or CR<sup>27</sup>;

$X^{31}$  is N or CR<sup>31</sup>;

- 25  $X^{32}$  is N or CR<sup>32</sup>;

$X^{33}$  is N or CR<sup>33</sup>;

wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N; wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each Cy is independently selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from  $R^{Cy}$ ;

each  $R^{Cy}$  is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, and NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of  $R^{Cy}$  is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, and NR<sup>c1</sup>R<sup>d1</sup>;

$R^7$ ,  $R^8$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{31}$ , and  $R^{32}$  are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;

$R^9$ ,  $R^{27}$ , and  $R^{33}$  are each independently selected from H, halo, OR<sup>a2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $R^9$ ,  $R^{27}$ , and  $R^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>m</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, and C(O)OR<sup>a2</sup>;

$R^{X3}$  and  $R^{Z3}$  are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of  $R^{X3}$  and  $R^{Z3}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>c2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>c2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>;

$R^{W1}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4 R<sup>'</sup>;

each R<sup>'</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, and NR<sup>c3</sup>R<sup>d3</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, and C<sub>6-10</sub> aryl of R<sup>'</sup> is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, and NR<sup>c3</sup>R<sup>d3</sup>;

each R<sup>a1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl; and

q is an integer selected from 1, 2, 3, 4, 5, and 6;

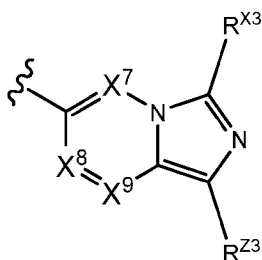
wherein when B is formula (c) or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

In some embodiments, provided herein is a compound of Formula (I), or a  
5 pharmaceutically acceptable salt thereof, wherein:

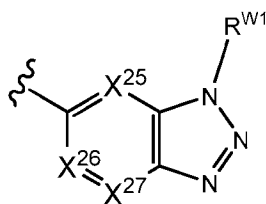
Q is NH;

A is Cy;

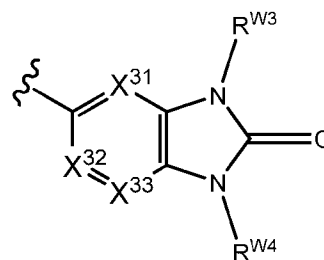
B is a group of formula (c), formula (i), or formula (k):



(c)



(i)



(k);

X<sup>7</sup> is CR<sup>7</sup>;

10 X<sup>8</sup> is CR<sup>8</sup>;

X<sup>9</sup> is CR<sup>9</sup>;

X<sup>25</sup> is CR<sup>25</sup>;

X<sup>26</sup> is CR<sup>26</sup>;

X<sup>27</sup> is CR<sup>27</sup>;

15 X<sup>31</sup> is CR<sup>31</sup>;

X<sup>32</sup> is CR<sup>32</sup>;

X<sup>33</sup> is CR<sup>33</sup>;

each Cy is independently selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered  
heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently  
20 selected from R<sup>Cy</sup>;

each R<sup>Cy</sup> is independently selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, and CN;

R<sup>7</sup>, R<sup>8</sup>, R<sup>25</sup>, R<sup>26</sup>, R<sup>31</sup>, and R<sup>32</sup> are each independently selected from H and halo;

R<sup>9</sup>, R<sup>27</sup>, and R<sup>33</sup> are each independently selected from H, halo, and 4-10 membered  
heterocycloalkyl, wherein said 4-10 membered heterocycloalkyl of R<sup>9</sup>, R<sup>27</sup>, and R<sup>33</sup> are each  
25 optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> alkyl,  
C(O)NR<sup>c2</sup>R<sup>d2</sup>, (CH<sub>2</sub>)<sub>m</sub>OR<sup>a2</sup>, and C(O)R<sup>b2</sup>;

$R^{X3}$  and  $R^{Z3}$  are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of  $R^{X3}$  and  $R^{Z3}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from  $C_{1-6}$  haloalkyl;

$R^{W1}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from H,  $C_{1-6}$  alkyl,  $C_{3-7}$  cycloalkyl, and 5-membered heteroaryl, wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{3-7}$  cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4  $R'$ ;

each  $R'$  is independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkynyl, and  $C_{1-6}$  haloalkyl, wherein the  $C_{1-6}$  alkyl of  $R'$  is optionally substituted with 1, 2, or 3 groups independently selected from  $OR^{a3}$ ;

each  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ , and  $R^{a3}$  is independently selected from H and  $C_{1-6}$  alkyl; and  $q$  is 1;

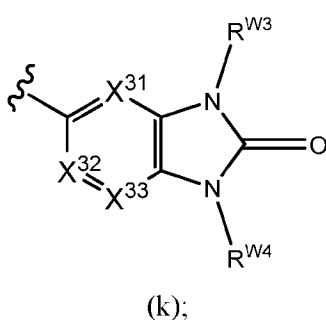
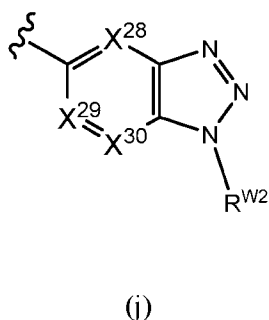
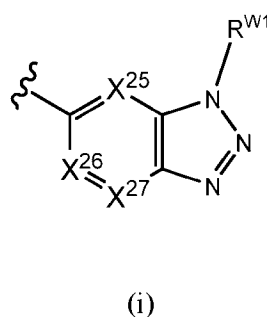
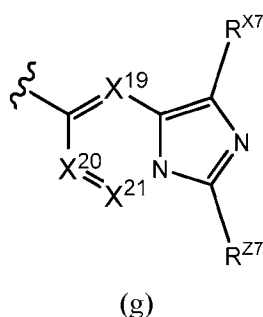
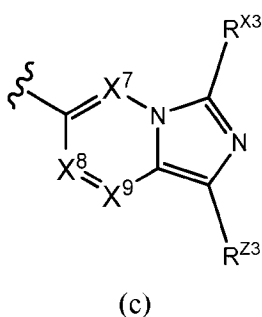
wherein when  $B$  is formula (c) or formula (k), then  $A$  is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, wherein:

$Q$  is NH;

$A$  is Cy or Cy- $C_{1-4}$  alkyl-;

$B$  is of formula (c), formula (g), formula (i), formula (j), or formula (k):



$X^7$  is N or  $CR^7$ ;

- $X^8$  is N or  $CR^8$ ;  
 $X^9$  is N or  $CR^9$ ;  
 $X^{19}$  is N or  $CR^{19}$ ;  
 $X^{20}$  is N or  $CR^{20}$ ;  
5  $X^{21}$  is N or  $CR^{21}$ ;  
 $X^{25}$  is N or  $CR^{25}$ ;  
 $X^{26}$  is N or  $CR^{26}$ ;  
 $X^{27}$  is N or  $CR^{27}$ ;  
 $X^{28}$  is N or  $CR^{28}$ ;  
10  $X^{29}$  is N or  $CR^{29}$ ;  
 $X^{30}$  is N or  $CR^{30}$ ;  
 $X^{31}$  is N or  $CR^{31}$ ;  
 $X^{32}$  is N or  $CR^{32}$ ;  
 $X^{33}$  is N or  $CR^{33}$ ;  
15 wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;  
wherein no more than two of  $X^{19}$ ,  $X^{20}$ , and  $X^{21}$  are simultaneously N;  
wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;  
wherein no more than two of  $X^{28}$ ,  $X^{29}$ , and  $X^{30}$  are simultaneously N;  
wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;  
20 each Cy is independently selected from C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>;  
each R<sup>Cy</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>,  
25 C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>Cy</sup> is optionally substituted by 1, 2, or 3 substituents  
30 independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>,

$R^7$ ,  $R^8$ ,  $R^{19}$ ,  $R^{20}$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{28}$ ,  $R^{29}$ ,  $R^{31}$ , and  $R^{32}$  are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;

$R^9$ ,  $R^{21}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each independently selected from H, halo, OR<sup>a2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $R^9$ ,  $R^{21}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

$R^{X3}$ ,  $R^{X7}$ ,  $R^{Z3}$ , and  $R^{Z7}$  are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of  $R^{X3}$ ,  $R^{X7}$ ,  $R^{Z3}$ , and  $R^{Z7}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>.

$R^{W1}$ ,  $R^{W2}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4 R<sup>'</sup>;

each R<sup>'</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, and C<sub>6-10</sub> aryl of R<sup>'</sup> is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>.

each  $R^{a1}$ ,  $R^{b1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{b3}$ ,  $R^{c3}$ , and  $R^{d3}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, , wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of  $R^{a1}$ ,  $R^{b1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{b3}$ ,  $R^{c3}$ , and  $R^{d3}$  is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from

5 halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>c4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>c4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

each  $R^{a4}$ ,  $R^{b4}$ ,  $R^{c4}$ , and  $R^{d4}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl, wherein said C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl are each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkyl, and C<sub>1-6</sub> haloalkoxy; and

each  $R^e$ ,  $R^{e1}$ ,  $R^{e2}$ ,  $R^{e3}$ , and  $R^{e4}$  is independently selected from H, C<sub>1-4</sub> alkyl, and CN;

wherein when B is formula (c), formula (g), or formula (k), then A is not 1-

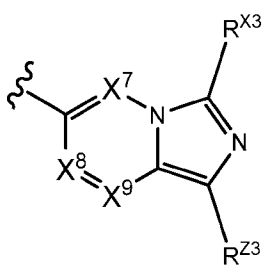
15 methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, wherein:

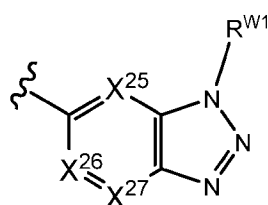
Q is NH;

A is Cy or Cy-C<sub>1-4</sub> alkyl-;

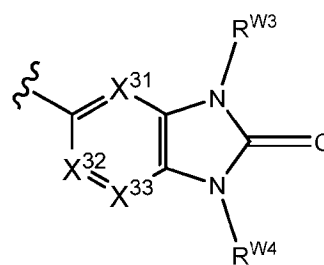
20 B is a group of formula (c), formula (i) or formula (k):



(c)



(i)



(k);

$X^7$  is N or CR<sup>7</sup>;

$X^8$  is N or CR<sup>8</sup>;

$X^9$  is N or CR<sup>9</sup>;

$X^{25}$  is N or CR<sup>25</sup>;

25  $X^{26}$  is N or CR<sup>26</sup>;

$X^{27}$  is N or CR<sup>27</sup>;

$X^{31}$  is N or CR<sup>31</sup>;

$X^{32}$  is N or  $CR^{32}$ ;

$X^{33}$  is N or  $CR^{33}$ ;

wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N; wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

5 wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each Cy is independently selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from  $R^{Cy}$ ;

each  $R^{Cy}$  is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>,  $OR^{a1}$ , and  $NR^{c1}R^{d1}$ , wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of  $R^{Cy}$  is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>,  $OR^{a1}$ , and  $NR^{c1}R^{d1}$ ;

$R^7$ ,  $R^8$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{31}$ , and  $R^{32}$  are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;

15  $R^9$ ,  $R^{27}$ , and  $R^{33}$  are each independently selected from H, halo,  $OR^{a2}$ ,  $NR^{c2}R^{d2}$ , C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $R^9$ ,  $R^{27}$ , and  $R^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>,  $OR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ , and  $C(O)OR^{a2}$ ;

20  $R^{X3}$  and  $R^{Z3}$  are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of  $R^{X3}$  and  $R^{Z3}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ ;

$R^{W1}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4  $R^*$ ;

30 each  $R^*$  is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>,  $OR^{a3}$ , and  $NR^{c3}R^{d3}$ , wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, and C<sub>6-10</sub> aryl of  $R^*$  is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>,  $OR^{a3}$ , and  $NR^{c3}R^{d3}$ ;



each  $R^{a1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{c3}$ , and  $R^{d3}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl;

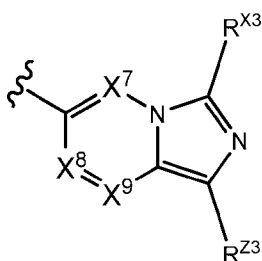
wherein when B is formula (c) or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

- 5 In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, wherein:

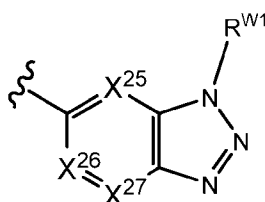
Q is NH;

A is Cy;

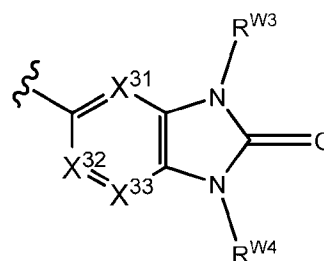
B is a group of formula (c), formula (i), or formula (k):



(c)



(i)



(k);

10  $X^7$  is CR<sup>7</sup>;

$X^8$  is CR<sup>8</sup>;

$X^9$  is CR<sup>9</sup>;

$X^{25}$  is CR<sup>25</sup>;

$X^{26}$  is CR<sup>26</sup>;

15  $X^{27}$  is CR<sup>27</sup>;

$X^{31}$  is CR<sup>31</sup>;

$X^{32}$  is CR<sup>32</sup>;

$X^{33}$  is CR<sup>33</sup>;

- 20 each Cy is independently selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>;

each R<sup>Cy</sup> is independently selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, and CN;

R<sup>7</sup>, R<sup>8</sup>, R<sup>25</sup>, R<sup>26</sup>, R<sup>31</sup>, and R<sup>32</sup> are each independently selected from H and halo;

- 25 R<sup>9</sup>, R<sup>27</sup>, and R<sup>33</sup> are each independently selected from H, halo, and 4-10 membered heterocycloalkyl, wherein said 4-10 membered heterocycloalkyl of R<sup>9</sup>, R<sup>27</sup>, and R<sup>33</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> alkyl, C(O)NR<sup>c2</sup>R<sup>d2</sup>, and C(O)R<sup>b2</sup>;

$R^{X3}$  and  $R^{Z3}$  are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of  $R^{X3}$  and  $R^{Z3}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from  $C_{1-6}$  haloalkyl;

$R^{W1}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from  $C_{1-6}$  alkyl and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4  $R'$ ;

each  $R'$  is independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkynyl, and  $C_{1-6}$  haloalkyl, wherein the  $C_{1-6}$  alkyl of  $R'$  is optionally substituted with 1, 2, or 3 groups independently selected from  $OR^{a3}$ ;

each  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ , and  $R^{a3}$  is independently selected from H and  $C_{1-6}$  alkyl; wherein when B is formula (c) or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

In some embodiments, when B is formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (k); A is Cy; and Cy is  $C_{3-7}$  cycloalkyl, then Cy is substituted with 0, 2, 3, 4, or 5 substituents independently selected from  $R^{Cy}$ .

In some embodiments, when B is formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (k); and A is Cy; then Cy is  $C_{4-7}$  cycloalkyl substituted with 1, 2, 3, 4, or 5 substituents independently selected from  $R^{Cy}$ .

In some embodiments, A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl. In some embodiments, A is not 1-methylcyclopropyl. In some embodiments, A is not 1-cyanocyclopropyl. In some embodiments, A is not 1-(fluoromethyl)cyclopropyl.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, selected from:

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-(2-methoxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-(2-methoxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1-(2-propynyl)-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

- 3-{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonylamino}-3-oxetanecarbonitrile;
- {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1-(2-propynyl)-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;
- 5 {7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;
- {7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;
- 10 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-(4-isobutyryl-1-piperazinyl)-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;
- 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-(4-isobutyryl-1-piperazinyl)-1,3-dihydro-1,3-benzimidazol-2-one;
- 1-(4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1H-1,2,3-benzotriazol-4-yl}-1-piperazinyl)-2-methyl-1-propanone;
- 15 1-(4-{1-[5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1H-1,2,3-benzotriazol-4-yl}-1-piperazinyl)-2-methyl-1-propanone;
- 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;
- 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-1,3-dihydro-1,3-benzimidazol-2-one;
- 20 one;
- 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-3-(2,2,2-trifluoroethyl)-1,3-dihydro-1,3-benzimidazol-2-one;
- 25 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-8-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-methyloxetan-3-yl)imidazo[1,5-a]pyridine-6-sulfonamide;
- 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-1,3-dihydro-1,3-benzimidazol-2-one;
- 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;
- 30 {7-[(R)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;
- {7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

- {7-(2,5-diazabicyclo[4.1.0]hept-2-yl)-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;
- {7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-1-cyclopropyl-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;
- 5 N-(1-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-(3-methyl-3-oxetanylaminosulfonyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl}-3-azepanyl)2-methylpropionamide;
- {7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;
- 10 {7-[(R)-4-(N,N-dimethylcarbamoyl)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;
- {7-[1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;
- 15 N,N-dimethyl-4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-(2-hydroxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl}-1-piperazinecarboxamide;
- {7-[1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;
- 20 N,N-dimethyl-4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-(2-hydroxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl}-1,2,3,6-tetrahydro-1-pyridinecarboxamide;
- 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{1-[(1-methoxycyclopropyl)carbonyl]-1,2,3,6-tetrahydro-4-pyridyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one;
- 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]-1,3-dihydro-1,3-benzimidazol-2-one;
- 30 {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-(2-oxa-7-aza-7-spiro[3.5]nonyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-3-azetidiny)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one;

4-{(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl}-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

{7-[(R)-4-(N,N-dimethylcarbamoyl)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(R)-3-(methoxymethyl)-1-piperazinyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-

(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(S)-3-(methoxymethyl)-1-piperazinyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-3-azetidiny)carbonyl]-1-piperazinyl}-3-methyl-1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-1,3-dihydro-2H-1,3-benzimidazol-2-one;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(2S,6S)-2,6-dimethyl-1,2,3,6-tetrahydro-4-pyridyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

5 {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-[(R)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-[2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

10 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

15 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

3-(2-aminoethyl)-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-(4-isobutyryl-1-piperazinyl)-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

20 {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-3-methyl-4-(N,N-dimethylcarbamoyl)-1-piperazinyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

25 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-[(3-methoxy-1-methyl-3-azetidiny)carbonyl]-3-methyl-1-piperazinyl]-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{1-[(1-methoxycyclopropyl)carbonyl]-1,2,3,6-tetrahydro-4-pyridyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one;

30 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-1-methyl-3-azetidiny)carbonyl]-1-piperazinyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-7-(1,2,3,6-tetrahydro-4-pyridyl)-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(S)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-3-methyl-4-(N-methylcarbamoyl)-1-piperazinyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(S)-2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-(1-isobutyryl-1,2,3,6-tetrahydro-4-pyridyl)-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclobutyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-methyl-4-{4-[(R)-1-methyl-2-azetidiny]carbonyl}-1-piperazinyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[4-(2-methoxy-2-methylpropionyl)-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(1-(1-(2-hydroxyethoxy)cyclopropane-1-carbonyl)-1,2,3,6-tetrahydropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-(4-(1-ethoxycyclopropane-1-carbonyl)piperazin-1-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

10 1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-4-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1H-benzo[d][1,2,3]triazole-6-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-((3R,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

15 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-7-(4-(1-(2-fluoroethyl)-3-methoxyazetidine-3-carbonyl)piperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-((3S,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

(S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-methoxycyclopropane-1-carbonyl)-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

25 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-((2S,6S)-2,6-dimethylmorpholino)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

(S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-methoxycyclobutane-1-carbonyl)-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

30 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(3-methoxyoxetane-3-carbonyl)piperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;



(S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(2-methoxy-2-methylpropanoyl)-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-(4-(1-(2-(dimethylamino)ethoxy)cyclopropane-1-carbonyl)piperazin-1-yl)-1-methyl-N-(3-methyloxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-(methoxy-d3)cyclopropane-1-carbonyl)piperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N-dimethyl-3,6-dihydropyridine-1(2H)-carboxamide;

4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,2-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide; and

4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,6-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, selected from:

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-(2-methoxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-(2-methoxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1-(2-propynyl)-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

3-{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonylamino}-3-oxetanecarbonitrile;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1-(2-propynyl)-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

- {7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;
- {7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;
- 5 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-(4-isobutyryl-1-piperazinyl)-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;
- 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-(4-isobutyryl-1-piperazinyl)-1,3-dihydro-1,3-benzimidazol-2-one;
- 1-(4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1H-1,2,3-benzotriazol-4-yl}-1-piperazinyl)-2-methyl-1-propanone;
- 10 1-(4-{1-[5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1H-1,2,3-benzotriazol-4-yl}-1-piperazinyl)-2-methyl-1-propanone;
- 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;
- 15 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-1,3-dihydro-1,3-benzimidazol-2-one;
- 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-3-(2,2,2-trifluoroethyl)-1,3-dihydro-1,3-benzimidazol-2-one;
- 20 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-8-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-methylloxetan-3-yl)imidazo[1,5-a]pyridine-6-sulfonamide;
- 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-1,3-dihydro-1,3-benzimidazol-2-one;
- 25 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;
- {7-[(R)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;
- {7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;
- 30 {7-(2,5-diazabicyclo[4.1.0]hept-2-yl)-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-1-cyclopropyl-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

5 N-(1-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-(3-methyl-3-oxetanylaminosulfonyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl}-3-azepanyl)2-methylpropionamide;

{7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

10 {7-[(R)-4-(N,N-dimethylcarbamoyl)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{7-[1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

15 N,N-dimethyl-4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-(2-hydroxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl}-1-piperazinecarboxamide;

20 {7-[1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

N,N-dimethyl-4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-(2-hydroxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl}-1,2,3,6-tetrahydro-1-pyridinecarboxamide;

25 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{1-[(1-methoxycyclopropyl)carbonyl]-1,2,3,6-tetrahydro-4-pyridyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]-1,3-dihydro-1,3-benzimidazol-2-one;

30 {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-(2-oxa-7-aza-7-spiro[3.5]nonyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-3-azetidiny)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one;

4-{(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl}-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

{7-[(R)-4-(N,N-dimethylcarbamoyl)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(R)-3-(methoxymethyl)-1-piperazinyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-

(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(S)-3-(methoxymethyl)-1-piperazinyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-3-azetidiny)carbonyl]-1-piperazinyl}-3-methyl-1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-1,3-dihydro-2H-1,3-benzimidazol-2-one;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(2S,6S)-2,6-dimethyl-1,2,3,6-tetrahydro-4-pyridyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

5 {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-[(R)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-[2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

10 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

15 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

3-(2-aminoethyl)-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-(4-isobutyryl-1-piperazinyl)-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

20 {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-3-methyl-4-(N,N-dimethylcarbamoyl)-1-piperazinyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

25 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-[(3-methoxy-1-methyl-3-azetidiny)carbonyl]-3-methyl-1-piperazinyl]-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{1-[(1-methoxycyclopropyl)carbonyl]-1,2,3,6-tetrahydro-4-pyridyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one;

30 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-1-methyl-3-azetidiny)carbonyl]-1-piperazinyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-7-(1,2,3,6-tetrahydro-4-pyridyl)-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(S)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-3-methyl-4-(N-methylcarbamoyl)-1-piperazinyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(S)-2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-(1-isobutyryl-1,2,3,6-tetrahydro-4-pyridyl)-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclobutyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-methyl-4-(4-{[(R)-1-methyl-2-azetidiny]carbonyl}-1-piperazinyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one; and

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[4-(2-methoxy-2-methylpropionyl)-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, selected from:

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-(2-methoxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-(2-methoxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1-(2-propynyl)-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

3-{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonylamino}-3-oxetanecarbonitrile;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1-(2-propynyl)-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-(4-isobutyryl-1-piperazinyl)-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-(4-isobutyryl-1-piperazinyl)-1,3-dihydro-1,3-benzimidazol-2-one;

1-(4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1H-1,2,3-benzotriazol-4-yl}-1-piperazinyl)-2-methyl-1-propanone;

1-(4-{1-[5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1H-1,2,3-benzotriazol-4-yl}-1-piperazinyl)-2-methyl-1-propanone;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-3-(2,2,2-trifluoroethyl)-1,3-dihydro-1,3-benzimidazol-2-one; and

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-8-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-methyloxetan-3-yl)imidazo[1,5-a]pyridine-6-sulfonamide.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, selected from:

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

{7-[(R)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{7-(2,5-diazabicyclo[4.1.0]hept-2-yl)-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-1-cyclopropyl-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

N-(1-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-(3-methyl-3-oxetanylaminosulfonyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl}-3-azepanyl)2-methylpropionamide;

{7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{7-[(R)-4-(N,N-dimethylcarbamoyl)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{7-[1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;



N,N-dimethyl-4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-(2-hydroxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl]-1-piperazinecarboxamide;

5 7-[1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

N,N-dimethyl-4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-(2-hydroxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl]-1,2,3,6-tetrahydro-1-pyridinecarboxamide;

10 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{1-[(1-methoxycyclopropyl)carbonyl]-1,2,3,6-tetrahydro-4-pyridyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]-1,3-dihydro-1,3-benzimidazol-2-one;

15 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-(2-oxa-7-aza-7-spiro[3.5]nonyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

20 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one;

25 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-3-azetidyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one;

4-{(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl}-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

{7-[(R)-4-(N,N-dimethylcarbamoyl)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

5 {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(R)-3-(methoxymethyl)-1-piperazinyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(S)-3-(methoxymethyl)-1-piperazinyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

10 6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-3-azetidynyl)carbonyl]-1-piperazinyl}-3-methyl-1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]-1,3-dihydro-2H-1,3-benzimidazol-2-one;

15 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-isobutryl-3-methyl-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(S)-4-isobutryl-3-methyl-1-piperazinyl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

20 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(S)-4-isobutryl-3-methyl-1-piperazinyl]-1,3-dihydro-2H-1,3-benzimidazol-2-one;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(2S,6S)-2,6-dimethyl-1,2,3,6-tetrahydro-4-pyridyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

25 {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-[(R)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-[2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

30 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

3-(2-aminoethyl)-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-(4-isobutyryl-1-piperazinyl)-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-3-methyl-4-(N,N-dimethylcarbamoyl)-1-piperazinyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-[(3-methoxy-1-methyl-3-azetidiny)carbonyl]-3-methyl-1-piperazinyl]-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{1-[(1-methoxycyclopropyl)carbonyl]-1,2,3,6-tetrahydro-4-pyridyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-1-methyl-3-azetidiny)carbonyl]-1-piperazinyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-7-(1,2,3,6-tetrahydro-4-pyridyl)-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(S)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

5 {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-3-methyl-4-(N-methylcarbamoyl)-1-piperazinyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(S)-2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

10 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-(1-isobutyryl-1,2,3,6-tetrahydro-4-pyridyl)-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclobutyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-methyl-4-(4-{[(R)-1-methyl-2-azetidiny]carbonyl}-1-piperazinyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one; and

20 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[4-(2-methoxy-2-methylpropionyl)-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,2-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide; and

25 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,6-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide.

In some embodiments, provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, selected from:

30 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(1-(1-(2-hydroxyethoxy)cyclopropane-1-carbonyl)-1,2,3,6-tetrahydropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-(4-(1-ethoxycyclopropane-1-carbonyl)piperazin-1-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-4-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1H-benzo[d][1,2,3]triazole-6-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-((3R,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-7-(4-(1-(2-fluoroethyl)-3-methoxyazetidine-3-carbonyl)piperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-((3S,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

(S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-methoxycyclopropane-1-carbonyl)-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-((2S,6S)-2,6-dimethylmorpholino)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

(S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-methoxycyclobutane-1-carbonyl)-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(3-methoxyoxetane-3-carbonyl)piperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

(S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(2-methoxy-2-methylpropanoyl)-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-(4-(1-(2-(dimethylamino)ethoxy)cyclopropane-1-carbonyl)piperazin-1-yl)-1-methyl-N-(3-methyloxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-(methoxy-d3)cyclopropane-1-carbonyl)piperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide; and

4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N-dimethyl-3,6-dihydropyridine-1(2H)-carboxamide.

It is further appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, can also be provided in combination in a single embodiment. Conversely, various features of the invention which are, for brevity, described in the context of a single embodiment, can also be provided separately or in any suitable subcombination.

At various places in the present specification, substituents of compounds of the invention are disclosed in groups or in ranges. It is specifically intended that the invention include each and every individual subcombination of the members of such groups and ranges. For example, the term “C<sub>1-6</sub> alkyl” is specifically intended to individually disclose methyl, ethyl, C<sub>3</sub> alkyl, C<sub>4</sub> alkyl, C<sub>5</sub> alkyl, and C<sub>6</sub> alkyl.

At various places in the present specification various aryl, heteroaryl, cycloalkyl, and heterocycloalkyl rings are described. Unless otherwise specified, these rings can be attached to the rest of the molecule at any ring member as permitted by valency. For example, the term “pyridinyl,” “pyridyl,” or “a pyridine ring” may refer to a pyridin-2-yl, pyridin-3-yl, or pyridin-4-yl ring.

The term “n-membered,” where “n” is an integer, typically describes the number of ring-forming atoms in a moiety where the number of ring-forming atoms is “n”. For example, piperidinyl is an example of a 6-membered heterocycloalkyl ring, pyrazolyl is an example of a 5-membered heteroaryl ring, pyridyl is an example of a 6-membered heteroaryl ring, and 1,2,3,4-tetrahydro-naphthalene is an example of a 10-membered cycloalkyl group.

For compounds of the invention in which a variable appears more than once, each variable can be a different moiety independently selected from the group defining the variable. For example, where a structure is described having two R groups that are simultaneously present on the same compound, the two R groups can represent different moieties independently selected from the group defined for R.

As used herein, the phrase “optionally substituted” means unsubstituted or substituted.

As used herein, the term “substituted” means that a hydrogen atom is replaced by a non-hydrogen group. It is to be understood that substitution at a given atom is limited by valency.

As used herein, the term “C<sub>i-j</sub>,” where i and j are integers, employed in combination with a chemical group, designates a range of the number of carbon atoms in the chemical group with i-j defining the range. For example, C<sub>1-6</sub> alkyl refers to an alkyl group having 1, 2, 3, 4, 5, or 6 carbon atoms.

As used herein, the term “alkyl,” employed alone or in combination with other terms, refers to a saturated hydrocarbon group that may be straight-chain or branched. In some embodiments, the alkyl group contains 1 to 7, 1 to 6, 1 to 4, or 1 to 3 carbon atoms. Examples of alkyl moieties include, but are not limited to, chemical groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, *sec*-butyl, *tert*-butyl, n-pentyl, 2-methyl-1-butyl, 3-pentyl, n-hexyl, 1,2,2-trimethylpropyl, n-heptyl, and the like. In some embodiments, the alkyl group is methyl, ethyl, or propyl.

As used herein, “alkenyl,” employed alone or in combination with other terms, refers to an alkyl group having one or more carbon-carbon double bonds. In some embodiments, the alkenyl moiety contains 2 to 6 or 2 to 4 carbon atoms. Example alkenyl groups include, but are not limited to, ethenyl, n-propenyl, isopropenyl, n-butenyl, *sec*-butenyl, and the like.

As used herein, “alkynyl,” employed alone or in combination with other terms, refers to an alkyl group having one or more carbon-carbon triple bonds. Example alkynyl groups include, but are not limited to, ethynyl, propyn-1-yl, propyn-2-yl, and the like. In some embodiments, the alkynyl moiety contains 2 to 6 or 2 to 4 carbon atoms.

As used herein, “halo” or “halogen,” employed alone or in combination with other terms, includes fluoro, chloro, bromo, and iodo. In some embodiments, halo is F or Cl.

As used herein, the term “haloalkyl,” employed alone or in combination with other terms, refers to an alkyl group having up to the full valency of halogen atom substituents, which may either be the same or different. In some embodiments, the halogen atoms are fluoro atoms. In some embodiments, the alkyl group has 1 to 6 or 1 to 4 carbon atoms. Example haloalkyl groups include CF<sub>3</sub>, C<sub>2</sub>F<sub>5</sub>, CHF<sub>2</sub>, CCl<sub>3</sub>, CHCl<sub>2</sub>, C<sub>2</sub>Cl<sub>5</sub>, and the like.

As used herein, the term “alkoxy,” employed alone or in combination with other terms, refers to a group of formula -O-alkyl. Example alkoxy groups include methoxy, ethoxy, propoxy (e.g., n-propoxy and isopropoxy), t-butoxy, and the like. In some embodiments, the alkyl group has 1 to 6 or 1 to 4 carbon atoms.

As used herein, “haloalkoxy,” employed alone or in combination with other terms, refers to a group of formula -O-(haloalkyl). In some embodiments, the alkyl group has 1 to 6 or 1 to 4 carbon atoms. An example haloalkoxy group is -OCF<sub>3</sub>.

As used herein, “amino,” employed alone or in combination with other terms, refers  
5 to NH<sub>2</sub>.

As used herein, the term “cycloalkyl,” employed alone or in combination with other terms, refers to a non-aromatic cyclic hydrocarbon including cyclized alkyl and alkenyl groups. Cycloalkyl groups can include mono- or polycyclic (e.g., having 2, 3, or 4 fused, bridged, or spiro rings) ring systems. Also included in the definition of cycloalkyl are  
10 moieties that have one or more aromatic rings (e.g., aryl or heteroaryl rings) fused (i.e., having a bond in common with) to the cycloalkyl ring, for example, benzo derivatives of cyclopentane, cyclohexene, cyclohexane, and the like, or pyrido derivatives of cyclopentane or cyclohexane. Ring-forming carbon atoms of a cycloalkyl group can be optionally substituted by oxo. Cycloalkyl groups also include cycloalkylidenes. The term “cycloalkyl”  
15 also includes bridgehead cycloalkyl groups (e.g., non-aromatic cyclic hydrocarbon moieties containing at least one bridgehead carbon, such as adamantan-1-yl) and spirocycloalkyl groups (e.g., non-aromatic hydrocarbon moieties containing at least two rings fused at a single carbon atom, such as spiro[2.5]octane and the like). In some embodiments, the cycloalkyl group has 3 to 10 ring members, or 3 to 7 ring members. In some embodiments, the  
20 cycloalkyl group is monocyclic or bicyclic. In some embodiments, the cycloalkyl group is monocyclic. In some embodiments, the cycloalkyl group is a C<sub>3-7</sub> monocyclic cycloalkyl group. Example cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclopentenyl, cyclohexenyl, cyclohexadienyl, cycloheptatrienyl, norbornyl, norpinyl, norcarnyl, tetrahydronaphthalenyl, octahydronaphthalenyl, indanyl, and the like. In  
25 some embodiments, the cycloalkyl group is cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

As used herein, the term “heterocycloalkyl,” employed alone or in combination with other terms, refers to a non-aromatic ring or ring system, which may optionally contain one or more alkenylene or alkynylene groups as part of the ring structure, which has at least one  
30 heteroatom ring member independently selected from nitrogen, sulfur, oxygen, and phosphorus. Heterocycloalkyl groups can include mono- or polycyclic (e.g., having 2, 3 or 4 fused, bridged, or spiro rings) ring systems. In some embodiments, the heterocycloalkyl group is a monocyclic or bicyclic group having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, sulfur and oxygen. Also included in the definition of heterocycloalkyl



are moieties that have one or more aromatic rings (e.g., aryl or heteroaryl rings) fused (i.e., having a bond in common with) to the non-aromatic heterocycloalkyl ring, for example, 1,2,3,4-tetrahydro-quinoline and the like. Heterocycloalkyl groups can also include bridgehead heterocycloalkyl groups (e.g., a heterocycloalkyl moiety containing at least one  
5 bridgehead atom, such as azaadamantan-1-yl and the like) and spiroheterocycloalkyl groups (e.g., a heterocycloalkyl moiety containing at least two rings fused at a single atom, such as [1,4-dioxo-8-aza-spiro[4.5]decan-N-yl] and the like). In some embodiments, the heterocycloalkyl group has 3 to 10 ring-forming atoms, 4 to 10 ring-forming atoms, or about 3 to 8 ring forming atoms. In some embodiments, the heterocycloalkyl group has 2 to 20  
10 carbon atoms, 2 to 15 carbon atoms, 2 to 10 carbon atoms, or about 2 to 8 carbon atoms. In some embodiments, the heterocycloalkyl group has 1 to 5 heteroatoms, 1 to 4 heteroatoms, 1 to 3 heteroatoms, or 1 to 2 heteroatoms. The carbon atoms or heteroatoms in the ring(s) of the heterocycloalkyl group can be oxidized to form a carbonyl, an N-oxide, or a sulfonyl group (or other oxidized linkage) or a nitrogen atom can be quaternized. In some embodiments, the  
15 heterocycloalkyl portion is a C<sub>2-7</sub> monocyclic heterocycloalkyl group. In some embodiments, the heterocycloalkyl group is a morpholine ring, pyrrolidine ring, piperazine ring, piperidine ring, tetrahydropyran ring, tetrahydropyridine, azetidine ring, or tetrahydrofuran ring.

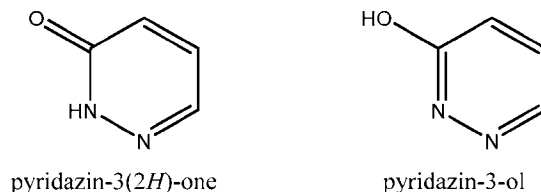
As used herein, the term “aryl,” employed alone or in combination with other terms, refers to a monocyclic or polycyclic (e.g., a fused ring system) aromatic hydrocarbon moiety,  
20 such as, but not limited to, phenyl, 1-naphthyl, 2-naphthyl, and the like. In some embodiments, aryl groups have from 6 to 10 carbon atoms or 6 carbon atoms. In some embodiments, the aryl group is a monocyclic or bicyclic group. In some embodiments, the aryl group is phenyl or naphthyl.

As used herein, the term “heteroaryl,” employed alone or in combination with other  
25 terms, refers to a monocyclic or polycyclic (e.g., a fused ring system) aromatic hydrocarbon moiety, having one or more heteroatom ring members independently selected from nitrogen, sulfur and oxygen. In some embodiments, the heteroaryl group is a monocyclic or a bicyclic group having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, sulfur and oxygen. Example heteroaryl groups include, but are not limited to, pyridyl, pyrimidinyl,  
30 pyrazinyl, pyridazinyl, triazinyl, furyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrol, oxazolyl, benzofuryl, benzothienyl, benzthiazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, indazolyl, 1,2,4-thiadiazolyl, isothiazolyl, purinyl, carbazolyl, benzimidazolyl, indolinyl, pyrrolyl, azolyl, quinolinyl, isoquinolinyl, benzisoxazolyl, imidazo[1,2-b]thiazolyl or the like. The carbon atoms or heteroatoms in the ring(s) of the heteroaryl group can be oxidized to

form a carbonyl, an N-oxide, or a sulfonyl group (or other oxidized linkage) or a nitrogen atom can be quaternized, provided the aromatic nature of the ring is preserved. In some embodiments, the heteroaryl group has from 3 to 10 carbon atoms, from 3 to 8 carbon atoms, from 3 to 5 carbon atoms, from 1 to 5 carbon atoms, or from 5 to 10 carbon atoms. In some  
5   embodiments, the heteroaryl group contains 3 to 14, 4 to 12, 4 to 8, 9 to 10, or 5 to 6 ring-forming atoms. In some embodiments, the heteroaryl group has 1 to 4, 1 to 3, or 1 to 2 heteroatoms.

The compounds described herein can be asymmetric (*e.g.*, having one or more stereocenters). All stereoisomers, such as enantiomers and diastereomers, are intended unless  
10   otherwise indicated. Compounds of the present invention that contain asymmetrically substituted carbon atoms can be isolated in optically active or racemic forms. Methods on how to prepare optically active forms from optically inactive starting materials are known in the art, such as by resolution of racemic mixtures or by stereoselective synthesis. Geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds  
15   described herein, and all such stable isomers are contemplated in the present invention. Cis and trans geometric isomers of the compounds of the present invention may be isolated as a mixture of isomers or as separated isomeric forms.

Compounds of the invention also include tautomeric forms. Tautomeric forms result from the swapping of a single bond with an adjacent double bond together with the  
20   concomitant migration of a proton. Tautomeric forms include prototropic tautomers which are isomeric protonation states having the same empirical formula and total charge. Example prototropic tautomers include ketone – enol pairs, amide - imidic acid pairs, lactam – lactim pairs, enamine – imine pairs, and annular forms where a proton can occupy two or more positions of a heterocyclic system, for example, 1H- and 3H-imidazole, 1H-, 2H- and 4H-  
25   1,2,4-triazole, 1H- and 2H- isoindole, and 1H- and 2H-pyrazole. Tautomeric forms can be in equilibrium or sterically locked into one form by appropriate substitution. An example of tautomeric forms, pyridazin-3(2H)-one and pyridazin-3-ol, is depicted below:



Compounds of the invention also include all isotopes of atoms occurring in the  
30   intermediates or final compounds. Isotopes include those atoms having the same atomic

number but different mass numbers. For example, isotopes of hydrogen include tritium and deuterium. In some embodiments, the compounds of the invention include at least one deuterium atom.

The term, "compound," as used herein is meant to include all stereoisomers,  
5 geometric isomers, tautomers, and isotopes of the structures depicted, unless otherwise specified.

All compounds, and pharmaceutically acceptable salts thereof, can be found together with other substances such as water and solvents (e.g., in the form of hydrates and solvates) or can be isolated.

10 In some embodiments, the compounds of the invention, or salts thereof, are substantially isolated. By "substantially isolated" is meant that the compound is at least partially or substantially separated from the environment in which it was formed or detected. Partial separation can include, for example, a composition enriched in the compounds of the invention. Substantial separation can include compositions containing at least about 50%, at  
15 least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 97%, or at least about 99% by weight of the compounds of the invention, or salt thereof. Methods for isolating compounds and their salts are routine in the art.

As used herein, and unless otherwise specified, the term "about", when used in connection with a numeric value or range of values which is provided to describe a particular  
20 solid form (e.g., a specific temperature or temperature range, such as describing a melting, dehydration, or glass transition; a mass change, such as a mass change as a function of temperature or humidity; a solvent or water content, in terms of, for example, mass or a percentage; or a peak position, such as in analysis by, for example, <sup>13</sup>C NMR, DSC, TGA and XRPD), indicate that the value or range of values may deviate to an extent deemed  
25 reasonable to one of ordinary skill in the art while still describing the particular solid form.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or  
30 complication, commensurate with a reasonable benefit/risk ratio.

The present invention also includes pharmaceutically acceptable salts of the compounds described herein. As used herein, "pharmaceutically acceptable salts" refers to derivatives of the disclosed compounds wherein the parent compound is modified by converting an existing acid or base moiety to its salt form. Examples of pharmaceutically

acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like. The pharmaceutically acceptable salts of the present invention include the non-toxic salts of the parent compound formed, for example, from non-toxic inorganic or organic acids.

- 5 The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two. Lists of suitable salts are found in *Remington's*  
10 *Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, Pa., 1985, p. 1418 and *Journal of Pharmaceutical Science*, 66, 2 (1977), each of which is incorporated herein by reference in its entirety.

#### Synthesis

- 15 Compounds of the invention, including salts thereof, can be prepared using known organic synthesis techniques and can be synthesized according to any of numerous possible synthetic routes.

- The reactions for preparing compounds of the invention can be carried out in suitable solvents which can be readily selected by one of skill in the art of organic synthesis. Suitable  
20 solvents can be substantially nonreactive with the starting materials (reactants), the intermediates, or products at the temperatures at which the reactions are carried out, e.g., temperatures which can range from the solvent's freezing temperature to the solvent's boiling temperature. A given reaction can be carried out in one solvent or a mixture of more than one solvent. Depending on the particular reaction step, suitable solvents for a particular reaction  
25 step can be selected by the skilled artisan.

- Preparation of compounds of the invention can involve the protection and deprotection of various chemical groups. The need for protection and deprotection, and the selection of appropriate protecting groups, can be readily determined by one skilled in the art. The chemistry of protecting groups can be found, for example, in T.W. Greene and P.G.M.  
30 Wuts, *Protective Groups in Organic Synthesis*, 3rd. Ed., Wiley & Sons, Inc., New York (1999), which is incorporated herein by reference in its entirety.

Reactions can be monitored according to any suitable method known in the art. For example, product formation can be monitored by spectroscopic means, such as nuclear magnetic resonance spectroscopy (e.g.,  $^1\text{H}$  or  $^{13}\text{C}$ ), infrared spectroscopy, spectrophotometry

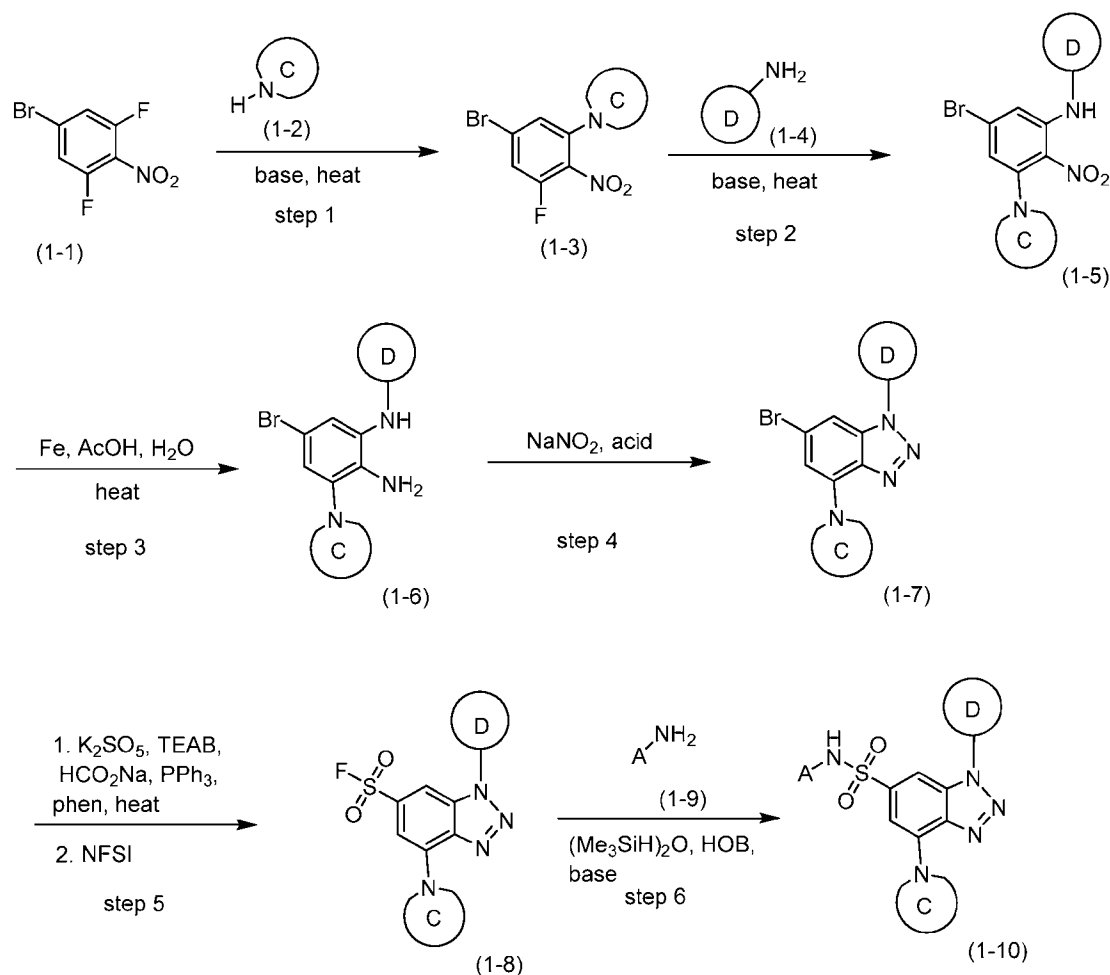
(e.g., UV-visible), or mass spectrometry, or by chromatography such as high performance liquid chromatography (HPLC) or thin layer chromatography.

The expressions, “ambient temperature,” “room temperature,” and “RT”, as used herein, are understood in the art, and refer generally to a temperature, *e.g.* a reaction temperature, that is about the temperature of the room in which the reaction is carried out, for example, a temperature from about 20 °C to about 30 °C.

Compounds of Formula I can be prepared according to numerous preparatory routes known in the literature. Example synthetic methods for preparing compounds of the invention are provided in the Schemes below. Unless noted otherwise, all substituents are as defined herein.

In the process depicted in Scheme 1, an appropriately substituted, aryl fluoride-containing compound of Formula (1-1) is substituted with amine compound (1-2) in the presence of a base and heat to form the aryl compound of Formula (1-3). The compound of Formula (1-3) is substituted with amine compound (1-4) in the presence of a base and heat to form the nitro compound of Formula (1-5). The nitro compound of Formula (1-5) is reduced in the presence of iron and acid to form amine compound of Formula (1-6). The compound of Formula (1-6) is cyclized in the presence of sodium nitrite and acid to form triazole compound of Formula (1-7). The compound of Formula (1-7) is reacted with a palladium catalyst like palladium acetate, K<sub>2</sub>SO<sub>5</sub> and then N-fluorobenzenesulfonimide to form sulfonyl fluoride compound of Formula (1-8). The compound of Formula (1-8) is substituted with amine compound of Formula (1-9) to form sulfonamide compound of Formula (1-9).

**Scheme 1**



wherein:

Ring C is an N-containing 5-10 membered heteroaryl or N-containing 4-10 membered heterocycloalkyl, wherein said 5-10 membered heteroaryl and 4-10 membered

- 5 heterocycloalkyl are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, and
- 10

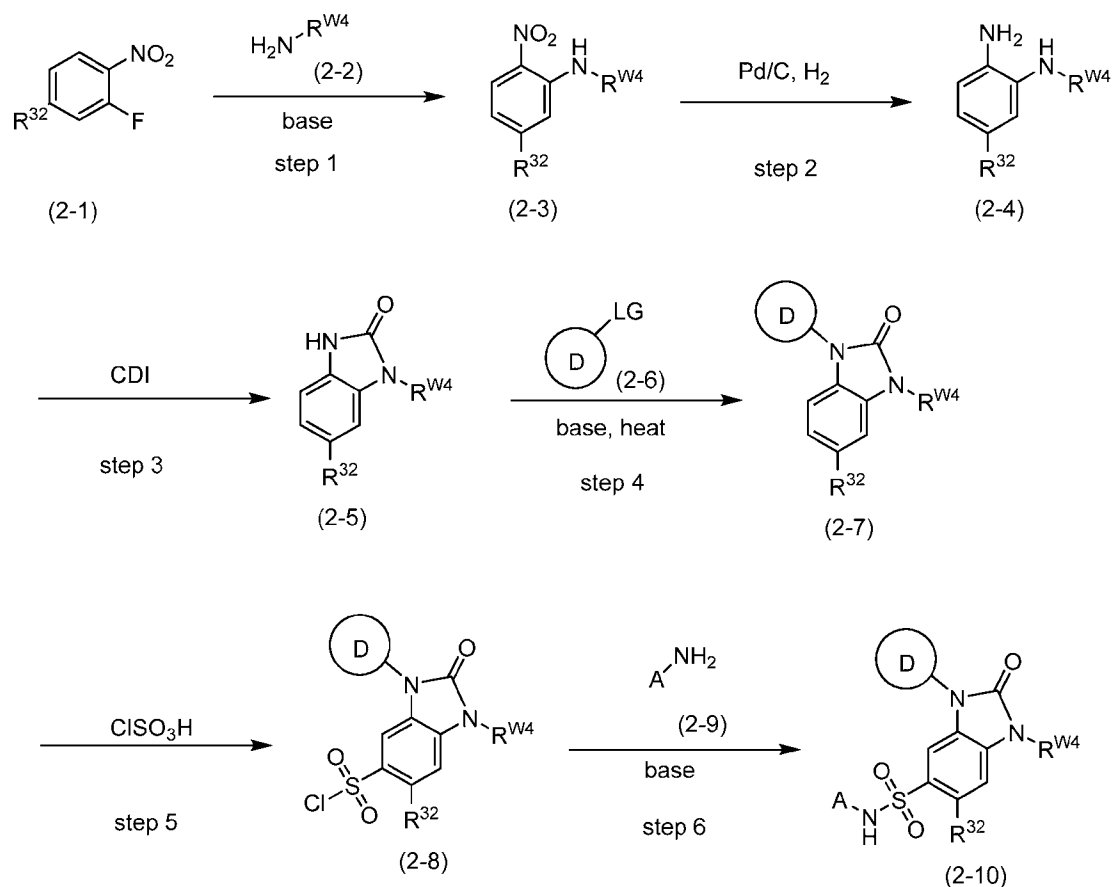
Ring D is 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4 R<sup>1</sup>.

In the process depicted in Scheme 1, an appropriately substituted, aryl fluoride-containing compound of Formula (2-1) is substituted with amine compound (2-2) in the

- 15 presence of a base to form the aryl compound of Formula (2-3). The compound of Formula

(2-3) is reduced to form amine compound of Formula (2-4). The compound of Formula (2-4) is cyclized with 1,1'-carbonyldiimidazole to form benzimidazole compound of Formula (2-5). The compound of Formula (2-5) is substituted with a compound of Formula (2-6) in the presence of base and heat to form the compound of Formula (2-7). The compound of Formula (2-7) is substituted with chlorosulfonic acid to form sulfonyl chloride compound of Formula (2-8). The compound of Formula (2-8) is substituted with a compound of Formula (2-9) in the presence of base to form sulfonamide compound of Formula (2-10).

### Scheme 2



10 wherein:

Ring D is 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4  $\text{R}'$ ;

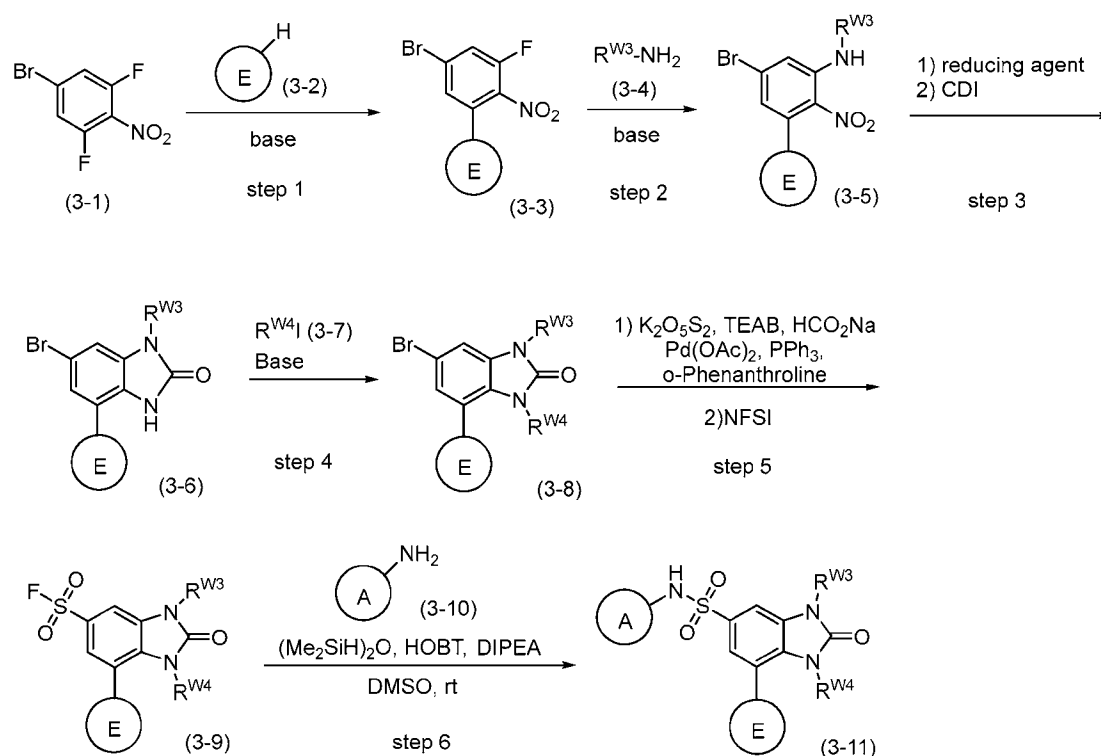
and

LG is a leaving group, such as halo.

In the process depicted in Scheme 3, an appropriately substituted, aryl fluoride-containing compound of Formula (3-1) is substituted with an appropriately substituted heterocycloalkyl (3-2, e.g., piperidinyl) in the presence of a base to form the aryl compound of Formula (3-3). The aryl fluoride containing-compound of Formula (3-3) is substituted with

amine compound (3-4) to form aryl compound of Formula (3-5). The compound of Formula (3-5) is reduced and cyclized to form the compound of Formula (3-6). The compound of Formula (3-6) is substituted with a compound of Formula (3-7) in the presence of a base to form compound of Formula (3-8). The compound of Formula (3-8) is reacted with a palladium catalyst like palladium acetate,  $K_2SO_5$  and then N-fluorobenzenesulfonimide to form sulfonyl fluoride compound of Formula (3-9). The compound of Formula (3-9) is substituted with amine compound of Formula (3-10) to form sulfonamide compound of Formula (3-11).

### Scheme 3



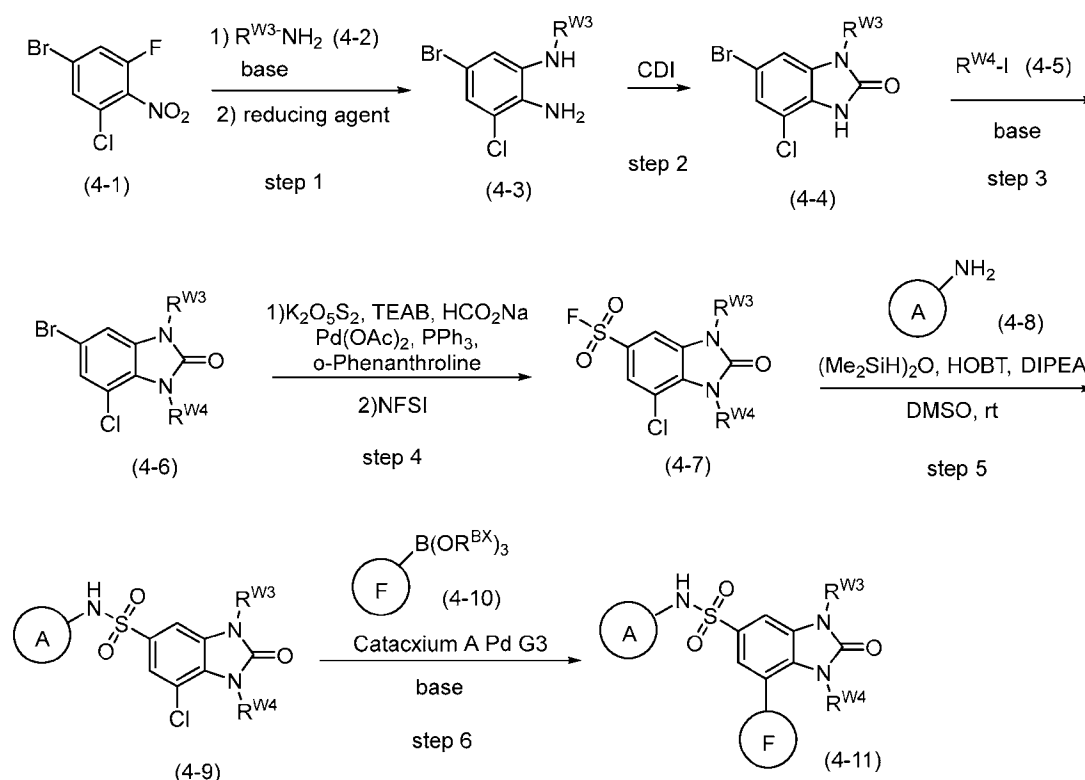
10

Ring E is an N-containing 5-10 membered heteroaryl or N-containing 4-10 membered heterocycloalkyl, wherein said 5-10 membered heteroaryl and 4-10 membered heterocycloalkyl are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ .

15



In the process depicted in Scheme 4, an appropriately substituted, aryl fluoride-containing compound of Formula (4-1) is substituted with an amine compound of Formula (4-2) to form aryl compound of Formula (4-3). The compound of Formula (4-3) is cyclized to form the aryl compound of Formula (4-4). The compound of Formula (4-4) is substituted with a compound of Formula (4-5) to form benzimidazolone compound of Formula (4-6). The compound of Formula (4-6) is reacted with a palladium catalyst like palladium acetate,  $K_2SO_5$  and then N-fluorobenzenesulfonimide to form sulfonyl fluoride compound of Formula (4-7). The compound of Formula (4-7) is substituted with amine compound of Formula (4-8) to form sulfonamide compound of Formula (4-9). The compound of Formula (4-9) is substituted with borate compound of Formula (4-10, e.g., a tetrahydropyridinyl substituted with a borate moiety) in the presence of a palladium catalyst and base to form sulfonamide compound of Formula (4-11).

**Scheme 4**

Ring F is  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10

membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>q</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>,  
 C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>,  
 NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c</sup>C(O)OR<sup>a2</sup>, NR<sup>c</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>,  
 NR<sup>c</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and  
 5 S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>; and

each R<sup>BX</sup> is independently selected from H and C<sub>1-6</sub> alkyl or the two R<sup>BX</sup>s can be joined in ring and optionally substituted.

### Methods of Use

10 Compounds of the invention can inhibit the activity of PARG. For example, the compounds of the invention can be used to inhibit activity of PARG in a cell or in an individual or patient in need of inhibition of the enzyme by administering an inhibiting amount of a compound of the invention to the cell, individual, or patient. In some embodiments, the PARG is PARG1.

15 As PARG inhibitors, the compounds of the invention are useful in the treatment of various diseases or disorders associated with abnormal expression or activity of PARG and diseases and disorders sensitive to the accumulation of ADP-ribose that results from treatment with PARG inhibitors. For example, the compounds of the invention are useful in the treatment of cancer.

20 In some embodiments, the cancer is a cellular stress-dependent cancer.

In some embodiments, the cancer exhibits cancer dependent transcriptional gene misregulation.

In some embodiments, the cancer is selected from lung cancer, colon cancer, breast cancer, ovarian cancer, gastric cancer, prostate cancer, liver cancer, pancreatic cancer, brain  
 25 cancer, skin cancer, bladder cancer, esophageal cancer, head and neck cancer, kidney cancer, rectal cancer, stomach cancer, thyroid cancer, uterine cancer, mantle cell lymphoma, and renal cell carcinoma.

As used herein, the term “cell” is meant to refer to a cell that is *in vitro*, *ex vivo* or *in vivo*. In some embodiments, an *ex vivo* cell can be part of a tissue sample excised from an  
 30 organism such as a mammal. In some embodiments, an *in vitro* cell can be a cell in a cell culture. In some embodiments, an *in vivo* cell is a cell living in an organism such as a mammal.

As used herein, the term “contacting” refers to the bringing together of indicated moieties in an *in vitro* system or an *in vivo* system. For example, “contacting” PARG or

“contacting” a cell with a compound of the invention includes the administration of a compound of the present invention to an individual or patient, such as a human, having PARG, as well as, for example, introducing a compound of the invention into a sample containing a cellular or purified preparation containing PARG.

5           As used herein, the term “individual” or “patient,” used interchangeably, refers to mammals, and particularly humans. Typically, the individual or patient is in need of treatment.

          As used herein, the phrase “therapeutically effective amount” refers to the amount of active compound or pharmaceutical agent that elicits the biological or medicinal response in a  
10   tissue, system, animal, individual or human that is being sought by a researcher, veterinarian, medical doctor or other clinician.

          As used herein the term “treating” or “treatment” refers to 1) inhibiting the disease in an individual who is experiencing or displaying the pathology or symptomatology of the disease (*i.e.*, arresting further development of the pathology and/or symptomatology), or 2)  
15   ameliorating the disease in an individual who is experiencing or displaying the pathology or symptomatology of the disease (*i.e.*, reversing the pathology and/or symptomatology).

          As used herein the term “preventing” or “prevention” refers to preventing the disease in an individual who may be predisposed to the disease but does not yet experience or display the pathology or symptomatology of the disease.

20

#### Combination Therapy

          One or more additional pharmaceutical agents or treatment methods such as, for example, chemotherapeutics or other anti-cancer agents, immune enhancers, immunosuppressants, immunotherapies, radiation, anti-tumor and anti-viral vaccines,  
25   cytokine therapy (*e.g.*, IL2, GM-CSF, *etc.*), and/or kinase (tyrosine or serine/threonine), epigenetic or signal transduction inhibitors can be used in combination with the compounds of the present invention. The agents can be combined with the present compounds in a single dosage form, or the agents can be administered simultaneously or sequentially as separate dosage forms.

30           Suitable agents for use in combination with the compounds of the present invention for the treatment of cancer include chemotherapeutic agents, targeted cancer therapies, immunotherapies or radiation therapy. Compounds of this invention may be effective in combination with anti-hormonal agents for treatment of breast cancer and other tumors. Suitable examples are anti-estrogen agents including but not limited to tamoxifen and

toremifene, aromatase inhibitors including but not limited to letrozole, anastrozole, and exemestane, adrenocorticosteroids (e.g. prednisone), progestins (e.g. megastrol acetate), and estrogen receptor antagonists (e.g. fulvestrant). Suitable anti-hormone agents used for treatment of prostate and other cancers may also be combined with compounds of the present invention. These include anti-androgens including but not limited to flutamide, bicalutamide, and nilutamide, luteinizing hormone-releasing hormone (LHRH) analogs including leuprolide, goserelin, triptorelin, and histrelin, LHRH antagonists (e.g. degarelix), androgen receptor blockers (e.g. enzalutamide) and agents that inhibit androgen production (e.g. abiraterone).

Angiogenesis inhibitors may be efficacious in some tumors in combination with the compounds of the present invention. These include antibodies against VEGF or VEGFR, or kinase inhibitors of VEGFR. Antibodies or other therapeutic proteins against VEGF include bevacizumab and aflibercept. Inhibitors of VEGFR kinases and other anti-angiogenesis inhibitors include but are not limited to sunitinib, sorafenib, axitinib, cediranib, pazopanib, regorafenib, brivanib, and vandetanib

Suitable chemotherapeutic or other anti-cancer agents for use in combination with the compounds of the present invention include, for example, alkylating agents (including, without limitation, nitrogen mustards, ethylenimine derivatives, alkyl sulfonates, nitrosoureas and triazenes) such as uracil mustard, chlormethine, cyclophosphamide (Cytosan<sup>TM</sup>), ifosfamide, melphalan, chlorambucil, pipobroman, triethylene-melamine, triethylenethio-phosphoramine, busulfan, carmustine, lomustine, streptozocin, dacarbazine, and temozolomide.

Additional anti-cancer agent(s) for use in combination with the compounds of the present invention include DNA damage or cell cycle check point inhibitors, including ATR, ATM, Wee1, CHK1, CHK2, Pol Theta inhibitors.

Other anti-cancer agent(s) for use in combination with the compounds of the present invention include antibody therapeutics to checkpoint or costimulatory molecules such as CTLA-4, PD-1, PD-L1 or 4-1BB, respectively, or antibodies to cytokines (IL-10, TGF- $\beta$ , etc.). Exemplary cancer immunotherapy antibodies include pembrolizumab, ipilimumab, nivolumab, atezolizumab and durvalumab. Additional anti-cancer agent(s) for use in combination with the compounds of the present invention include antibody therapeutics directed to surface molecules of hematological cancers such as ofatumumab, rituximab, and alemtuzumab.

Methods for the safe and effective administration of most of these chemotherapeutic agents are known to those skilled in the art. In addition, their administration is described in the standard literature. For example, the administration of many of the chemotherapeutic agents is described in the "Physicians' Desk Reference" (PDR, e.g., 1996 edition, Medical Economics Company, Montvale, NJ), the disclosure of which is incorporated herein by  
5 reference as if set forth in its entirety.

#### Pharmaceutical Formulations and Dosage Forms

When employed as pharmaceuticals, the compounds of the invention can be  
10 administered in the form of pharmaceutical compositions. A pharmaceutical composition refers to a combination of a compound of the invention, or its pharmaceutically acceptable salt, and at least one pharmaceutically acceptable carrier. These compositions can be prepared in a manner well known in the pharmaceutical art, and can be administered by a variety of routes, depending upon whether local or systemic treatment is desired and upon the area to be  
15 treated. Administration may be oral, topical (including ophthalmic and to mucous membranes including intranasal, vaginal and rectal delivery), pulmonary (*e.g.*, by inhalation or insufflation of powders or aerosols, including by nebulizer; intratracheal, intranasal, epidermal and transdermal), ocular, or parenteral.

This invention also includes pharmaceutical compositions which contain, as the active  
20 ingredient, one or more of the compounds of the invention above in combination with one or more pharmaceutically acceptable carriers. In making the compositions of the invention, the active ingredient is typically mixed with an excipient, diluted by an excipient or enclosed within such a carrier in the form of, for example, a capsule, sachet, paper, or other container. When the excipient serves as a diluent, it can be a solid, semi-solid, or liquid material, which  
25 acts as a vehicle, carrier or medium for the active ingredient. Thus, the compositions can be in the form of tablets, pills, powders, lozenges, sachets, cachets, elixirs, suspensions, emulsions, solutions, syrups, aerosols (as a solid or in a liquid medium), ointments containing, for example, up to 10 % by weight of the active compound, soft and hard gelatin capsules, suppositories, sterile injectable solutions, and sterile packaged powders.

30 The compositions can be formulated in a unit dosage form. The term "unit dosage form" refers to a physically discrete unit suitable as unitary dosages for human subjects and other mammals, each unit containing a predetermined quantity of active material calculated to produce the desired therapeutic effect, in association with a suitable pharmaceutical excipient.

The active compound can be effective over a wide dosage range and is generally administered in a pharmaceutically effective amount. It will be understood, however, that the amount of the compound actually administered will usually be determined by a physician, according to the relevant circumstances, including the condition to be treated, the chosen  
5 route of administration, the actual compound administered, the age, weight, and response of the individual patient, the severity of the patient's symptoms, and the like.

For preparing solid compositions such as tablets, the principal active ingredient is mixed with a pharmaceutical excipient to form a solid pre-formulation composition containing a homogeneous mixture of a compound of the present invention. When referring  
10 to these pre-formulation compositions as homogeneous, the active ingredient is typically dispersed evenly throughout the composition so that the composition can be readily subdivided into equally effective unit dosage forms such as tablets, pills and capsules. This solid pre-formulation is then subdivided into unit dosage forms of the type described above.

The tablets or pills of the present invention can be coated or otherwise compounded to  
15 provide a dosage form affording the advantage of prolonged action. For example, the tablet or pill can comprise an inner dosage and an outer dosage component, the latter being in the form of an envelope over the former. The two components can be separated by an enteric layer which serves to resist disintegration in the stomach and permit the inner component to pass intact into the duodenum or to be delayed in release. A variety of materials can be used for  
20 such enteric layers or coatings, such materials including a number of polymeric acids and mixtures of polymeric acids with such materials as shellac, cetyl alcohol, and cellulose acetate.

The liquid forms in which the compounds and compositions of the present invention can be incorporated for administration orally or by injection include aqueous solutions,  
25 suitably flavored syrups, aqueous or oil suspensions, and flavored emulsions with edible oils such as cottonseed oil, sesame oil, coconut oil, or peanut oil, as well as elixirs and similar pharmaceutical vehicles.

Compositions for inhalation or insufflation include solutions and suspensions in pharmaceutically acceptable, aqueous or organic solvents, or mixtures thereof, and powders.  
30 The liquid or solid compositions may contain suitable pharmaceutically acceptable excipients as described supra. In some embodiments, the compositions are administered by the oral or nasal respiratory route for local or systemic effect. Compositions in can be nebulized by use of inert gases. Nebulized solutions may be breathed directly from the nebulizing device or the nebulizing device can be attached to a face masks tent, or intermittent positive pressure

breathing machine. Solution, suspension, or powder compositions can be administered orally or nasally from devices which deliver the formulation in an appropriate manner.

The amount of compound or composition administered to a patient will vary depending upon what is being administered, the purpose of the administration, such as prophylaxis or therapy, the state of the patient, the manner of administration, and the like. In therapeutic applications, compositions can be administered to a patient already suffering from a disease in an amount sufficient to cure or at least partially arrest the symptoms of the disease and its complications. Effective doses will depend on the disease condition being treated as well as by the judgment of the attending clinician depending upon factors such as the severity of the disease, the age, weight and general condition of the patient, and the like.

The compositions administered to a patient can be in the form of pharmaceutical compositions described above. These compositions can be sterilized by conventional sterilization techniques, or may be sterile filtered. Aqueous solutions can be packaged for use as is, or lyophilized, the lyophilized preparation being combined with a sterile aqueous carrier prior to administration.

The therapeutic dosage of the compounds of the present invention can vary according to, for example, the particular use for which the treatment is made, the manner of administration of the compound, the health and condition of the patient, and the judgment of the prescribing physician. The proportion or concentration of a compound of the invention in a pharmaceutical composition can vary depending upon a number of factors including dosage, chemical characteristics (e.g., hydrophobicity), and the route of administration. The dosage is likely to depend on such variables as the type and extent of progression of the disease or disorder, the overall health status of the particular patient, the relative biological efficacy of the compound selected, formulation of the excipient, and its route of administration. Effective doses can be extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

The compounds of the invention can also be formulated in combination with one or more additional active ingredients which can include any pharmaceutical agent such as anti-viral agents, anti-cancer agents, vaccines, antibodies, immune enhancers, immune suppressants, anti-inflammatory agents and the like.

## EXAMPLES

Definitions: ACN (acetonitrile); AcOH (acetic acid); d (doublet); DCM (dichloromethane); DIBAL-H (diisobutylaluminium hydride); DIEA (N,N-diisopropylethylamine); DMF (N,N-

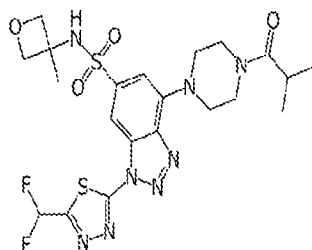
dimethylformamide); DMSO (dimethylsulfoxide); DMSO-*d*<sub>6</sub> (deuterated dimethylsulfoxide); EA (ethyl acetate); equiv (equivalents); ESI (electrospray ionization); EtOAc (ethyl acetate); EtOH (ethanol); g (gram); h (hour); HCl (hydrochloric acid); HOBT (hydroxybenzotriazole); <sup>1</sup>H NMR (proton nuclear magnetic resonance); Hz (hertz); IPA (iso-propyl alcohol); L (liter);

5 LCMS (liquid chromatography-mass spectrometry); LiCl (lithium chloride); LiOH (lithium hydroxide); M (molar); m (multiplet); MeOH (methanol); mg (milligrams); MHz (megahertz); min (minutes); mL (milliliters), mmol (millimoles); m/z (mass per charge); NBS (N-bromo succinimide); NFSI (N-fluorodi(benzenesulfonyl)amine); nm (nanometers); Pd-PEPPSI-IPent (dichloro[1,3-bis(2,6-di-3-pentylphenyl)imidazol-2-ylidene](3-

10 chloropyridyl)palladium(II)); PE (petroleum ether); PPh<sub>3</sub> (triphenylphosphine); ppm (parts per million); prep-HPLC (preparative high-performance liquid chromatography); q (quartet); RT (room temperature); RT (retention time); s (singlet); TEA (triethylamine); TEAB (tetraethylammonium bromide); THF (tetrahydrofuran); t (triplet); TLC (thin layer chromatography); UV (ultraviolet); and v/v (volume/volume).

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**Example 1: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-(3-methyloxetan-3-yl)-7-[4-(2-methylpropanoyl)piperazin-1-yl]-1,2,3-benzotriazole-5-sulfonamide**



20 *Step 1: N-(5-bromo-3-fluoro-2-nitrophenyl)-5-(difluoromethyl)-1,3,4-thiadiazol-2-amine.*

To a mixture of 5-bromo-1,3-difluoro-2-nitrobenzene (4 g, 16.808 mmol, 1 equiv), 5-(difluoromethyl)-1,3,4-thiadiazol-2-amine (3.05 g, 20.17 mmol, 1.2 equiv) and Cs<sub>2</sub>CO<sub>3</sub> (6.57 g, 20.17 mmol, 1.2 equiv) in DMF (40 mL) was stirred at 100 °C for 16 h. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The

25 resulting mixture was diluted with H<sub>2</sub>O (200 mL). The resulting mixture was extracted with EA (3×150 mL). The combined organic layers were washed with brine (2 × 200 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:1) to



afford N-(5-bromo-3-fluoro-2-nitrophenyl)-5-(difluoromethyl)-1,3,4-thiadiazol-2-amine (2.2 g, 31.91%) as a yellow solid. LCMS (ES, m/z): 372, 374 [M+H]<sup>+</sup>

*Step 2: 1-[4-(5-bromo-3-{[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl] amino}-2-nitrophenyl) piperazin-1-yl]-2-methylpropan-1-one.*

A mixture of 1-[4-(5-bromo-3-fluoro-2-nitrophenyl)piperazin-1-yl]-2-methylpropan-1-one (2 g, 5.345 mmol, 1 equiv), 5-(difluoromethyl)-1,3,4-thiadiazol-2-amine (0.97 g, 6.414 mmol, 1.2 equiv) and Cs<sub>2</sub>CO<sub>3</sub> (5.22 g, 16.035 mmol, 3 equiv) in THF (20 mL) was stirred at 70 °C for 16 h. The reaction was monitored by LCMS. The mixture was allowed to cool  
10 down to room temperature. The resulting mixture was diluted with H<sub>2</sub>O (150 mL). The resulting mixture was extracted with EA (3 × 100 mL). The combined organic layers were washed with brine (2 × 200 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:1) to afford 1-[4-(5-bromo-3-{[5-(difluoromethyl)-  
15 1,3,4-thiadiazol-2-yl] amino}-2-nitrophenyl) piperazin-1-yl]-2-methylpropan-1-one (800 mg, 26.66%) as a dark yellow solid. LCMS (ES, m/z): 505, 507[M+H]<sup>+</sup>

*Step 3: 1-[4-(2-amino-5-bromo-3-{[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl] amino} phenyl) piperazin-1-yl]-2-methylpropan-1-one.*

To a stirred mixture of 1-[4-(5-bromo-3-{[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl] amino}-2-nitrophenyl) piperazin-1-yl]-2-methylpropan-1-one (800 mg, 1.583 mmol, 1 equiv) in EA (10 mL) was added HOAc (3 mL), Fe powder (397.84 mg, 7.124 mmol, 4 equiv) and H<sub>2</sub>O (3 mL). The resulting mixture was stirred for 2 h at 70 °C. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The  
25 resulting mixture was diluted with H<sub>2</sub>O (100 mL). The resulting mixture was extracted with EA (3 × 80 mL). The combined organic layers were washed with brine (150 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:1) to afford 1-[4-(2-amino-5-bromo-3-{[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl] amino} phenyl) piperazin-1-yl]-2-methylpropan-1-one (600 mg, 71.76%) as a brown solid. LCMS (ES, m/z):  
30 475, 477 [M+H]<sup>+</sup>

*Step 4: 1-(4-{6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1,2,3-benzotriazol-4-yl}piperazin-1-yl)-2-methylpropan-1-one.*

To a stirred solution of 1-[4-(2-amino-5-bromo-3-{[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl] amino} phenyl) piperazin-1-yl]-2-methylpropan-1-one (600 mg, 1.262 mmol, 1 equiv) in conc. HCl (6 mL) was slowly added NaNO<sub>2</sub> (104.50 mg, 1.514 mmol, 1.2 equiv) at 0 °C. The resulting mixture was stirred for 2 h at room temperature. The reaction  
5 was monitored by LCMS. The mixture was basified to pH 10 with NaOH (1M). The resulting mixture was extracted with EA (3×80 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:1) to afford 1-(4-{6-bromo-1-[5-(difluoromethyl)-  
10 1,3,4-thiadiazol-2-yl]-1,2,3- benzotriazol-4-yl}piperazin-1-yl)-2-methylpropan-1-one (400 mg, 70.37%) as a yellow solid. LCMS (ES, m/z): 486, 488 [M+H]<sup>+</sup>

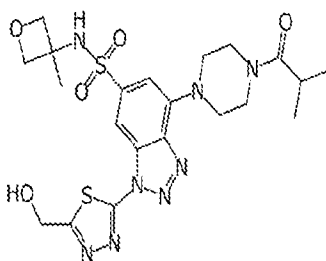
*Step 5: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[4-(2-methylpropanoyl)piperazin-1-yl]-1,2,3- benzotriazole-5-sulfonyl fluoride.*

To a stirred mixture of 1-(4-{6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-  
1,2,3- benzotriazol-4-yl}piperazin-1-yl)-2-methylpropan-1-one (600 mg, 1.234 mmol, 1  
equiv) in DMSO (10 mL) was added dipotassium sulfinosulfonate (548.56 mg, 2.468 mmol,  
2 equiv), tetraethylazanium bromide (285.20 mg, 1.357 mmol, 1.1 equiv), sodium formate  
(251.71 mg, 3.702 mmol, 3 equiv), PPh<sub>3</sub> (97.08 mg, 0.370 mmol, 0.3 equiv), phen (66.70 mg,  
20 0.370 mmol, 0.3 equiv) and palladium acetate (27.70 mg, 0.123 mmol, 0.1 equiv) at room  
temperature. The resulting mixture was stirred for 4 h at 70 °C under nitrogen atmosphere.  
The mixture was allowed to cool down to room temperature. To the above mixture was added  
the solution of NFSI (778.05 mg, 2.468 mmol, 2 equiv) in THF (2 mL) dropwise at room  
temperature. The resulting mixture was stirred for additional 2 h at room temperature. The  
25 reaction was monitored by LCMS. The resulting mixture was diluted with H<sub>2</sub>O (100 mL).  
The resulting mixture was extracted with EA (3×80 mL). The combined organic layers were  
washed with brine (2×100 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate  
was concentrated under reduced pressure. The residue was purified by silica gel column  
chromatography, eluted with PE/EA (1:1) to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-  
30 yl]-7-[4-(2-methylpropanoyl)piperazin-1-yl]-1,2,3- benzotriazole-5-sulfonyl fluoride (300  
mg, 50%) as a yellow solid. LCMS (ES, m/z): 490 [M+H]<sup>+</sup>

*Step 6: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-(3-methyloxetan-3-yl)-7-[4-(2-methylpropanoyl)piperazin-1-yl]-1,2,3-benzotriazole-5-sulfonamide.*

To a stirred solution of 1-(4-{6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl] - 1,2,3-benzotriazol-4-yl} piperazin-1-yl)-2-methylpropan-1-one (100 mg, 0.206 mmol, 1 equiv) and 3-methyloxetan-3-amine (35.83 mg, 0.412 mmol, 2 equiv) in DMSO (2 mL) were added HOBT (2.78 mg, 0.021 mmol, 0.1 equiv), [(dimethylsilyl)oxy] dimethylsilane (55.24 mg, 0.412 mmol, 2 equiv) and DIEA (132.88 mg, 1.030 mmol, 5 equiv) in portions at room temperature. The reaction was stirred at room temperature for 2 h. The reaction was monitored by LCMS. The resulting mixture was diluted with H<sub>2</sub>O (30 mL). The resulting mixture was extracted with EA (3×20 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The product was purified by prep-HPLC with the following conditions: (Column: XBridge Prep OBD C18 Column, 30\*150 mm, 5μm; Mobile Phase A: Water(10mmol/L NH<sub>4</sub>HCO<sub>3</sub>), Mobile Phase B: ACN; Flow rate: 60 mL/min mL/min; Gradient: 32%B to 62%B in 7 min; Wave Length: 254nm/220nm nm; RT1(min): 6.22) to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-(3-methyloxetan-3-yl)-7-[4-(2-methylpropanoyl)piperazin-1-yl]-1,2,3-benzotriazole-5-sulfonamide (45.3 mg, 39.26%) as a yellow solid. LCMS (ES, m/z): 557.15[M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, Chloroform-d) δ=8.40 (s, 1H), 7.29-6.89 (m, 2H), 5.75 (s, 1H), 4.77 (d, J=6.3 Hz, 2H), 4.36 (d, J=6.6 Hz, 2H), 4.11-3.78 (m, 8H), 2.95-2.78 (m, 1H), 1.65 (s, 3H), 1.19 (d, J=6.9 Hz, 6H).

**Example 2: 3-[5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl]-N-(3-methyloxetan-3-yl)-7-[4-(2-methylpropanoyl)piperazin-1-yl]-1,2,3-benzotriazole-5-sulfonamide**



*Step 1: 1-[4-(5-bromo-3-fluoro-2-nitrophenyl)piperazin-1-yl]-2-methylpropan-1-one.*

A solution of 5-bromo-1,3-difluoro-2-nitrobenzene (4 g, 16.808 mmol, 1 equiv), 2-methyl-1-(piperazin-1-yl)propan-1-one (2.63 g, 16.808 mmol, 1 equiv) and Cs<sub>2</sub>CO<sub>3</sub> (16.43 g, 50.424 mmol, 3 equiv) in DMF (40 mL) was stirred for overnight at 100 °C. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The

resulting mixture was diluted with water (120 mL). The resulting mixture was extracted with EtOAc (3×100 mL). The combined organic layers were washed with brine (3×100 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:1) to afford 1-[4-(5-bromo-3-fluoro-2-nitrophenyl)piperazin-1-yl]-2-methylpropan-1-one (5 g, 71.55%) as a yellow solid. LCMS (ESI, m/z): 374, 376[M+H]<sup>+</sup>.

*Step 2: ethyl 5-({5-bromo-3-[4-(2-methylpropanoyl)piperazin-1-yl]-2-nitrophenyl}amino)-1,3,4-thiadiazole-2-carboxylate.*

A solution of 1-[4-(5-bromo-3-fluoro-2-nitrophenyl)piperazin-1-yl]-2-methylpropan-1-one (4 g, 10.689 mmol, 1 equiv), ethyl 5-amino-1,3,4-thiadiazole-2-carboxylate (1.67 g, 9.620 mmol, 0.9 equiv) and Cs<sub>2</sub>CO<sub>3</sub> (10.45 g, 32.067 mmol, 3 equiv) in DMF (40 mL) was stirred for overnight at 70 °C. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The resulting mixture was diluted with water (150 mL). The resulting mixture was extracted with EtOAc (3 x 120 mL). The combined organic layers were washed with brine (2 x 150 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:1) to afford ethyl 5-({5-bromo-3-[4-(2-methylpropanoyl)piperazin-1-yl]-2-nitrophenyl}amino)-1,3,4-thiadiazole-2-carboxylate (3.8 g, 60.67%) as a yellow solid. LCMS (ESI, m/z): 527, 529 [M+H]<sup>+</sup>.

*Step 3: ethyl 5-({2-amino-5-bromo-3-[4-(2-methylpropanoyl)piperazin-1-yl] phenyl}amino)-1,3,4-thiadiazole-2-carboxylate.*

A mixture of ethyl 5-({5-bromo-3-[4-(2-methylpropanoyl)piperazin-1-yl]-2-nitrophenyl}amino)-1,3,4-thiadiazole-2-carboxylate (4.5 g, 8.533 mmol, 1 equiv) and Fe powder (1.91 g, 34.132 mmol, 4 equiv) in a mixed solvent of EA (40 mL), H<sub>2</sub>O (10 mL) and AcOH (3 mL) was stirred for 2 h at 70 °C. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The resulting mixture was filtered, the filter cake was washed with EtOAc (3 x 10 mL). The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with DCM/MeOH (10:1) to afford ethyl 5-({2-amino-5-bromo-3-[4-(2-methylpropanoyl)piperazin-1-yl] phenyl}amino)-1,3,4-thiadiazole-2-carboxylate (2 g, 42.41%) as a yellow solid. LCMS (ESI, m/z): 497, 499 [M+H]<sup>+</sup>.

*Step 4: ethyl 5-{6-bromo-4-[4-(2-methylpropanoyl)piperazin-1-yl]-1,2,3-benzotriazol-1-yl}-1,3,4-thiadiazole-2-carboxylate.*

To a stirred solution of ethyl 5-({2-amino-5-bromo-3-[4-(2-methylpropanoyl)piperazin-1-yl]phenyl} amino)-1,3,4-thiadiazole-2-carboxylate (2 g, 4.021 mmol, 1 equiv) in HCl (20 mL, 2M) was added NaNO<sub>2</sub> (0.35 g, 5.026 mmol, 1.25 equiv) in portions at 0 °C. The resulting mixture was stirred for 16 h at room temperature. The reaction was monitored by LCMS. The resulting mixture was diluted with water (50 mL). The mixture was extracted with EtOAc (3 x 80 mL). The combined organic layers were washed with brine (2 x 100 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:1) to afford ethyl 5-{6-bromo-4-[4-(2-methylpropanoyl)piperazin-1-yl]-1,2,3-benzotriazol-1-yl}-1,3,4-thiadiazole-2-carboxylate (700 mg, 30.82%) as a white solid. LCMS (ESI, m/z): 508, 510 [M+H]<sup>+</sup>.

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*Step 5: 1-(4-{6-bromo-1-[5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl]-1,2,3-benzotriazol-4-yl}piperazin-1-yl)-2-methylpropan-1-one.*

To a stirred solution of ethyl 5-{6-bromo-4-[4-(2-methylpropanoyl)piperazin-1-yl]-1,2,3-benzotriazol-1-yl}-1,3,4-thiadiazole-2-carboxylate (500 mg, 0.983 mmol, 1 equiv) in DCM (10 mL) was added DIBAL-H (1 M in DCM, 1.97 mL, 1.966 mmol, 2 equiv) at -78 °C under nitrogen atmosphere. The resulting mixture was stirred for 4 h at room temperature under nitrogen atmosphere. The reaction was monitored by LCMS. The reaction was quenched by the addition of potassium sodium tartrate (aq., 50 mL) at 0 °C. The resulting mixture was extracted with DCM (3 x 80 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:1) to afford 1-(4-{6-bromo-1-[5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl]-1,2,3-benzotriazol-4-yl}piperazin-1-yl)-2-methylpropan-1-one (200 mg, 39.25%) as a light yellow oil. LCMS (ESI, m/z): 466, 468[M+H]<sup>+</sup>.

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*Step 6: 1-(4-[6-bromo-1-(5-{[(tert-butyl)dimethylsilyl]oxy)methyl}-1,3,4-thiadiazol-2-yl]-1,2,3-benzotriazol-4-yl]piperazin-1-yl)-2-methylpropan-1-one.*

To a stirred mixture of 1-(4-{6-bromo-1-[5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl]-1,2,3-benzotriazol-4-yl}piperazin-1-yl)-2-methylpropan-1-one (200 mg, 0.429 mmol, 1

equiv) and imidazole (58.39 mg, 0.858 mmol, 2 equiv) in DCM (5 mL) was added TBSCl (96.96 mg, 0.643 mmol, 1.5 equiv) at 0 °C. The resulting mixture was stirred for 3 h at room temperature. The resulting mixture was diluted with DCM (30 mL). The resulting mixture was washed with water (3 x 20 mL). The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:1) to afford 1-{4-[6-bromo-1-(5-{[(tert-butyldimethylsilyl)oxy]methyl}-1,3,4-thiadiazol-2-yl)-1,2,3-benzotriazol-4-yl]piperazin-1-yl}-2-methylpropan-1-one (200 mg, 72.29%) as a yellow solid. LCMS (ESI, m/z): 580, 582 [M+H]<sup>+</sup>.

Step 7: 3-(5-{[(tert-butyldimethylsilyl)oxy]methyl}-1,3,4-thiadiazol-2-yl)-N-(3-methyloxetan-3-yl)-7-[4-(2-methylpropanoyl) piperazin-1-yl]-1,2,3-benzotriazole-5-sulfonamide.

A mixture of 1-{4-[6-bromo-1-(5-{[(tert-butyldimethylsilyl)oxy]methyl}-1,3,4-thiadiazol-2-yl)-1,2,3-benzotriazol-4-yl]piperazin-1-yl}-2-methylpropan-1-one (200 mg, 0.344 mmol, 1 equiv), TEAB (86.87 mg, 0.413 mmol, 1.2 equiv), HCOONa (70.28 mg, 1.032 mmol, 3 equiv), PPh<sub>3</sub> (27.10 mg, 0.103 mmol, 0.3 equiv), 1,10-phenanthroline (18.62 mg, 0.103 mmol, 0.3 equiv), Pd(OAc)<sub>2</sub> (7.73 mg, 0.034 mmol, 0.1 equiv) and K<sub>2</sub>S<sub>2</sub>O<sub>5</sub> (168.48 mg, 0.757 mmol, 2.2 equiv) in DMSO (5 mL) was stirred for 4 h at 70 °C under nitrogen atmosphere. To the above mixture was added 3-methyloxetan-3-amine (45.01 mg, 0.516 mmol, 1.5 equiv) and NBS (153.27 mg, 0.860 mmol, 2.5 equiv) in THF (2 mL) dropwise at 0 °C under nitrogen atmosphere. The final reaction mixture was stirred for 1 h at room temperature under nitrogen atmosphere. The reaction was monitored by LCMS. The resulting mixture was diluted with water (30 mL). The mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine (3 x 10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by Prep-TLC, eluted with PE/EA (1:3) to afford 3-(5-{[(tert-butyldimethylsilyl)oxy]methyl}-1,3,4-thiadiazol-2-yl)-N-(3-methyloxetan-3-yl)-7-[4-(2-methylpropanoyl) piperazin-1-yl]-1,2,3-benzotriazole-5-sulfonamide (50 mg, 20.07%) as a yellow solid. LCMS (ESI, m/z): 651 [M+H]<sup>+</sup>.

Step 8: 3-[5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl]-N-(3-methyloxetan-3-yl)-7-[4-(2-methylpropanoyl)piperazin-1-yl]-1,2,3-benzotriazole-5-sulfonamide.

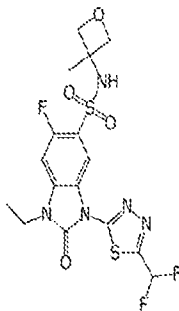
A solution of 3-(5-{[(tert-butyldimethylsilyl)oxy]methyl}-1,3,4-thiadiazol-2-yl)-N-(3-methyloxetan-3-yl)-7-[4-(2-methylpropanoyl)piperazin-1-yl]-1,2,3-benzotriazole-5-sulfonamide (40 mg, 0.061 mmol, 1 equiv) in THF (5 mL) was added HF-pyridine (1

mL) dropwise. The mixture was stirred for 3 h at room temperature. The reaction was monitored by LCMS. The resulting mixture was concentrated under reduced pressure. The crude product was purified by Prep-HPLC with the following conditions (Column: XBridge Shield RP 18 OBD Column, 30\*150 mm, 5 $\mu$ m; Mobile Phase A: Water (10mmol/L

- 5  $\text{NH}_4\text{HCO}_3$  + 0.1%  $\text{NH}_3\text{-H}_2\text{O}$ ), Mobile Phase B: ACN; Flow rate: 60 mL/min mL/min; Gradient: 23% B to 53% B in 7min; Wave Length: 254nm nm; RT1(min): 6.33) to afford 3-[5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl]-N-(3-methyloxetan-3-yl)-7-(4-propanoylpiperazin-1-yl)-1,2,3-benzotriazole-5-sulfonamide (2.6 mg, 8.08%) as a light-green solid. LCMS (ESI, m/z): 537.20  $[\text{M}+\text{H}]^+$ .  $^1\text{H}$  NMR (300 MHz, Chloroform- $d$ )  $\delta$ =8.41 (s, 1H), 7.16 (s, 1H), 5.68 (s, 1H), 5.17 (s, 2H), 4.77 (d, J = 6.6 Hz, 2H), 4.35 (d, J = 6.6 Hz, 2H), 4.04-3.98 (m, 2H), 3.95-3.79 (m, 6H), 3.03-2.97 (m, 1H), 2.95-2.80 (m, 1H), 1.66 (s, 3H), 1.19 (d, J = 6.6 Hz, 6H).
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**Example 3: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-benzodiazole-5-sulfonyl chloride**

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*Step 1: N-ethyl-5-fluoro-2-nitroaniline.*

- To a stirred mixture of 2,4-difluoro-1-nitro-benzene (3. g, 18.86 mmol, 1 equiv) and ethylamine (0.85 g, 18.86 mmol, 1 equiv) in 1,4-dioxane (50 mL) was added  $\text{K}_2\text{CO}_3$  (5.21 g, 37.71 mmol, 2 equiv) dropwise at room temperature. The reaction was monitored according to LCMS. The mixture was filtered. The filtrate was added with  $\text{H}_2\text{O}$  (100 mL) and extracted by EtOAc (100 mL x 3). The organic layer was combined, washed by brine (200 mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated. The residue was purified by silica gel column chromatography, eluted with PE / EA (1:1) to afford N-ethyl-5-fluoro-2-nitroaniline (1.5 g) as an off-white solid. LCMS (ESI, m/z): 185.10  $[\text{M}+\text{H}]^+$ .
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- 25

*Step 2: N1-ethyl-5-fluorobenzene-1,2-diamine.*

A mixture of N-ethyl-5-fluoro-2-nitroaniline (660 mg, 3.58 mmol, 1 equiv), Pd/C (381.37 mg, 0.36 mmol, 0.1 equiv, 10%) and H<sub>2</sub> (excess) in MeOH (10 mL) was stirred for 16h at room temperature. The resulting mixture was filtered, the filter cake was washed with MeOH (3 x 5 mL). To afford N1-ethyl-5-fluorobenzene-1,2-diamine) as an off-white solid. LCMS (ESI, m/z): 185.10 [M+H]<sup>+</sup>

*Step 3: 1-ethyl-6-fluoro-1,3-dihydro-2H-benzo[d]imidazol-2-one.*

A mixture of N1-ethyl-5-fluorobenzene-1,2-diamine (1.04 g, 6.754 mmol, 1 equiv) and CDI (1.10 g, 6.754 mmol, 1 equiv) in THF (30 mL) was stirred for 16 h at 60 °C. Water was added and the resulting mixture was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with water (3 x 50 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. LCMS (ESI, m/z): 181.05 [M+H]<sup>+</sup>.

*Step 4: 1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-5-fluoro-1,3-dihydro-2H-benzo[d]imidazol-2-one.*

A mixture of 1-ethyl-6-fluoro-3H-1,3-benzodiazol-2-one (500 mg, 2.775 mmol, 1 equiv), CuI (158.55 mg, 0.832 mmol, 0.3 equiv), K<sub>2</sub>CO<sub>3</sub> (1150.55 mg, 8.325 mmol, 3 equiv), (1S,2S)-N1,N2-dimethylcyclohexane-1,2-diamine (197.36 mg, 1.387 mmol, 0.5 equiv) and 2-bromo-5-(difluoromethyl)-1,3,4-thiadiazole (596.67 mg, 2.775 mmol, 1 equiv) in 1,4-dioxane (10 mL) was stirred for 4h at 80 °C. Add water, the resulting mixture was extracted with EtOAc (3 x10 mL). The combined organic layers were washed with water (3 x 10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. LCMS (ESI, m/z): 315.05 [M+H]<sup>+</sup>.

*Step 5: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-benzodiazole-5-sulfonyl chloride.*

The mixture of 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-5-fluoro-1,3-benzodiazol-2-one (30 mg, 0.095 mmol, 1 equiv) in HSO<sub>3</sub>Cl (0.5 mL, 7.595 mmol, 79.57 equiv) was stirred at 0 °C for 1 h under N<sub>2</sub> atmosphere. The desired product was detected by LCMS. The mixture was diluted by DCM (3 mL) and concentrated under reduced pressure. The procedure was repeated three times. The residue was diluted with EtOAc (5 mL) and quenched by ice. The organic was washed by brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-

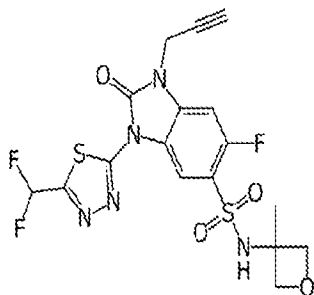


1,3-benzodiazole-5-sulfonyl chloride (30 mg, 76.14%) as yellow oil. LCMS (ESI, m/z): 412.95 [M+H]<sup>+</sup>

Step 6: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-N-(3-methyloxetan-3-yl)-2-oxo-1,3-benzodiazole-5-sulfonamide.

To the mixture of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-benzodiazole-5-sulfonyl chloride (25 mg, 0.061 mmol, 1 equiv) in DMF (1 mL, 12.922 mmol, 213.36 equiv) was added 3-methyloxetan-3-amine (7.91 mg, 0.091 mmol, 1.5 equiv) and TEA (12.26 mg, 0.122 mmol, 2 equiv). The mixture was stirred at room temperature for 16 h under nitrogen atmosphere. The desired product was detected by LCMS. The mixture was purified by Prep-HPLC with the following conditions (Column: XBridge Prep OBD C18 Column, 30\*150 mm, 5μm; Mobile Phase A: Water(10 mmol/L NH<sub>4</sub>HCO<sub>3</sub> + 0.1% NH<sub>3</sub>-H<sub>2</sub>O), Mobile Phase B: ACN; Flow rate: 60 mL/min; Gradient: 30% B to 60% B in 7 min, 60% B; Wave Length: 254 nm; RT1(min): 6; to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-N-(3-methyloxetan-3-yl)-2-oxo-1,3-benzodiazole-5-sulfonamide (3.7 mg, 13.18%) as a white solid. LCMS (ESI, m/z): 464.05 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ=8.79-8.64 (m, 2H), 7.50-7.88 (m, 2H), 4.64 (d, J=6.0 Hz, 2H), 4.17 (d, J = 6.4 Hz, 2H), 4.04-4.10 (m, 2H), 1.46 (s, 3H), 1.31 (d, J = 7.2 Hz, 3H).

**Example 4: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-(3-methyloxetan-3-yl)-2-oxo-1-(prop-2-yn-1-yl)-1,3-benzodiazole-5-sulfonamide**



Step 1: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-(3-methyloxetan-3-yl)-2-oxo-1H-1,3-benzodiazole-5-sulfonamide.

To a stirred solution of 3-methyloxetan-3-amine (90.58 mg, 1.040 mmol, 2 equiv) in DMF (1.5 mL) and TEA (0.5 mL, 3.597 mmol, 6.92 equiv) was added 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1H-1,3-benzodiazole-5-sulfonyl

chloride (200 mg, 0.520 mmol, 1 equiv) in DMF (1 mL) dropwise at 0 °C. The resulting mixture was stirred for 2 h at room temperature. The reaction was monitored by LCMS. Then water (30 mL) was added. The mixture was extracted with EA (3×20 mL), the combined organic layers were washed with brine (2 × 30 mL), dried over anhydrous

5 Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by silica gel column chromatography (eluting with 1:1 EA/PE) to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-(3-methyloxetan-3-yl)-2-oxo-1H-1,3-benzodiazole-5-sulfonamide (170 mg, 67.60%) as a yellow solid. LCMS (ESI, m/z): 436 [M+H]<sup>+</sup>.

10 *Step 2: N-{1-acetyl-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1,3-benzodiazol-5-ylsulfonyl}-N-(3-methyloxetan-3-yl)acetamide.*

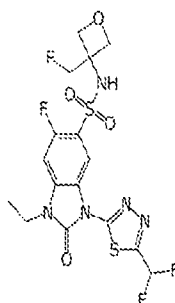
A mixture of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-(3-methyloxetan-3-yl)-2-oxo-1H-1,3-benzodiazole-5-sulfonamide (170 mg, 0.390 mmol, 1 equiv) and acetic anhydride (398.60 mg, 3.900 mmol, 10 equiv) in pyridine (3 mL) was stirred for 16 h at room temperature. The reaction was monitored by LCMS. Then water (30 mL) was added. The mixture was extracted with DCM (3 × 20 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated to afford N-{1-acetyl-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1,3-benzodiazol-5-ylsulfonyl}-N-(3-methyloxetan-3-yl)acetamide (150 mg, crude) as a yellow solid. LCMS (ESI, m/z): 520 [M+H]<sup>+</sup>.

*Step 3: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-(3-methyloxetan-3-yl)-2-oxo-1-(prop-2-yn-1-yl)-1,3-benzodiazole-5-sulfonamide.*

A mixture of N-{1-acetyl-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1,3-benzodiazol-5-ylsulfonyl}-N-(3-methyloxetan-3-yl)acetamide (50 mg, 0.096 mmol, 1 equiv), K<sub>2</sub>CO<sub>3</sub> (39.91 mg, 0.288 mmol, 3 equiv) and 3-bromoprop-1-yne (22.90 mg, 0.192 mmol, 2 equiv) in DMF (2 mL) was stirred for 16 h at 50 °C under N<sub>2</sub> atmosphere. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. Then NH<sub>3</sub>-H<sub>2</sub>O (2 mL) was added and stirred for 12 h. The reaction was monitored by LCMS. The mixture was added water (30 mL) and extracted with DCM (3 × 20 mL), the combined organic layers were washed with brine (30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by prep-HPLC with the following conditions: (Column: XBridge Prep OBD C18 Column, 30\*150 mm, 5μm; Mobile Phase A: Water (10 mmol/L NH<sub>4</sub>HCO<sub>3</sub> + 0.1% NH<sub>3</sub>-H<sub>2</sub>O), Mobile Phase B: ACN; Flow rate: 60

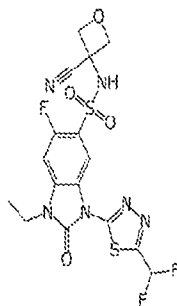
mL/min; Gradient: 30% B to 60% B in 7 min; WaveLength: 254 nm; RT1(min): 5.87) to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-(3-methyloxetan-3-yl)-2-oxo-1-(prop-2-yn-1-yl)-1,3-benzodiazole-5-sulfonamide (9.3 mg, 19.87%) as a yellow solid. LCMS (ESI, m/z): 474.05 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ=8.76-8.69 (m, 2H), 7.80-7.72 (m, 1H), 7.66-7.49 (m, 1H), 4.92 (s, 2H), 4.64 (d, J = 6.0 Hz, 2H), 4.18 (d, J = 6.4 Hz, 2H), 3.52 (s, 1H), 1.45 (s, 3H).

**Example 5: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide**



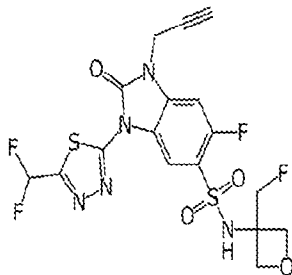
To the mixture of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-benzodiazole-5-sulfonyl chloride (30 mg, 0.073 mmol, 1 equiv) in DMF (1 mL) was added 3-(fluoromethyl)oxetan-3-amine hydrochloride (15.43 mg, 0.109 mmol, 1.5 equiv) and TEA (14.71 mg, 0.146 mmol, 2 equiv). The mixture was stirred at room temperature for 2 h. Desired product could be detected by LCMS. The mixture was purified by Prep-HPLC with the following conditions (Column: XBridge Prep Phenyl OBD Column, 19\*250 mm, 5μm; Mobile Phase A: Water(10 mmol/L NH<sub>4</sub>HCO<sub>3</sub> + 0.1% NH<sub>3</sub>-H<sub>2</sub>O), Mobile Phase B: ACN; Flow rate: 25 mL/min; Gradient: 35% B to 60% B in 10 min, 60% B; Wave Length: 254 nm; RT1(min): 8; to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide (3.2 mg, 9.08%) as a white solid. LCMS (ESI, m/z): 482.05 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ=8.96 (s, 1H), 8.73 (d, J=6.6 Hz, 1H), 7.89-7.42 (m, 2H), 4.69-4.60 (m, 3H), 4.58-4.53 (m, 1H), 4.38 (d, J=6.9 Hz, 2H), 4.05-3.98 (m, 2H), 1.31 (d, J=7.2 Hz, 3H).

**Example 6: N-(3-cyanooxetan-3-yl)-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-benzodiazole-5-sulfonamide**



To the mixture of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-benzodiazole-5-sulfonyl chloride (30 mg, 0.073 mmol, 1 equiv) in pyridine (2 mL) was added 3-aminooxetane-3-carbonitrile hydrochloride (14.67 mg, 0.109 mmol, 1.5 equiv). The mixture was stirred at room temperature for 2 h. Desired product could be detected by LCMS. The mixture was concentrated under reduced pressure. The crude product was purified by Prep-HPLC with the following conditions: (Column: XBridge Prep OBD C18 Column, 30\*150 mm, 5 $\mu$ m; Mobile Phase A: Water(10 mmol/L NH<sub>4</sub>HCO<sub>3</sub> + 0.1% NH<sub>3</sub>-H<sub>2</sub>O), Mobile Phase B: ACN; Flow rate: 60 mL/min; Gradient: 17% B to 47% B in 7 min, 47% B; Wave Length: 254 nm; RT1(min): 5.02; to afford N-(3-cyano-oxetan-3-yl)-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-benzodiazole-5-sulfonamide (9.8 mg, 27.67%) as an off-white semi-solid. LCMS (ESI, m/z): 475.05 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>)  $\delta$ =9.64 (s, 1H), 8.73 (d, J=6.6 Hz, 1H), 7.92-7.45 (m, 2H), 4.84 (d, J=7.2 Hz, 2H), 4.76 (d, J=7.2 Hz, 2H), 3.95-4.10 (m, 2H), 1.31 (t, J=7.2 Hz, 3H).

**Example 7: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-[3-(difluoromethyl)oxetan-3-yl]-2-oxo-1-(prop-2-yn-1-yl)-1,3-benzodiazole-5-sulfonamide**



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*Step 1: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1H-1,3-benzodiazole-5-sulfonyl chloride.*

A mixture of 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-5-fluoro-3H-1,3-benzodiazol-2-one (200 mg, 0.699 mmol, 1 equiv) in ClSO<sub>3</sub>H (1 mL) was stirred for 2 h at

60 °C. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The resulting mixture was diluted with EA (4 mL). The reaction was quenched by the addition of water (30 mL) at 0 °C. The mixture was extracted with EA (3 × 25 mL), the combined organic layers were washed with brine (30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1H-1,3-benzodiazole-5-sulfonyl chloride (200 mg, 74.40%) as a yellow solid. LCMS (ESI, m/z): 385 [M+H]<sup>+</sup>.

*Step 2: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1H-1,3-benzodiazole-5-sulfonamide.*

To a stirred solution of 3-(fluoromethyl)oxetan-3-amine hydrochloride (147.68 mg, 1.040 mmol, 2 equiv) in DMF (1.5 mL) and DIEA (0.5 mL) was added 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1H-1,3-benzodiazole-5-sulfonyl chloride (200 mg, 0.520 mmol, 1 equiv) in DMF (1 mL) dropwise at 0 °C. The resulting mixture was stirred for 2h at room temperature. The reaction was monitored by LCMS. Then water (30 mL) was added. The mixture was extracted with EA (3×20 mL), the combined organic layers were washed with brine (2×30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by silica gel column chromatography (eluting with 1:1 EA/PE) to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1H-1,3-benzodiazole-5-sulfonamide (20 mg, 6.79%) as a yellow solid. LCMS (ESI, m/z): 454 [M+H]<sup>+</sup>.

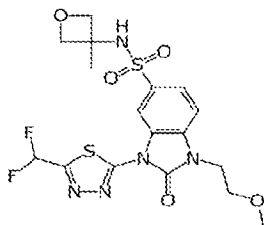
*Step 3: 1-acetyl-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide.*

A mixture of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1H-1,3-benzodiazole-5-sulfonamide (100 mg, 0.221 mmol, 1 equiv) and acetic anhydride (225.17 mg, 2.210 mmol, 10 equiv) in pyridine (3 mL) was stirred for 16 h at room temperature. The reaction was monitored by LCMS. Then water (20 mL) was added. The mixture was extracted with DCM (3 × 20 mL), the combined organic layers were washed with brine (30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated to afford 1-acetyl-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide (60 mg, 54.91%) as a yellow solid. LCMS (ESI, m/z): 538 [M+H]<sup>+</sup>.

Step 4: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1-(prop-2-yn-1-yl)-1,3-benzodiazole-5-sulfonamide.

A mixture of 1-acetyl-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide (60 mg, 0.121 mmol, 1 equiv), K<sub>2</sub>CO<sub>3</sub> (50.21 mg, 0.363 mmol, 3 equiv) and 3-bromoprop-1-yne (28.81 mg, 0.242 mmol, 2 equiv) in DMF (1 mL) was stirred for 16 h at 50 °C under N<sub>2</sub> atmosphere. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The reaction mixture was purified by prep-HPLC with the following conditions: (Column: XBridge Prep OBD C18 Column, 30\*150 mm, 5μm; Mobile Phase A: Water (10 mmol/L NH<sub>4</sub>HCO<sub>3</sub> + 0.1% NH<sub>3</sub>-H<sub>2</sub>O), Mobile Phase B: ACN; Flow rate: 60 mL/min; Gradient: 28% B to 58% B in 7 min; Wave Length: 254 nm; RT1(min): 5.48) to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1-(prop-2-yn-1-yl)-1,3-benzodiazole-5-sulfonamide (11.8 mg, 18.96%) as a white solid. LCMS (ESI, m/z): 492.05 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ=9.04 (s, 1H), 8.76 (d, J = 6.3 Hz, 1H), 7.84-7.46 (m, 2H), 4.92 (s, 2H), 4.69 (s, 1H), 4.67-4.60 (m, 2H), 4.54 (s, 1H), 4.37 (d, J = 7.2 Hz, 2H), 3.52 (s, 1H).

**Example 8: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-(2-methoxyethyl)-N-(3-methyloxetan-3-yl)-2-oxo-1,3-benzodiazole-5-sulfonamide**



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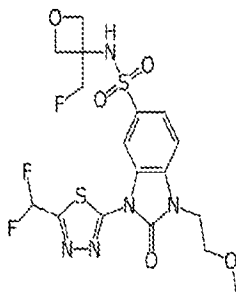
A solution of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-(2-methoxyethyl)-2-oxo-1,3-benzodiazole-5-sulfonyl chloride (50 mg, 0.118 mmol, 1 equiv) in DMF (2 mL) was added 3-methyloxetan-3-amine (20.51 mg, 0.236 mmol, 2 equiv) and DIEA (66.33 mg, 0.513 mmol, 3 equiv) dropwise at 0 °C. The resulting mixture was stirred for 2 h at room temperature. Desired product could be detected by LCMS. The resulting mixture was quenched with water (30 mL). The aqueous layer was extracted with EA (3 × 20 mL). The combined organic layers were washed by brine (30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by Prep-HPLC with the following condition: (Column: YMC-Actus Triart C18 ExRS, 30\*150

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mm, 5 $\mu$ m; Mobile Phase A: Water(10 mmol/L NH<sub>4</sub>HCO<sub>3</sub> + 0.1% NH<sub>3</sub>-H<sub>2</sub>O), Mobile Phase B: MeOH--HPLC; Flow rate: 60 mL/min; Gradient: 43% B to 63% B in 10 min, 63% B; Wave Length: 254 nm; RT1(min): 6.32; to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-(2-methoxyethyl)-N-(3-methyloxetan-3-yl)-2-oxo-1,3-benzodiazole-5-

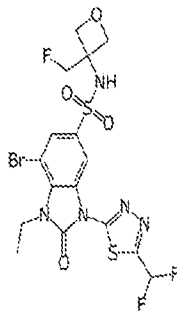
- 5 sulfonamide (15.5 mg, 27.61%) as a white solid. LCMS (ES, m/z): 476 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>)  $\delta$  8.81 (s, 1H), 8.38 (br, 1H), 7.84-7.80 (m, 1H), 7.79-7.47 (m, 2H), 4.55 (d, J = 6.0 Hz, 2H), 4.20 (t, J = 5.1 Hz, 2H), 4.11 (d, J = 6.3 Hz, 2H), 3.69 (t, J = 5.1 Hz, 2H), 3.25 (s, 3H), 1.45 (s, 3H).

10 **Example 9: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-N- (3-(fluoromethyl)oxetan-3-yl)-1-(2-methoxyethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide**



- A solution of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-(2-methoxyethyl)-2-oxo-1,3-benzodiazole-5-sulfonyl chloride (30 mg, 0.071 mmol, 1 equiv) in DMF (1 mL) was added 3-(fluoromethyl)oxetan-3-amine hydrochloride (20.16 mg, 0.142 mmol, 2 equiv) and DIEA (27.38 mg, 0.213 mmol, 3 equiv) dropwise at 0 °C. The resulting mixture was stirred for 2 h at room temperature. Desired product could be detected by LCMS. The solids was filtered and washed with EA (2  $\times$  5 mL). The filtration was concentrated. The residue was purified by Prep-HPLC with the following condition: (Column: XBridge Shield RP18 OBD Column, 30\*150 mm, 5 $\mu$ m; Mobile Phase A: Water(10 mmol/L NH<sub>4</sub>HCO<sub>3</sub>), Mobile Phase B: ACN; Flow rate: 60 mL/min; Gradient: 27% B to 57% B in 7 min, 57% B; Wave Length: 254 nm; RT1(min): 5.77; to afford 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-N- (3-(fluoromethyl)oxetan-3-yl)-1-(2-methoxyethyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide (7.3 mg, 20.97%) as a white solid. LCMS (ES, m/z): 494 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>)  $\delta$  8.82 (s, 1H), 7.86-7.82 (m, 1H), 7.81-7.46 (m, 2H), 6.63 (br, 1H), 4.71 (s, 1H), 4.55-4.52 (m, 3H), 4.35-4.32 (m, 2H), 4.21 (t, J = 7.2 Hz, 2H), 3.69 (t, J = 7.2 Hz, 2H), 3.25 (s, 3H).

**Example 10: 7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide**



5 *Step 1: 7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-benzodiazole-5-sulfonyl chloride.*

A solution of 4-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-1,3-benzodiazol-2-one (300 mg, 0.800 mmol, 1 equiv) in chlorosulfonic acid (2 mL) was stirred for 2 h at 60 °C. The reaction was quenched with H<sub>2</sub>O (30 mL) at 0 °C. The aqueous layer  
10 was extracted with EA (3×30 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure to afford 7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-benzodiazole-5-sulfonyl chloride (200 mg, crude). LCMS (ES, m/z): 473, 475[M+H]<sup>+</sup>

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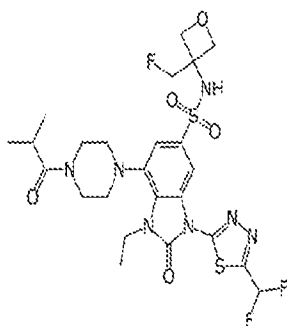
*Step 2: 7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide.*

A solution of 3-(fluoromethyl) oxetan-3-amine hydrochloride (29.89 mg, 0.212 mmol, 2 equiv) in DMF (2 mL) was added TEA (53.41 mg, 0.530 mmol, 5 equiv) and 7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-benzodiazole-5-sulfonyl  
20 chloride (50 mg, 0.106 mmol, 1 equiv) dropwise at 0 °C. The resulting mixture was stirred for additional 1 h at room temperature. The reaction was monitored by LCMS. The resulting mixture was diluted with H<sub>2</sub>O (30 mL). The resulting mixture was extracted with EA (3 × 20 mL). The combined organic layers were washed with saturation brine (2 × 30 mL), dried over  
25 anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by Prep-HPLC with the following conditions: (Column: Agilent ZORBAX SB-Aq, 21.2\*250mm 7μm; Mobile Phase A: Water (10 mmol/L NH<sub>4</sub>HCO<sub>3</sub> + 0.1% NH<sub>3</sub>-H<sub>2</sub>O), Mobile Phase B: ACN; Flow rate: 25 mL/min; Gradient: 45% B to 65% B in 7



min; Wave Length: 254 nm; RT1(min): 6.35) to afford 7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide (20.1 mg, 35.06%) as a white solid. LCMS (ES, m/z): 542, 544[M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ=9.00 (s, 1H), 8.91 (s, 1H), 7.95 (s, 1H), 7.64-7.46 (m, 1H), 4.73 (s, 1H), 4.57-4.54 (m, 3H), 4.37-4.30 (m, 4H), 1.38 (t, J = 6.9 Hz, 3H).

**Example 11: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-7-[4-(2-methylpropanoyl)piperazin-1-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide**



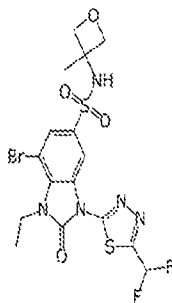
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To a stirred mixture of 7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide (450 mg, 0.830 mmol, 1 equiv) and 2-methyl-1-(piperazin-1-yl)propan-1-one (259.25 mg, 1.660 mmol, 2 equiv) in 1,4-dioxane (5 mL) was added Pd-PEPPSI-IPentCl (139.42 mg, 0.166 mmol, 0.2 equiv) in portions at room temperature under nitrogen atmosphere. The resulting mixture was stirred for 2 h at 90 °C under nitrogen atmosphere. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The resulting mixture was diluted with H<sub>2</sub>O (50 mL). The resulting mixture was extracted with EA (3 × 50 mL). The combined organic layers were washed with brine (2 × 50 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:1). The crude product was purified by Prep-HPLC with the following conditions: (Column: XSelect CSH Prep C18 OBD Column, 19\*250 mm, 5μm; Mobile Phase A: Water(0.1%FA), Mobile Phase B: ACN; Flow rate: 25 mL/min; Gradient: 43% B to 73% B in 7 min, 73% B; Wave Length: 254 nm; RT1(min): 6.78; Injection Volume: 0.8 mL; to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-7-[4-(2-methylpropanoyl)piperazin-1-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide (44.4 mg, 8.59%) as a white solid. LCMS (ES, m/z):

618.25 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ=8.81 (s, 1H), 8.74 (s, 1H), 7.79-7.50 (m, 2H), 4.70 (s, 1H), 4.59 (s, 1H), 4.57-4.50 (m, 3H), 4.38-4.25 (m, 4H), 4.14-4.07 (m, 1H), 3.45-3.34 (m, 1H), 3.14-3.06 (m, 2H), 3.03-2.91 (m, 1H), 2.90-2.72 (m, 3H), 1.39-1.32 (m, 3H), 1.12-0.99 (m, 6H).

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**Example 12: 7-bromo-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-methyloxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide**



10 *Step 1: 7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-benzodiazole-5-sulfonyl chloride.*

A solution of 4-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-1,3-benzodiazol-2-one (300 mg, 0.800 mmol, 1 equiv) in chlorosulfonic acid (2 mL) was stirred for 2 h at 60 °C. The reaction was quenched with H<sub>2</sub>O (30 mL) at 0 °C. The aqueous layer  
15 was extracted with EA (3×20 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure to afford 7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-benzodiazole-5-sulfonyl chloride (200 mg, crude). LCMS (ES, m/z): 473, 475[M+H]<sup>+</sup>

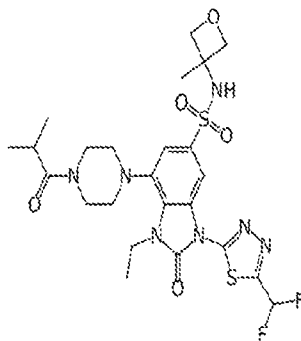
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*Step 2: 7-bromo-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-methyloxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.*

A solution of 3-methyloxetan-3-amine (165 mg, 1.899 mmol, 3 equiv) in DMF (1 mL) was treated with TEA (53 mg, 0.530 mmol, 5 equiv) for 5 min at 0 °C followed by the  
25 addition of 7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-benzodiazole-5-sulfonyl chloride (50 mg, 0.106 mmol, 1 equiv) dropwise at 0 °C. The resulting mixture was stirred for additional 1 h at 25 °C. The reaction was monitored by LCMS. The resulting mixture was quenched with water (30 mL). The aqueous layer was

extracted with EA (3 × 20 mL). The combined organic layers were washed by brine (30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by Prep-HPLC with the following conditions: (Column: Agilent ZORBAX SB-Aq, 21.2\*250mm 7μm; Mobile Phase A: Water(10 mmol/L NH<sub>4</sub>HCO<sub>3</sub> + 0.1% NH<sub>3</sub>-H<sub>2</sub>O), Mobile Phase B: ACN; Flow rate: 25 mL/min; Gradient: 45% B to 65% B in 7 min; Wave Length: 254 nm; RT1(min): 6.35) to afford 7-bromo-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-methyloxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide (24.5 mg, 28.22%) as a white solid. LCMS (ES, m/z): 524, 526[M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ 8.89 (s, 1H), 8.30 (s, 1H), 7.92 (s, 1H), 7.64-7.46 (m, 1H), 4.56 (d, J = 6.3 Hz, 2H), 4.37-4.30 (m, 2H), 4.15 (d, J = 6.6 Hz, 2H), 1.46 (s, 3H), 1.37 (t, J = 6.9 Hz, 3H).

**Example 13: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-(3-methyloxetan-3-yl)-7-[4-(2-methylpropanoyl) piperazin-1-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide**

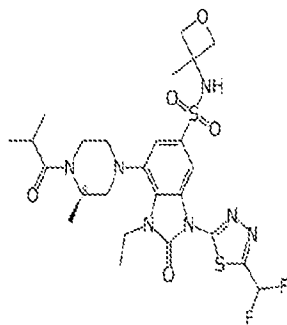


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To a stirred solution of 7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-(3-methyloxetan-3-yl)-2-oxo-1,3-benzodiazole-5-sulfonamide (500 mg, 0.954 mmol, 1 equiv) in dioxane (5 mL) was added Pd-PEPPSI-IPentCl (160.22 mg, 0.191 mmol, 0.2 equiv), Cs<sub>2</sub>CO<sub>3</sub> (932.05 mg, 2.862 mmol, 3 equiv) and 2-methyl-1-(piperazin-1-yl)propan-1-one (297.94 mg, 1.908 mmol, 2 equiv) at room temperature under nitrogen atmosphere. The resulting mixture was stirred for 2 h at 80 °C under nitrogen atmosphere. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The resulting mixture was diluted with H<sub>2</sub>O (50 mL). The filtrate was extracted with EA (3 × 50 mL). The combined organic layers were washed with brine (2×50 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The crude product was purified by Prep-HPLC with the following conditions: (Column: C18; Mobile Phase A: Water (10 mmol/L NH<sub>4</sub>HCO<sub>3</sub>), Mobile Phase B: ACN; Flow rate: 50

mL/min; Gradient: 45% B to 65% B in 10 min, 65% B; Wave Length: 254 nm; RT1(min): 6.35 to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-(3-methyloxetan-3-yl)-7-[4-(2-methylpropanoyl) piperazin-1-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide (50.9 mg, 8.64%) as a white solid. LCMS (ES, m/z): 600.20[M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ=8.72 (s, 1H), 8.45 (br, 1H), 7.86-7.43 (m, 2H), 4.58-4.49 (m, 3H), 4.35-4.07 (m, 5H), 3.42-3.33 (m, 1H), 3.18-3.07 (m, 2H), 3.01-2.68 (m, 4H), 1.45 (s, 3H), 1.34 (t, J=6.9 Hz, 3H), 1.12-0.98 (m, 6H).

**Example 14: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(methyl)oxetan-3-yl]-7-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide**



*Step 1: tert-butyl (2R)-4-(5-bromo-3-fluoro-2-nitrophenyl)-2-methylpiperazine-1-carboxylate.*

A mixture of 5-bromo-1,3-difluoro-2-nitrobenzene (10 g, 42.019 mmol, 1 equiv), Cs<sub>2</sub>CO<sub>3</sub> (34.23 g, 105.047 mmol, 2.5 equiv) and tert-butyl (2R)-2-methylpiperazine-1-carboxylate (8.42 mg, 0.042 mmol, 1 equiv) in DMF (100 mL) was stirred for 2 h at 100 °C. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The resulting mixture was diluted with water (1000 mL). The resulting mixture was washed with EA (3 x 600 mL). The combined organic layers were brine (2 x 800 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (3:1) to afford tert-butyl (2R)-4-(5-bromo-3-fluoro-2-nitrophenyl)-2-methylpiperazine-1-carboxylate (12.5 g, 71.12%) as a yellow oil. LCMS (ESI, m/z): 418, 420 [M+H]<sup>+</sup>

*Step 2: (3R)-1-(5-bromo-3-fluoro-2-nitrophenyl)-3-methylpiperazine.*

A solution tert-butyl (2R)-4-(5-bromo-3-fluoro-2-nitrophenyl)-2-methylpiperazine-1-carboxylate (12.5 g, 0.030 mol, 1 equiv) in HCl (4 M in dioxane, 100 mL) was stirred for 2 h at room temperature. The reaction was monitored by LCMS. The resulting mixture was concentrated under reduced pressure to afford (3R)-1-(5-bromo-3-fluoro-2-nitrophenyl)-3-methylpiperazine (14 g, crude) as a yellow oil. LCMS (ESI, m/z): 318, 320 [M+H]<sup>+</sup>.

*Step 3: 1-[(2R)-4-(5-bromo-3-fluoro-2-nitrophenyl)-2-methylpiperazin-1-yl]-2-methylpropan-1-one.*

Into a mixture of (3R)-1-(5-bromo-3-fluoro-2-nitrophenyl)-3-methylpiperazine (14 g, 44.005 mmol, 1 equiv) and TEA (13.36 g, 132.015 mmol, 3 equiv) in DCM (100 mL) was added isobutyryl chloride (9.38 g, 88.010 mmol, 2 equiv) dropwise at 0 °C. The resulting mixture was stirred for 2 h at room temperature. The reaction was monitored by LCMS. The reaction was quenched by the addition of water (600 mL). The aqueous layer was extracted with DCM (3 x 600 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:1) to afford 1-[(2R)-4-(5-bromo-3-fluoro-2-nitrophenyl)-2-methylpiperazin-1-yl]-2-methylpropan-1-one (10.5 g, 61.46%) as a yellow solid. LCMS (ESI, m/z): 388, 390 [M+H]<sup>+</sup>.

*Step 4: 1-[(2R)-4-(5-bromo-3-{[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino}-2-nitrophenyl)-2-methylpiperazin-1-yl]-2-methylpropan-1-one.*

A mixture of 1-[(2R)-4-(5-bromo-3-fluoro-2-nitrophenyl)-2-methylpiperazin-1-yl]-2-methylpropan-1-one (10.5 g, 27.045 mmol, 1 equiv), 5-(difluoromethyl)-1,3,4-thiadiazol-2-amine (4.90 g, 32.454 mmol, 1.2 equiv) and Cs<sub>2</sub>CO<sub>3</sub> (26.44 g, 81.135 mmol, 3 equiv) in DMF (100 mL) was stirred for 16 h at 70 °C. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The resulting mixture was diluted with ethyl acetate (1 L). The resulting mixture was washed with 2 x 600 mL of water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:1) to afford 1-[(2R)-4-(5-bromo-3-{[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino}-2-nitrophenyl)-2-methylpiperazin-1-yl]-2-methylpropan-1-one (9.5 g, 67.63%) as a yellow solid. LCMS (ESI, m/z): 519, 521 [M+H]<sup>+</sup>.

Step 5: 1-[(2R)-4-(2-amino-5-bromo-3-{[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino}phenyl)-2-methylpiperazin-1-yl]-2-methylpropan-1-one.

A mixture of 1-[(2R)-4-(5-bromo-3-{[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino}-2-nitrophenyl)-2-methylpiperazin-1-yl]-2-methylpropan-1-one (9.5 g, 18.291 mmol, 1 equiv) and B<sub>2</sub>(OH)<sub>4</sub> (6.56 g, 73.164 mmol, 4 equiv) in DMF (100 mL) was added 4-(pyridin-4-yl)pyridine (0.03 g, 0.192 mmol, 0.01 equiv) in portions at -50 °C. The resulting mixture was stirred for 2 h at room temperature. The reaction was monitored by LCMS. The resulting mixture was diluted with water (1 L). The resulting mixture was washed with EA (3 x 600 mL). The combined organic layers were brine (2 x 800 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (1:3) to afford 1-[(2R)-4-(2-amino-5-bromo-3-{[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino}phenyl)-2-methylpiperazin-1-yl]-2-methylpropan-1-one (7.3 g, 81.55%) as a yellow solid. LCMS (ESI, m/z): 489, 491 [M+H]<sup>+</sup>.

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Step 6: 6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-3H-1,3-benzodiazol-2-one.

A mixture of 1-[(2R)-4-(2-amino-5-bromo-3-{[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino}phenyl)-2-methylpiperazin-1-yl]-2-methylpropan-1-one (7.3 g, 14.917 mmol, 1 equiv) and CDI (4.84 g, 29.834 mmol, 2 equiv) in DMF (60 mL) was stirred for 16 h at 85 °C. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The resulting mixture was diluted with water (600 mL). The resulting mixture was washed with EA (3 x 300 mL). The combined organic layers were washed with brine (2 x 500 mL) dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The crude product was re-crystallized from EA/MeOH (20:5) to afford 6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-3H-1,3-benzodiazol-2-one (3.2787 g, 41.06%) as an off-white solid. LCMS (ESI, m/z): 515, 517 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>) δ=12.22 (s, 1H), 8.19 (d, J = 1.5 Hz, 1H), 7.80-7.44 (m, 1H), 7.07 (d, J = 1.8 Hz, 1H), 4.76-3.33 (m, 4H), 3.15-2.98 (m, 2H), 2.97-2.81 (m, 1H), 2.51-2.31 (m, 1H), 1.35-1.15 (m, 3H), 1.03 (d, J = 6.6 Hz, 6H).

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Step 7: 6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-1,3-benzodiazol-2-one.

A mixture of 6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-3H-1,3-benzodiazol-2-one (250 mg, 0.485 mmol, 1 equiv), bromoethane (105.71 mg, 0.970 mmol, 2 equiv) and Cs<sub>2</sub>CO<sub>3</sub> (395.12 mg, 1.212 mmol, 2.5 equiv) in DMF (8 mL) was stirred for 16 h at 70 °C. The reaction was monitored by LCMS. The mixture was allowed to cool down to room temperature. The resulting mixture was diluted with water (100 mL). The resulting mixture was washed with EA (3 x 80 mL). The combined organic layers were washed with brine (2 x 120 mL) dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (3:1) to afford 6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-1,3-benzodiazol-2-one (120 mg, 45.52%) as a yellow solid. LCMS (ESI, m/z): 543, 545[M+H]<sup>+</sup>.

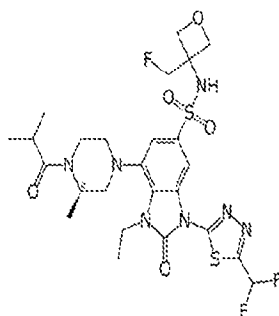
*Step 8: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-2-oxo-1,3-benzodiazole-5-sulfonyl fluoride.*

A mixture of 6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-1,3-benzodiazol-2-one (150 mg, 0.276 mmol, 1 equiv), potassium metabisulfite (122.73 mg, 0.552 mmol, 2 equiv), tetraethylazanium bromide (63.81 mg, 0.304 mmol, 1.1 equiv), sodium formate (56.31 mg, 0.828 mmol, 3 equiv), PPh<sub>3</sub> (21.72 mg, 0.083 mmol, 0.3 equiv), phen (14.92 mg, 0.083 mmol, 0.3 equiv) and Pd(OAc)<sub>2</sub> (6.20 mg, 0.028 mmol, 0.1 equiv) in DMSO (3 mL) was stirred for 4 h at 70 °C under nitrogen atmosphere. To the above mixture was added NFSI (174.08 mg, 0.552 mmol, 2 equiv) in THF (1 mL) dropwise at 0 °C. The resulting mixture was stirred for additional 1 h at room temperature. The reaction was monitored by LCMS. The resulting mixture was diluted with water (80 mL). The resulting mixture was washed with EA (3 x 60 mL). The combined organic layers were washed with brine (2 x 100 mL) dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE / EA (1:1) to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-2-oxo-1,3-benzodiazole-5-sulfonyl fluoride (100 mg, 66.28%) as a white solid. LCMS (ESI, m/z): 547[M+H]<sup>+</sup>.

Step 9: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-N-(3-methyloxetan-3-yl)-2-oxo-1,3-benzodiazole-5-sulfonamide.

A mixture of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-2-oxo-1,3-benzodiazole-5-sulfonyl fluoride (100 mg, 0.183 mmol, 1 equiv), 3-methyloxetan-3-amine (31.88 mg, 0.366 mmol, 2 equiv), HOBt (49.44 mg, 0.366 mmol, 2 equiv), DIEA (70.94 mg, 0.549 mmol, 3 equiv) and [(dimethylsilyl)oxy]dimethylsilane (49.15 mg, 0.366 mmol, 2 equiv) in DMSO (2 mL) was stirred for 2 h at room temperature. The reaction was monitored by LCMS. The resulting mixture was diluted with water (60 mL). The resulting mixture was washed with EA (3 x 50 mL). The combined organic layers were washed with brine (2 x 80 mL) dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The crude product was purified by Prep-HPLC with the following conditions (Column: XBridge BEH Shield RP18 Column, 19\*250 mm, 5µm; Mobile Phase A: Water(10mmol/L NH<sub>4</sub>HCO<sub>3</sub>), Mobile Phase B: ACN; Flow rate: 25 mL/min mL/min; Gradient: 41%B to 71%B in 7 min; Wave Length: 254nm/220nm nm; RT1(min): 6.53) to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-N-(3-methyloxetan-3-yl)-2-oxo-1,3-benzodiazole-5-sulfonamide (32.7 mg, 28.98%) as a white solid. LCMS (ESI, m/z): 614 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ=8.73 (s, 1H), 8.47 (s, 1H), 7.78-7.51 (m, 2H), 4.81-3.89 (m, 8H), 3.57-2.87 (m, 5H), 2.67-2.50 (m, 1H), 1.45-1.42 (m, 4H), 1.34 (t, J = 6.8 Hz, 3H), 1.27 (d, J = 6.8 Hz, 2H), 1.11-0.99 (m, 6H).

**Example 15: 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-7-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-2-oxo-1,3-benzodiazole-5-sulfonamide**





A mixture of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-2-oxo-1,3-benzodiazole-5-sulfonyl fluoride (100 mg, 0.183 mmol, 1 equiv), HOBT (169.82 mg, 0.458 mmol, 2.5 equiv), 3-(fluoromethyl)oxetan-3-amine (38.46 mg, 0.366 mmol, 2 equiv), DIEA (70.94 mg, 0.549 mmol, 3 equiv) and

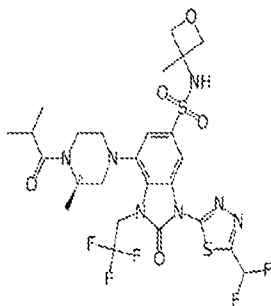
5 [(dimethylsilyl)oxy]dimethylsilane (147.45 mg, 1.098 mmol, 6 equiv) in DMSO (2 mL) was stirred for 2 h at room temperature. The reaction was monitored by LCMS. The resulting mixture was diluted with ethyl acetate (60 mL). The residue was washed with water (4 x 30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the filtrate was concentrated under reduced pressure. The crude product was purified by Prep-HPLC with the following

10 conditions (Column: XBridge BEH Shield RP18 Column, 19\*250 mm, 5μm; Mobile Phase A: Water(10mmol/L NH<sub>4</sub>HCO<sub>3</sub>), Mobile Phase B: ACN; Flow rate: 25 mL/min mL/min; Gradient: 45%B to 75%B in 7 min; Wave Length: 254nm/220nm nm; RT1(min): 6.55) to afford 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-7-[(3R)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]-2-oxo-1,3-benzodiazole-5-

15 sulfonamide (30.7 mg, 26.52%) as a white solid. LCMS (ESI, m/z): 632.25[M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ=8.83 (s, 1H), 8.75 (s, 1H), 7.78-7.51 (m, 2H), 4.81–4.49 (m, 10H), 3.65–2.87 (m, 5H), 2.67-2.51 (m, 1H), 1.43-1.23 (m, 6H), 1.11-0.99 (m, 6H).

**Example 16: 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-3-(2,2,2-trifluoroethyl)-1,3-dihydro-1,3-benzimidazol-2-one**

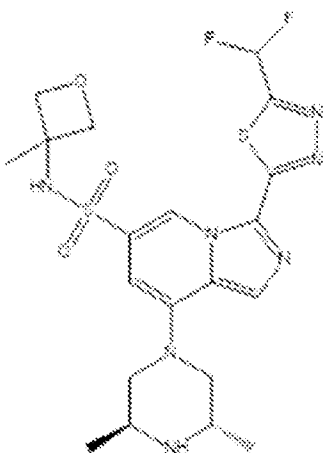
20



MS (m/z): 668.00[M+H]<sup>+</sup>. <sup>1</sup>H NMR (400MHz DMSO-d<sub>6</sub>) δ=8.78 (s, 1H) 8.54 (s, 1H), 7.87 (s, 1H), 7.79-7.53 (m, 1H), 5.42-5.18 (m, 2H) 4.86-3.91 (m, 6H), 5.51-3.18 (m, 1H), 3.12-2.89.

25

**Example 17: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-8-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-methyloxetan-3-yl)imidazo[1,5-a]pyridine-6-sulfonamide**



*Step 1: (5-bromo-3-chloropyridin-2-yl)methanamine.*

5 To an oven-dried flask was added compound 5-bromo-3-chloropyridinonitrile (20.00 g, 91.97 mmol) and DCE (200 mL) at r. t. Then the DIBALH (275.92 mmol, 276 mL) was added dropwise at 0 °C under N<sub>2</sub> atmosphere. The reaction mixture was then stirred at r. t. for 20 hours until the reaction completed (detected with LC-MS). The resulting solution was diluted with NH<sub>4</sub>Cl (aq) carefully, followed by added 2 N NaOH to adjust the pH to 12. The mixture was extracted with DCM (200 mL X 3) and the combined organic phase was washed with brine, dried with anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo* to give compound (5-bromo-3-chloropyridin-2-yl)methanamine (crude), which was used for the next step without further purification.

15 *Step 2: ethyl 2-(((5-bromo-3-chloropyridin-2-yl)methyl)amino)-2-oxoacetate*

To a mixture of (5-bromo-3-chloropyridin-2-yl)methanamine (13.50 g, 60.95 mmol) and DIPEA (15.76 g, 121.91 mmol, 21.23 mL) in DCM (200 mL) was added ethyl 2-chloro-2-oxoacetate **3** (9.99 g, 73.14 mmol) dropwise at 0 °C. The reaction mixture was stirred at r. t. for 1 hour. Once the reaction completed (detected by LC-MS), the resulting mixture was diluted with water (100 mL) before extracted with DCM (200 mL X 3). The organic phase were combined, washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and the filtrate was concentrated *in vacuo*. The remaining residue was purified by silica-gel c. c. to give ethyl 2-(((5-bromo-3-chloropyridin-2-yl)methyl)amino)-2-oxoacetate (11.6 g, 36.07 mmol, 59.18% yield) as a yellow solid.

25

*Step 3: ethyl 6-bromo-8-chloroimidazo[1,5-a]pyridine-3-carboxylate*

To a mixture of 2-(((5-bromo-3-chloropyridin-2-yl)methyl)amino)-2-oxoacetate (11.60 g, 36.07 mmol) in POCl<sub>3</sub> (60 mL) was added P<sub>2</sub>O<sub>5</sub> (15.36 g, 108.22 mmol) at 0 °C carefully. Then the mixture was stirred at 110 °C for 2 hours till the reaction completed (monitored with LC-MS). The mixture was concentrated *in vacuo* to afford a yellow solid, which was then dissolved in EA (100 mL). The organic phase was washed with water, NaHCO<sub>3</sub> (aq) and brine. Then the combined organic phase was concentrated *in vacuo* to afford ethyl 6-bromo-8-chloroimidazo[1,5-a]pyridine-3-carboxylate (10.70 g, 35.25 mmol, 97.72% yield) as a yellow solid.

10

*Step 4: 6-bromo-8-chloroimidazo[1,5-a]pyridine-3-carbohydrazide*

To a solution of ethyl 6-bromo-8-chloroimidazo[1,5-a]pyridine-3-carboxylate (10.70 g, 35.25 mmol) in ethanol (120 mL) was added NH<sub>2</sub>NH<sub>2</sub> (11.30 g, 352.51 mmol) under 0 °C, and the resulting mixture was stirred at 80 °C for 2 hours. After 2 hours, LC-MS analysis showed the completion of reaction. The reaction mixture was cooled to 0 °C and filtered. The solid was washed with ethanol (100 mL), and dried to afford the 6-bromo-8-chloroimidazo[1,5-a]pyridine-3-carbohydrazide (8.0 g, 27.63 mmol, 78.39% yield) as an off-white solid.

15

*Step 5: 6-bromo-8-chloro-N'-(2,2-difluoroacetyl)imidazo[1,5-a]pyridine-3-carbohydrazide*

To a mixture of 6-bromo-8-chloroimidazo[1,5-a]pyridine-3-carbohydrazide (8.00 g, 27.63 mmol) in ethanol (120 mL) was added ethyl 2,2-difluoroacetate **7** (34.29 g, 276.32 mmol) and DBU (8.40 g, 55.26 mmol). The mixture was stirred at 100 °C for 2 hours till the reaction completed (detected by LC-MS). The mixture was concentrated *in vacuo*, and the residue was washed with PET/EtOH (5:1) 3 times to afford the 6-bromo-8-chloro-N'-(2,2-difluoroacetyl)imidazo[1,5-a]pyridine-3-carbohydrazide (10.0 g, 27.21 mmol, 98.47% yield) as a yellow solid.

25

*Step 6: 2-(6-bromo-8-chloroimidazo[1,5-a]pyridin-3-yl)-5-(difluoromethyl)-1,3,4-thiadiazole*

To a mixture of 6-bromo-8-chloro-N'-(2,2-difluoroacetyl)imidazo[1,5-a]pyridine-3-carbohydrazide (10.00 g, 27.21 mmol) in toluene (110 mL) was added the Lawesson's reagent (12.11 g, 29.93 mmol) at r. t, and the resulting mixture was stirred at 120 °C for 2 hours under N<sub>2</sub> till reaction completed (detected by LC-MS). The solvent was evaporated almost completely. Methanol (100 mL) was then added and the mixture was stirred at 70 °C

30

for 30 minutes. The mixture was then cooled to 0°C and filtered to afford 2-(6-bromo-8-chloroimidazo[1,5-a]pyridin-3-yl)-5-(difluoromethyl)-1,3,4-thiadiazole (7.1 g, 19.42 mmol, 71.38% yield) as an off-white solid.

5 *Step 7: 2-(6-(benzylthio)-8-chloroimidazo[1,5-a]pyridin-3-yl)-5-(difluoromethyl)-1,3,4-thiadiazole*

To a mixture of 2-(6-bromo-8-chloroimidazo[1,5-a]pyridin-3-yl)-5-(difluoromethyl)-1,3,4-thiadiazole (7.10 g, 19.42 mmol) and phenylmethanethiol (2.65 g, 21.36 mmol) in dioxane (120 mL) was added the Pd<sub>2</sub>(dba)<sub>3</sub> (888.51 mg, 971.05 μmol), XantPhos (1.12 g, 1.94 mmol) and DIPEA (7.53 g, 58.26 mmol, 10.15 mL). Then the mixture was stirred at 90  
10 °C for 4 hours under N<sub>2</sub> till the reaction completed (detected by LC-MS). The solvent was evaporated almost completely. The crude product was washed with MeCN (50 mL) to afford the 2-(6-(benzylthio)-8-chloroimidazo[1,5-a]pyridin-3-yl)-5-(difluoromethyl)-1,3,4-thiadiazole (7.6 g, 18.59 mmol, 95.71% yield) as a yellow solid.

15

*Step 8: 2-(6-(benzylthio)-8-chloro-1-iodoimidazo[1,5-a]pyridin-3-yl)-5-(difluoromethyl)-1,3,4-thiadiazole*

To a mixture of 2-(6-(benzylthio)-8-chloroimidazo[1,5-a]pyridin-3-yl)-5-(difluoromethyl)-1,3,4-thiadiazole (7.60 g, 18.59 mmol) in MeCN (60 mL) was added AcOH  
20 (2.5 mL) at r. t. Then the NIS (8.36 g, 37.18 mmol) was added at 0 °C. The resulting mixture was then stirred at 20 °C for 16 hours till the reaction completed (monitored by LC-MS). The mixture was filtered to afford the 2-(6-(benzylthio)-8-chloro-1-iodoimidazo[1,5-a]pyridin-3-yl)-5-(difluoromethyl)-1,3,4-thiadiazole (7.5 g, 14.02 mmol, 75.45% yield) as a yellow solid.

25 *Step 9: 8-chloro-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-iodoimidazo[1,5-a]pyridine-6-sulfonyl chloride*

To a mixture of compound (4.36 g, 8.15 mmol) in acetic acid (30 mL) and water (6 mL) were added NCS (2.72 g, 20.38 mmol) and 2 drops of HCl in ice bath. The resulting mixture was stirred at r. t. for 30 minutes. The reaction mixture was clear first and then a  
30 precipitate appeared. LC-MS analysis showed the reaction was completed. Then the mixture was added ice cold water (70 mL) and filtered. The filtrate was combined and dried by lyophilization to afford 8-chloro-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-iodoimidazo[1,5-a]pyridine-6-sulfonyl chloride (245.97 mg, 2.82 mmol).

Step 10: 8-chloro-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-iodo-N-(3-methyloxetan-3-yl)imidazo[1,5-a]pyridine-6-sulfonamide

To a flask were added 3-methyloxetan-3-amine (245.97 mg, 2.82 mmol), THF (4 mL) and water (2 mL). The NaHCO<sub>3</sub> (395.27 mg, 4.71 mmol) was added at r. t. The mixture of compound (481 mg, 941.12 μmol) in MeCN (4 mL) was added into the solution at 0 °C. The resulting mixture was stirred at r. t. for 1 hour before it was monitored with LCMS. The mixture was extracted with EA (30 mL X 3), and the combined organic phase was washed with brine, dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and the filtrate was concentrated *in vacuo*. The residue was purified in a SOD C18 c. c. on a prep-MPLC to afford the 8-chloro-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-iodo-N-(3-methyloxetan-3-yl)imidazo[1,5-a]pyridine-6-sulfonamide (508.0 mg, 904.31 μmol, 96.09% yield) as a yellow solid.

Step 11: 2-(8-chloro-6-hydrosulfonylimidazo[1,5-a]pyridin-3-yl)-5-(difluoromethyl)-1,3,4-thiadiazole

To a solution of compound (508.00 mg, 904.31 μmol) in THF (15 mL) were added DIPEA (350.63 mg, 2.71 mmol, 472.55 μL) and Pd/C (100 mg) at r. t. Then the mixture was stirred at r. t. under H<sub>2</sub> atmosphere for 16 hours till the reaction completed (detected LC-MS). Then the mixture was filtered and the filtrate was concentrated *in vacuo* to afford a crude product, which was purified by a reverse phase prep-MPLC to afford the 2-(8-chloro-6-hydrosulfonylimidazo[1,5-a]pyridin-3-yl)-5-(difluoromethyl)-1,3,4-thiadiazole (150 mg, 344.15 μmol, 38.06% yield) as a yellow solid.

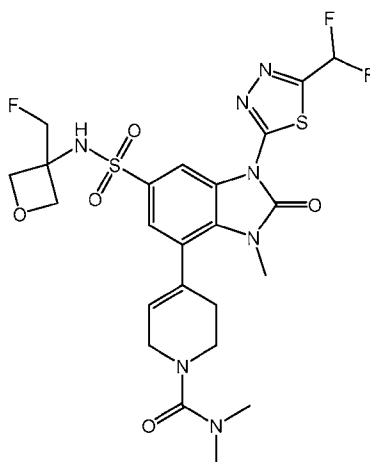
Step 12: tert-butyl (2S,6S)-4-(3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-6-(N-(3-methyloxetan-3-yl)sulfamoyl)imidazo[1,5-a]pyridin-8-yl)-2,6-dimethylpiperazine-1-carboxylate

To a mixture of compound (150.00 mg, 344.15 μmol) and tert-butyl (2S,6S)-2,6-dimethylpiperazine-1-carboxylate (147.51 mg, 688.30 μmol) in dioxane (8 mL) was added the Pd-PEPPSI-HeptCl (29.62 mg, 34.42 μmol) and Cs<sub>2</sub>CO<sub>3</sub> (338.64 mg, 1.03 mmol). Then the mixture was stirred at 100 °C for 3 hours under N<sub>2</sub> till the reaction completed (detected by LC-MS). The mixture was filtered and the solvent was evaporated almost completely to give tert-butyl (2S,6S)-4-(3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-6-(N-(3-methyloxetan-3-yl)sulfamoyl)imidazo[1,5-a]pyridin-8-yl)-2,6-dimethylpiperazine-1-carboxylate (crude) which was used for the next step without further purification.

Step 13: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-8-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-methyloxetan-3-yl)imidazo[1,5-a]pyridine-6-sulfonamide

To a solution of tert-butyl (2S,6S)-4-(3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-6-(N-(3-methyloxetan-3-yl)sulfamoyl)imidazo[1,5-a]pyridin-8-yl)-2,6-dimethylpiperazine-1-carboxylate (210.00 mg, 171.09  $\mu\text{mol}$ ) in DCM (10 mL) was added TFA (4 mL) at r. t. The reaction mixture was stirred at r. t for 1 hour till the reaction completed (monitored with LC-MS). The solvent was removed *in vacuo* to afford a crude product which was then purified by reverse phase prep-HPLC (base) to afford the 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-8-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-methyloxetan-3-yl)imidazo[1,5-a]pyridine-6-sulfonamide (21.3 mg, 41.43  $\mu\text{mol}$ , 24.22% yield, 99.9% purity) as a yellow solid. LC-MS  $m/z$ :  $[M+H]^+$  calcd. for  $C_{20}H_{26}F_2N_7O_3S_2^+$ : 514.1; found: 514.0.  $^1\text{H}$  NMR (400 MHz, Methanol- $d_4$ )  $\delta$  9.78 (s, 1H), 7.80 (s, 1H), 7.32 (t,  $J = 53.6$  Hz, 1H), 6.73 (s, 1H), 4.79 (dd,  $J = 6.0, 1.6$  Hz, 2H), 4.31 (d,  $J = 6.4$  Hz, 2H), 3.49-3.41 (m, 2H), 3.36 (dd,  $J = 12.0, 2.4$  Hz, 1H), 3.12 (dd,  $J = 11.6, 6.4$  Hz, 2H), 1.63 (s, 3H), 1.35 (d,  $J = 6.4$  Hz, 6H).

**Example 27: 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-6-(N-(3-(difluoromethyl)oxetan-3-yl)sulfamoyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N-dimethyl-5,6-dihydropyridine-1(2H)-carboxamide**



Step 1: N-(5-bromo-3-chloro-2-nitrophenyl)-5-(difluoromethyl)-1,3,4-thiadiazol-2-amine.

A mixture of 5-bromo-1-chloro-3-fluoro-2-nitro-benzene (5 g, 19.65 mmol), 5-(difluoromethyl)-1,3,4-thiadiazol-2-amine (4.45 g, 29.48 mmol) and  $\text{Cs}_2\text{CO}_3$  (12.81 g, 39.30 mmol) in DMSO (40 mL) was stirred at 90  $^\circ\text{C}$  for 3 h. Monitored by LCMS. The reaction mixture was diluted with water and extracted with EtOAc 3 times, the combined organic

phase was washed with water 3 times, dried by  $\text{Na}_2\text{SO}_4$ , filtered and concentrated, no further purification, the residue was used at next step directly. LCMS (ESI,  $m/z$ ): 385  $[\text{M}+\text{H}]^+$ .

*Step 2: 5-bromo-3-chloro-N1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)benzene-1,2-diamine.*

5 To a solution of N-(5-bromo-3-chloro-2-nitro-phenyl)-5-(difluoromethyl)-1,3,4-thiadiazol-2-amine (7.58 g, 19.66 mmol) in EtOH (60 mL) was added  $\text{NH}_4\text{Cl}$  (21.03 g, 393.18 mmol) and Zn (12.86 g, 196.59 mmol), the reaction mixture was stirred at 20 °C for 16 h. Monitored by LCMS. The reaction mixture was filtered, the filtrate was diluted with water and extracted with EtOAc 3 times, the combined organic phase was washed with brine,  
10 dried by  $\text{Na}_2\text{SO}_4$ , filtered and concentrated to give 5-bromo-3-chloro-N1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]benzene-1,2-diamine (7.1 g, crude) as a yellow solid. LCMS (ESI,  $m/z$ ): 355  $[\text{M}+\text{H}]^+$ .

*Step 3: 6-bromo-4-chloro-1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1H-benzo[d]imidazol-2(3H)-one.*

15 A mixture of 5-bromo-3-chloro-N1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]benzene-1,2-diamine (7.1 g, 19.97 mmol) and CDI (4.86 g, 29.95 mmol) in DMF (40 mL) was stirred at 20 °C for 1h. Monitored by LCMS. The reaction mixture was concentrated, the residue was purified by flash column to give 5-bromo-7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1H-benzimidazol-2-one (7 g, crude) as a brown solid.  
20 LCMS (ESI,  $m/z$ ): 381  $[\text{M}+\text{H}]^+$ .

*Step 4: 6-bromo-4-chloro-1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-methyl-1H-benzo[d]imidazol-2(3H)-one.*

25 To a solution of 5-bromo-7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1H-benzimidazol-2-one (2 g, 5.24 mmol) and  $\text{Cs}_2\text{CO}_3$  (3.42 g, 10.48 mmol) in DMF (20 mL) was added MeI (1.12 g, 7.86 mmol), the reaction mixture was stirred at 20 °C for 0.5 h. Monitored by LCMS. The reaction mixture was concentrated, the residue was purified by flash column to give 6-bromo-4-chloro-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-benzimidazol-2-one (1.3 g, 3.29 mmol, 62.70% yield) as a yellow solid. LCMS (ESI,  
30  $m/z$ ): 395  $[\text{M}+\text{H}]^+$ .

*Step 5: 7-chloro-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfinic acid.*

A mixture of 6-bromo-4-chloro-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-benzimidazol-2-one (1.3 g, 3.29 mmol), o-phenanthroline (88.82 mg, 492.91  $\mu$ mol), PPh<sub>3</sub> (129.29 mg, 492.91  $\mu$ mol), Pd(OAc)<sub>2</sub> (73.77 mg, 328.61  $\mu$ mol), HCO<sub>2</sub>Na (491.65 mg, 7.23 mmol), K<sub>2</sub>O<sub>5</sub>S<sub>2</sub> (1.46 g, 6.57 mmol) and TEAB (759.64 mg, 3.61 mmol) in DMSO (15 mL) under N<sub>2</sub> was heated at 70 °C for 1.5 h. Monitored by LCMS. No work up, the reaction mixture was used at next step directly. LCMS (ESI, m/z): 381 [M+H]<sup>+</sup>.

*Step 6: 7-chloro-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonyl fluoride.*

To a solution step 5 in DMSO (15 mL) and DMF (10 mL) at 0 °C was added NFSI (1.55 g, 4.92 mmol), the reaction mixture was stirred at 0 °C for 0.5 h. Monitored by LCMS. The reaction mixture was diluted with water and extracted with EtOAc 3 times, the combined organic phase was washed with water three times, then brine, dried by Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated, the residue was purified by flash column to give 7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-benzimidazole-5-sulfonyl fluoride (0.88 g, 2.21 mmol, 67.22% yield) as a yellow solid. LCMS (ESI, m/z): 399 [M+H]<sup>+</sup>.

*Step 7: 7-chloro-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.*

To a solution of 7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-benzimidazole-5-sulfonyl fluoride (350 mg, 877.70  $\mu$ mol), 3-(fluoromethyl)oxetan-3-amine (186.39 mg, 1.32 mmol, CL) and DIPEA (7.36 g, 56.95 mmol, 9.92 mL) in DMSO (25 mL) was added HOBT (177.89 mg, 1.32 mmol), followed by (Me<sub>2</sub>SiH)<sub>2</sub>O (109.28 mg, 813.58  $\mu$ mol) dropwise, the reaction mixture was stirred at 20 °C for 15 min. Monitored by LCMS. The reaction mixture was diluted with water and extracted with EtOAc 3 times, the combined organic phase was washed with water 3 times, dried by Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated, the residue was purified by flash column to give 7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-[3-(fluoromethyl)oxetan-3-yl]-1-methyl-2-oxo-benzimidazole-5-sulfonamide (190 mg, 392.67  $\mu$ mol, 44.74% yield) as a yellow solid. LCMS (ESI, m/z): 484 [M+H]<sup>+</sup>.

*Step 8: tert-butyl 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-5,6-dihydropyridine-1(2H)-carboxylate.*



A mixture of 7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-[3-(fluoromethyl)oxetan-3-yl]-1-methyl-2-oxo-benzimidazole-5-sulfonamide (190 mg, 392.67  $\mu\text{mol}$ ), tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-2H-pyridine-1-carboxylate (182.12 mg, 589.00  $\mu\text{mol}$ ), cataCXium A Pd G3 (28.60 mg, 39.27  $\mu\text{mol}$ ) and  
5  $\text{K}_3\text{PO}_4$  (166.70 mg, 785.33  $\mu\text{mol}$ ) in  $\text{H}_2\text{O}$  (1 mL) and t-BuOH (4 mL) under  $\text{N}_2$  was heated at 80 °C for 2 h. Monitored by LCMS. The reaction mixture was concentrated, the residue was purified by flash column to give tert-butyl 4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-3-methyl-2-oxo-benzimidazol-4-yl]-3,6-dihydro-2H-pyridine-1-carboxylate (140 mg, 221.99  $\mu\text{mol}$ , 56.53% yield) as a yellow solid. LCMS  
10 (ESI, m/z): 631  $[\text{M}+\text{H}]^+$ .

*Step 9: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-7-(1,2,3,6-tetrahydropyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.*

15 A mixture of tert-butyl 4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-3-methyl-2-oxo-benzimidazol-4-yl]-3,6-dihydro-2H-pyridine-1-carboxylate (140 mg, 221.99  $\mu\text{mol}$ ) in DCM (3 mL) and TFA (3 mL) was stirred at 20 °C for 1 h. Monitored by LCMS. The reaction mixture was concentrated to give 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-[3-(fluoromethyl)oxetan-3-yl]-1-methyl-2-oxo-7-(1,2,3,6-tetrahydropyridin-4-yl)benzimidazole-5-sulfonamide (143.09 mg, crude, TF) as a  
20 yellow oil. LCMS (ESI, m/z): 531  $[\text{M}+\text{H}]^+$ .

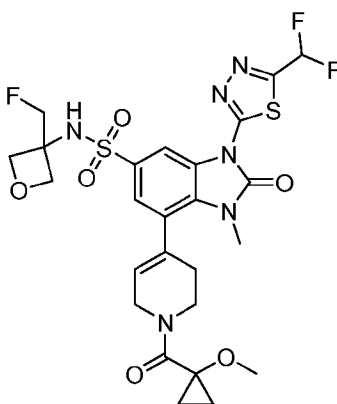
*Step 10: 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N-dimethyl-5,6-dihydropyridine-1(2H)-carboxamide.*

To a solution of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-[3-(fluoromethyl)oxetan-3-yl]-1-methyl-2-oxo-7-(1,2,3,6-tetrahydropyridin-4-yl)benzimidazole-5-sulfonamide (143.09 mg, 221.99  $\mu\text{mol}$ , TF) and TEA (449.27 mg, 4.44 mmol, 619.26  $\mu\text{L}$ ) in DCM (5 mL) was added N,N-dimethylcarbonyl chloride (119.36 mg, 1.11 mmol),  
30 the reaction mixture was stirred at 20 °C for 16 h. Monitored by LCMS. The reaction mixture was concentrated, the residue was purified by prep-HPLC (Base) to give 4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-3-methyl-2-oxo-benzimidazol-4-yl]-N,N-dimethyl-3,6-dihydro-2H-pyridine-1-carboxamide (49.9 mg, 82.86  $\mu\text{mol}$ , 37.33% yield, 99.9% purity) as a white solid. LCMS (ESI, m/z): 602.5

[M+H]<sup>+</sup>. <sup>1</sup>H NMR (600 MHz, Chloroform-*d*) δ 9.03 (d, *J* = 1.8 Hz, 1H), 7.63 (d, *J* = 1.8 Hz, 1H), 7.06 (t, *J* = 53.4 Hz, 1H), 5.83 (m, 1H), 5.65 (s, 1H), 4.82 – 4.74 (m, 3H), 4.71 (s, 1H), 4.48 – 4.41 (m, 2H), 3.98 (d, *J* = 3.6 Hz, 2H), 3.59 (s, 3H), 3.52 (t, *J* = 5.4 Hz, 2H), 2.91 (s, 6H), 2.52 (s, 2H).

5

**Example 31: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-7-(1-(1-methoxycyclopropanecarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide**



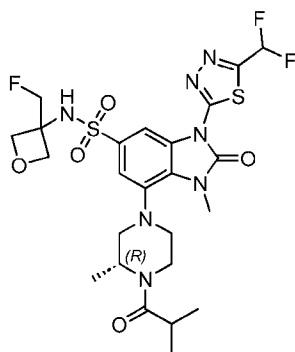
10

To a stirred solution of 1-methoxycyclopropanecarboxylic acid (22.98 mg, 197.91 μmol) in DMSO (2.89 mL) was added HATU (75.21 mg, 197.91 μmol) and DIPEA (85.26 mg, 659.70 μmol, 114.91 μL), the resulting reaction mixture was stirred at rt for 10 min before 1-methoxycyclopropanecarboxylic acid (22.98 mg, 197.91 μmol) was added. After the reaction was finished which was monitored by LCMS, then the mixture was purified by the reversed phase chromatograph to give 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-7-(1-(1-methoxycyclopropanecarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide (43 mg, 67.85 μmol, 51.43% yield, 99.2% purity). LCMS (ESI, *m/z*): 629.0 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (600 MHz, DMSO) δ 8.4 (s, 1H), 8.84 (s, 1H), 7.78 – 7.52 (m, 2H), 5.97 (s, 1H), 4.69 (s, 1H), 4.60 (s, 1H), 4.53 (dd, *J* = 6.7, 3.4 Hz, 2H), 4.34 (d, *J* = 6.8 Hz, 2H), 4.20 – 3.77 (m, 4H), 3.48 (s, 3H), 3.26 (s, 3H), 2.52 (m, 2H), 1.03 (m, 2H), 0.97 (m, 2H).

20

**Example 43: (R)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-isobutyryl-3-methylpiperazin-1-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide**

25



*Step 1: (R)-tert-butyl 4-(5-bromo-3-fluoro-2-nitrophenyl)-2-methylpiperazine-1-carboxylate*

A mixture of 5-bromo-1,3-difluoro-2-nitro-benzene (20 g, 84.04 mmol), tert-butyl  
 5 (2R)-2-methylpiperazine-1-carboxylate (16.83 g, 84.04 mmol) and DIPEA (21.72 g, 168.08  
 mmol, 29.28 mL) in DMSO (150 mL) was stirred at 80 °C for 16 h. Monitored by LCMS.  
 The reaction mixture was diluted with water and extracted with EtOAc 3 times, the combined  
 organic phase was washed with water three times, then brine, dried by Na<sub>2</sub>SO<sub>4</sub>, filtered and  
 concentrated to give tert-butyl rac-(2R)-4-(5-bromo-3-fluoro-2-nitro-phenyl)-2-methyl-  
 10 piperazine-1-carboxylate (35.15 g, crude) as a yellow oil. LCMS (ESI, m/z): 418 [M+H]<sup>+</sup>.

*Step 2: (R)-tert-butyl 4-(5-bromo-3-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)amino)-2-nitrophenyl)-2-methylpiperazine-1-carboxylate.*

A mixture of tert-butyl (2R)-4-(5-bromo-3-fluoro-2-nitro-phenyl)-2-methyl-  
 15 piperazine-1-carboxylate (32 g, 76.51 mmol), 5-(difluoromethyl)-1,3,4-thiadiazol-2-amine  
 (13.88 g, 91.81 mmol) and Cs<sub>2</sub>CO<sub>3</sub> (49.86 g, 153.02 mmol) in DMSO (200 mL) was stirred  
 at 90 °C for 16 h. Monitored by LCMS. The reaction mixture was diluted with water and  
 extracted with EtOAc 3 times, the combined organic phase was washed with water three  
 times, then brine, dried by Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to give tert-butyl (2R)-4-[5-  
 20 bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]-2-nitro-phenyl]-2-methyl-  
 piperazine-1-carboxylate (42.03 g, crude) as a yellow oil. LCMS (ESI, m/z): 549 [M+H]<sup>+</sup>.

*Step 3: (R)-tert-butyl 4-(2-amino-5-bromo-3-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)amino)phenyl)-2-methylpiperazine-1-carboxylate.*

To a solution of tert-butyl (2R)-4-[5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-  
 25 yl]amino]-2-nitro-phenyl]-2-methyl-piperazine-1-carboxylate (42.02 g, 76.49 mmol) and  
 NH<sub>4</sub>Cl (81.83 g, 1.53 mol) in EtOH (400 mL) was added Zn (50.01 g, 764.85 mmol), the

reaction mixture was stirred at 20 °C for 2 h. Monitored by LCMS. The reaction mixture was filtered and concentrated, the residue was diluted with water and extracted with EtOAc 2 times, the combined organic phase was dried by Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to give tert-butyl (2R)-4-[2-amino-5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]phenyl]-2-methyl-piperazine-1-carboxylate (39.73 g, crude) as a yellow oil. LCMS (ESI, m/z): 519 [M+H]<sup>+</sup>.

*Step 4: (R)-tert-butyl 4-(6-bromo-1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-2-methylpiperazine-1-carboxylate.*

10 A mixture of tert-butyl (2R)-4-[2-amino-5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]phenyl]-2-methyl-piperazine-1-carboxylate (39.73 g, 76.49 mmol) and CDI (18.60 g, 114.74 mmol) in DMF (250 mL) was stirred at 20 °C for 1 h. Monitored by LCMS. The reaction mixture was concentrated to give tert-butyl rac-(2R)-4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-2-oxo-3H-benzimidazol-4-yl]-2-methyl-piperazine-1-  
15 carboxylate (41.72 g, crude) as a yellow oil. LCMS (ESI, m/z): 545 [M+H]<sup>+</sup>.

*Step 5: (R)-tert-butyl 4-(6-bromo-1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-2-methylpiperazine-1-carboxylate.*

To a solution of tert-butyl (2R)-4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-2-oxo-3H-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (10 g, 18.34 mmol) and Cs<sub>2</sub>CO<sub>3</sub> (11.95 g, 36.67 mmol) in DMF (80 mL) was added MeI (2.60 g, 18.34 mmol), the reaction mixture was stirred at 20 °C for 1 h. Monitored by LCMS. The reaction mixture was concentrated, the residue was purified by flash column to give tert-butyl (2R)-4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-2-oxo-benzimidazol-4-yl]-2-methyl-  
25 piperazine-1-carboxylate (8 g, crude) as a yellow solid. LCMS (ESI, m/z): 559 [M+H]<sup>+</sup>.

*Step 6: 7-((R)-4-(tert-butoxycarbonyl)-3-methylpiperazin-1-yl)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfinic acid.*

A mixture of tert-butyl rac-(2R)-4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (8 g, 14.30 mmol), o-phenanthroline (386.55 mg, 2.15 mmol), PPh<sub>3</sub> (562.63 mg, 2.15 mmol), Pd(OAc)<sub>2</sub> (321.05 mg, 1.43 mmol), HCO<sub>2</sub>Na (1.95 g, 28.60 mmol), K<sub>2</sub>O<sub>5</sub>S<sub>2</sub> (6.99 g, 31.46 mmol) and TEAB (4.51 g, 21.45 mmol) in DMSO (80 mL) was heated at 70 °C under N<sub>2</sub> for 3 h.

Monitored by LCMS. No work up, the reaction mixture was used at next step directly. LCMS (ESI, m/z): 545 [M+H]<sup>+</sup>.

5 *Step 7: (R)-tert-butyl 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-6-(fluorosulfonyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-2-methylpiperazine-1-carboxylate.*

To a solution of step 6 in DMSO (80) and DMF (40 mL) was added NFSI (4.16 g, 21.46 mmol) at 0 °C, the reaction mixture was stirred at 0 °C for 0.5 h. Monitored by LCMS. The reaction mixture was diluted with water and extracted with EtOAc 3 times, the combined organic phase was washed with water three times, then brine, dried by Na<sub>2</sub>SO<sub>4</sub>, filtered and  
10 concentrated, the residue was purified by flash column to give tert-butyl (2R)-4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluorosulfonyl-3-methyl-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (6 g, crude) as a yellow solid. LCMS (ESI, m/z): 563[M+H]<sup>+</sup>.

15 *Step 8: (R)-tert-butyl 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-2-methylpiperazine-1-carboxylate.*

To a solution of tert-butyl (2R)-4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluorosulfonyl-3-methyl-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (0.25  
20 g, 444.38 μmol), 3-(fluoromethyl)oxetan-3-amine (75.49 mg, 533.25 μmol, CL) and DIPEA (574.31 mg, 4.44 mmol, 774.01 μL) in DMSO (3 mL) was added HOBt (90.07 mg, 666.57 μmol), followed by (Me<sub>2</sub>SiH)<sub>2</sub>O (5.97 mg, 44.44 μmol), the reaction mixture was stirred at 25 °C for 16 h. Monitored by LCMS. The reaction mixture was purified by MPLC (acid) to give tert-butyl (2R)-4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[[3-(  
25 (fluoromethyl)oxetan-3-yl)sulfamoyl]-3-methyl-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (0.19 g, 293.35 μmol, 66.01% yield) as a yellow solid. LCMS (ESI, m/z): 648[M+H]<sup>+</sup>.

30 *Step 9: (R)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-7-(3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.*

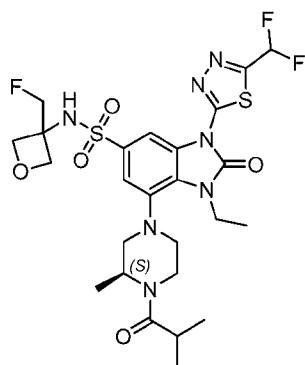
A mixture of tert-butyl (2R)-4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[[3-(fluoromethyl)oxetan-3-yl)sulfamoyl]-3-methyl-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (0.19 g, 293.35 μmol) in DCM (3 mL) and TFA (3 mL) was stirred at 25 °C for 1 h. Monitored by LCMS. The reaction mixture was concentrated to give

3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-[3-(fluoromethyl)oxetan-3-yl]-1-methyl-2-oxo-7-[(3R)-3-methylpiperazin-1-yl]benzimidazole-5-sulfonamide (194.08 mg, crude, TF) as a yellow oil. LCMS (ESI, m/z): 548[M+H]<sup>+</sup>.

- 5 *Step 10: (R)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-isobutyryl-3-methylpiperazin-1-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.*

To a solution of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-[3-(fluoromethyl)oxetan-3-yl]-1-methyl-2-oxo-7-[(3R)-3-methylpiperazin-1-yl]benzimidazole-5-sulfonamide (194.08 mg, 293.35 μmol, TF), and TEA (593.68 mg, 5.87 mmol, 818.31 μL) in DCM (3.17 mL) at 0 °C was added 2-methylpropanoyl chloride (62.51 mg, 586.70 μmol) dropwise, the reaction mixture was stirred at 0 °C for 1 h. Monitored by LCMS. The reaction mixture was purified by prep-HPLC (Base) to give 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-[3-(fluoromethyl)oxetan-3-yl]-1-methyl-2-oxo-7-[(3R)-3-methyl-4-(2-methylpropanoyl) piperazin-1-yl]benzimidazole-5-sulfonamide (89.5 mg, 144.76 μmol, 49.35% yield, 99.9% purity) as a white solid. LCMS (ESI, m/z): 618.5[M+H]<sup>+</sup>. <sup>1</sup>H NMR (600 MHz, Chloroform-*d*) δ 8.92 (d, *J* = 1.8 Hz, 1H), 7.68 (d, *J* = 15.6 Hz, 1H), 7.06 (t, *J* = 53.4 Hz, 1H), 5.81 (s, 1H), 5.04 (s, 0.5H), 4.80 – 4.74 (m, 3H), 4.70 (d, *J* = 1.2 Hz, 1H), 4.61 (d, *J* = 13.2 Hz, 0.5H), 4.44 (d, *J* = 7.2 Hz, 2H), 4.37 (s, 0.5H), 3.96 (d, *J* = 2.4 Hz, 3H), 3.84 (d, *J* = 13.2 Hz, 0.5H), 3.67 (t, *J* = 12.6 Hz, 0.5H), 3.27 (d, *J* = 10.8 Hz, 0.5H), 3.24 – 3.11 (m, 2H), 3.02 (dd, *J* = 26.4, 11.4 Hz, 1H), 2.90 – 2.65 (m, 2H), 1.50 (d, *J* = 6.6 Hz, 1.5H), 1.37 (d, *J* = 6.6 Hz, 1.5H), 1.23 (d, *J* = 6.6 Hz, 1.5H), 1.19 (d, *J* = 6.6 Hz, 3H), 1.14 (d, *J* = 6.6 Hz, 1.5H).

- 25 **Example 45: (S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-isobutyryl-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide**



Step 1: *tert-butyl (S)-4-(5-bromo-3-fluoro-2-nitrophenyl)-2-methylpiperazine-1-carboxylate.*

To a solution of 5-bromo-1,3-difluoro-2-nitro-benzene (2.87 g, 12.06 mmol) in DMF  
 5 (10 mL) was added DIPEA (3.12 g, 24.12 mmol, 4.20 mL) and *tert-butyl rac-(2S)-2-*  
*methylpiperazine-1-carboxylate* (2.67 g, 13.33 mmol). And then the mixture was stirred at  
 70 °C for 3 hours. After 3 hrs, LCMS analysis showed the complete consumption of 5-  
 bromo-1,3-difluoro-2-nitro-benzene (2.87 g, 12.06 mmol). Water was added and the crude  
 product suspension was extracted twice with ethyl acetate. The combined organic layers were  
 10 washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated. After  
 filtration, the filtrate was concentrated under reduced pressure. The residue was obtained *tert-*  
*butyl rac-(2S)-4-(5-bromo-3-fluoro-2-nitro-phenyl)-2-methyl-piperazine-1-carboxylate* (5.04  
 g, crude) as yellow oil. LCMS: 418 [M+H]<sup>+</sup>

Step 2: *tert-butyl (S)-4-(5-bromo-3-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)amino)-2-nitrophenyl)-2-methylpiperazine-1-carboxylate.*

To a solution of *tert-butyl rac-(2S)-4-(5-bromo-3-fluoro-2-nitro-phenyl)-2-methyl-*  
*piperazine-1-carboxylate* (5.04 g, 12.05 mmol) in DMF (10 mL) was added Cs<sub>2</sub>CO<sub>3</sub> (7.83 g,  
 24.10 mmol) and 5-(difluoromethyl)-1,3,4-thiadiazol-2-amine (1.82 g, 12.05 mmol). And  
 20 then the mixture was stirred at 70 °C for 3 hours. After 3 hrs, LCMS analysis showed the  
 complete consumption of *tert-butyl rac-(2S)-4-(5-bromo-3-fluoro-2-nitro-phenyl)-2-methyl-*  
*piperazine-1-carboxylate* (5.04 g, 12.05 mmol). Water was added and the crude product  
 suspension was extracted twice with ethyl acetate. The combined organic layers were washed  
 with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated. After filtration, the  
 25 filtrate was concentrated under reduced pressure. The residue was obtained *tert-butyl rac-*  
*(2S)-4-[5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]-2-nitro-phenyl]-2-*  
*methyl-piperazine-1-carboxylate* (6.62 g, crude) as yellow solid. LCMS: 418 [M+H]<sup>+</sup>

Step 3: *tert-butyl (S)-4-(2-amino-5-bromo-3-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)amino)phenyl)-2-methylpiperazine-1-carboxylate.*

To a mixture of *tert-butyl rac-(2S)-4-[5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]-2-nitro-phenyl]-2-methyl-piperazine-1-carboxylate* (6.62 g, 12.05 mmol) in EtOH (20 mL) was added the Zn (7.88 g, 120.50 mmol), NH<sub>4</sub>Cl (12.89 g, 241.00 mmol). And then the mixture was stirred at 25 °C for 3 hours. After 3 hrs, LCMS analysis showed the complete consumption of *tert-butyl rac-(2S)-4-[5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]-2-nitro-phenyl]-2-methyl-piperazine-1-carboxylate* (6.62 g, 12.05 mmol). The reaction mixture was purified by Prep-HPLC and dried by hyophilization to give *tert-butyl rac-(2S)-4-[2-amino-5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]phenyl]-2-methyl-piperazine-1-carboxylate* (6.26 g, crude) as yellow solid. LCMS: 519 [M+H]<sup>+</sup>.

Step 4: *tert-butyl (S)-4-(6-bromo-1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-2-methylpiperazine-1-carboxylate.*

To a solution of *tert-butyl (2S)-4-[2-amino-5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]phenyl]-2-methyl-piperazine-1-carboxylate* (6.26 g, 12.05 mmol) in DMF (10 mL) was added CDI (2.60 g, 18.08 mmol). And then the mixture was stirred at 25 °C for 3 hours. After 3 hrs, LCMS analysis showed the complete consumption of *tert-butyl (2S)-4-[2-amino-5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]phenyl]-2-methyl-piperazine-1-carboxylate* (6.26 g, 12.05 mmol). Water was added and the crude product suspension was extracted twice with ethyl acetate. The combined organic layers were washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated. After filtration, the filtrate was concentrated under reduced pressure. The residue was obtained *tert-butyl (2S)-4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-2-oxo-3H-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate* (6.57 g, crude) as yellow solid. LCMS: 545 [M+H]<sup>+</sup>.

Step 5: *tert-butyl (S)-4-(6-bromo-1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-2-methylpiperazine-1-carboxylate.*

To a solution of *tert-butyl (2S)-4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-2-oxo-3H-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate* (6.57 g, 12.05 mmol) in DMF (10 mL) was added EtBr (5.25 g, 48.18 mmol), K<sub>2</sub>CO<sub>3</sub> (3.32 g, 24.09 mmol). And then the mixture was stirred at 25 °C for 16 hours. After 16 hrs, LCMS analysis showed the



complete consumption of tert-butyl (2S)-4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-2-oxo-3H-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (6.57 g, 12.05 mmol). Water was added and the crude product suspension was extracted twice with ethyl acetate. The combined organic layers were washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated. The residue was purified by flash chromatography (DCM/MeOH 100:1→50:1→10:1) to give tert-butyl (2S)-4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (3.0 g, 5.23 mmol, 43.43% yield) as white solid. LCMS: 573[M+H]<sup>+</sup>.

Step 6: 7-((S)-4-(tert-butoxycarbonyl)-3-methylpiperazin-1-yl)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfinic acid.

To a mixture of tert-butyl (2S)-4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (3 g, 5.23 mmol) in DMSO (25 mL) was added the 1,10 phenanthroline (141.41 mg, 784.72 μmol), K<sub>2</sub>O<sub>5</sub>S<sub>2</sub> (2.33 g, 10.46 mmol), CHNaO<sub>2</sub> (782.63 mg, 11.51 mmol), PPh<sub>3</sub> (205.82 mg, 784.72 μmol), TEAB (1.85 g, 5.75 mmol) and Pd(OCOCH<sub>3</sub>)<sub>2</sub> (118 mg). And then the mixture was stirred at 70 °C for 4 hrs under N<sub>2</sub>. After 4 hrs, LCMS analysis showed the complete consumption of tert-butyl (2S)-4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (3 g, 5.23 mmol). The reaction mixture was used for the next step without further purification. LCMS: 559[M+H]<sup>+</sup>.

Step 7: tert-butyl (S)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(fluorosulfonyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-2-methylpiperazine-1-carboxylate.

To a solution of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-7-[(3S)-4-tert-butoxycarbonyl-3-methyl-piperazin-1-yl]benzimidazole-5-sulfinic acid (2.92 g, 5.23 mmol) in DMSO (10 mL) was added NFSI (2.47 g, 7.84 mmol). And then the mixture was stirred at 0 °C for 0.2 hour. After 0.2 hr, LCMS analysis showed the complete consumption of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-7-[(3S)-4-tert-butoxycarbonyl-3-methyl-piperazin-1-yl]benzimidazole-5-sulfinic acid (2.92 g, 5.23 mmol). Water was added and the crude product suspension was extracted twice with ethyl acetate. The combined organic layers were washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated. The residue was purified by flash chromatography (DCM/ MeOH 100:1→50:1→10:1) to give tert-butyl (2S)-4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-

ethyl-6-fluorosulfonyl-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (1.15 g, 1.99 mmol, 38.15% yield) as white solid. LCMS: 577[M+H]<sup>+</sup>.

Step 8: *tert*-butyl (S)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-2-methylpiperazine-1-carboxylate.

To a mixture of *tert*-butyl (2S)-4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-fluorosulfonyl-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (800 mg, 1.39 mmol) and 3-(fluoromethyl)oxetan-3-amine (218.75 mg, 2.08 mmol) in DMSO (3 mL) was added the (Me<sub>2</sub>SiH)<sub>2</sub>O (18.59 mg, 138.74 μmol), HOBt (281.20 mg, 2.08 mmol) and DIPEA (268.96 mg, 2.08 mmol, 362.49 μL). And then the mixture was stirred at 25 °C for 16 hours. After 16 hrs, LCMS analysis showed the complete consumption of 3-(fluoromethyl)oxetan-3-amine (218.75 mg, 2.08 mmol). The reaction mixture was purified by Prep-HPLC and dried by hyophilization to give *tert*-butyl (2S)-4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (900 mg, 1.36 mmol, 98.03% yield) as a white solid. LCMS: 662[M+H]<sup>+</sup>.

Step 9: (S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.

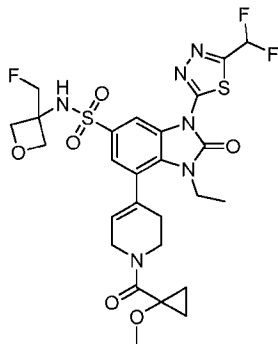
To a solution of *tert*-butyl (2S)-4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (490 mg, 740.50 μmol) in DCM (3 mL) was added TFA (1.69 g, 14.81 mmol). And then the mixture was stirred at room temperature for 0.5 hour. After 0.5 hr, TLC analysis (DCM/ MeOH = 10:1) showed the complete consumption of *tert*-butyl (2S)-4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-2-oxo-benzimidazol-4-yl]-2-methyl-piperazine-1-carboxylate (490 mg, 740.50 μmol, TFA salt). The reaction mixture was evaporated. The residue was used for the next step without further purification. LCMS: 562 [M+H]<sup>+</sup>.

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Step 10: (S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-isobutyryl-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.

To a mixture of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-7-[(3S)-3-methylpiperazin-1-yl]benzimidazole-5-sulfonamide (415 mg, 738.96  $\mu\text{mol}$ ) in DCM (3 mL) was added the TFA (252.77 mg, 2.22 mmol). And then the mixture was stirred at 25 °C for 0.5 hours. After 0.5 hr, LCMS analysis showed the complete consumption of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-7-[(3S)-3-methylpiperazin-1-yl]benzimidazole-5-sulfonamide (415 mg, 738.96  $\mu\text{mol}$ ). The reaction mixture was purified by Prep-HPLC and dried by lyophilization to give 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-7-[(3S)-3-methyl-4-(2-methylpropanoyl)piperazin-1-yl]benzimidazole-5-sulfonamide (211 mg, 331.02  $\mu\text{mol}$ , 44.80% yield, 99.1% purity) as a white solid. LCMS: 632.5[M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  8.81 (s, 1H), 8.75 (d, *J* = 1.7 Hz, 1H), 7.91 – 7.40 (m, 2H), 4.81 (s, 0.5H), 4.69 (s, 1H), 4.58 (s, 1H), 4.53 (dd, *J* = 6.8, 3.5 Hz, 2H), 4.43 (m, 2H), 4.33 (m, 3.5H), 3.90 (d, *J* = 13.4 Hz, 0.5H), 3.57 (t, *J* = 12.3 Hz, 0.5H), 3.24 – 3.21 (m, 0.5H), 3.16 – 3.08 (m, 2H), 3.03 (t, *J* = 12.4 Hz, 1H), 2.91 (m, 1H), 2.67 – 2.60 (m, 0.5H) 1.49 – 1.21 (m, 6H), 1.05 (td, *J* = 20.6, 6.7 Hz, 6H).

**Example 55: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(1-(1-methoxycyclopropanecarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.**



*Step 1: 6-bromo-4-chloro-1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-1H-benzo[d]imidazol-2(3H)-one.*

To a solution of 5-bromo-7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1H-benzimidazol-2-one (4 g, 10.48 mmol) and Cs<sub>2</sub>CO<sub>3</sub> (6.83 g, 20.97 mmol) in DMF (30 mL) was added EtI (1.96 g, 12.58 mmol), the reaction mixture was stirred at 25 °C for 3 h. Monitored by LCMS. The reaction mixture was concentrated, the residue was purified by

flash column to give 6-bromo-4-chloro-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-benzimidazol-2-one (3.4 g, crude) as a yellow solid. LCMS (ESI, m/z): 409[M+H]<sup>+</sup>.

Step 2: 7-chloro-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-2-oxo-2,3-dihydro-1H-benzof[d]imidazole-5-sulfonic acid.

A mixture of 6-bromo-4-chloro-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-benzimidazol-2-one (3.4 g, 8.30 mmol), o-phenanthroline (224.36 mg, 1.25 mmol), PPh<sub>3</sub> (326.55 mg, 1.25 mmol), Pd(OAc)<sub>2</sub> (186.34 mg, 830.00 μmol), HCO<sub>2</sub>Na (1.24 g, 18.26 mmol), K<sub>2</sub>O<sub>5</sub>S<sub>2</sub> (3.69 g, 16.60 mmol) and TEAB (1.92 g, 9.13 mmol) in DMSO (30 mL) under N<sub>2</sub> was heated at 70 °C for 3 h. Monitored by LCMS. No work up, the reaction mixture was used at next step directly. LCMS (ESI, m/z): 395[M+H]<sup>+</sup>.

Step 3: 7-chloro-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-2-oxo-2,3-dihydro-1H-benzof[d]imidazole-5-sulfonyl fluoride.

To a solution of step 2 in DMF (10 mL) and DMSO (30 mL) at 0 °C was added NFSI (3.93 g, 12.46 mmol), the reaction mixture was stirred at 0 °C for 30 min. Monitored by LCMS. The reaction mixture was diluted with water and extracted with EtOAc 3 times, the combined organic phase was washed with water three times, then brine, dried by Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated, the residue was purified by flash column to give 7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-benzimidazole-5-sulfonyl fluoride (2.3 g, crude) as a yellow solid. LCMS (ESI, m/z): 413[M+H]<sup>+</sup>.

Step 4: 7-chloro-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzof[d]imidazole-5-sulfonamide.

To a solution of 7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-benzimidazole-5-sulfonyl fluoride (1.3 g, 3.15 mmol), 3-(fluoromethyl)oxetan-3-amine (445.85 mg, 3.15 mmol) and DIPEA (4.07 g, 31.49 mmol, 5.49 mL) in DMSO (15 mL) was added HOBt (638.29 mg, 4.72 mmol), followed by (Me<sub>2</sub>SiH)<sub>2</sub>O (42.30 mg, 314.93 μmol), the reaction mixture was stirred at 25 °C for 16 h. Monitored by LCMS. The reaction mixture was diluted with water and extracted with EtOAc 3 times, the combined organic phase was washed with water three times, then brine, dried by Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated, the residue was purified by flash column to give 7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-

benzimidazole-5-sulfonamide (0.78 g, 1.57 mmol, 49.74% yield) as a yellow solid. LCMS (ESI, m/z): 498[M+H]<sup>+</sup>.

Step 5: *tert*-butyl 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-5,6-dihydropyridine-1(2H)-carboxylate.

A mixture of 7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-benzimidazole-5-sulfonamide (0.1 g, 200.84 μmol), *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-2H-pyridine-1-carboxylate (74.52 mg, 241.01 μmol), cataCXium A Pd G<sub>3</sub> (14.63 mg, 20.08 μmol) and K<sub>3</sub>PO<sub>4</sub> (42.63 mg, 200.84 μmol) in H<sub>2</sub>O (0.2 mL) and *t*-BuOH (0.8 mL) under N<sub>2</sub> was heated at 80 °C for 2 h. Monitored by LCMS. The reaction mixture was concentrated, the residue was purified by flash column to give *tert*-butyl 4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-2-oxo-benzimidazol-4-yl]-3,6-dihydro-2H-pyridine-1-carboxylate (0.12 g, 186.14 μmol, 92.68% yield) as a light yellow solid. LCMS (ESI, m/z): 645[M+H]<sup>+</sup>.

Step 6: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-2-oxo-7-(1,2,3,6-tetrahydropyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.

A mixture *tert*-butyl 4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-2-oxo-benzimidazol-4-yl]-3,6-dihydro-2H-pyridine-1-carboxylate (0.12 g, 186.14 μmol) in DCM (3 mL) and TFA (3 mL) was stirred at 25 °C for 1 h. Monitored by LCMS. The reaction mixture was concentrated to give 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-7-(1,2,3,6-tetrahydropyridin-4-yl)benzimidazole-5-sulfonamide (122.59 mg, crude, TF) as a yellow solid. LCMS (ESI, m/z): 545[M+H]<sup>+</sup>.

Step 7: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(1-(1-methoxycyclopropanecarbonyl)-1,2,3,6-tetrahydropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.

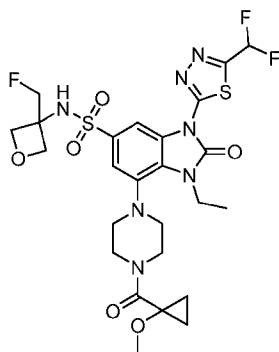
To a solution of 1-methoxycyclopropanecarboxylic acid (25.94 mg, 223.37 μmol), 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-7-(1,2,3,6-tetrahydropyridin-4-yl)benzimidazole-5-sulfonamide (122.59 mg, 186.14 μmol, TF) and DIPEA (240.57 mg, 1.86 mmol, 324.21 μL) in DMF (2 mL) was added HATU

(84.93 mg, 223.37  $\mu$ mol) at 0 °C, the reaction mixture was stirred at 0 °C for 30 min.

Monitored by LCMS. The reaction mixture was purified by MPLC to give 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-7-[1-(1-methoxycyclopropanecarbonyl)-3,6-dihydro-2H-pyridin-4-yl]-2-oxo-benzimidazole-5-sulfonamide (38.3 mg, 59.30  $\mu$ mol, 31.86% yield, 99.5% purity) as a white solid. LCMS (ESI, m/z): 643.1[M+H]<sup>+</sup>. <sup>1</sup>H NMR (600 MHz, Chloroform-*d*)  $\delta$  9.11 (d, *J* = 1.8 Hz, 1H), 7.63 (d, *J* = 1.8 Hz, 1H), 7.06 (t, *J* = 53.4 Hz, 1H), 5.92 (s, 1H), 5.46 (s, 1H), 4.86 – 4.77 (m, 3H), 4.74 (s, 1H), 4.65 – 4.40 (m, 3H), 4.29 (s, 1H), 4.23 – 3.85 (m, 4H), 3.37 (s, 3H), 2.57 (s, 2H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.17 (s, 2H), 1.02 (d, *J* = 3.0 Hz, 2H).

10

**Example 57: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-methoxycyclopropane-1-carbonyl)piperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide**



15

*Step 1: tert-butyl 4-(5-bromo-3-fluoro-2-nitrophenyl)piperazine-1-carboxylate.*

To a solution of 5-bromo-1,3-difluoro-2-nitrobenzene (10 g, 42.02 mmol) in DMF (20 mL) was added DIPEA (10.86 g, 84.04 mmol, 14.64 mL) and tert-butyl piperazine-1-carboxylate (8.61 g, 46.22 mmol). And then the mixture was stirred at 25°C for 3 hours.

20 After 3 hrs, LCMS analysis showed the complete consumption of 5-bromo-1,3-difluoro-2-nitrobenzene (10 g, 42.02 mmol). Water was added and the crude product suspension was extracted twice with ethyl acetate. The combined organic layers were washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated. After filtration, the filtrate was concentrated under reduced pressure. The residue was obtained tert-butyl 4-(5-bromo-3-fluoro-2-nitrophenyl)piperazine-1-carboxylate (16.99 g, crude) as yellow solid. LCMS: 404 [M+H]<sup>+</sup>.

25

Step 2: *tert-butyl 4-(5-bromo-3-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)amino)-2-nitrophenyl)piperazine-1-carboxylate.*

To a solution of *tert-butyl 4-(5-bromo-3-fluoro-2-nitro-phenyl)piperazine-1-carboxylate* (16.99 g, 42.03 mmol) in DMF (20 mL) was added  $\text{Cs}_2\text{CO}_3$  (27.32 g, 84.06 mmol) and 5-(difluoromethyl)-1,3,4-thiadiazol-2-amine (6.35 g, 42.03 mmol). And then the mixture was stirred at 70 °C for 3 hours. After 3 hrs, LCMS analysis showed the complete consumption of *tert-butyl 4-(5-bromo-3-fluoro-2-nitro-phenyl)piperazine-1-carboxylate* (16.99 g, 42.03 mmol). Water was added and the crude product suspension was extracted twice with ethyl acetate. The combined organic layers were washed with water, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and the solvent was evaporated. After filtration, the filtrate was concentrated under reduced pressure. The residue was obtained *tert-butyl 4-(5-bromo-3-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)amino)-2-nitrophenyl)piperazine-1-carboxylate* (22.55 g, crude) as yellow solid. LCMS: 535  $[\text{M}+\text{H}]^+$ .

Step 3: *tert-butyl 4-(2-amino-5-bromo-3-((5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)amino)phenyl)piperazine-1-carboxylate.*

To a solution of *tert-butyl 4-[5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]-2-nitro-phenyl]piperazine-1-carboxylate* (22.5 g, 42.03 mmol) in EtOH (20 mL) was added Zn (27.48 g, 420.28 mmol) and  $\text{NH}_4\text{Cl}$  (44.96 g, 840.55 mmol). And then the mixture was stirred at 25°C for 3 hours. After 3 hrs, LCMS analysis showed the complete consumption of *tert-butyl 4-[5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]-2-nitro-phenyl]piperazine-1-carboxylate* (22.5 g, 42.03 mmol). Water was added and the crude product suspension was extracted twice with ethyl acetate. The combined organic layers were washed with water, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and the solvent was evaporated. After filtration, the filtrate was concentrated under reduced pressure. The residue was obtained *tert-butyl 4-[2-amino-5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]phenyl]piperazine-1-carboxylate* (21.24 g, crude) as yellow solid. LCMS: 505  $[\text{M}+\text{H}]^+$ .

Step 4: *tert-butyl 4-(6-bromo-1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)piperazine-1-carboxylate.*

To a solution of *tert-butyl 4-[2-amino-5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]phenyl]piperazine-1-carboxylate* (21.24 g, 42.03 mmol) in DMF (20 mL) was added CDI (10.22 g, 63.04 mmol). And then the mixture was stirred at 25°C for 3

hours. After 16 hrs, LCMS analysis showed the complete consumption of tert-butyl 4-[2-amino-5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]phenyl]piperazine-1-carboxylate (21.24 g, 42.03 mmol). Water was added and the crude product suspension was extracted twice with ethyl acetate. The combined organic layers were washed with water,  
5 dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated. After filtration, the filtrate was concentrated under reduced pressure. The residue was obtained tert-butyl 4-[2-amino-5-bromo-3-[[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]amino]phenyl]piperazine-1-carboxylate (21.24 g, crude) as yellow solid. LCMS: 531 [M+H]<sup>+</sup>.

10 *Step 5: tert-butyl 4-(6-bromo-1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)piperazine-1-carboxylate.*

To a solution of tert-butyl 4-(6-bromo-1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)piperazine-1-carboxylate (21.24 g, 39.97 mmol) in DMF (20 mL) was added EtBr (17.42 g, 159.89 mmol). And then the mixture was stirred  
15 at 25 °C for 16 hours. After 16 hrs, LCMS analysis showed the complete consumption of tert-butyl 4-(6-bromo-1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)piperazine-1-carboxylate (21.24 g, 39.97 mmol). Water was added and the crude product suspension was extracted twice with ethyl acetate. The combined organic layers were washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was  
20 evaporated. The residue was purified by flash chromatography (DCM/ MeOH 100:1→50:1→10:1) to give tert-butyl 4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-2-oxo-benzimidazol-4-yl]piperazine-1-carboxylate (3.8 g, 6.79 mmol, 16.99% yield) as white solid. LCMS: 559[M+H]<sup>+</sup>.

25 *Step 6: 7-(4-(tert-butoxycarbonyl)piperazin-1-yl)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonic acid.*

To a mixture of tert-butyl 4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-2-oxo-benzimidazol-4-yl]piperazine-1-carboxylate (3.8 g, 6.79 mmol) in DMSO (10 mL) was added the 1,10 ferroin (183.62 mg, 1.02 mmol) , K<sub>2</sub>O<sub>5</sub>S<sub>2</sub> (3.02 g, 13.59 mmol) ,  
30 NaCHO<sub>2</sub> (1.02 g, 14.94 mmol), PPh<sub>3</sub> (267.25 mg, 1.02 mmol) , TEAB (4.38 g, 13.59 mmol), and Pd(OAc)<sub>2</sub> (153 mg, 679.85 μmol). And then the mixture was stirred at 70 °C for 3 hrs under N<sub>2</sub>. After 3 hrs , LCMS analysis showed the complete consumption of tert-butyl 4-[6-bromo-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-2-oxo-benzimidazol-4-



yl]piperazine-1-carboxylate (3.8 g, 6.79 mmol). The residue was used for the next step without further purification. LCMS: 545 [M+H]<sup>+</sup>.

Step 7: *tert-butyl 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(fluorosulfonyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)piperazine-1-carboxylate*.

To a solution of 7-(4-*tert*-butoxycarbonylpiperazin-1-yl)-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-benzimidazole-5-sulfinic acid (3.7 g, 6.79 mmol) in DMSO (10 mL) was added NFSI (1.98 g, 10.19 mmol). And then the mixture was stirred at 0 °C for 0.1 hour. After 0.1 hr, LCMS analysis showed the complete consumption of 7-(4-*tert*-butoxycarbonylpiperazin-1-yl)-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-benzimidazole-5-sulfinic acid (3.7 g, 6.79 mmol). Water was added and the crude product suspension was extracted twice with ethyl acetate. The combined organic layers were washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated. The residue was purified by flash chromatography (DCM/ MeOH 100:1→50:1→10:1) to give *tert*-butyl 4-[1-5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-fluorosulfonyl-2-oxo-benzimidazol-4-yl]piperazine-1-carboxylate (1.2 g, 2.13 mmol, 31.40% yield) as white solid. LCMS (ESI, m/z): 563 [M+H]<sup>+</sup>.

Step 8: *tert-butyl 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)piperazine-1-carboxylate*.

To a mixture of *tert*-butyl 4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-fluorosulfonyl-2-oxo-benzimidazol-4-yl]piperazine-1-carboxylate (400 mg, 711.00 μmol) and 3-(fluoromethyl)oxetan-3-amine (74.73 mg, 711.00 μmol) in DMSO (3 mL) was added the DIPEA (643.23 mg, 4.98 mmol, 866.89 μL), HOBt (144.11 mg, 1.07 mmol) and (Me<sub>2</sub>SiH)<sub>2</sub>O (9.53 mg, 71.10 μmol). And then the mixture was stirred at 25°C for 16 hours. After 16 hrs, LCMS analysis showed the complete consumption of 3-(fluoromethyl)oxetan-3-amine (74.73 mg, 711.00 μmol). Water was added and the crude product suspension was extracted twice with ethyl acetate. The combined organic layers were washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was evaporated. The residue was purified by flash chromatography (DCM/ MeOH 100:1→50:1→10:1) to give *tert*-butyl 4-[3-ethyl-1-[5-(1-fluoroethyl)-1,3,4-thiadiazol-2-yl]-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-2-oxo-benzimidazol-4-yl]piperazine-1-carboxylate (150 mg, 233.02 μmol, 32.77% yield) as white solid. LCMS: 648[M+H]<sup>+</sup>.

Step 9: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-2-oxo-7-(piperazin-1-yl)-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.

To a solution of tert-butyl 4-[3-ethyl-1-[5-(1-fluoroethyl)-1,3,4-thiadiazol-2-yl]-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-2-oxo-benzimidazol-4-yl]piperazine-1-carboxylate (150 mg, 233.02  $\mu$ mol) in DCM (3 mL) was added TFA (531.38 mg, 4.66 mmol). And then the mixture was stirred at 25°C for 0.5 hour. After 0.5 hr, TLC analysis (DCM: MeOH = 10:1) showed the complete consumption of tert-butyl 4-[3-ethyl-1-[5-(1-fluoroethyl)-1,3,4-thiadiazol-2-yl]-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-2-oxo-benzimidazol-4-yl]piperazine-1-carboxylate (150 mg, 233.02  $\mu$ mol). The reaction mixture was evaporated. The residue was used for the next step without further purification. LCMS: 548[M+H]<sup>+</sup>.

Step 10: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-methoxycyclopropane-1-carbonyl)piperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.

To a mixture of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-7-piperazin-1-yl-benzimidazole-5-sulfonamide (127 mg, 231.93  $\mu$ mol) and 1-methoxycyclopropanecarboxylic acid (40.40 mg, 347.90  $\mu$ mol) in DMF (3 mL) was added the DIPEA (59.95 mg, 463.86  $\mu$ mol, 80.80  $\mu$ L), HATU (132.20 mg, 347.90  $\mu$ mol). And then the mixture was stirred at 20 °C for 3 hrs. After 3 hrs, LCMS analysis showed the complete consumption of 1-methoxycyclopropanecarboxylic acid (40.40 mg, 347.90  $\mu$ mol). The reaction mixture was purified by Prep-HPLC and dried by hyophilization to give 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-7-[4-(1-methoxycyclopropanecarbonyl)piperazin-1-yl]-2-oxo-benzimidazole-5-sulfonamide (107 mg, 165.55  $\mu$ mol, 71.38% yield, 99.9% purity) as a white solid. LCMS: 646.5[M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, Methanol-*d*<sub>4</sub>)  $\delta$  8.93 (m, 1H), 7.81 (t, *J* = 1.9 Hz, 1H), 7.28 (t, *J* = 53.4 Hz, 1H), 4.71 (m, 3H), 4.59 (m, 3H), 4.45 (m, 4H), 3.38 (s, 3H), 3.23 (d, *J* = 11.6 Hz, 2H), 3.00 (m, 2H), 1.44 (t, *J* = 7.0 Hz, 3H), 1.12-1.05 (m, 2H), 1.04 – 0.97 (m, 2H).

**Example 60: rel-(R)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,6-trimethyl-5,6-dihydropyridine-1(2H)-carboxamide;**

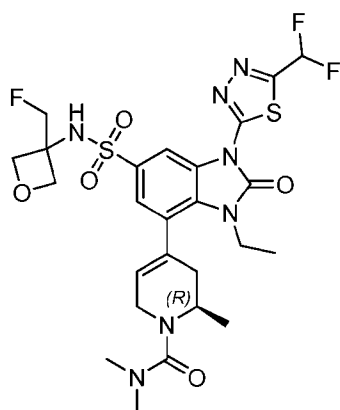
**Example 61:** rel-(R)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,2-trimethyl-5,6-dihydropyridine-1(2H)-carboxamide;

**Example 62:** rel-(R)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,6-trimethyl-5,6-dihydropyridine-1(2H)-carboxamide;

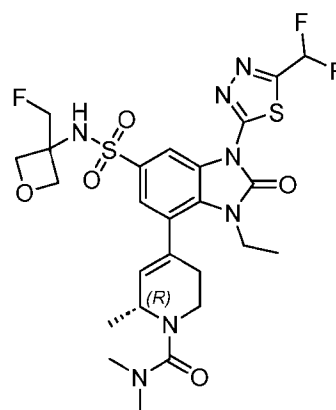
**Example 64:** rel-(R)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,2-trimethyl-5,6-dihydropyridine-1(2H)-carboxamide;

**Example 84:** 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,2-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide; and

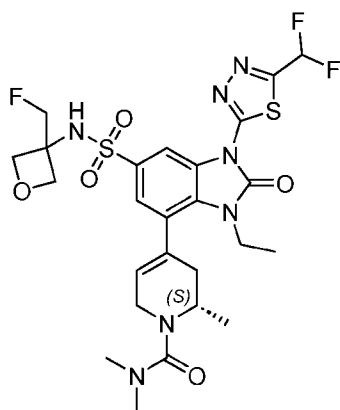
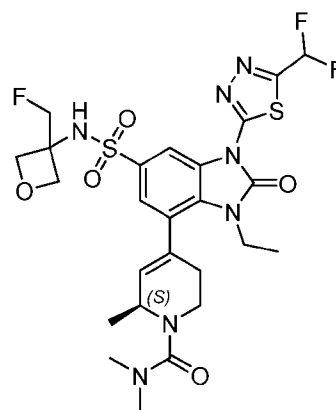
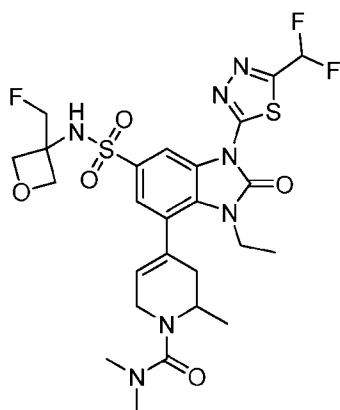
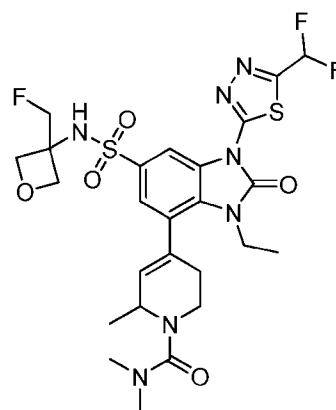
**Example 85:** 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,6-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide



**Example 60**



**Example 61**

**Example 62****Example 64****Example 84****Example 85**

Step 1: *tert*-butyl 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-6-methyl-3,6-dihydropyridine-1(2H)-carboxylate and *tert*-butyl 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-2-methyl-3,6-dihydropyridine-1(2H)-carboxylate

A mixture of 7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-2-oxo-benzimidazole-5-sulfonamide (205.80 mg, 413.33  $\mu$ mol), *tert*-butyl 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)piperidine-1-carboxylate (159.82 mg, 496.00  $\mu$ mol), cataCXium A Pd G<sub>3</sub> (30.10 mg, 41.33  $\mu$ mol) and K<sub>3</sub>PO<sub>4</sub> (175.47 mg, 826.66  $\mu$ mol) in H<sub>2</sub>O (0.4 mL) and *t*-BuOH (1.6 mL) under N<sub>2</sub> was heated at 80 °C for 2 h. Monitored by LCMS. The reaction mixture was concentrated, the residue was purified by flash column to give a mixture of *tert*-butyl 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-6-methyl-3,6-dihydropyridine-1(2H)-carboxylate and *tert*-butyl 4-(1-

(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-2-methyl-3,6-dihydropyridine-1(2H)-carboxylate (0.29 g, crude) as a light yellow solid. LCMS (ESI, m/z): 659[M+H]<sup>+</sup>.

5 *Step 2: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(6-methyl-1,2,3,6-tetrahydropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide and 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(2-methyl-1,2,3,6-tetrahydropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide*

10 A mixture of tert-butyl 4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-2-oxo-benzimidazol-4-yl]-2-methyl-3,6-dihydro-2H-pyridine-1-carboxylate, 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-6-methyl-3,6-dihydropyridine-1(2H)-carboxylate (0.29 g, 440.25 μmol) in DCM (2 mL) and  
15 TFA (2 mL) was stirred at 25 °C for 1 h. Monitored by LCMS. The reaction mixture was concentrated to give a mixture of 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(6-methyl-1,2,3,6-tetrahydropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide and 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(2-methyl-1,2,3,6-tetrahydropyridin-4-yl)-2-oxo-  
20 2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide. (296.12 mg, crude, TFA salt) as a yellow oil. LCMS (ESI, m/z): 559[M+H]<sup>+</sup>.

*Step 3: rel-(R)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,6-trimethyl-5,6-dihydropyridine-1(2H)-carboxamide;*  
25 *rel-(R)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,2-trimethyl-5,6-dihydropyridine-1(2H)-carboxamide;*  
*rel-(R)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,6-trimethyl-5,6-dihydropyridine-1(2H)-carboxamide; and*  
30 *rel-(R)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,2-trimethyl-5,6-dihydropyridine-1(2H)-carboxamide.*

To a solution of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-7-(2-methyl-1,2,3,6-tetrahydropyridin-4-yl)-2-oxo-benzimidazole-5-sulfonamide and 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-N-[3-(fluoromethyl)oxetan-3-yl]-7-(6-methyl-1,2,3,6-tetrahydropyridin-4-yl)-2-oxo-benzimidazole-5-sulfonamide (296.12 mg, 440.25  $\mu$ mol, TF) and TEA (890.98 mg, 8.80 mmol, 1.23 mL) in DCM (4 mL) was added N,N-dimethylcarbonyl chloride (236.72 mg, 2.20 mmol), the reaction mixture was stirred at 25 °C for 16 h. Monitored by LCMS. The reaction mixture was concentrated, the residue was purified by MPLC to give a white solid, then SFC to give

10

*Lowest retention compound (Example 60):*

rel-(R)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,2-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide (9.5 mg, 15.07  $\mu$ mol, 34.24% yield, 99.9% purity) as a white solid. Column: CHIRALPAK AD-3, Mobile Phase A: IPA(0.1%DEA):CO<sub>2</sub>=25:75, Flow rate: 1.0mL/min, Gradient: isocratic, Injection Volume: 1  $\mu$ L, Retention time: 2.796 min. LCMS (ESI, m/z): 630 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (600 MHz, Chloroform-*d*)  $\delta$  9.08 (s, 1H), 7.57 (s, 1H), 7.06 (t, *J* = 53.4 Hz, 1H), 5.85 (s, 1H), 5.57 (s, 1H), 4.80 (m, 3H), 4.73 (s, 1H), 4.46 (d, *J* = 6.6 Hz, 2H), 4.19 (m, 3H), 4.01 (m, 1H), 3.88 (s, 1H), 2.90 (m, 7H), 2.12 (s, 1H), 1.40 – 1.24 (m, 6H).

20

This compound was isolated substantially as a single enantiomer and tentatively assigned (R) stereochemistry.

*Second lowest retention compound (Example 61):*

rel-(R)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,2-trimethyl-5,6-dihydropyridine-1(2H)-carboxamide (33.2 mg, 52.67  $\mu$ mol, 29.91% yield, 99.9% purity) as a white solid. Column: CHIRALPAK AD-3, Mobile Phase A: IPA(0.1%DEA):CO<sub>2</sub>=25:75, Flow rate: 1.0mL/min, Gradient: isocratic, Injection Volume: 3  $\mu$ L, Retention time: 3.127 min LCMS (ESI, m/z): 630[M+H]<sup>+</sup>. <sup>1</sup>H NMR (600 MHz, Chloroform-*d*)  $\delta$  9.07 (s, 1H), 7.62 (m, 1H), 7.06 (t, *J* = 53.4 Hz, 1H), 5.86 (s, 1H), 5.63 (s, 1H), 4.81 (s, 3H), 4.73 (s, 1H), 4.50 – 4.36 (m, 3H), 4.13 (s, 2H), 3.76 (s, 1H), 3.27 (s, 1H), 2.92 (s, 6H), 2.76 (s, 1H), 2.23 (d, *J* = 15.6 Hz, 1H), 1.38 (s, 3H), 1.29 (s, 3H).

30

This compound was isolated substantially as a single enantiomer and tentatively assigned (R) stereochemistry.

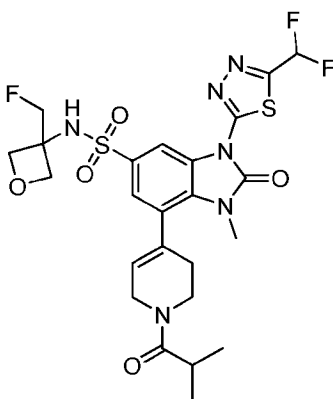
*Third lowest retention compound (Example 62):*

- 5 rel-(R)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,2-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide (8.1 mg, 12.85  $\mu$ mol, 29.19% yield, 99.9% purity) as a white solid. Column: CHIRALPAK AD-3, Mobile Phase A: IPA(0.1%DEA):CO<sub>2</sub>=25:75, Flow rate: 1.0mL/min, Gradient: isocratic, Injection Volume: 3  $\mu$ L. Retention time: 4.794 min. LCMS (ESI, m/z): 630[M+H]<sup>+</sup>. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  8.97 – 8.76 (m, 2H), 7.65 (t, *J* = 53.4 Hz, 1H), 7.52 (d, *J* = 1.8 Hz, 1H), 5.91 (s, 1H), 4.68 (s, 1H), 4.61 (s, 1H), 4.55 (m, 2H), 4.35 (d, *J* = 7.2 Hz, 2H), 4.11 (m, 1H), 4.04 (s, 2H), 3.90 (d, *J* = 18.6 Hz, 1H), 3.80 (d, *J* = 18.6 Hz, 1H), 2.99 – 2.86 (m, 1H), 2.80 (s, 6H), 2.14 (d, *J* = 16.8 Hz, 1H), 1.26 (d, *J* = 7.2 Hz, 3H), 1.19 (t, *J* = 7.2 Hz, 3H).
- 15 This compound was isolated substantially as a single enantiomer and tentatively assigned (S) stereochemistry.

*Fourth lowest retention compound (Example 64):*

- 20 rel-(R)-4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,6-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide (38.8 mg, 60.69  $\mu$ mol, 34.47% yield, 98.5% purity) as a white solid. Column: CHIRAL ART Cellulose-C, Mobile Phase A: IPA(0.1%DEA):CO<sub>2</sub>=30:70, Flow rate: 1.0mL/min, Gradient: isocratic, Injection Volume: 5  $\mu$ L, Retention time: 7.912 min. LCMS (ESI, m/z): 630[M+H]<sup>+</sup>. <sup>1</sup>H NMR (600 MHz, Chloroform-*d*)  $\delta$  9.07 (d, *J* = 1.8 Hz, 1H), 7.62 (d, *J* = 1.8 Hz, 1H), 7.06 (t, *J* = 53.4 Hz, 1H), 5.85 (d, *J* = 3.6 Hz, 1H), 5.69 (s, 1H), 4.80 (m, 3H), 4.72 (s, 1H), 4.46 (d, *J* = 7.2 Hz, 2H), 4.40 (s, 1H), 4.12 (m, 2H), 3.75 (m, 1H), 3.30 – 3.21 (m, 1H), 2.91 (s, 6H), 2.81 – 2.68 (m, 1H), 2.22 (d, *J* = 17.4 Hz, 1H), 1.38 (d, *J* = 7.2 Hz, 3H), 1.29 (s, 3H).
- 25 This compound was isolated substantially as a single enantiomer and tentatively assigned (S) stereochemistry.
- 30

**Example 65: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-7-(1-isobutryl-1,2,3,6-tetrahydropyridin-4-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide**



Step 1: *tert*-butyl 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-5,6-dihydropyridine-1(2H)-carboxylate.

A mixture of 7-chloro-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-[3-(fluoromethyl)oxetan-3-yl]-1-methyl-2-oxo-benzimidazole-5-sulfonamide (0.08 g, 165.33  $\mu$ mol), *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-2H-pyridine-1-carboxylate (61.35 mg, 198.40  $\mu$ mol), cataCXium A Pd G<sub>3</sub> (12.04 mg, 16.53  $\mu$ mol) and K<sub>3</sub>PO<sub>4</sub> (70.19 mg, 330.67  $\mu$ mol) in H<sub>2</sub>O (0.2 mL) and *t*-BuOH (0.8 mL) under N<sub>2</sub> was heated at 80 °C for 2 h. Monitored by LCMS. The reaction mixture was concentrated, the residue was purified by flash column to give *tert*-butyl 4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-3-methyl-2-oxo-benzimidazol-4-yl]-3,6-dihydro-2H-pyridine-1-carboxylate (0.07 g, 111.00  $\mu$ mol, 67.13% yield) as a light yellow solid. LCMS (ESI, *m/z*): 631[M+H]<sup>+</sup>.

Step 2: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-7-(1,2,3,6-tetrahydropyridin-4-yl)-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide.

A mixture of *tert*-butyl 4-[1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[[3-(fluoromethyl)oxetan-3-yl]sulfamoyl]-3-methyl-2-oxo-benzimidazol-4-yl]-3,6-dihydro-2H-pyridine-1-carboxylate (0.07 g, 111.00  $\mu$ mol) in DCM (1 mL) and TFA (1 mL) was stirred at 25 °C for 1 h. Monitored by LCMS. The reaction mixture was concentrated to give 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-[3-(fluoromethyl)oxetan-3-yl]-1-methyl-2-oxo-7-(1,2,3,6-tetrahydropyridin-4-yl)benzimidazole-5-sulfonamide (71.54 mg, crude, TFA salt) as a yellow oil. LCMS (ESI, *m/z*): 531[M+H]<sup>+</sup>.

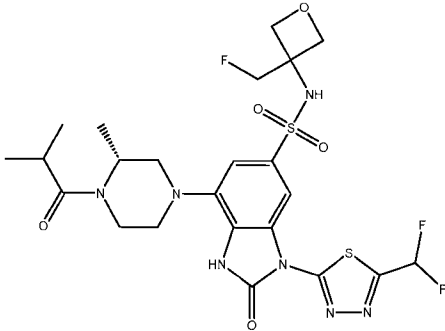
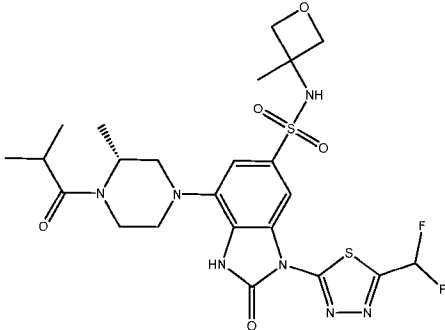
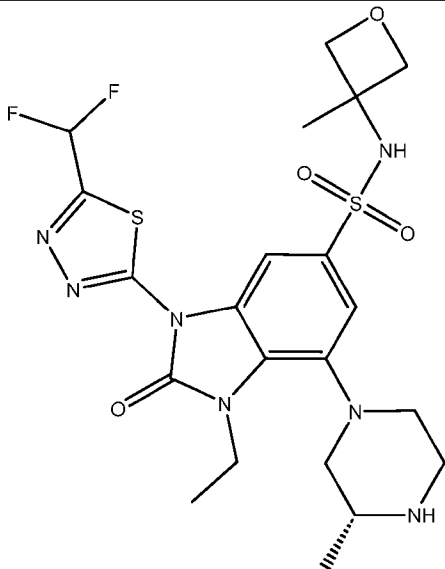


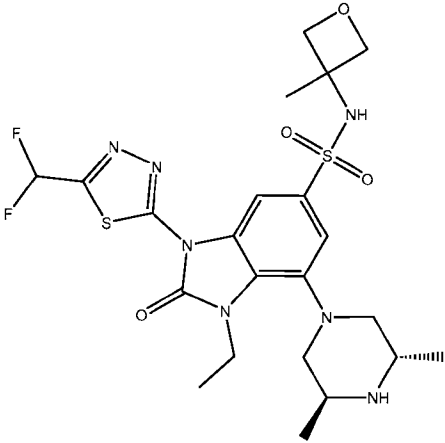
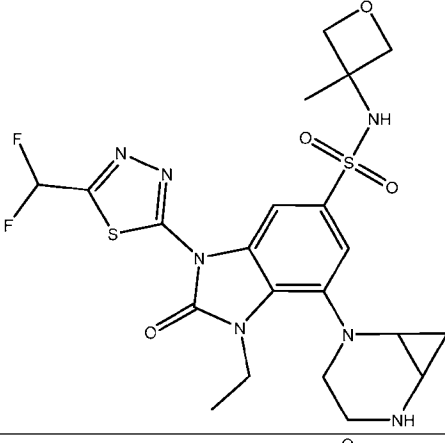
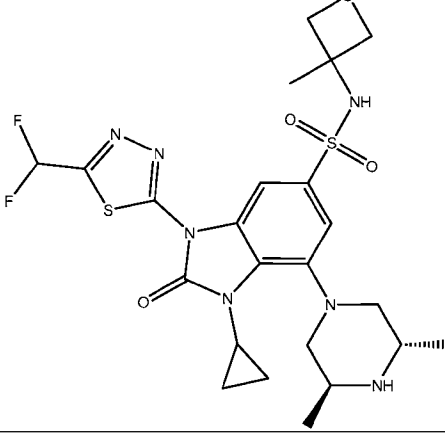
Step 3: 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-7-(1-isobutyryl-1,2,3,6-tetrahydropyridin-4-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzof[d]imidazole-5-sulfonamide.

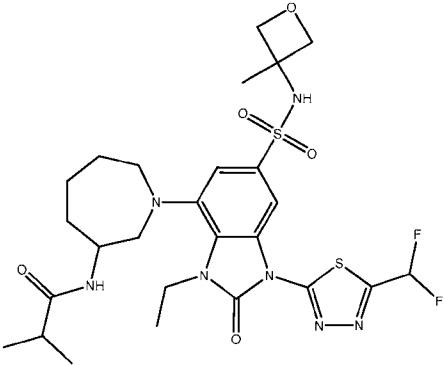
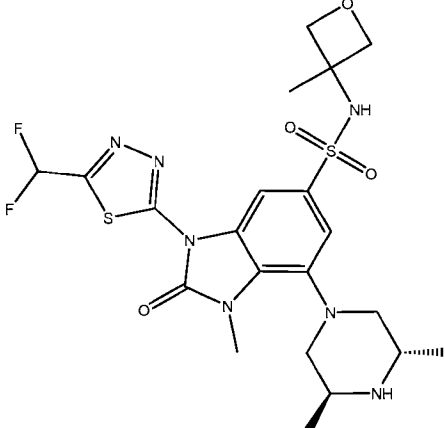
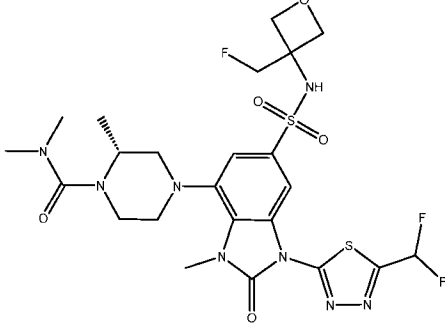
5 To a solution of 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-[3-(fluoromethyl)oxetan-3-yl]-1-methyl-2-oxo-7-(1,2,3,6-tetrahydropyridin-4-yl)benzimidazole-5-sulfonamide (71.54 mg, 110.99  $\mu$ mol, TFA salt) and TEA (224.62 mg, 2.22 mmol, 309.61  $\mu$ L) in DCM (1 mL) at 0 °C was added 2-methylpropanoyl chloride (11.83 mg, 110.99  $\mu$ mol) in DCM (200  $\mu$ L) dropwise, the reaction mixture was stirred at 0 °C for 2 h. Monitored  
10 by LCMS. The reaction mixture was concentrated, the residue was purified by MPLC (base) to give 3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-N-[3-(fluoromethyl)oxetan-3-yl]-1-methyl-7-[1-(2-methylpropanoyl)-3,6-dihydro-2H-pyridin-4-yl]-2-oxo-benzimidazole-5-sulfonamide (21.3 mg, 35.04  $\mu$ mol, 31.57% yield, 98.8% purity) as a white solid. LCMS (ESI, m/z): 601.5[M+H]<sup>+</sup>. <sup>1</sup>H NMR (600 MHz, Chloroform-*d*)  $\delta$  9.04 (d, *J* = 1.8 Hz, 1H),  
15 7.63 (s, 1H), 7.06 (t, *J* = 53.4 Hz, 1H), 5.87 (d, *J* = 30.6 Hz, 1H), 5.68 (s, 1H), 4.81 – 4.75 (m, 3H), 4.71 (s, 1H), 4.45 (d, *J* = 7.2 Hz, 2H), 4.29 (m, 2H), 3.86 – 3.70 (m, 2H), 3.57 (s, 3H), 2.88 (s, 1H), 2.51 (m, 2H), 1.20 (d, *J* = 6.6 Hz, 6H).

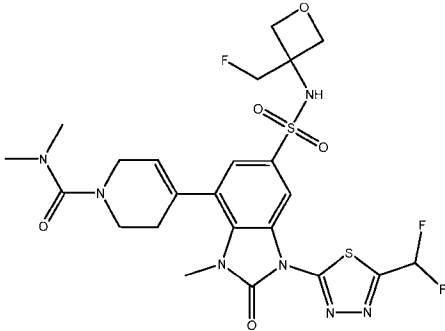
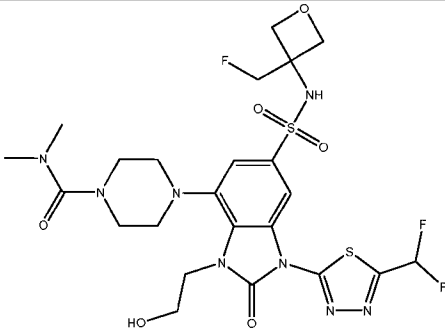
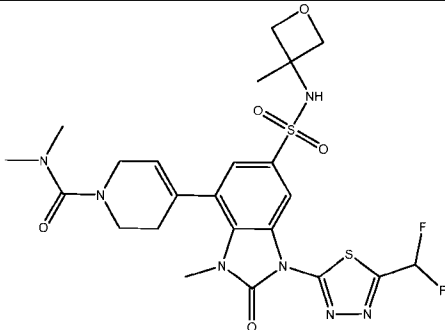
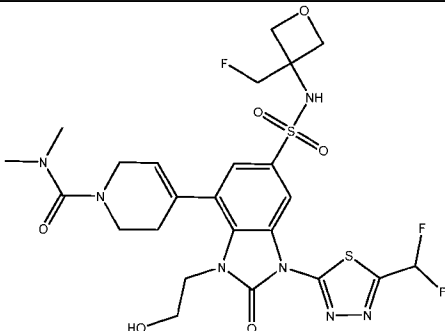
The chemical name, structure, and mass spectrometry [M+H]<sup>+</sup> data for example nos.  
20 18–67 and 69–83 is provided in Table 1. The compounds of Table 1 were prepared by methods analogous to those described for the compounds of Examples 1–17, 27, 31, 43, 45, 55, 57, 60–62, and 64.

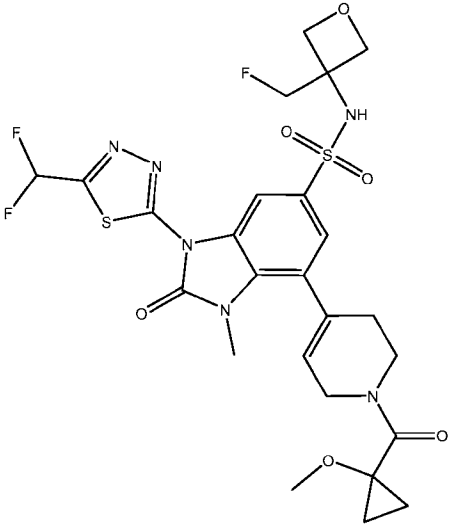
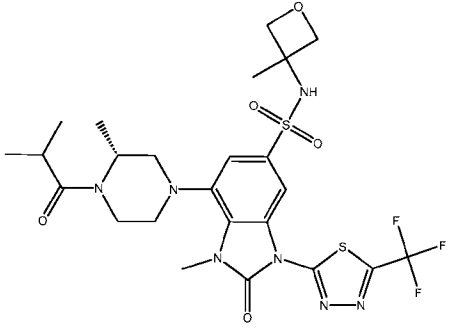
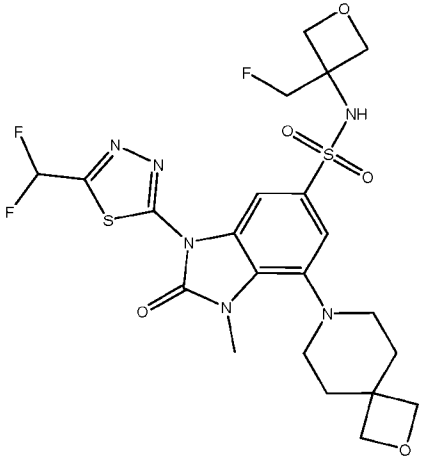
**Table 1. Name, Structure, and Mass Spectrometry [M+H]<sup>+</sup> for Example Nos. 18–67 and**  
25 **70–83**

| Ex. No. | Compound Name                                                                                                                                                            | Compound Structure                                                                   | Mass Spectrometry<br>[M + H] <sup>+</sup> (m/z) |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------------------------|
| 18      | 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-1,3-dihydro-1,3-benzimidazol-2-one |    | 604.1                                           |
| 19      | 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one         |   | 586.1                                           |
| 20      | {7-[(R)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine          |  | 544.1                                           |

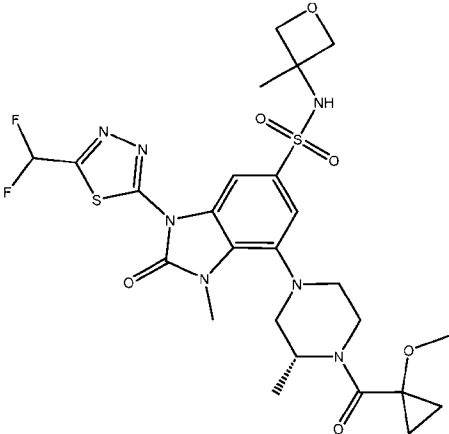
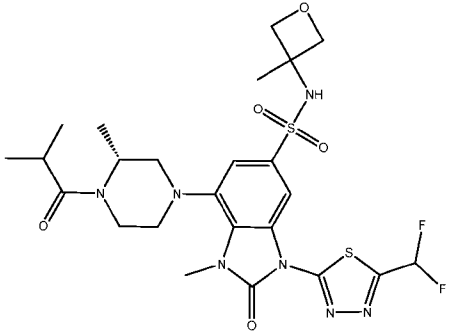
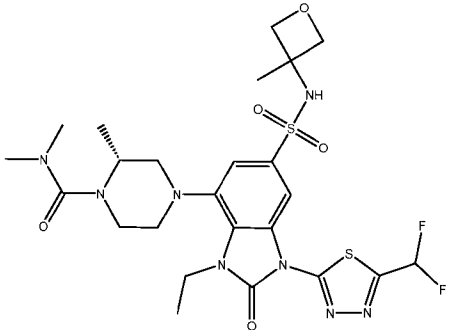
| Ex. No. | Compound Name                                                                                                                                                                                                                 | Compound Structure                                                                   | Mass Spectrometry<br>[M + H] <sup>+</sup> (m/z) |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------------------------|
| 21      | {7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine                                                       |    | 558.5                                           |
| 22      | {7-(2,5-diazabicyclo[4.1.0]hept-2-yl)-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine<br><br>This compound was isolated as a racemic mixture. |   | 542.4                                           |
| 23      | {7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-1-cyclopropyl-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine                                                 |  | 570.5                                           |

| Ex. No. | Compound Name                                                                                                                                                                                     | Compound Structure                                                                   | Mass Spectrometry [M + H] <sup>+</sup> (m/z) |
|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------|
| 24      | N-(1-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-(3-methyl-3-oxetanylaminosulfonyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl]-3-azepanyl}2-methylpropionamide                          |    | 628.2                                        |
| 25      | {7-[(3S,5S)-3,5-dimethyl-1-piperaziny]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine                           |   | 544.5                                        |
| 26      | {7-[(R)-4-(N,N-dimethylcarbamoyl)-3-methyl-1-piperaziny]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine |  | 619.1                                        |

| Ex. No. | Compound Name                                                                                                                                                                                                  | Compound Structure                                                                   | Mass Spectrometry [M + H] <sup>+</sup> (m/z) |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------|
| 27      | {7-[1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine           |    | 602.5                                        |
| 28      | N,N-dimethyl-4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-(2-hydroxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl]-1-piperazinecarboxamide                  |   | 635.0                                        |
| 29      | {7-[1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine                   |  | 584.5                                        |
| 30      | N,N-dimethyl-4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-(2-hydroxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl]-1,2,3,6-tetrahydro-1-pyridinecarboxamide |  | 632.0                                        |

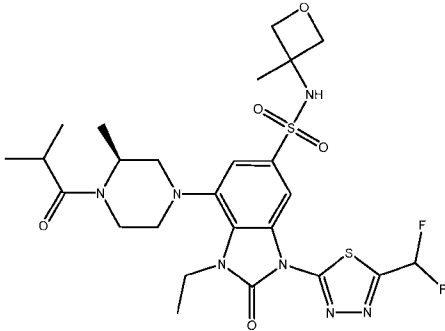
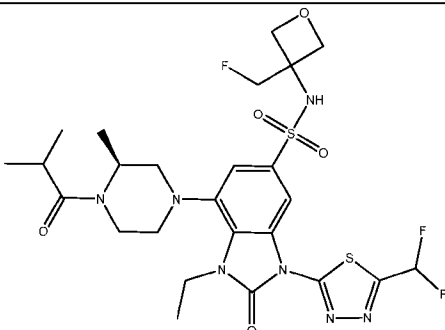
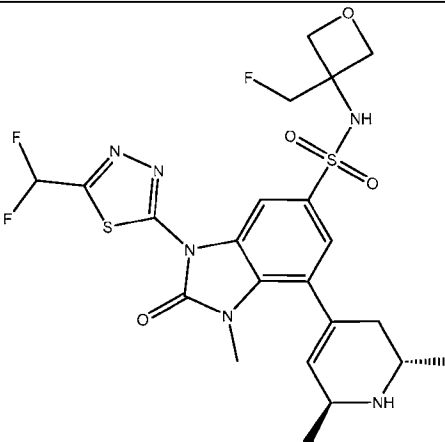
| Ex. No. | Compound Name                                                                                                                                                                                             | Compound Structure                                                                   | Mass Spectrometry [M + H] <sup>+</sup> (m/z) |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------|
| 31      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{1-[(1-methoxycyclopropyl)carbonyl]-1,2,3,6-tetrahydro-4-pyridyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one |    | 629.0                                        |
| 32      | 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]-1,3-dihydro-1,3-benzimidazol-2-one                                |   | 618.1                                        |
| 33      | {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-(2-oxa-7-aza-7-spiro[3.5]nonyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine                               |  | 575.0                                        |

| Ex. No. | Compound Name                                                                                                                                                                                | Compound Structure | Mass Spectrometry [M + H] <sup>+</sup> (m/z) |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------|
| 34      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one           |                    | 614.1                                        |
| 35      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one   |                    | 632.0                                        |
| 36      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-3-azetidynyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one |                    | 647.5                                        |

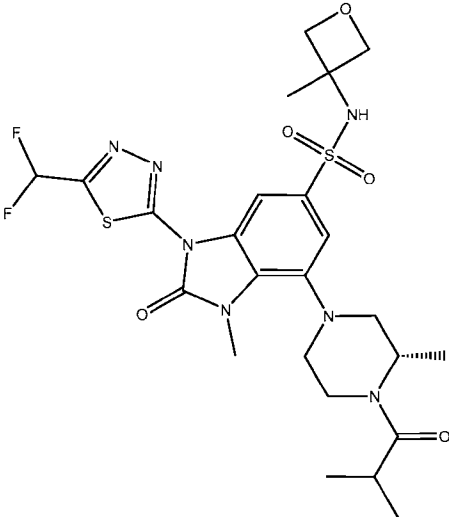
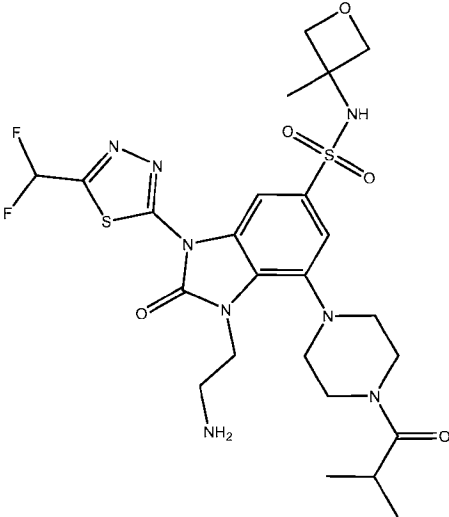
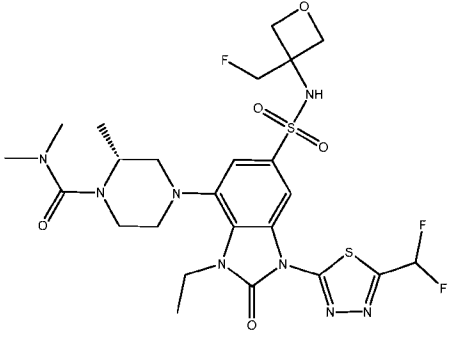
| Ex. No. | Compound Name                                                                                                                                                                                   | Compound Structure                                                                   | Mass Spectrometry<br>[M + H] <sup>+</sup> (m/z) |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------------------------|
| 37      | 4-[(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one |    | 628.0                                           |
| 38      | 4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one                       |   | 600.5                                           |
| 39      | {7-[(R)-4-(N,N-dimethylcarbamoyl)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine       |  | 615.5                                           |



| Ex. No. | Compound Name                                                                                                                                                                                   | Compound Structure | Mass Spectrometry<br>[M + H] <sup>+</sup> (m/z) |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------|
| 40      | {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(R)-3-(methoxymethyl)-1-piperazinyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine            |                    | 578.5                                           |
| 41      | {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(S)-3-(methoxymethyl)-1-piperazinyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine            |                    | 578.5                                           |
| 42      | 6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-3-azetidiny)carbonyl]-1-piperazinyl}-3-methyl-1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]-1,3-dihydro-2H-1,3-benzimidazol-2-one |                    | 665.3                                           |
| 43      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one            |                    | 618.5                                           |

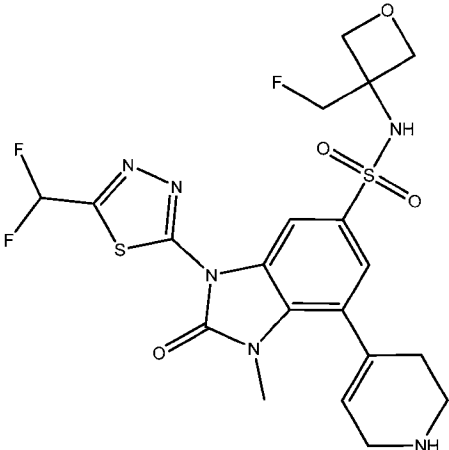
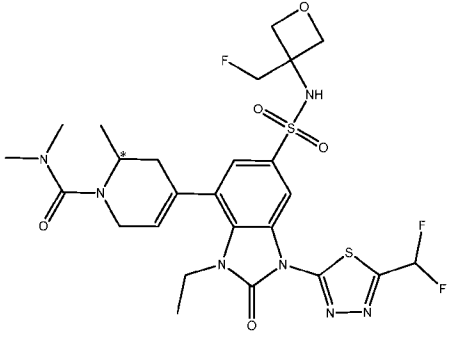
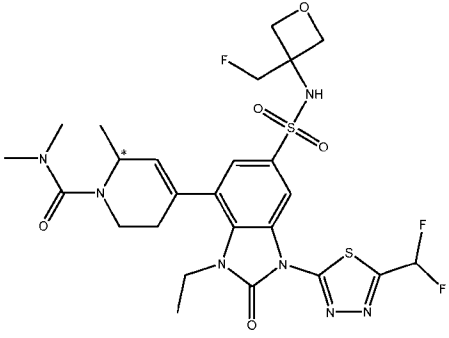
| Ex. No. | Compound Name                                                                                                                                                                                      | Compound Structure                                                                   | Mass Spectrometry<br>[M + H] <sup>+</sup> (m/z) |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------------------------|
| 44      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one                        |    | 614.5                                           |
| 45      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-1,3-dihydro-2H-1,3-benzimidazol-2-one                |   | 632.5                                           |
| 46      | {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(2S,6S)-2,6-dimethyl-1,2,3,6-tetrahydro-4-pyridyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine |  | 559.4                                           |

| Ex. No. | Compound Name                                                                                                                                                                                                                                                                   | Compound Structure | Mass Spectrometry<br>[M + H] <sup>+</sup> (m/z) |
|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------|
| 47      | <p>{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-[6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine</p> <p>This compound was isolated as a racemic mixture.</p> |                    | 616.5                                           |
| 48      | <p>{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-[2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine</p> <p>This compound was isolated as a racemic mixture.</p> |                    | 616.5                                           |
| 49      | <p>1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one</p>                                                                        |                    | 642.5                                           |

| Ex. No. | Compound Name                                                                                                                                                                                        | Compound Structure                                                                   | Mass Spectrometry [M + H] <sup>+</sup> (m/z) |
|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------|
| 50      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one                         |    | 600.0                                        |
| 51      | 3-(2-aminoethyl)-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-(4-isobutyryl-1-piperazinyl)-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one                              |   | 615.3                                        |
| 52      | {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-3-methyl-4-(N,N-dimethylcarbamoyl)-1-piperazinyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine |  | 633.1                                        |

| Ex. No. | Compound Name                                                                                                                                                                                                       | Compound Structure | Mass Spectrometry [M + H] <sup>+</sup> (m/z) |
|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------|
| 53      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one          |                    | 646.0                                        |
| 54      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-[(3-methoxy-1-methyl-3-azetidiny)carbonyl]-3-methyl-1-piperazinyl]-1,3-dihydro-2H-1,3-benzimidazol-2-one |                    | 689.1                                        |
| 55      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{1-[(1-methoxycyclopropyl)carbonyl]-1,2,3,6-tetrahydro-4-pyridyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one         |                    | 643.1                                        |

| Ex. No. | Compound Name                                                                                                                                                                                         | Compound Structure | Mass Spectrometry [M + H] <sup>+</sup> (m/z) |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------|
| 56      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one                  |                    | 628.5                                        |
| 57      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one          |                    | 646.5                                        |
| 58      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-1-methyl-3-azetidyl)carbonyl]-1-piperazinyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one |                    | 675.1                                        |

| Ex. No. | Compound Name                                                                                                                                                                                                                                                                                                                           | Compound Structure                                                                   | Mass Spectrometry [M + H] <sup>+</sup> (m/z) |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------|
| 59      | {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-7-(1,2,3,6-tetrahydro-4-pyridyl)-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine                                                                                                                                                           |    | 531.0                                        |
| 60      | {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine P1 least polar<br><br>This compound was isolated substantially as either the (R) or (S) enantiomer at the * carbon. |   | 630.1                                        |
| 61      | {3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine                                                                                                                     |  | 630.1                                        |

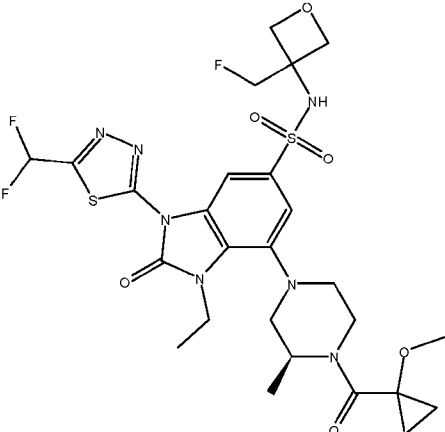
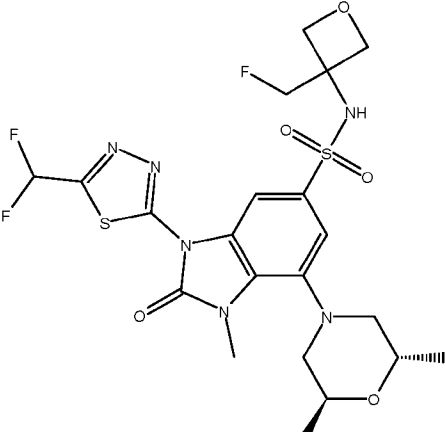
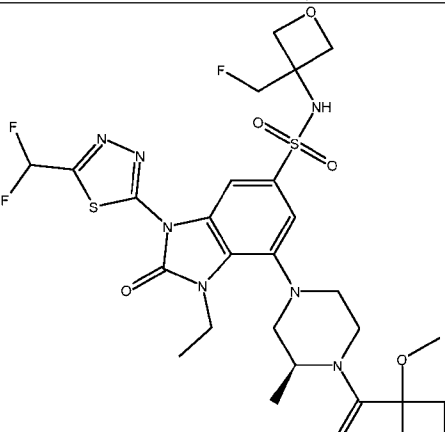
| Ex. No. | Compound Name                                                                                                                                                                                                                                                                                                                   | Compound Structure | Mass Spectrometry [M + H] <sup>+</sup> (m/z) |
|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------|
|         | This compound was isolated substantially as either the (R) or (S) enantiomer at the * carbon.                                                                                                                                                                                                                                   |                    |                                              |
| 62      | <p>{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(S)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine</p> <p>This compound was isolated substantially as either the (R) or (S) enantiomer at the * carbon.</p> |                    | 630.1                                        |
| 63      | <p>{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-3-methyl-4-(N-methylcarbamoyl)-1-piperazinyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine</p>                                                                                                                         |                    | 619.0                                        |
| 64      | <p>{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(S)-2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine</p>                                                                                                      |                    | 630.2                                        |

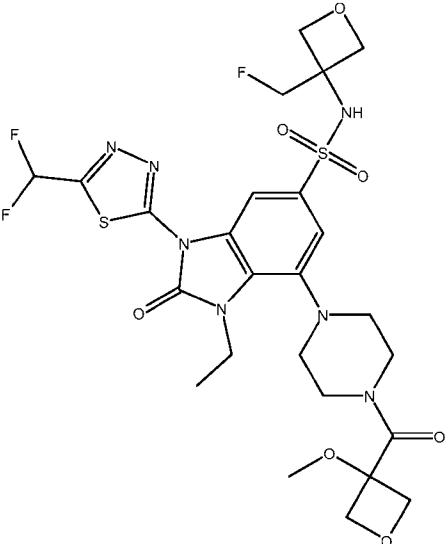
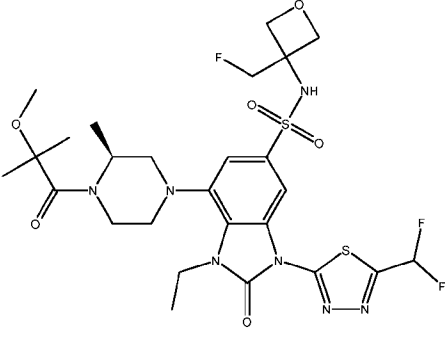
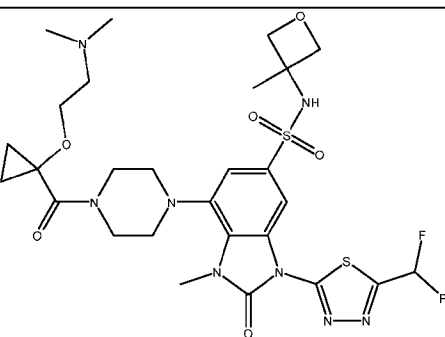


| Ex. No. | Compound Name                                                                                                                                                                                   | Compound Structure | Mass Spectrometry [M + H] <sup>+</sup> (m/z) |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------|
|         | This compound was isolated substantially as either the (R) or (S) enantiomer at the * carbon.                                                                                                   |                    |                                              |
| 65      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-(1-isobutyl-1,2,3,6-tetrahydro-4-pyridyl)-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one            |                    | 601.5                                        |
| 66      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclobutyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one    |                    | 646.1                                        |
| 67      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-methyl-4-{4-[(R)-1-methyl-2-azetidiny]carbonyl}-1-piperazinyl-1,3-dihydro-2H-1,3-benzimidazol-2-one |                    | 631.5                                        |

| Ex. No. | Compound Name                                                                                                                                                                                                               | Compound Structure | Mass Spectrometry [M + H] <sup>+</sup> (m/z) |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------|
| 69      | 1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[4-(2-methoxy-2-methylpropionyl)-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one                                  |                    | 634.5                                        |
| 70      | 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(1-(1-(2-hydroxyethoxy)cyclopropane-1-carbonyl)-1,2,3,6-tetrahydropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide |                    | 673.0                                        |
| 71      | 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-(4-(1-ethoxycyclopropane-1-carbonyl)piperazin-1-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide                             |                    | 660.1                                        |
| 72      | 1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-4-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1H-benzo[d][1,2,3]triazole-6-sulfonamide                                                                |                    | 533.5                                        |

| Ex. No. | Compound Name                                                                                                                                                                                                   | Compound Structure | Mass Spectrometry<br>[M + H] <sup>+</sup> (m/z) |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------|
| 73      | 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-((3R,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide                               |                    | 562.4                                           |
| 74      | 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-7-(4-(1-(2-fluoroethyl)-3-methoxyazetidine-3-carbonyl)piperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide |                    | 707.1                                           |
| 75      | 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-((3S,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide                               |                    | 562.2                                           |

| Ex. No. | Compound Name                                                                                                                                                                                                 | Compound Structure                                                                   | Mass Spectrometry<br>[M + H] <sup>+</sup> (m/z) |
|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------------------------|
| 76      | (S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-methoxycyclopropane-1-carbonyl)-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide |    | 660.2                                           |
| 77      | 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-((2S,6S)-2,6-dimethylmorpholino)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide                                 |   | 563.1                                           |
| 78      | (S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-methoxycyclobutane-1-carbonyl)-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide  |  | 674.1                                           |

| Ex. No. | Compound Name                                                                                                                                                                                               | Compound Structure                                                                   | Mass Spectrometry<br>[M + H] <sup>+</sup> (m/z) |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------------------------|
| 79      | 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(3-methoxyoxetane-3-carbonyl)piperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide                 |    | 660.0 [M-H] <sup>-</sup>                        |
| 80      | (S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(2-methoxy-2-methylpropanoyl)-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide    |   | 662.5                                           |
| 81      | 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-(4-(1-(2-(dimethylamino)ethoxy)cyclopropane-1-carbonyl)piperazin-1-yl)-1-methyl-N-(3-methyloxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide |  | 671.5                                           |

| Ex. No. | Compound Name                                                                                                                                                                                          | Compound Structure | Mass Spectrometry<br>[M + H] <sup>+</sup> (m/z) |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------|
| 82      | 3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-(methoxy-d3)cyclopropane-1-carbonyl)piperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide  |                    | 649.5                                           |
| 83      | 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N-dimethyl-3,6-dihydropyridine-1(2H)-carboxamide    |                    | 616.5                                           |
| 84      | 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,2-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide |                    |                                                 |
| 85      | 4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,6-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide |                    |                                                 |

**Example A. Inhibition of PARG TFMU Assay**

The ability of the compounds of the Examples to inhibit PARG activity in 4-(trifluoromethyl)umbelliferone (TFMU) assay was determined as described below. PARG inhibitors were added into 384 well plate for a 10-point dose response curve at 1:3 dilutions.

- 5 TFMU PARG substrate and PARG (250 pM or 2 nM) were then added to the plate to initiate enzymatic reaction. After incubation with the reagent, luminescence was read. IC<sub>50</sub> values were calculated using set control points for 100% inhibition as no enzyme and 0% inhibition 250 pM or 2 nM of PARG enzyme.

- Compounds of the present disclosure showed IC<sub>50</sub> values in the following ranges: \*\*\*\* =  
 10 IC<sub>50</sub> < 50 nM; \*\*\* = 50 nM ≤ IC<sub>50</sub> < 500 nM; \*\* = 500 nM ≤ IC<sub>50</sub> < 5000 nM; \* = 5000 nM ≤ IC<sub>50</sub>.

Data obtained for the Example compounds using the TFMU assay described in Example A is provided in Table A.

**Table A**

| Example No. | PARG TFMU Assay (IC <sub>50</sub> nM) |
|-------------|---------------------------------------|
| 1           | ****                                  |
| 2           | ****                                  |
| 3           | ****                                  |
| 4           | ****                                  |
| 5           | ****                                  |
| 6           | ****                                  |
| 7           | ****                                  |
| 8           | ****                                  |
| 9           | ****                                  |
| 10          | ****                                  |
| 11          | ****                                  |
| 12          | ****                                  |
| 13          | ****                                  |
| 14          | ****                                  |
| 15          | ****                                  |
| 16          | ****                                  |
| 17          | ****                                  |
| 18          | ****                                  |
| 19          | ****                                  |
| 20          | ****                                  |
| 22          | ****                                  |
| 26          | ****                                  |
| 27          | ****                                  |
| 28          | ****                                  |
| 29          | ****                                  |
| 30          | ****                                  |
| 31          | ****                                  |
| 32          | ****                                  |

| Example No. | PARG TFMU Assay (IC <sub>50</sub> nM) |
|-------------|---------------------------------------|
| 33          | *****                                 |
| 34          | *****                                 |
| 35          | *****                                 |
| 36          | *****                                 |
| 37          | *****                                 |
| 38          | *****                                 |
| 39          | *****                                 |
| 40          | *****                                 |
| 41          | *****                                 |
| 42          | *****                                 |
| 43          | *****                                 |
| 44          | *****                                 |
| 45          | *****                                 |
| 46          | *****                                 |
| 47          | *****                                 |
| 48          | *****                                 |
| 49          | *****                                 |
| 50          | *****                                 |
| 51          | *****                                 |
| 52          | *****                                 |
| 53          | *****                                 |
| 54          | *****                                 |
| 55          | *****                                 |
| 56          | *****                                 |
| 57          | *****                                 |
| 58          | *****                                 |
| 59          | *****                                 |
| 60          | *****                                 |
| 61          | *****                                 |
| 62          | *****                                 |
| 63          | *****                                 |
| 64          | *****                                 |
| 65          | *****                                 |
| 66          | *****                                 |
| 67          | *****                                 |
| 69          | *****                                 |
| 70          | *****                                 |
| 71          | *****                                 |
| 72          | *****                                 |
| 73          | *****                                 |
| 74          | *****                                 |
| 75          | *****                                 |
| 76          | *****                                 |
| 77          | ***                                   |



| Example No. | PARG TFMU Assay (IC <sub>50</sub> nM) |
|-------------|---------------------------------------|
| 78          | ****                                  |
| 79          | ****                                  |
| 80          | ****                                  |
| 81          | ****                                  |
| 82          | ****                                  |

#### Example B. Inhibition of PARG Cellular Viability Assay

HCC1806 cells were plated in 384 well cell culture plates and incubated at 37 °C 5% CO<sub>2</sub>. PARG inhibitors were added starting at 20 μM for a 10-point dose response curve at 1:2 dilutions. The compounds were added to the plate for 168 h and then the percentage of viable cells was assessed either by CyQUANT kit (Invitrogen) for examples 1, 3, 8–9, 11, and 13 or Cell-Titer Glo kit (Promega) for examples 15 and 16 following the instructions of the respective manufacturer.

Compounds of the present disclosure showed IC<sub>50</sub> values in the following ranges:

\*\*\* denotes: IC<sub>50</sub> < 10 μM;

\*\* denotes: 10 μM ≤ IC<sub>50</sub> ≤ 100 μM; and

\* denotes: 100 μM < IC<sub>50</sub>.

Data obtained for the Example compounds using the cell viability cellular assay described in Example B is provided in Table B.

**Table B**

| Example No. | HCC1806 viability assay (IC <sub>50</sub> μM) |
|-------------|-----------------------------------------------|
| 1           | ***                                           |
| 3           | ***                                           |
| 8           | **                                            |
| 9           | ***                                           |
| 11          | ***                                           |
| 13          | ***                                           |
| 15          | ***                                           |
| 16          | ***                                           |
| 26          | ***                                           |
| 27          | ***                                           |
| 29          | ***                                           |

#### Example C. Cellular accumulation of ADP ribose assay using JESS Automated Western Blot System

To measure cellular PARG activity in response to PARG inhibitors, poly-ADP ribose accumulation was measured in cells treated with inhibitors at three specific concentrations for 24 h.

Briefly, HCC1806 cells were seeded onto plates (day 0) and the following day (day 1) media was replaced with media containing inhibitors at three concentrations (100 nM, 500 nM, and 1000 nM) or DMSO alone as a control. Cells were incubated at 37 °C for 24 h in a CO<sub>2</sub> incubator. The following day (day 2), cells were washed with PBS, lysed with lysis buffer containing 50 mM TrisHCl, 100 mM NaCl, 1% Tritonx-100, 5 mM MgCl<sub>2</sub>, 1 mM DTT, protease inhibitors, and olaparib. The protein concentration of lysates was determined and normalized. Samples were prepared for loading into the JESS assay plates according to manufacturer's instructions. Mono- and Poly-ADP ribose levels were quantitated using respective primary and secondary antibodies.

Compounds of the present disclosure showed percent vehicle control values in the following ranges:

\*\*\* denotes: percent vehicle control > 1000%;

\*\* denotes: 200% < percent vehicle control ≤ 1000%; and

\* denotes: percent vehicle control ≤ 200%.

Data obtained for the Example compounds using the ADP ribose assay described in Example C is provided in Table C.

**Table C**

| Example No. | Percent Vehicle Control |        |         |                        |        |         |
|-------------|-------------------------|--------|---------|------------------------|--------|---------|
|             | PanMAR                  |        |         | Poly-/Mono- ADP Ribose |        |         |
|             | 100 nM                  | 500 nM | 1000 nM | 100 nM                 | 500 nM | 1000 nM |
| 11          | *                       | **     | **      | *                      | ***    | ***     |
| 13          | *                       | **     | **      | *                      | ***    | ***     |
| 14          | **                      | **     | **      | **                     | ***    | ***     |

#### **Example D. Cell Viability assay in HCC1428 cells using Cell-Titer-Glo**

##### **1. Cell Seeding**

1.1 The cells were passaged as per ATCC guidelines. The cells were split in log growth into 384 well plates the night before performing the assay. Three experimental replicates were performed for each assay.

##### **2. Compound preparation and treatment**

2.1 The compound dilutions were prepared in fresh tissue culture media to achieve 10 doses with 1:2 fold dilution steps. These dilutions were made at 2X the final dilution.

2.2 The media was removed from the 384 well plate and 30 µl fresh media was dispensed per well into the plate.

2.3 30 µl of the 2X dilutions made in step 2.1 were dispensed. The doses were transferred for each experimental replicate at the same time.

2.4 The plate was shaken at a plate shaker for 2 minutes and returned to the incubator.

### 3. Detection

3.1 After 7 days, the plate was removed from the incubator and equilibrated at room temperature for 15 minutes.

5 3.2 The Cell Titer Glo reagents were thawed to equilibrate to room temperature before the experiment.

40 µl of reagent from CellCounting Lite®2.0 luminescent Cell Viability Assay Kit was added into each well to be detected. The contents were mixed for 2 minutes on an orbital shaker to induce cell lysis. Then the plates were placed at room temperature for 10 min followed by  
10 reading on CLARIOstar Plus.

### 4. Data analysis

4.1 The inhibition activity was calculated following the formula below:

15 
$$\text{Inhibition (\%)} = 100\% \times (Lum_{vehicle} - Lum_{sample}) / (Lum_{vehicle} - Lum_{blank})$$

4.2 The IC<sub>50</sub> was calculated by fitting the Curve using GraphPad Prism software:  
GraphPad Prism software.

$$Y = \text{Bottom} + (\text{Top} - \text{Bottom}) / (1 + 10^{((\text{LogIC}_{50} - X) * \text{HillSlope}))}$$

Compounds of the present disclosure showed IC<sub>50</sub> values in the following ranges:

20 \*\*\* denotes: IC<sub>50</sub> < 0.5 µM;

\*\* denotes: 0.5 µM ≤ IC<sub>50</sub> ≤ 1.5 µM; and

\* denotes: 1.5 µM < IC<sub>50</sub>.

Data obtained for the Example compounds using the cell viability assay described in Example D is provided in Table D.

25 **Table D.**

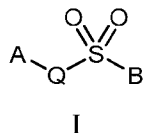
| Example No. | HCC1428 viability assay (IC <sub>50</sub> µM) |
|-------------|-----------------------------------------------|
| 26          | ***                                           |
| 27          | ***                                           |
| 28          | *                                             |
| 29          | ***                                           |
| 30          | ***                                           |
| 31          | ***                                           |
| 32          | ***                                           |
| 33          | **                                            |
| 34          | ***                                           |
| 35          | ***                                           |
| 36          | **                                            |
| 37          | ***                                           |
| 38          | ***                                           |
| 39          | ***                                           |
| 40          | **                                            |

|    |     |
|----|-----|
| 42 | *   |
| 43 | *** |
| 44 | *** |
| 45 | *** |
| 46 | **  |
| 47 | *** |
| 48 | *** |
| 49 | *** |
| 50 | *** |
| 52 | *** |
| 53 | *** |
| 54 | *** |
| 55 | *** |
| 56 | *** |
| 57 | *** |
| 58 | *** |
| 71 | *** |
| 72 | *** |
| 74 | *** |
| 78 | *** |
| 79 | *** |
| 80 | *** |
| 82 | *** |
| 83 | *** |

Various modifications of the invention, in addition to those described herein, will be apparent to those skilled in the art from the foregoing description. Such modifications are also intended to fall within the scope of the appended claims. Each reference, including all  
5 patent, patent applications, and publications, cited in the present application is incorporated herein by reference in its entirety.

**What is claimed is:**

1. A compound of Formula I:

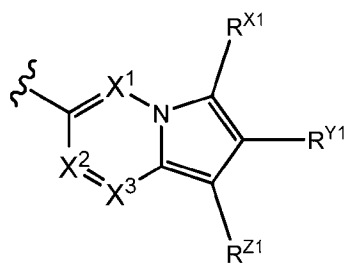


or a pharmaceutically acceptable salt thereof, wherein:

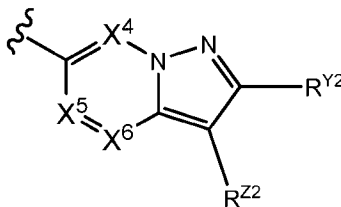
Q is NH or CH<sub>2</sub>;

A is C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, Cy, or Cy-C<sub>1-4</sub> alkyl-, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of A are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a</sup>, SR<sup>a</sup>, C(O)R<sup>b</sup>, C(O)NR<sup>c</sup>R<sup>d</sup>, C(O)OR<sup>a</sup>, OC(O)R<sup>b</sup>, OC(O)NR<sup>c</sup>R<sup>d</sup>, C(=NR<sup>c</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(=NR<sup>c</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(O)R<sup>b</sup>, NR<sup>c</sup>C(O)OR<sup>a</sup>, NR<sup>c</sup>C(O)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>S(O)R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>, S(O)R<sup>b</sup>, S(O)NR<sup>c</sup>R<sup>d</sup>, S(O)<sub>2</sub>R<sup>b</sup>, and S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>,

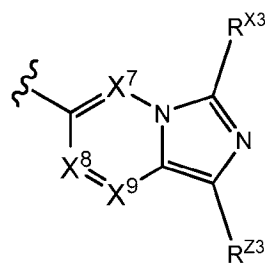
B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), formula (h), formula (i), formula (j), or formula (k):



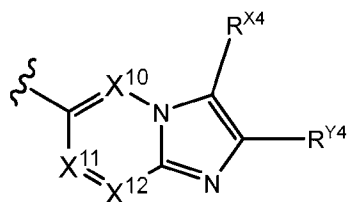
(a)



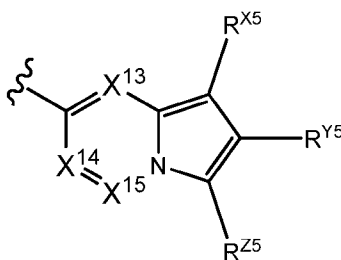
(b)



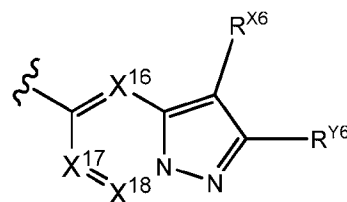
(c)



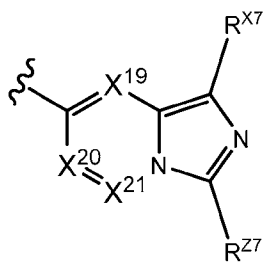
(d)



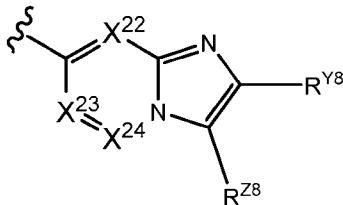
(e)



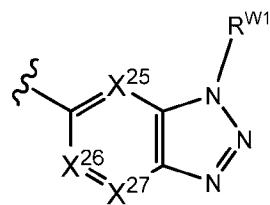
(f)



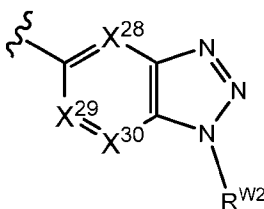
(g)



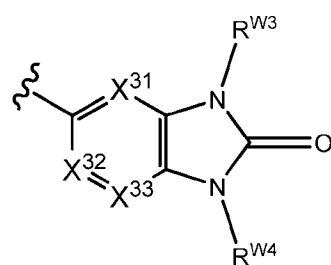
(h)



(i)



(j)



(k);

X<sup>1</sup> is N or CR<sup>1</sup>;

X<sup>2</sup> is N or CR<sup>2</sup>;

X<sup>3</sup> is N or CR<sup>3</sup>;

X<sup>4</sup> is N or CR<sup>4</sup>;

X<sup>5</sup> is N or CR<sup>5</sup>;

X<sup>6</sup> is N or CR<sup>6</sup>;

X<sup>7</sup> is N or CR<sup>7</sup>;

X<sup>8</sup> is N or CR<sup>8</sup>;

X<sup>9</sup> is N or CR<sup>9</sup>;

X<sup>10</sup> is N or CR<sup>10</sup>;

X<sup>11</sup> is N or CR<sup>11</sup>;

X<sup>12</sup> is N or CR<sup>12</sup>;

X<sup>13</sup> is N or CR<sup>13</sup>;

X<sup>14</sup> is N or CR<sup>14</sup>;

X<sup>15</sup> is N or CR<sup>15</sup>;

X<sup>16</sup> is N or CR<sup>16</sup>;

X<sup>17</sup> is N or CR<sup>17</sup>;

X<sup>18</sup> is N or CR<sup>18</sup>;

$X^{19}$  is N or  $CR^{19}$ ;

$X^{20}$  is N or  $CR^{20}$ ;

$X^{21}$  is N or  $CR^{21}$ ;

$X^{22}$  is N or  $CR^{22}$ ;

$X^{23}$  is N or  $CR^{23}$ ;

$X^{24}$  is N or  $CR^{24}$ ;

$X^{25}$  is N or  $CR^{25}$ ;

$X^{26}$  is N or  $CR^{26}$ ;

$X^{27}$  is N or  $CR^{27}$ ;

$X^{28}$  is N or  $CR^{28}$ ;

$X^{29}$  is N or  $CR^{29}$ ;

$X^{30}$  is N or  $CR^{30}$ ;

$X^{31}$  is N or  $CR^{31}$ ;

$X^{32}$  is N or  $CR^{32}$ ;

$X^{33}$  is N or  $CR^{33}$ ;

wherein no more than two of  $X^1$ ,  $X^2$ , and  $X^3$  are simultaneously N;

wherein no more than two of  $X^4$ ,  $X^5$ , and  $X^6$  are simultaneously N;

wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;

wherein no more than two of  $X^{10}$ ,  $X^{11}$ , and  $X^{12}$  are simultaneously N;

wherein no more than two of  $X^{13}$ ,  $X^{14}$ , and  $X^{15}$  are simultaneously N;

wherein no more than two of  $X^{16}$ ,  $X^{17}$ , and  $X^{18}$  are simultaneously N;

wherein no more than two of  $X^{19}$ ,  $X^{20}$ , and  $X^{21}$  are simultaneously N;

wherein no more than two of  $X^{22}$ ,  $X^{23}$ , and  $X^{24}$  are simultaneously N;

wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

wherein no more than two of  $X^{28}$ ,  $X^{29}$ , and  $X^{30}$  are simultaneously N;

wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each Cy is independently selected from  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from  $R^{Cy}$ ;

each  $R^{Cy}$  is independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,

$\text{NR}^{\text{c1}}\text{S}(\text{O})\text{R}^{\text{b1}}$ ,  $\text{NR}^{\text{c1}}\text{S}(\text{O})_2\text{R}^{\text{b1}}$ ,  $\text{NR}^{\text{c1}}\text{S}(\text{O})_2\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{S}(\text{O})\text{R}^{\text{b1}}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b1}}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ , wherein the  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl of  $\text{R}^{\text{Cy}}$  is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN,  $\text{NO}_2$ ,  $\text{OR}^{\text{a1}}$ ,  $\text{SR}^{\text{a1}}$ ,  $\text{C}(\text{O})\text{R}^{\text{b1}}$ ,  $\text{C}(\text{O})\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a1}}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b1}}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{C}(=\text{NR}^{\text{e1}})\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{NR}^{\text{c1}}\text{C}(=\text{NR}^{\text{e1}})\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{NR}^{\text{c1}}\text{C}(\text{O})\text{R}^{\text{b1}}$ ,  $\text{NR}^{\text{c1}}\text{C}(\text{O})\text{OR}^{\text{a1}}$ ,  $\text{NR}^{\text{c1}}\text{C}(\text{O})\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{NR}^{\text{c1}}\text{S}(\text{O})\text{R}^{\text{b1}}$ ,  $\text{NR}^{\text{c1}}\text{S}(\text{O})_2\text{R}^{\text{b1}}$ ,  $\text{NR}^{\text{c1}}\text{S}(\text{O})_2\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{S}(\text{O})\text{R}^{\text{b1}}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b1}}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c1}}\text{R}^{\text{d1}}$ .

$\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^7$ ,  $\text{R}^8$ ,  $\text{R}^{10}$ ,  $\text{R}^{11}$ ,  $\text{R}^{13}$ ,  $\text{R}^{14}$ ,  $\text{R}^{16}$ ,  $\text{R}^{17}$ ,  $\text{R}^{19}$ ,  $\text{R}^{20}$ ,  $\text{R}^{22}$ ,  $\text{R}^{23}$ ,  $\text{R}^{25}$ ,  $\text{R}^{26}$ ,  $\text{R}^{28}$ ,  $\text{R}^{29}$ ,  $\text{R}^{31}$ , and  $\text{R}^{32}$  are each independently selected from H, halo, and  $\text{C}_{1-4}$  alkyl;

$\text{R}^3$ ,  $\text{R}^6$ ,  $\text{R}^9$ ,  $\text{R}^{12}$ ,  $\text{R}^{15}$ ,  $\text{R}^{18}$ ,  $\text{R}^{21}$ ,  $\text{R}^{24}$ ,  $\text{R}^{27}$ ,  $\text{R}^{30}$ , and  $\text{R}^{33}$  are each independently selected from H, halo,  $\text{OR}^{\text{a2}}$ ,  $\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{C}_{6-10}$  aryl,  $\text{C}_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said  $\text{C}_{6-10}$  aryl,  $\text{C}_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $\text{R}^3$ ,  $\text{R}^6$ ,  $\text{R}^9$ ,  $\text{R}^{12}$ ,  $\text{R}^{15}$ ,  $\text{R}^{18}$ ,  $\text{R}^{21}$ ,  $\text{R}^{24}$ ,  $\text{R}^{27}$ ,  $\text{R}^{30}$ , and  $\text{R}^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$  haloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $(\text{CH}_2)_q\text{OR}^{\text{a2}}$ ,  $\text{OR}^{\text{a2}}$ ,  $\text{SR}^{\text{a2}}$ ,  $\text{C}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{C}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a2}}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{C}(=\text{NR}^{\text{e2}})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c2}}\text{C}(=\text{NR}^{\text{e2}})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c2}}\text{C}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{NR}^{\text{c2}}\text{C}(\text{O})\text{OR}^{\text{a2}}$ ,  $\text{NR}^{\text{c2}}\text{C}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c2}}\text{S}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{NR}^{\text{c2}}\text{S}(\text{O})_2\text{R}^{\text{b2}}$ ,  $\text{NR}^{\text{c2}}\text{S}(\text{O})_2\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{S}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b2}}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ .

$\text{R}^{\text{X1}}$ ,  $\text{R}^{\text{X3}}$ ,  $\text{R}^{\text{X4}}$ ,  $\text{R}^{\text{X5}}$ ,  $\text{R}^{\text{X6}}$ ,  $\text{R}^{\text{X7}}$ ,  $\text{R}^{\text{Y1}}$ ,  $\text{R}^{\text{Y2}}$ ,  $\text{R}^{\text{Y4}}$ ,  $\text{R}^{\text{Y5}}$ ,  $\text{R}^{\text{Y6}}$ ,  $\text{R}^{\text{Y8}}$ ,  $\text{R}^{\text{Z1}}$ ,  $\text{R}^{\text{Z2}}$ ,  $\text{R}^{\text{Z3}}$ ,  $\text{R}^{\text{Z5}}$ ,  $\text{R}^{\text{Z7}}$ , and  $\text{R}^{\text{Z8}}$  are each independently selected from H, halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl, and 5-membered heteroaryl, wherein said  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl, and 5-membered heteroaryl of  $\text{R}^{\text{X1}}$ ,  $\text{R}^{\text{X3}}$ ,  $\text{R}^{\text{X4}}$ ,  $\text{R}^{\text{X5}}$ ,  $\text{R}^{\text{X6}}$ ,  $\text{R}^{\text{X7}}$ ,  $\text{R}^{\text{Y1}}$ ,  $\text{R}^{\text{Y2}}$ ,  $\text{R}^{\text{Y4}}$ ,  $\text{R}^{\text{Y5}}$ ,  $\text{R}^{\text{Y6}}$ ,  $\text{R}^{\text{Y8}}$ ,  $\text{R}^{\text{Z1}}$ ,  $\text{R}^{\text{Z2}}$ ,  $\text{R}^{\text{Z3}}$ ,  $\text{R}^{\text{Z5}}$ ,  $\text{R}^{\text{Z7}}$ , and  $\text{R}^{\text{Z8}}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$  haloalkyl,  $\text{C}_{6-10}$  aryl,  $\text{C}_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{\text{a2}}$ ,  $\text{SR}^{\text{a2}}$ ,  $\text{C}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{C}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a2}}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{C}(=\text{NR}^{\text{e2}})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c2}}\text{C}(=\text{NR}^{\text{e2}})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c2}}\text{C}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{NR}^{\text{c2}}\text{C}(\text{O})\text{OR}^{\text{a2}}$ ,  $\text{NR}^{\text{c2}}\text{C}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c2}}\text{S}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{NR}^{\text{c2}}\text{S}(\text{O})_2\text{R}^{\text{b2}}$ ,  $\text{NR}^{\text{c2}}\text{S}(\text{O})_2\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{S}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b2}}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ .



$R^{W1}$ ,  $R^{W2}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4  $R'$ ;

each  $R'$  is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of  $R'$  is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>;

each  $R^a$ ,  $R^b$ ,  $R^c$ ,  $R^d$ ,  $R^{a1}$ ,  $R^{b1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{b3}$ ,  $R^{c3}$ , and  $R^{d3}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of  $R^a$ ,  $R^b$ ,  $R^c$ ,  $R^d$ ,  $R^{a1}$ ,  $R^{b1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{b3}$ ,  $R^{c3}$ , and  $R^{d3}$  is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>;

or  $R^c$  and  $R^d$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>,

$C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ;

or  $R^{c1}$  and  $R^{d1}$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ;

or  $R^{c2}$  and  $R^{d2}$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ;

or  $R^{c3}$  and  $R^{d3}$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ;

or  $R^{c4}$  and  $R^{d4}$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ;

each  $R^{a4}$ ,  $R^{b4}$ ,  $R^{c4}$ , and  $R^{d4}$  is independently selected from H,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, wherein said  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl are

each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino,  $\text{NHC}_{1-4}$  alkyl,  $\text{N}(\text{C}_{1-4}$  alkyl)<sub>2</sub>, halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{1-6}$  alkoxy,  $\text{C}_{1-6}$  haloalkyl, and  $\text{C}_{1-6}$  haloalkoxy;

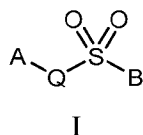
each  $\text{R}^e$ ,  $\text{R}^{e1}$ ,  $\text{R}^{e2}$ ,  $\text{R}^{e3}$ , and  $\text{R}^{e4}$  is independently selected from H,  $\text{C}_{1-4}$  alkyl, and CN;

and

q is an integer selected from 1, 2, 3, 4, 5, and 6;

wherein when B is formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

2. A compound of Formula I:

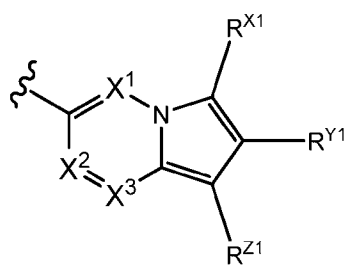


or a pharmaceutically acceptable salt thereof, wherein:

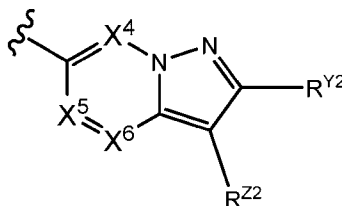
Q is NH or  $\text{CH}_2$ ;

A is  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl, Cy, or  $\text{Cy-C}_{1-4}$  alkyl-, wherein said  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl, and  $\text{C}_{2-6}$  alkynyl of A are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$  haloalkyl,  $\text{C}_{6-10}$  aryl,  $\text{C}_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^a$ ,  $\text{SR}^a$ ,  $\text{C}(\text{O})\text{R}^b$ ,  $\text{C}(\text{O})\text{NR}^c\text{R}^d$ ,  $\text{C}(\text{O})\text{OR}^a$ ,  $\text{OC}(\text{O})\text{R}^b$ ,  $\text{OC}(\text{O})\text{NR}^c\text{R}^d$ ,  $\text{C}(=\text{NR}^e)\text{NR}^c\text{R}^d$ ,  $\text{NR}^c\text{C}(=\text{NR}^e)\text{NR}^c\text{R}^d$ ,  $\text{NR}^c\text{R}^d$ ,  $\text{NR}^c\text{C}(\text{O})\text{R}^b$ ,  $\text{NR}^c\text{C}(\text{O})\text{OR}^a$ ,  $\text{NR}^c\text{C}(\text{O})\text{NR}^c\text{R}^d$ ,  $\text{NR}^c\text{S}(\text{O})\text{R}^b$ ,  $\text{NR}^c\text{S}(\text{O})_2\text{R}^b$ ,  $\text{NR}^c\text{S}(\text{O})_2\text{NR}^c\text{R}^d$ ,  $\text{S}(\text{O})\text{R}^b$ ,  $\text{S}(\text{O})\text{NR}^c\text{R}^d$ ,  $\text{S}(\text{O})_2\text{R}^b$ , and  $\text{S}(\text{O})_2\text{NR}^c\text{R}^d$ ,

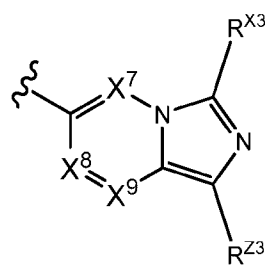
B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), formula (h), formula (i), formula (j), or formula (k):



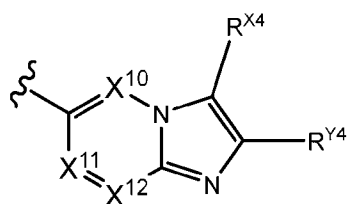
(a)



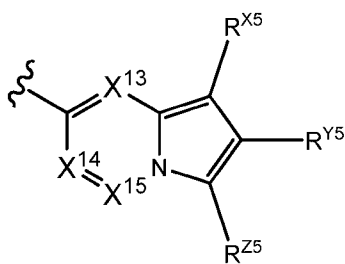
(b)



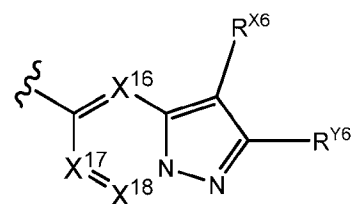
(c)



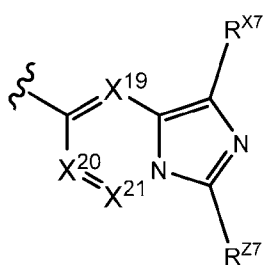
(d)



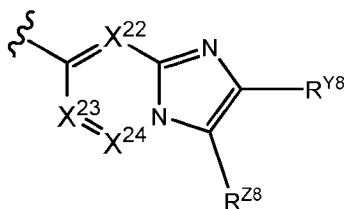
(e)



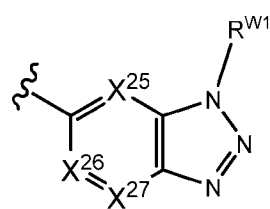
(f)



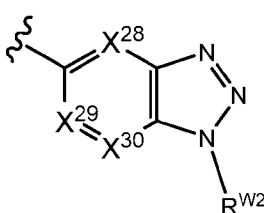
(g)



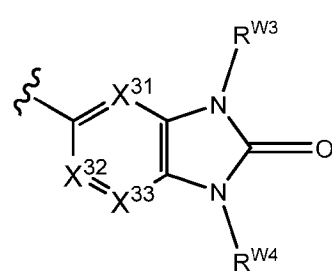
(h)



(i)



(j)



(k);

$X^1$  is N or CR<sup>1</sup>;

$X^2$  is N or CR<sup>2</sup>;

$X^3$  is N or CR<sup>3</sup>;

$X^4$  is N or CR<sup>4</sup>;

$X^5$  is N or CR<sup>5</sup>;

$X^6$  is N or CR<sup>6</sup>;

$X^7$  is N or CR<sup>7</sup>;

$X^8$  is N or CR<sup>8</sup>;

$X^9$  is N or CR<sup>9</sup>;

$X^{10}$  is N or CR<sup>10</sup>;

$X^{11}$  is N or CR<sup>11</sup>;

$X^{12}$  is N or CR<sup>12</sup>;

$X^{13}$  is N or CR<sup>13</sup>;

$X^{14}$  is N or CR<sup>14</sup>;

$X^{15}$  is N or CR<sup>15</sup>;

$X^{16}$  is N or CR<sup>16</sup>;

$X^{17}$  is N or CR<sup>17</sup>;

$X^{18}$  is N or CR<sup>18</sup>;

$X^{19}$  is N or CR<sup>19</sup>;

$X^{20}$  is N or CR<sup>20</sup>;

$X^{21}$  is N or CR<sup>21</sup>;

$X^{22}$  is N or CR<sup>22</sup>;

$X^{23}$  is N or CR<sup>23</sup>;

$X^{24}$  is N or CR<sup>24</sup>;

$X^{25}$  is N or CR<sup>25</sup>;

$X^{26}$  is N or CR<sup>26</sup>;

$X^{27}$  is N or CR<sup>27</sup>;

$X^{28}$  is N or CR<sup>28</sup>;

$X^{29}$  is N or CR<sup>29</sup>;

$X^{30}$  is N or CR<sup>30</sup>;

$X^{31}$  is N or CR<sup>31</sup>;

$X^{32}$  is N or CR<sup>32</sup>;

$X^{33}$  is N or CR<sup>33</sup>;

wherein no more than two of  $X^1$ ,  $X^2$ , and  $X^3$  are simultaneously N;

wherein no more than two of  $X^4$ ,  $X^5$ , and  $X^6$  are simultaneously N;

wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;

wherein no more than two of  $X^{10}$ ,  $X^{11}$ , and  $X^{12}$  are simultaneously N;

wherein no more than two of  $X^{13}$ ,  $X^{14}$ , and  $X^{15}$  are simultaneously N;

wherein no more than two of  $X^{16}$ ,  $X^{17}$ , and  $X^{18}$  are simultaneously N;

wherein no more than two of  $X^{19}$ ,  $X^{20}$ , and  $X^{21}$  are simultaneously N;

wherein no more than two of  $X^{22}$ ,  $X^{23}$ , and  $X^{24}$  are simultaneously N;

wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

wherein no more than two of  $X^{28}$ ,  $X^{29}$ , and  $X^{30}$  are simultaneously N;

wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each Cy is independently selected from C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>;

each R<sup>Cy</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>Cy</sup> is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>;

R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>13</sup>, R<sup>14</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>19</sup>, R<sup>20</sup>, R<sup>22</sup>, R<sup>23</sup>, R<sup>25</sup>, R<sup>26</sup>, R<sup>28</sup>, R<sup>29</sup>, R<sup>31</sup>, and R<sup>32</sup> are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;

R<sup>3</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>12</sup>, R<sup>15</sup>, R<sup>18</sup>, R<sup>21</sup>, R<sup>24</sup>, R<sup>27</sup>, R<sup>30</sup>, and R<sup>33</sup> are each independently selected from H, halo, OR<sup>a2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of R<sup>3</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>12</sup>, R<sup>15</sup>, R<sup>18</sup>, R<sup>21</sup>, R<sup>24</sup>, R<sup>27</sup>, R<sup>30</sup>, and R<sup>33</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>q</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>;

R<sup>X1</sup>, R<sup>X3</sup>, R<sup>X4</sup>, R<sup>X5</sup>, R<sup>X6</sup>, R<sup>X7</sup>, R<sup>Y1</sup>, R<sup>Y2</sup>, R<sup>Y4</sup>, R<sup>Y5</sup>, R<sup>Y6</sup>, R<sup>Y8</sup>, R<sup>Z1</sup>, R<sup>Z2</sup>, R<sup>Z3</sup>, R<sup>Z5</sup>, R<sup>Z7</sup>, and R<sup>Z8</sup> are each independently selected from H, halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl of R<sup>X1</sup>, R<sup>X3</sup>, R<sup>X4</sup>, R<sup>X5</sup>, R<sup>X6</sup>, R<sup>X7</sup>, R<sup>Y1</sup>, R<sup>Y2</sup>, R<sup>Y4</sup>, R<sup>Y5</sup>, R<sup>Y6</sup>, R<sup>Y8</sup>, R<sup>Z1</sup>, R<sup>Z2</sup>, R<sup>Z3</sup>, R<sup>Z5</sup>, R<sup>Z7</sup>, and R<sup>Z8</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from

halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>,

R<sup>W1</sup>, R<sup>W2</sup>, R<sup>W3</sup>, and R<sup>W4</sup> are each independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4 R' ;

each R' is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R' is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>,

each R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>a1</sup>, R<sup>b1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>b3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>a1</sup>, R<sup>b1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>b3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected

from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

or R<sup>c</sup> and R<sup>d</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

or R<sup>c1</sup> and R<sup>d1</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

or R<sup>c2</sup> and R<sup>d2</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

or R<sup>c3</sup> and R<sup>d3</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

or R<sup>c4</sup> and R<sup>d4</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,



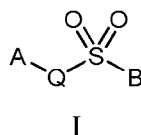
each  $R^{a4}$ ,  $R^{b4}$ ,  $R^{c4}$ , and  $R^{d4}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl are each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkyl, and C<sub>1-6</sub> haloalkoxy;

each  $R^e$ ,  $R^{e1}$ ,  $R^{e2}$ ,  $R^{e3}$ , and  $R^{e4}$  is independently selected from H, C<sub>1-4</sub> alkyl, and CN; and

q is an integer selected from 1, 2, 3, 4, 5, and 6;

wherein when B is formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

3. A compound of Formula I:

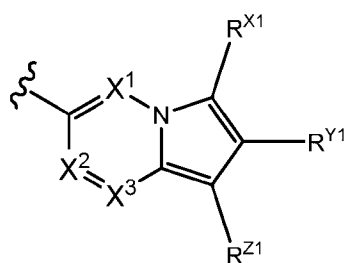


or a pharmaceutically acceptable salt thereof, wherein:

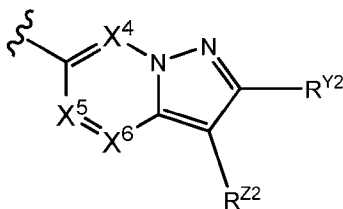
Q is NH or CH<sub>2</sub>;

A is C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, Cy, or Cy-C<sub>1-4</sub> alkyl-, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of A are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a</sup>, SR<sup>a</sup>, C(O)R<sup>b</sup>, C(O)NR<sup>c</sup>R<sup>d</sup>, C(O)OR<sup>a</sup>, OC(O)R<sup>b</sup>, OC(O)NR<sup>c</sup>R<sup>d</sup>, C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(=NR<sup>e</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>C(O)R<sup>b</sup>, NR<sup>c</sup>C(O)OR<sup>a</sup>, NR<sup>c</sup>C(O)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>S(O)R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>R<sup>b</sup>, NR<sup>c</sup>S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>, S(O)R<sup>b</sup>, S(O)NR<sup>c</sup>R<sup>d</sup>, S(O)<sub>2</sub>R<sup>b</sup>, and S(O)<sub>2</sub>NR<sup>c</sup>R<sup>d</sup>,

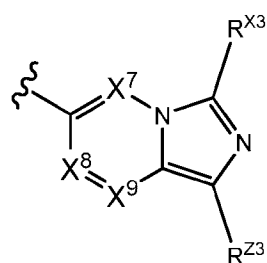
B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), formula (h), formula (i), formula (j), or formula (k):



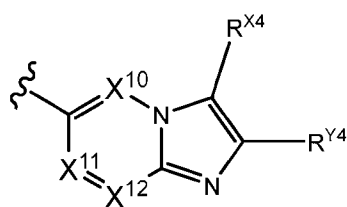
(a)



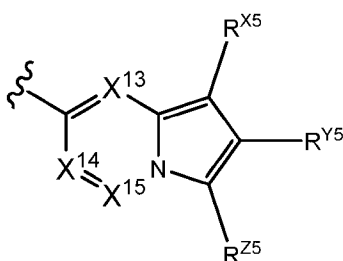
(b)



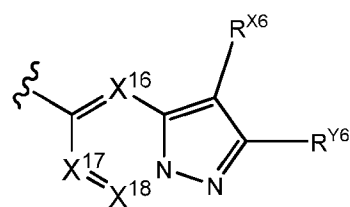
(c)



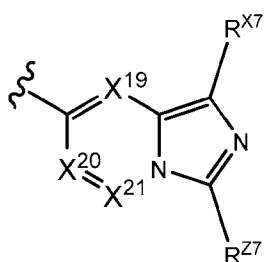
(d)



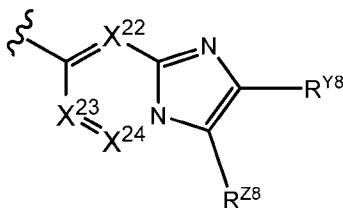
(e)



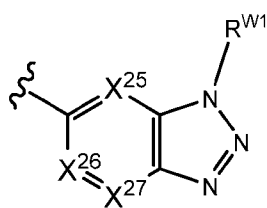
(f)



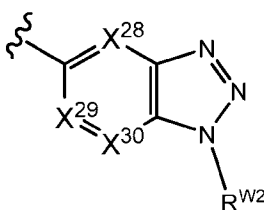
(g)



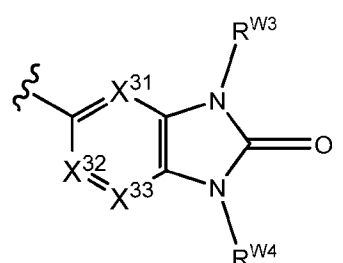
(h)



(i)



(j)



(k);

$X^1$  is N or  $CR^1$ ;

$X^2$  is N or  $CR^2$ ;

$X^3$  is N or  $CR^3$ ;

$X^4$  is N or  $CR^4$ ;

$X^5$  is N or  $CR^5$ ;

$X^6$  is N or  $CR^6$ ;

$X^7$  is N or  $CR^7$ ;

$X^8$  is N or  $CR^8$ ;

$X^9$  is N or  $CR^9$ ;

$X^{10}$  is N or  $CR^{10}$ ;

$X^{11}$  is N or  $CR^{11}$ ;

$X^{12}$  is N or  $CR^{12}$ ;

$X^{13}$  is N or  $CR^{13}$ ;

$X^{14}$  is N or  $CR^{14}$ ;

$X^{15}$  is N or  $CR^{15}$ ;

$X^{16}$  is N or  $CR^{16}$ ;

$X^{17}$  is N or  $CR^{17}$ ;

$X^{18}$  is N or  $CR^{18}$ ;

$X^{19}$  is N or  $CR^{19}$ ;

$X^{20}$  is N or  $CR^{20}$ ;

$X^{21}$  is N or  $CR^{21}$ ;

$X^{22}$  is N or  $CR^{22}$ ;

$X^{23}$  is N or  $CR^{23}$ ;

$X^{24}$  is N or  $CR^{24}$ ;

$X^{25}$  is N or  $CR^{25}$ ;

$X^{26}$  is N or  $CR^{26}$ ;

$X^{27}$  is N or  $CR^{27}$ ;

$X^{28}$  is N or  $CR^{28}$ ;

$X^{29}$  is N or  $CR^{29}$ ;

$X^{30}$  is N or  $CR^{30}$ ;

$X^{31}$  is N or  $CR^{31}$ ;

$X^{32}$  is N or  $CR^{32}$ ;

$X^{33}$  is N or  $CR^{33}$ ;

wherein no more than two of  $X^1$ ,  $X^2$ , and  $X^3$  are simultaneously N;

wherein no more than two of  $X^4$ ,  $X^5$ , and  $X^6$  are simultaneously N;

wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;

wherein no more than two of  $X^{10}$ ,  $X^{11}$ , and  $X^{12}$  are simultaneously N;

wherein no more than two of  $X^{13}$ ,  $X^{14}$ , and  $X^{15}$  are simultaneously N;

wherein no more than two of  $X^{16}$ ,  $X^{17}$ , and  $X^{18}$  are simultaneously N;

wherein no more than two of  $X^{19}$ ,  $X^{20}$ , and  $X^{21}$  are simultaneously N;

wherein no more than two of  $X^{22}$ ,  $X^{23}$ , and  $X^{24}$  are simultaneously N;

wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

wherein no more than two of  $X^{28}$ ,  $X^{29}$ , and  $X^{30}$  are simultaneously N;

wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each Cy is independently selected from C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>;

each R<sup>Cy</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>Cy</sup> is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>;

R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>13</sup>, R<sup>14</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>19</sup>, R<sup>20</sup>, R<sup>22</sup>, R<sup>23</sup>, R<sup>25</sup>, R<sup>26</sup>, R<sup>28</sup>, R<sup>29</sup>, R<sup>31</sup>, and R<sup>32</sup> are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;

R<sup>3</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>12</sup>, R<sup>15</sup>, R<sup>18</sup>, R<sup>21</sup>, R<sup>24</sup>, R<sup>27</sup>, R<sup>30</sup>, and R<sup>33</sup> are each independently selected from H, halo, OR<sup>a2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of R<sup>3</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>12</sup>, R<sup>15</sup>, R<sup>18</sup>, R<sup>21</sup>, R<sup>24</sup>, R<sup>27</sup>, R<sup>30</sup>, and R<sup>33</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>,

$\text{NR}^{\text{c2}}\text{C}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{NR}^{\text{c}}\text{C}(\text{O})\text{OR}^{\text{a2}}$ ,  $\text{NR}^{\text{c}}\text{C}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c}}\text{S}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{NR}^{\text{c2}}\text{S}(\text{O})_2\text{R}^{\text{b2}}$ ,  
 $\text{NR}^{\text{c2}}\text{S}(\text{O})_2\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{S}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b2}}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ;  
 $\text{R}^{\text{X1}}$ ,  $\text{R}^{\text{X3}}$ ,  $\text{R}^{\text{X4}}$ ,  $\text{R}^{\text{X5}}$ ,  $\text{R}^{\text{X6}}$ ,  $\text{R}^{\text{X7}}$ ,  $\text{R}^{\text{Y1}}$ ,  $\text{R}^{\text{Y2}}$ ,  $\text{R}^{\text{Y4}}$ ,  $\text{R}^{\text{Y5}}$ ,  $\text{R}^{\text{Y6}}$ ,  $\text{R}^{\text{Y8}}$ ,  $\text{R}^{\text{Z1}}$ ,  $\text{R}^{\text{Z2}}$ ,  $\text{R}^{\text{Z3}}$ ,  $\text{R}^{\text{Z5}}$ ,  $\text{R}^{\text{Z7}}$ ,  
 and  $\text{R}^{\text{Z8}}$  are each independently selected from H, halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl, and 5-  
 membered heteroaryl, wherein said  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl, and 5-membered heteroaryl of  
 $\text{R}^{\text{X1}}$ ,  $\text{R}^{\text{X3}}$ ,  $\text{R}^{\text{X4}}$ ,  $\text{R}^{\text{X5}}$ ,  $\text{R}^{\text{X6}}$ ,  $\text{R}^{\text{X7}}$ ,  $\text{R}^{\text{Y1}}$ ,  $\text{R}^{\text{Y2}}$ ,  $\text{R}^{\text{Y4}}$ ,  $\text{R}^{\text{Y5}}$ ,  $\text{R}^{\text{Y6}}$ ,  $\text{R}^{\text{Y8}}$ ,  $\text{R}^{\text{Z1}}$ ,  $\text{R}^{\text{Z2}}$ ,  $\text{R}^{\text{Z3}}$ ,  $\text{R}^{\text{Z5}}$ ,  $\text{R}^{\text{Z7}}$ , and  $\text{R}^{\text{Z8}}$   
 are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from  
 halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$  haloalkyl,  $\text{C}_{6-10}$  aryl,  $\text{C}_{3-7}$  cycloalkyl, 5-10  
 membered heteroaryl, 4-10 membered heterocycloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl-  
 $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl,  
 $\text{CN}$ ,  $\text{NO}_2$ ,  $\text{OR}^{\text{a2}}$ ,  $\text{SR}^{\text{a2}}$ ,  $\text{C}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{C}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a2}}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  
 $\text{C}(=\text{NR}^{\text{c2}})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c2}}\text{C}(=\text{NR}^{\text{c2}})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c2}}\text{C}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{NR}^{\text{c2}}\text{C}(\text{O})\text{OR}^{\text{a2}}$ ,  
 $\text{NR}^{\text{c2}}\text{C}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{NR}^{\text{c2}}\text{S}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{NR}^{\text{c2}}\text{S}(\text{O})_2\text{R}^{\text{b2}}$ ,  $\text{NR}^{\text{c2}}\text{S}(\text{O})_2\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  $\text{S}(\text{O})\text{R}^{\text{b2}}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ,  
 $\text{S}(\text{O})_2\text{R}^{\text{b2}}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c2}}\text{R}^{\text{d2}}$ ;

R<sup>W1</sup>, R<sup>W2</sup>, R<sup>W3</sup>, and R<sup>W4</sup> are each independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4 R<sup>z</sup>;

each R' is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R' is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>;

each R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>a1</sup>, R<sup>b1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>b3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub>

alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>a1</sup>, R<sup>b1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>b3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

or R<sup>c</sup> and R<sup>d</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

or R<sup>c1</sup> and R<sup>d1</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

or R<sup>c2</sup> and R<sup>d2</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

or R<sup>c3</sup> and R<sup>d3</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>.

or  $R^{c4}$  and  $R^{d4}$ , together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,  $C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ,

each  $R^{a4}$ ,  $R^{b4}$ ,  $R^{c4}$ , and  $R^{d4}$  is independently selected from H,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, wherein said  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl are each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy,  $C_{1-6}$  haloalkyl, and  $C_{1-6}$  haloalkoxy; and

each  $R^e$ ,  $R^{e1}$ ,  $R^{e2}$ ,  $R^{e3}$ , and  $R^{e4}$  is independently selected from H,  $C_{1-4}$  alkyl, and CN;

wherein when B is formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein Q is NH.

5. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein Q is  $CH_2$ .

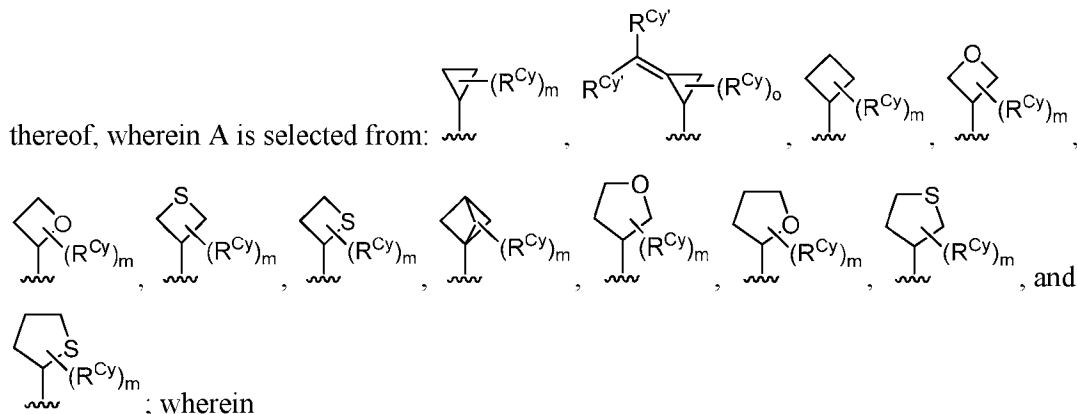
6. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein A is Cy.

7. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein A is selected from  $C_{3-7}$  cycloalkyl and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from  $R^{Cy}$ .

8. The compound of any one of claims 1-7, or a pharmaceutically acceptable salt thereof, wherein A is C<sub>3-7</sub> cycloalkyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>.
9. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, wherein A is cyclopropyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>.
10. The compound of any one of claims 7-9, or a pharmaceutically acceptable salt thereof, wherein at least one R<sup>Cy</sup> is C<sub>1-6</sub> alkyl.
11. The compound of any one of claims 7-9, or a pharmaceutically acceptable salt thereof, wherein at least one R<sup>Cy</sup> is methyl.
12. The compound of any one of claims 7-9, or a pharmaceutically acceptable salt thereof, wherein at least one R<sup>Cy</sup> is CN.
13. The compound of any one of claims 7-9, or a pharmaceutically acceptable salt thereof, wherein the cyclopropyl is substituted with methyl and CN.
14. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein A is 4-10 membered heterocycloalkyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>.
15. The compound of any one of claims 1-6 and 14, or a pharmaceutically acceptable salt thereof, wherein A is oxetanyl optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>.
16. The compound of claim 14 or 15, or a pharmaceutically acceptable salt thereof, wherein at least one R<sup>Cy</sup> is C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, or CN.
17. The compound of claim 14 or 15, or a pharmaceutically acceptable salt thereof, wherein at least one R<sup>Cy</sup> is methyl, fluoromethyl, or CN.



18. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt

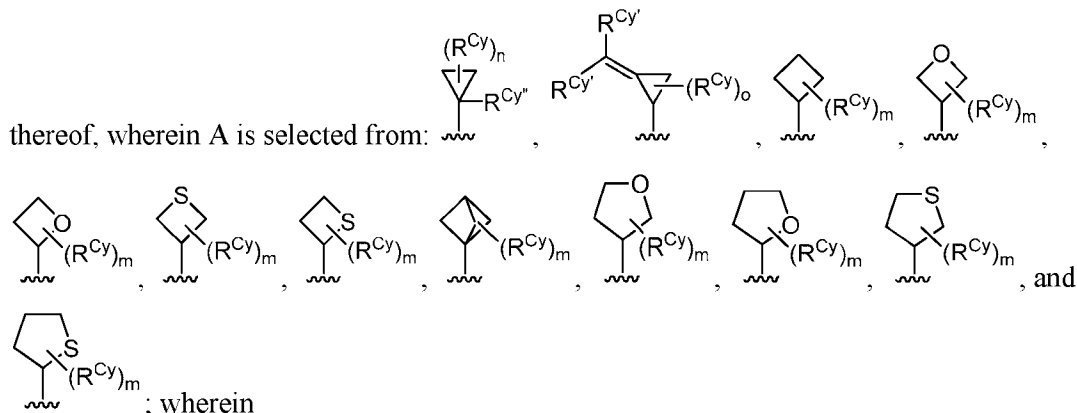


each  $R^{Cy'}$  is selected from from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

$m$  is an integer selected from 0, 1, 2, 3, 4, and 5; and

$o$  is an integer selected from 0, 1, 2, and 3.

19. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt



each  $R^{Cy'}$  is selected from from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

$R^{Cy''}$  is selected from halo,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,

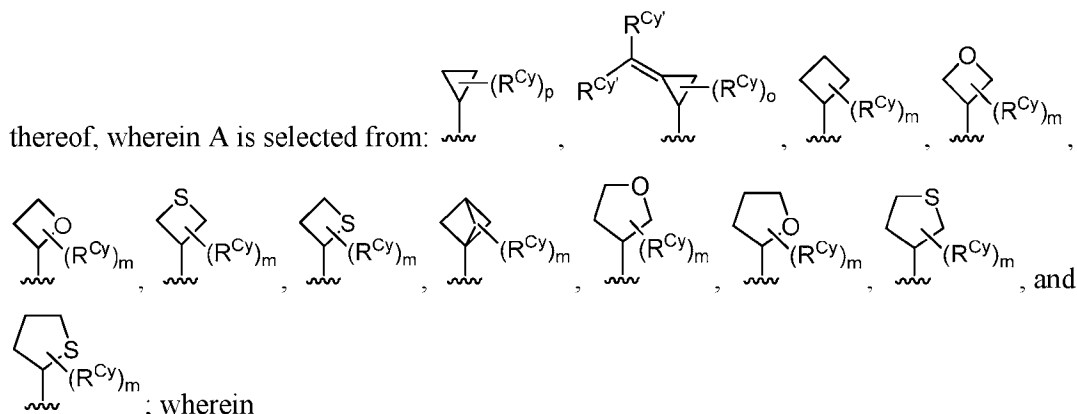
$C(=NR^{c1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{c1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ , wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl of  $R^{Cy}$  is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{c1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{c1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

m is an integer selected from 0, 1, 2, 3, 4, and 5;

n is an integer selected from 0, 1, 2, 3, and 4; and

o is an integer selected from 0, 1, 2, and 3.

20. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt



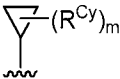
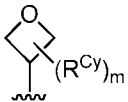
each  $R^{Cy'}$  is selected from from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{c1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{c1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

m is an integer selected from 0, 1, 2, 3, 4, and 5;

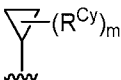
o is an integer selected from 0, 1, 2, and 3; and

p is an integer selected from 0, 2, 3, 4, and 5.

21. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt

thereof, wherein A is selected from:  and ; and  
m is an integer selected from 0, 1, 2, 3, 4, and 5.

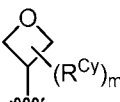
22. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt

thereof, wherein A is: ; and  
m is an integer selected from 0, 1, 2, 3, 4, and 5.

23. The compound of claim 22, or a pharmaceutically acceptable salt thereof, wherein m is an integer selected from 0, 2, 3, 4, and 5.

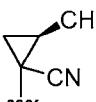
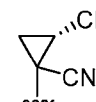
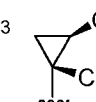
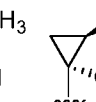
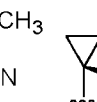
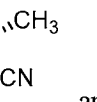
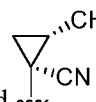
24. The compound of claim 22, or a pharmaceutically acceptable salt thereof, wherein m is 2.

25. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt

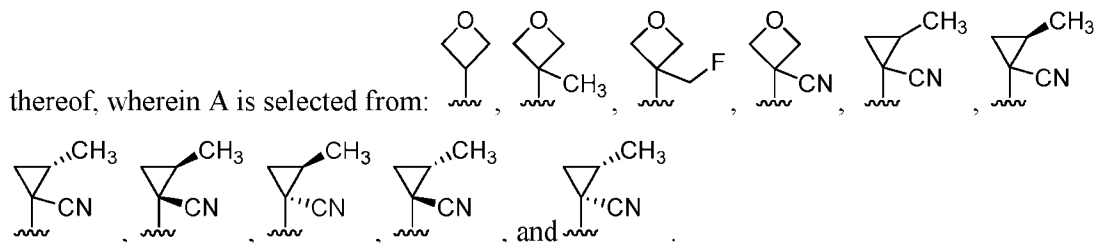
thereof, wherein A is selected from: ; and  
m is an integer selected from 0, 1, 2, 3, 4, and 5.

26. The compound of claim 25, or a pharmaceutically acceptable salt thereof, wherein m is 1.

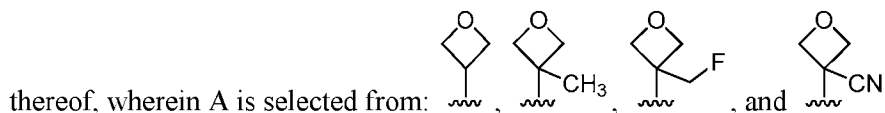
27. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt

thereof, wherein A is selected from: , , , , , ,  
, , , , , , and .

28. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt



29. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt

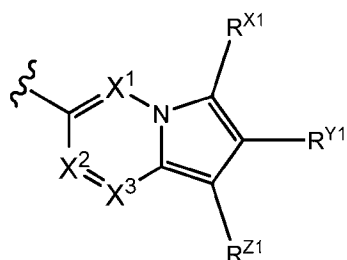


30. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein each  $R^{Cy}$  is independently selected from halo, C<sub>2-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>2-6</sub> haloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of  $R^{Cy}$  is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>.

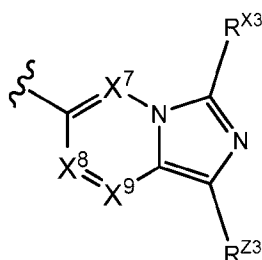
31. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein each  $R^{Cy}$  is independently selected from halo, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>2-6</sub>

alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>Cy</sup> is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>.

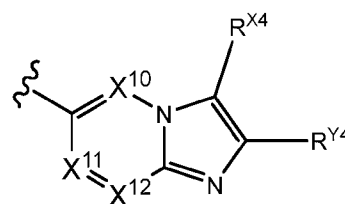
32. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein B is of formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), formula (i), or formula (k):



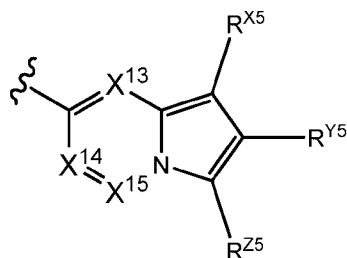
(a)



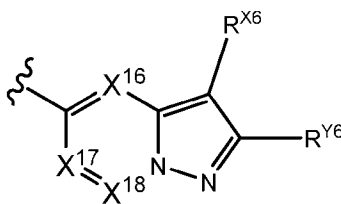
(c)



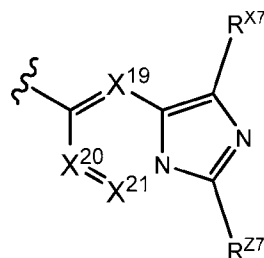
(d)



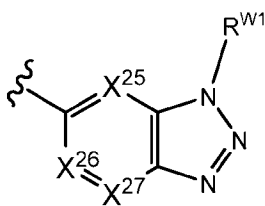
(e)



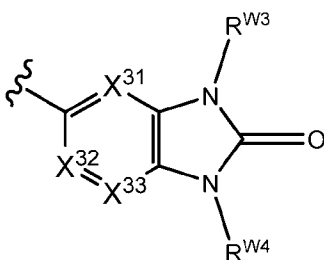
(f)



(g)

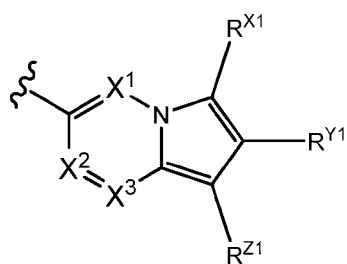


(i)

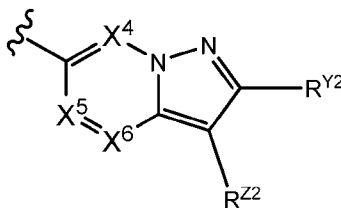


(k).

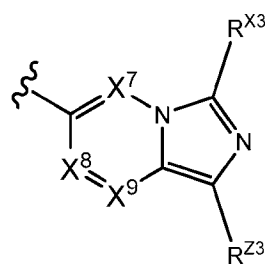
33. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (h):



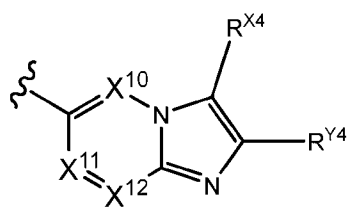
(a)



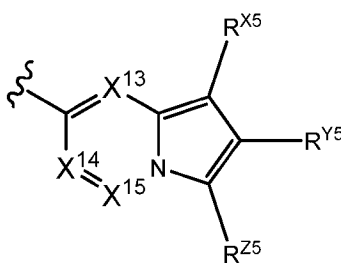
(b)



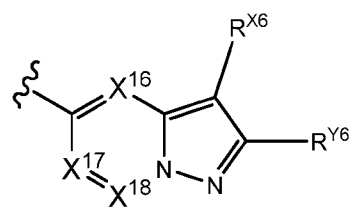
(c)



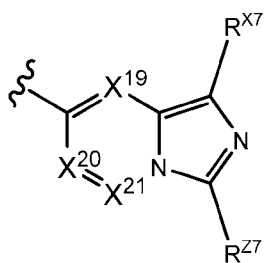
(d)



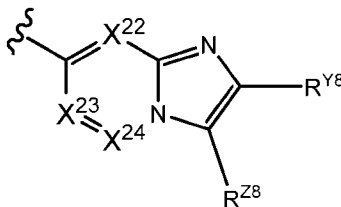
(e)



(f)

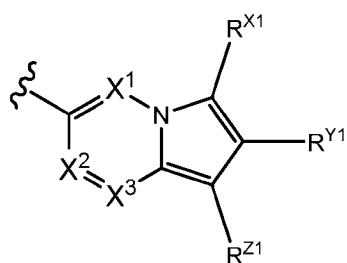


(g)

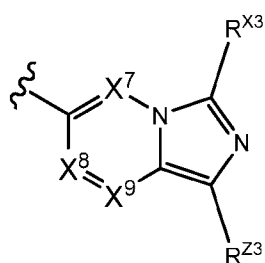


(h).

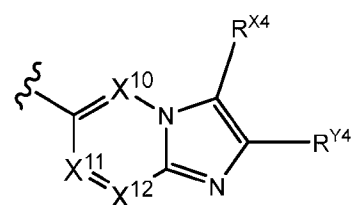
34. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (h):



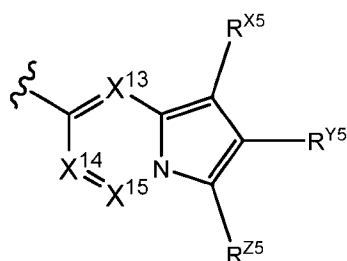
(a)



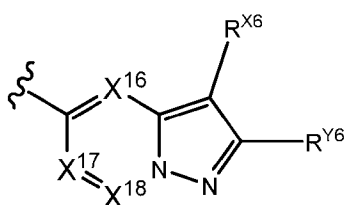
(c)



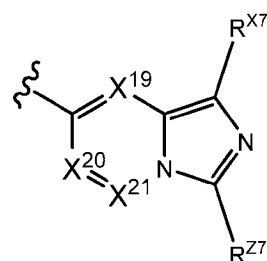
(d)



(e)

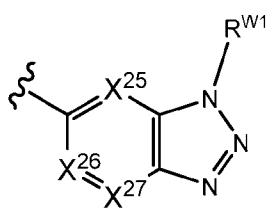


(f)

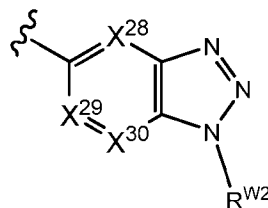


(g).

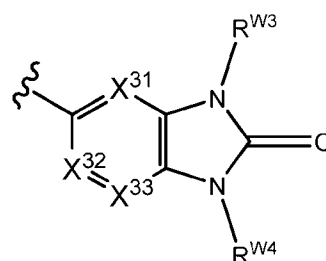
35. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein B is of formula (i), formula (j), or formula (k):



(i)

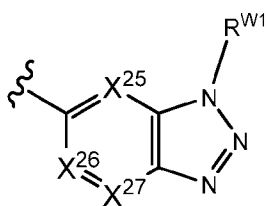


(j)

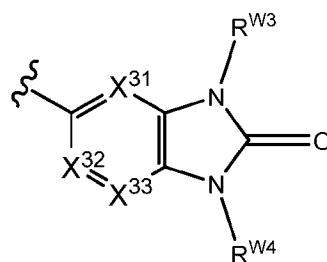


(k).

36. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein B is of formula (i) or formula (k):

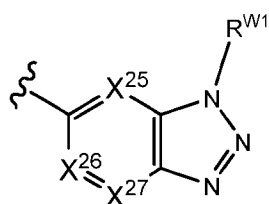


(i)



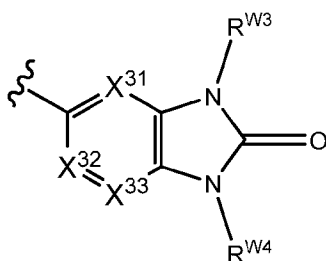
(k).

37. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein B is of formula (i):



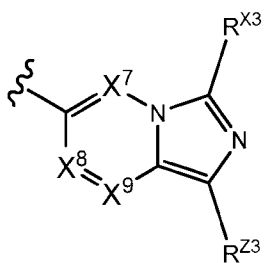
(i).

38. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein B is of formula (k):

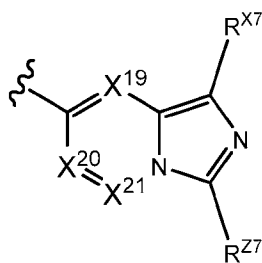


(k).

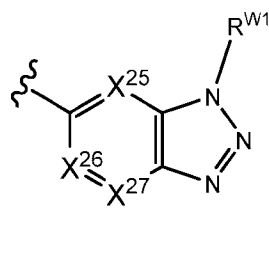
39. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein B is of formula (c), formula (g), formula (i), formula (j), or formula (k):



(c)

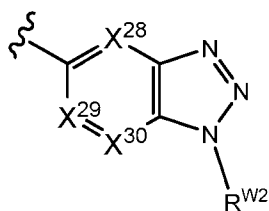


(g)

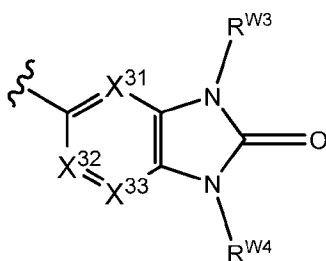


(i)



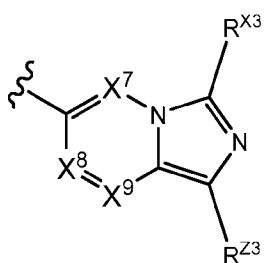


(j)

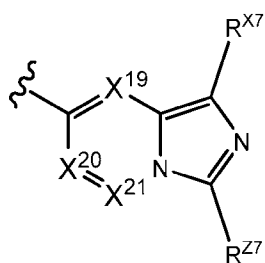


(k).

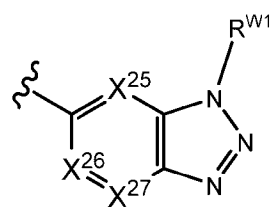
40. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein B is of formula (c), formula (g), formula (i), or formula (k):



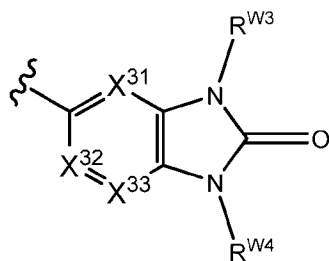
(c)



(g)

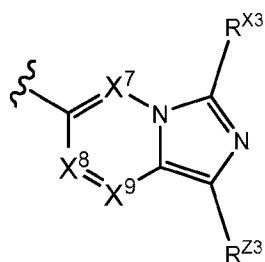


(i)



(k).

41. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein B is of formula (c):



(c).

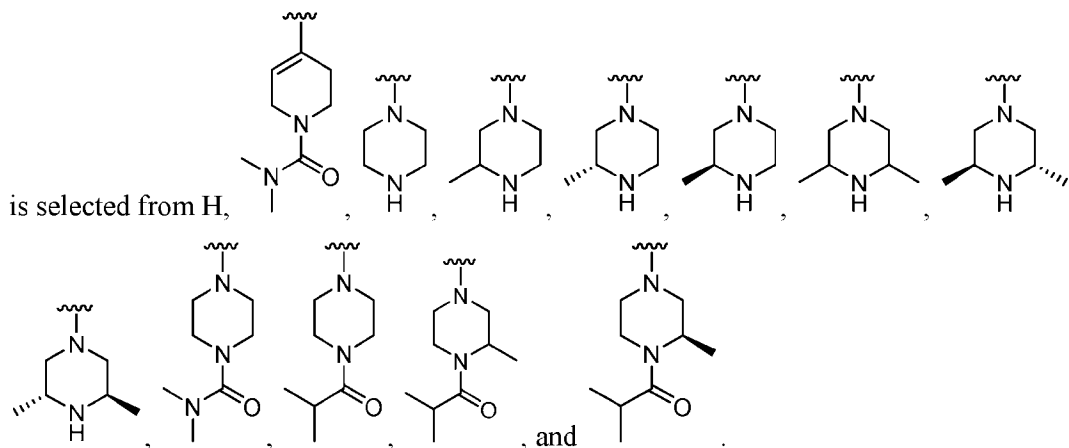
42. The compound of claim 41, or a pharmaceutically acceptable salt thereof, wherein  $X^7$  is  $CR^7$ ,  $X^8$  is  $CR^8$ , and  $X^9$  is  $CR^9$ .

43. The compound of claim 42, or a pharmaceutically acceptable salt thereof, wherein  $R^7$  is H.

44. The compound of claim 42, or a pharmaceutically acceptable salt thereof, wherein  $R^8$  is selected from H, fluoro, and bromo.

45. The compound of claim 42, or a pharmaceutically acceptable salt thereof, wherein  $R^9$  is selected from H and 4-10 membered heterocycloalkyl, wherein said 4-10 membered heterocycloalkyl is optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ ,  $NR^cS(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ .

46. The compound of claim 42, or a pharmaceutically acceptable salt thereof, wherein  $R^9$

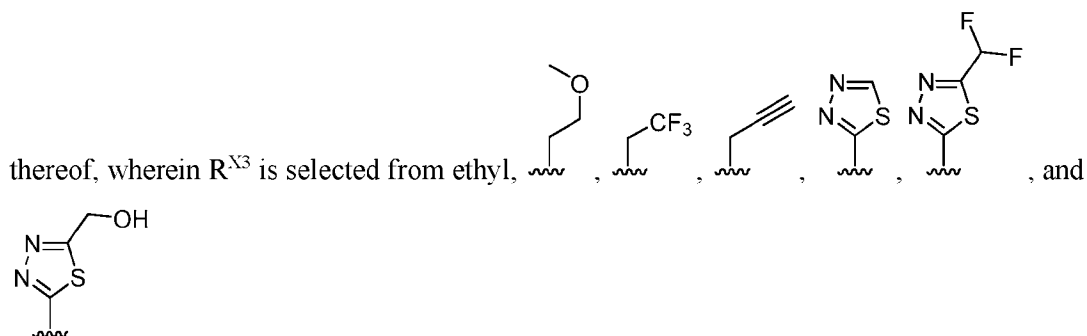


47. The compound of any one of claims 41-46, or a pharmaceutically acceptable salt thereof, wherein  $R^{X3}$  is selected from  $C_{1-6}$  alkyl and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4  $R'$ .

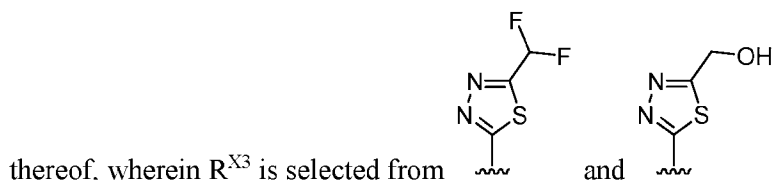
48. The compound of any one of claims 41-46, or a pharmaceutically acceptable salt thereof, wherein  $R^{X3}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4  $R'$ , selected from halo,  $OR^{a3}$ , and CN.

49. The compound of any one of claims 41-46, or a pharmaceutically acceptable salt thereof, wherein  $R^{X3}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  $C_{1-6}$  alkyl.

50. The compound of any one of claims 41-46, or a pharmaceutically acceptable salt



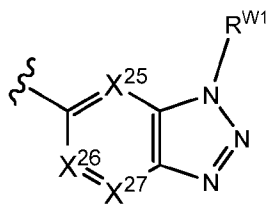
51. The compound of any one of claims 41-46, or a pharmaceutically acceptable salt



52. The compound of any one of claims 41-46, or a pharmaceutically acceptable salt thereof, wherein  $R^{Z3}$  is selected from H and halo.

53. The compound of any one of claims 41-46, or a pharmaceutically acceptable salt thereof, wherein  $R^{Z3}$  is selected from H and chloro.

54. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein B is of formula (i):



(i).

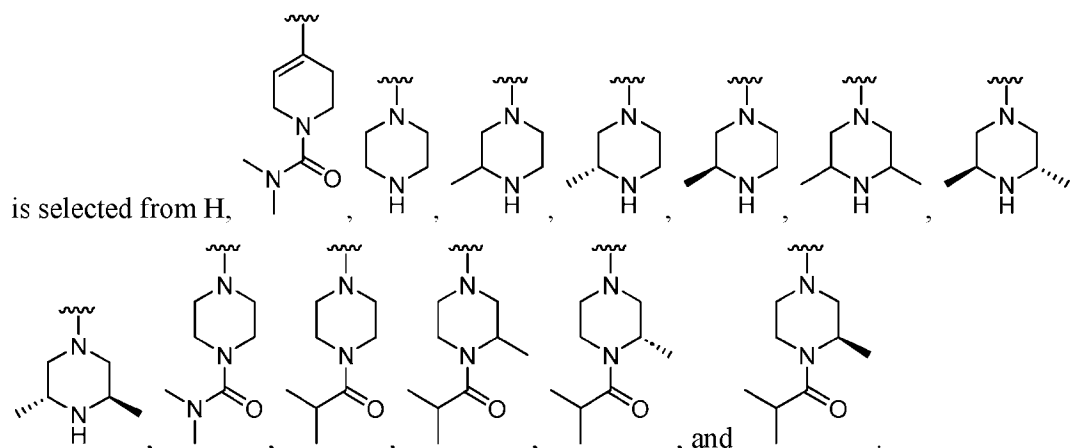
55. The compound of claim 54, or a pharmaceutically acceptable salt thereof, wherein  $X^{25}$  is  $CR^{25}$ ,  $X^{26}$  is  $CR^{26}$ , and  $X^{27}$  is  $CR^{27}$ .

56. The compound of claim 55, or a pharmaceutically acceptable salt thereof, wherein  $R^{25}$  is H.

57. The compound of claim 55, or a pharmaceutically acceptable salt thereof, wherein  $R^{26}$  is selected from H, fluoro, and bromo.

58. The compound of claim 55, or a pharmaceutically acceptable salt thereof, wherein  $R^{27}$  is selected from H and 4-10 membered heterocycloalkyl, wherein said 4-10 membered heterocycloalkyl is optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ ,  $NR^cS(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ .

59. The compound of claim 55, or a pharmaceutically acceptable salt thereof, wherein  $R^{27}$

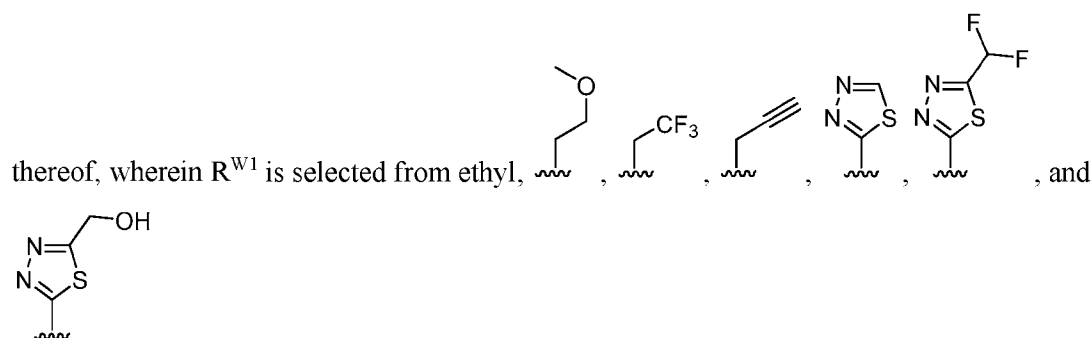


60. The compound of any one of claims 54-59, or a pharmaceutically acceptable salt thereof, wherein  $R^{W1}$  is selected from  $C_{1-6}$  alkyl and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4  $R'$ .

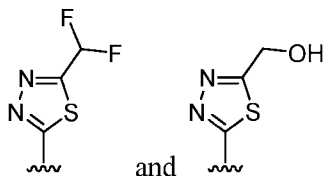
61. The compound of any one of claims 54-59, or a pharmaceutically acceptable salt thereof, wherein  $R^{W1}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4  $R'$ , selected from halo,  $OR^{a3}$ , and CN.

62. The compound of any one of claims 54-59, or a pharmaceutically acceptable salt thereof, wherein  $R^{W1}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  $C_{1-6}$  alkyl.

63. The compound of any one of claims 54-59, or a pharmaceutically acceptable salt



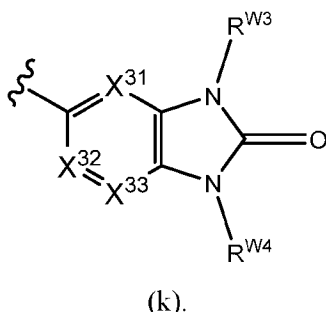
64. The compound of any one of claims 54-59, or a pharmaceutically acceptable salt



thereof, wherein  $R^{W1}$  is selected from

and

65. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein B is a group of formula (k):



66. The compound of claim 65, or a pharmaceutically acceptable salt thereof, wherein  $X^{31}$  is  $CR^{31}$ ,  $X^{32}$  is  $CR^{32}$ , and  $X^{33}$  is  $CR^{33}$ .

67. The compound of claim 66, or a pharmaceutically acceptable salt thereof, wherein  $R^{31}$  is H.

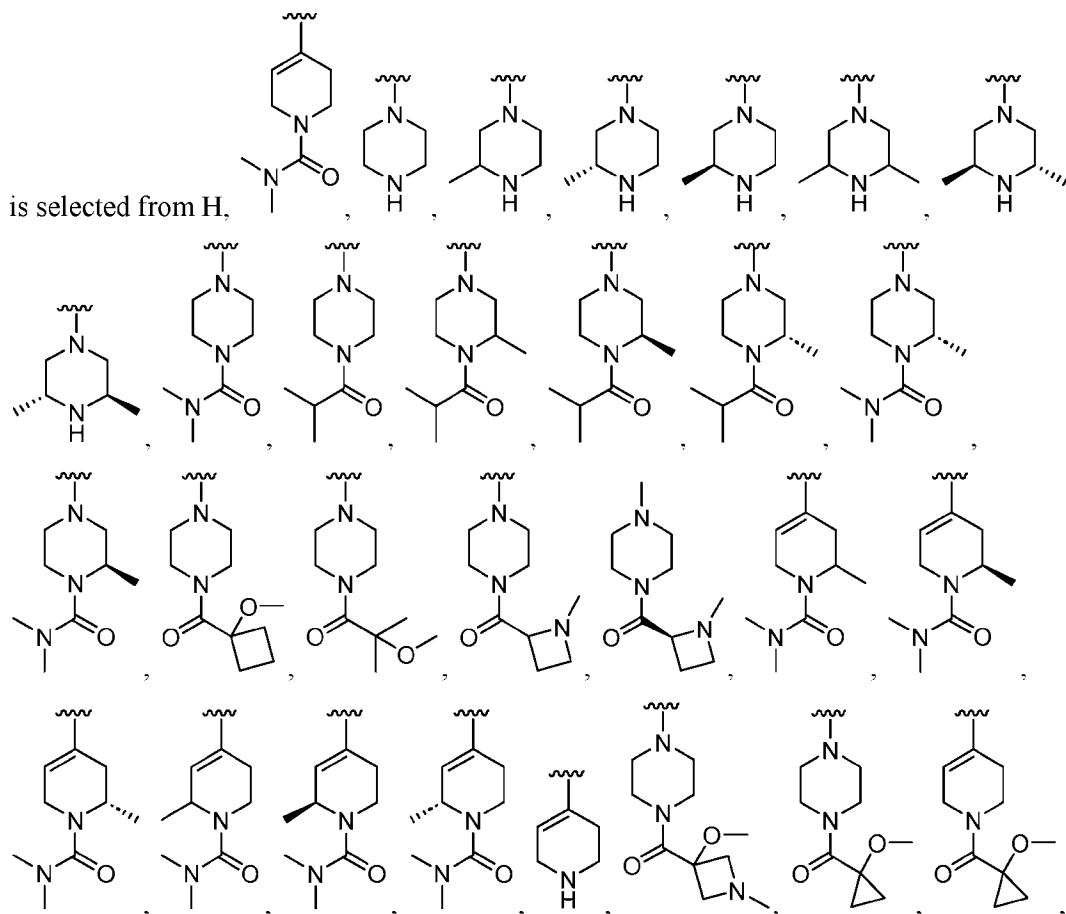
68. The compound of claim 66, or a pharmaceutically acceptable salt thereof, wherein  $R^{32}$  is selected from H, fluoro, and bromo.

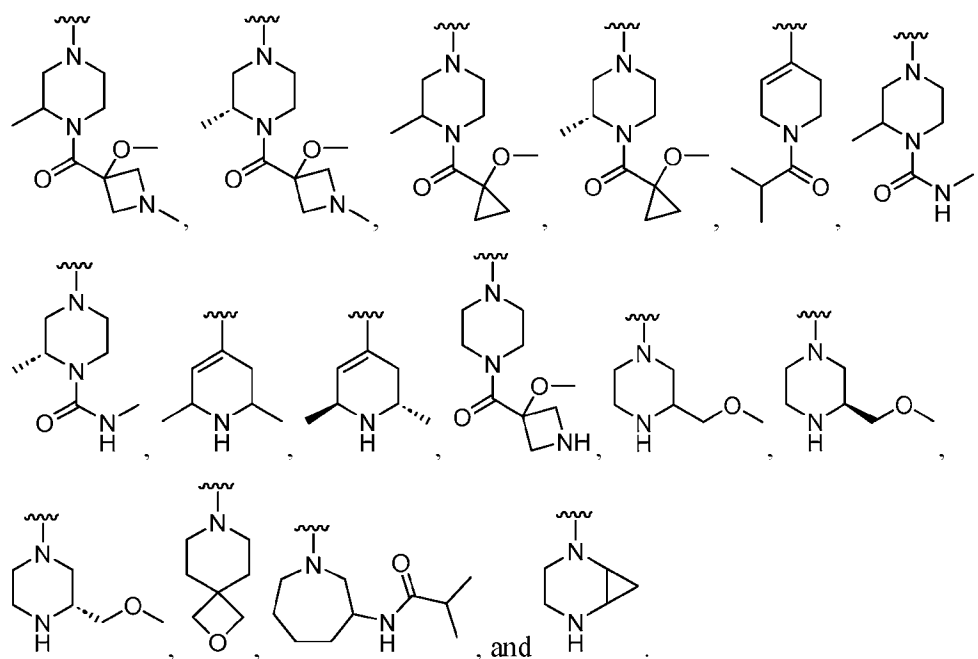
69. The compound of claim 66, or a pharmaceutically acceptable salt thereof, wherein  $R^{33}$  is selected from H, halo,  $OR^{a2}$ ,  $NR^{c2}R^{d2}$ ,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $R^3$ ,  $R^6$ ,  $R^9$ ,  $R^{12}$ ,  $R^{15}$ ,  $R^{18}$ ,  $R^{21}$ ,  $R^{24}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $(CH_2)_mOR^{a2}$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{c2})NR^{c2}R^{d2}$ ,

$\text{NR}^{\text{c}2}\text{C}(=\text{NR}^{\text{c}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  
 $\text{NR}^{\text{c}2}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  
 $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ .

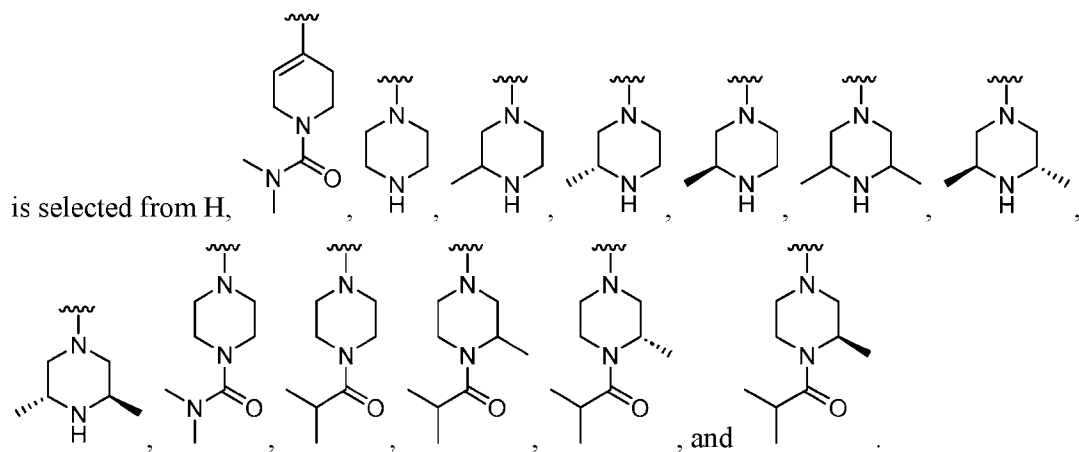
70. The compound of claim 66, or a pharmaceutically acceptable salt thereof, wherein  $\text{R}^{\text{c}3}$  is selected from H and 4-10 membered heterocycloalkyl, wherein said 4-10 membered heterocycloalkyl is optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $\text{C}_{1-6}$  alkyl,  $\text{C}_{2-6}$  alkenyl,  $\text{C}_{2-6}$  alkynyl,  $\text{C}_{1-6}$  haloalkyl,  $\text{C}_{6-10}$  aryl- $\text{C}_{1-4}$  alkyl,  $\text{C}_{3-7}$  cycloalkyl- $\text{C}_{1-4}$  alkyl, 5-10 membered heteroaryl- $\text{C}_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $\text{C}_{1-4}$  alkyl, CN,  $\text{NO}_2$ ,  $\text{OR}^{\text{a}2}$ ,  $\text{SR}^{\text{a}2}$ ,  $\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{OC}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{OC}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{C}(=\text{NR}^{\text{c}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(=\text{NR}^{\text{c}2})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{OR}^{\text{a}2}$ ,  $\text{NR}^{\text{c}2}\text{C}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{R}^{\text{b}2}$ ,  $\text{NR}^{\text{c}2}\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})\text{R}^{\text{b}2}$ ,  $\text{S}(\text{O})\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ ,  $\text{S}(\text{O})_2\text{R}^{\text{b}2}$ , and  $\text{S}(\text{O})_2\text{NR}^{\text{c}2}\text{R}^{\text{d}2}$ .

71. The compound of claim 66, or a pharmaceutically acceptable salt thereof, wherein  $\text{R}^{\text{c}3}$

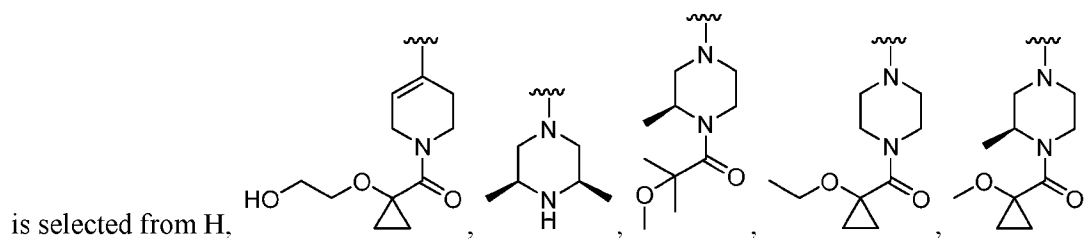




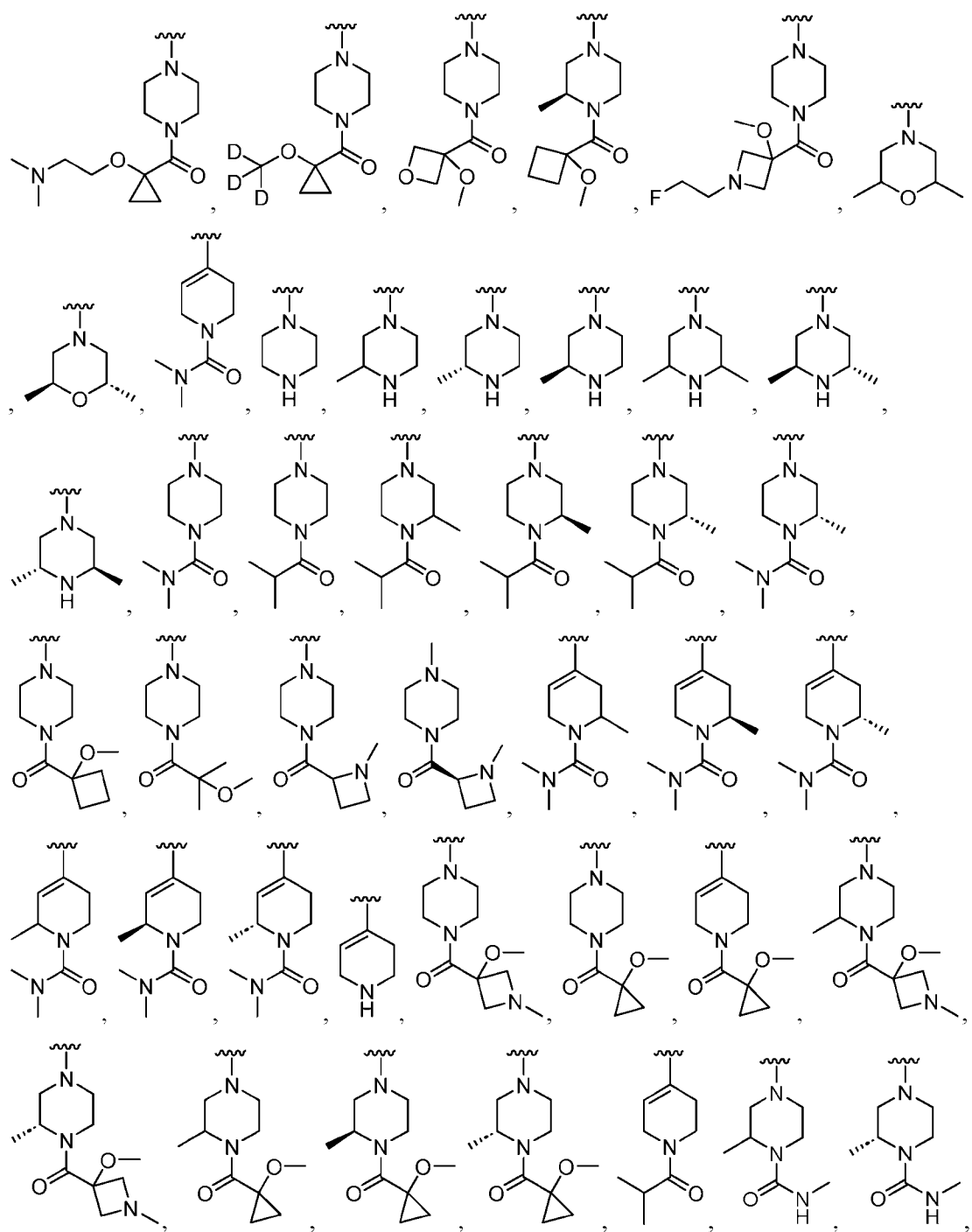
72. The compound of claim 66, or a pharmaceutically acceptable salt thereof, wherein R<sup>33</sup>

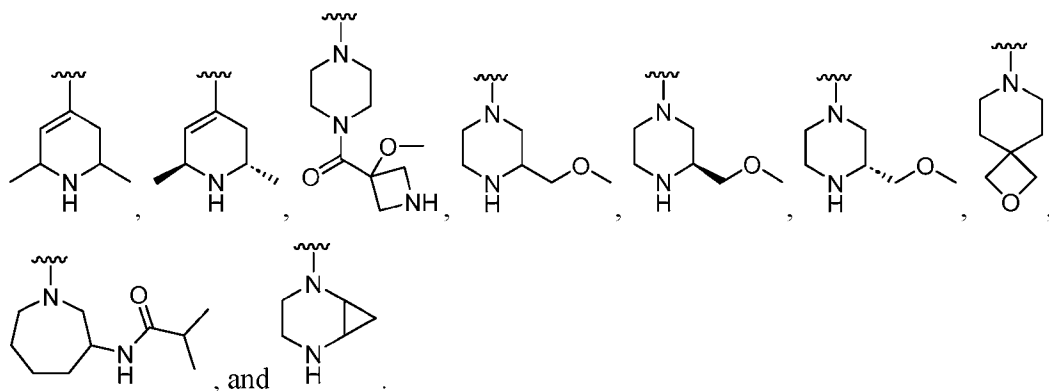


73. The compound of claim 66, or a pharmaceutically acceptable salt thereof, wherein R<sup>33</sup>

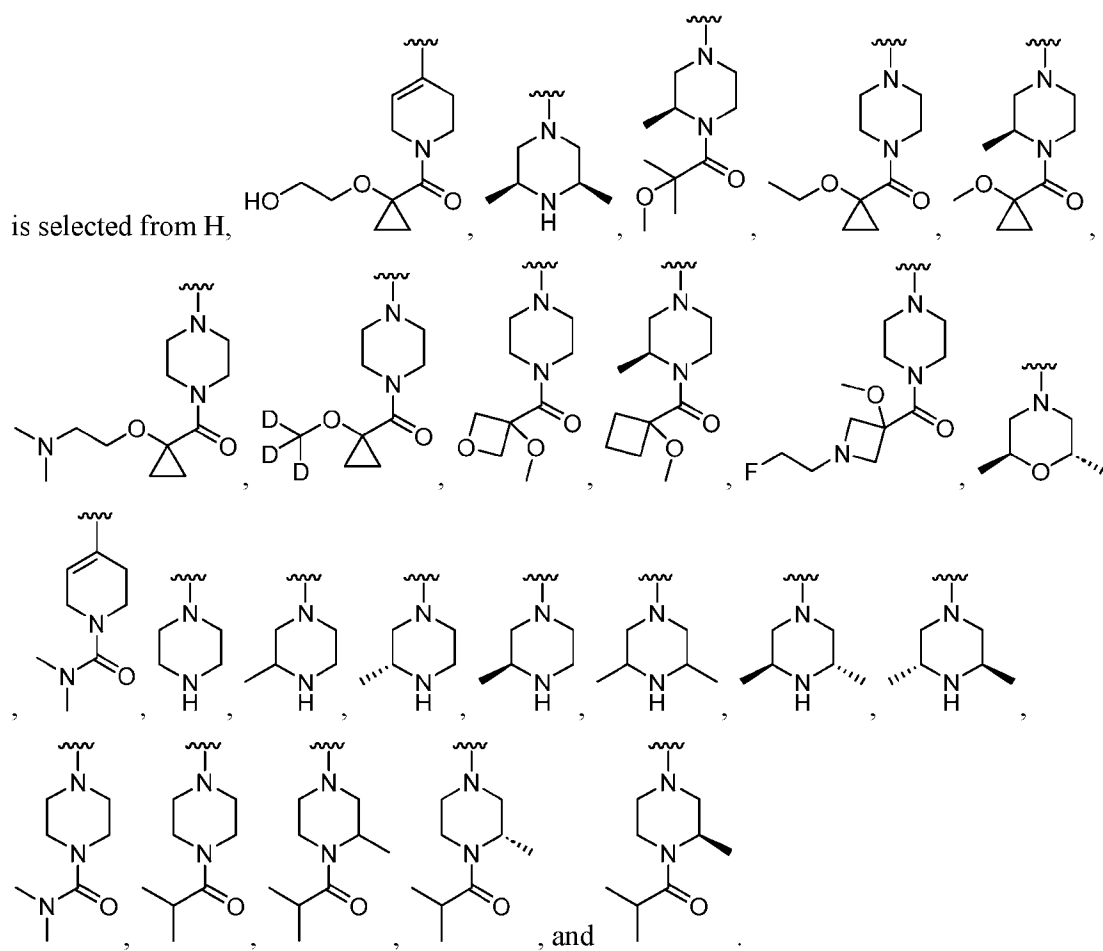








74. The compound of claim 66, or a pharmaceutically acceptable salt thereof, wherein R<sup>33</sup>



75. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein R<sup>W3</sup> and R<sup>W4</sup> are selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl,

and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4 R<sup>7</sup>.

76. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein R<sup>W3</sup> and R<sup>W4</sup> are selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4 R<sup>7</sup>.

77. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein R<sup>W3</sup> and R<sup>W4</sup> are selected from C<sub>1-6</sub> alkyl and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4 R<sup>7</sup>.

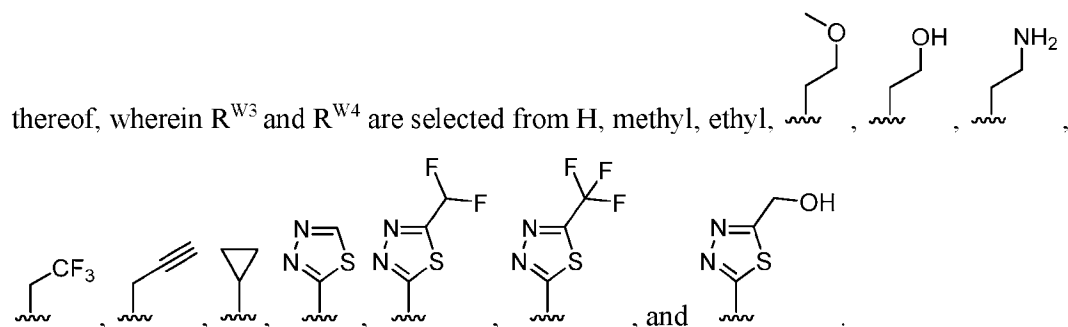
78. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein R<sup>W3</sup> and R<sup>W4</sup> are C<sub>1-6</sub> alkyl optionally substituted with 1, 2, 3, or 4 R<sup>7</sup>, selected from halo, OR<sup>a3</sup>, and CN.

79. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein R<sup>W3</sup> and R<sup>W4</sup> are 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4 C<sub>1-6</sub> alkyl.

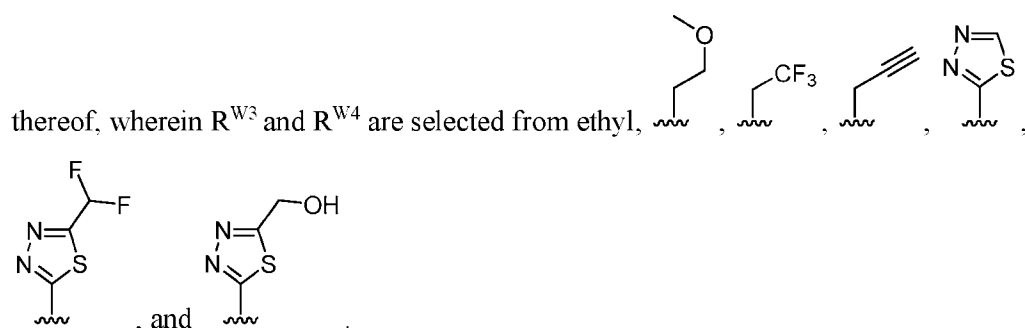
80. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, at least one of R<sup>W3</sup> and R<sup>W4</sup> is 1,3,4-thiadiazolyl optionally substituted with 1 R<sup>7</sup>.

81. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, at least one of R<sup>W3</sup> and R<sup>W4</sup> is 1,3,4-thiadiazolyl optionally substituted with difluoromethyl, trifluoromethyl, or methanol.

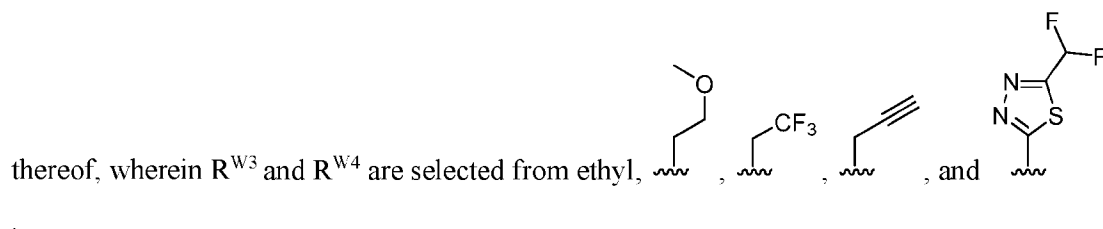
82. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt



83. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt



84. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt



85. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein:

$R^{W3}$  is selected from H,  $C_{1-6}$  alkyl, and  $C_{3-7}$  cycloalkyl, wherein the  $C_{1-6}$  alkyl and  $C_{3-7}$  cycloalkyl are optionally substituted with 1, 2, 3, or 4  $R'$ ; and

$R^{W4}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  $R'$ .

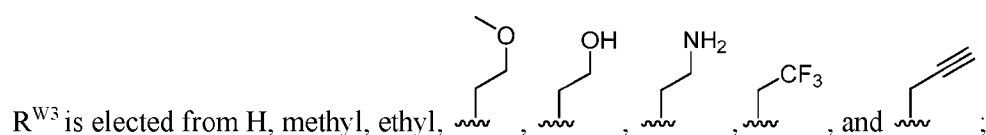
86. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein  $R^{W3}$  is  $C_{1-6}$  alkyl and  $R^{W4}$  is 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4  $R'$ .

87. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein  $R^{W3}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4  $R^*$ , selected from halo,  $OR^{a3}$ ,  $NR^{c3}R^{d3}$ , and CN.

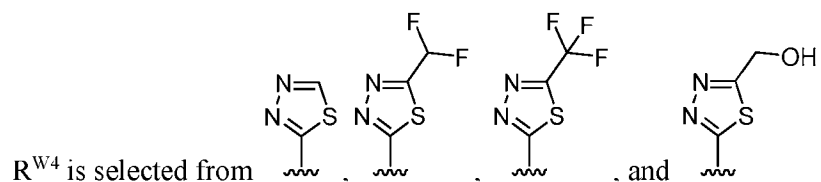
88. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein  $R^{W3}$  is  $C_{1-6}$  alkyl optionally substituted with 1, 2, 3, or 4  $R^*$ , selected from halo,  $OR^{a3}$ , and CN.

89. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein  $R^{W4}$  is 5-membered heteroaryl optionally substituted with 1, 2, 3, or 4  $C_{1-6}$  alkyl.

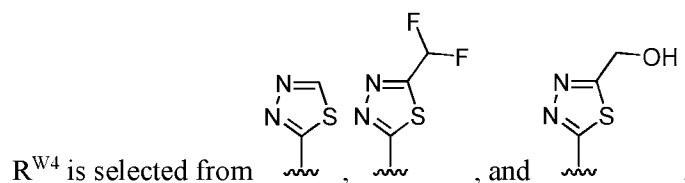
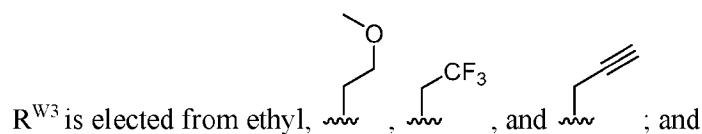
90. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein:



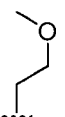
and

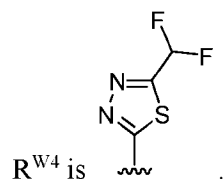


91. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein:

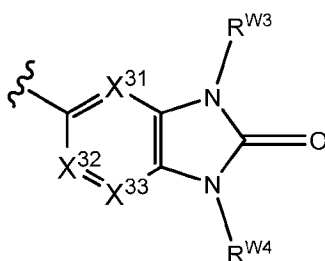
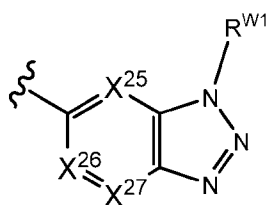
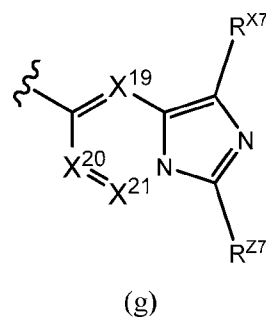
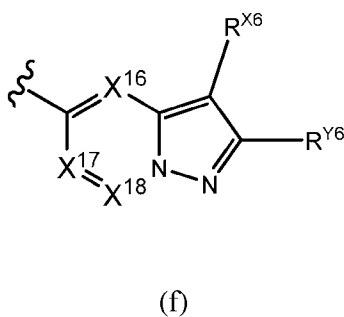
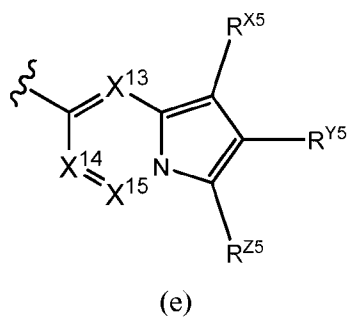
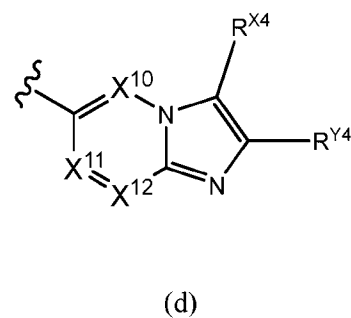
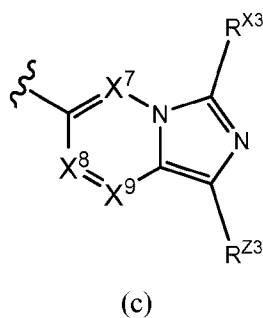
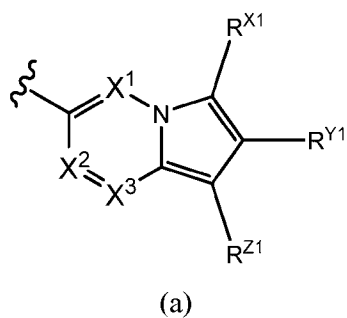


92. The compound of any one of claims 65-73, or a pharmaceutically acceptable salt thereof, wherein:

$R^{W3}$  is selected from ethyl, , , ; and

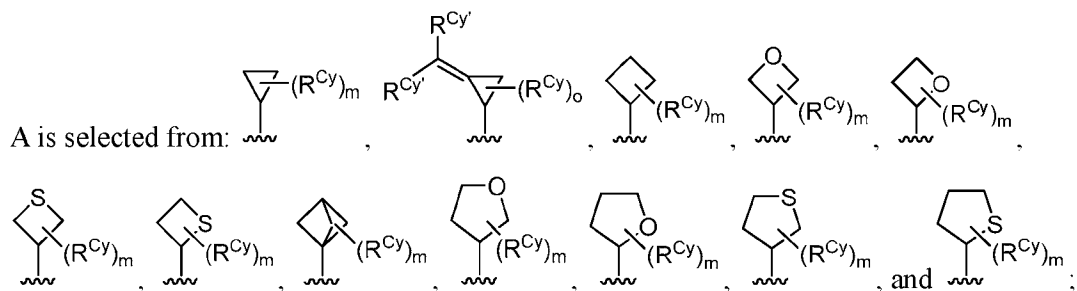


93. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein B is of formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), formula (i), or formula (k):



(i)

(k);

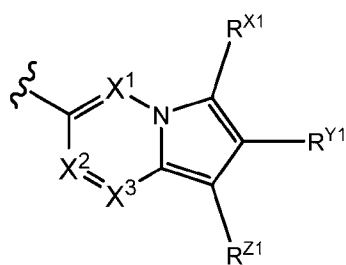


each  $R^{Cy'}$  is selected from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{c1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{c1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

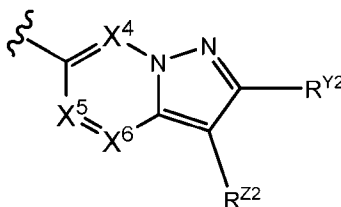
$m$  is an integer selected from 0, 1, 2, 3, 4, and 5; and

$o$  is an integer selected from 0, 1, 2, and 3.

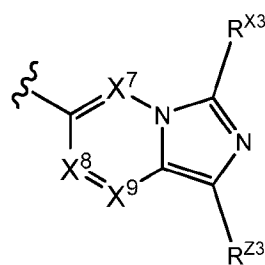
94. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (h):



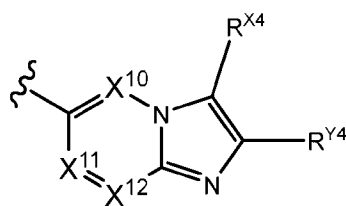
(a)



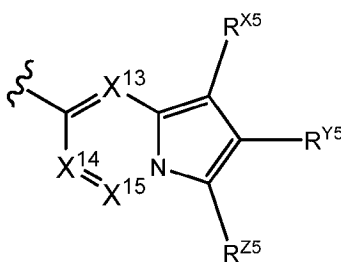
(b)



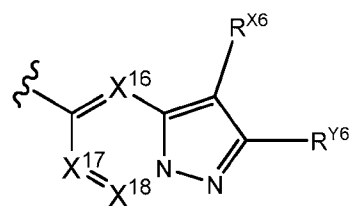
(c)



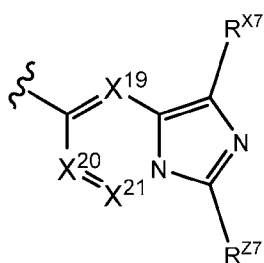
(d)



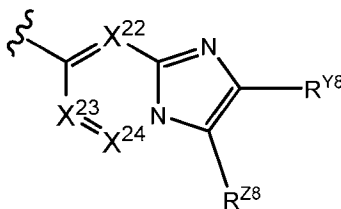
(e)



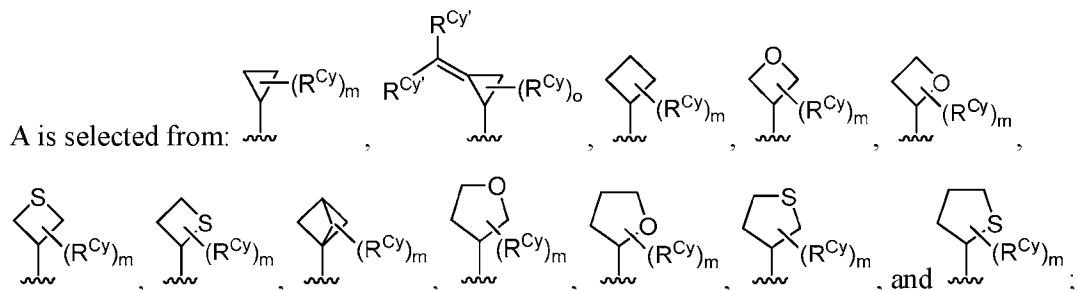
(f)



(g)



(h);



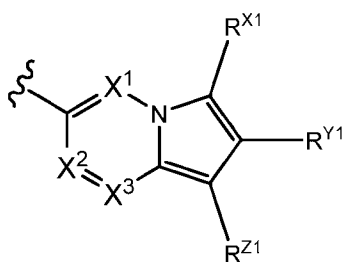
wherein

each  $R^{Cy'}$  is selected from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

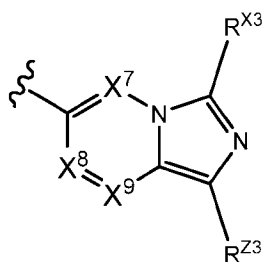
m is an integer selected from 0, 1, 2, 3, 4, and 5; and

o is an integer selected from 0, 1, 2, and 3.

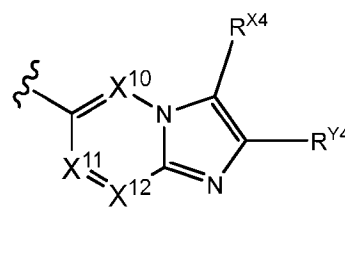
95. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein B is of formula (a), formula (b), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (h):



(a)

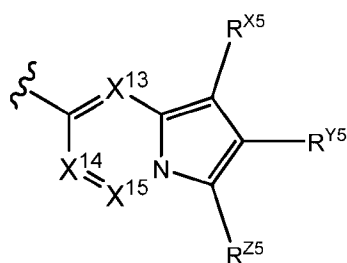


(c)

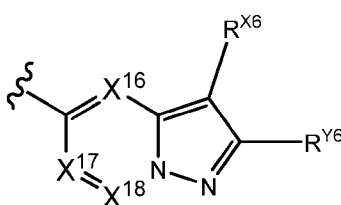


(d)

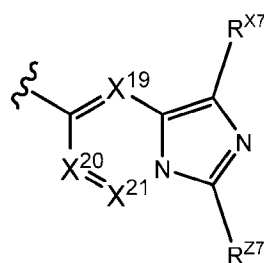




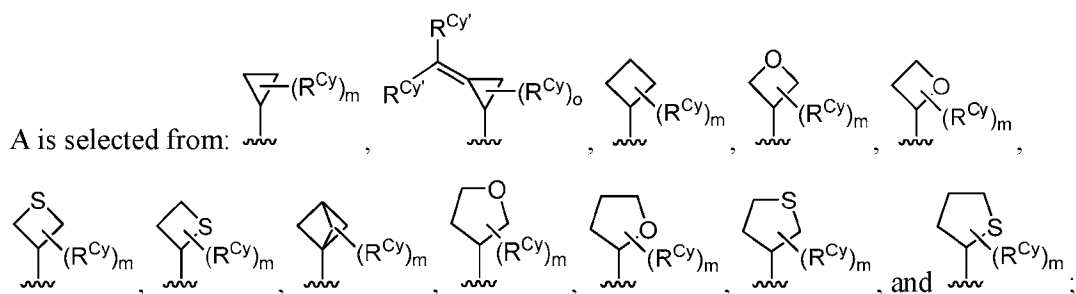
(e)



(f)



(g);



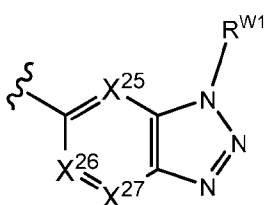
wherein

each  $R^{Cy'}$  is selected from from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

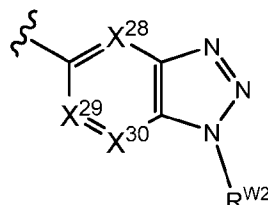
$m$  is an integer selected from 0, 1, 2, 3, 4, and 5; and

$o$  is an integer selected from 0, 1, 2, and 3.

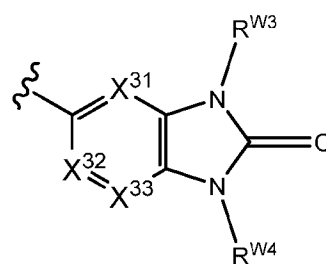
96. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein B is of formula (i), formula (j), or formula (k):



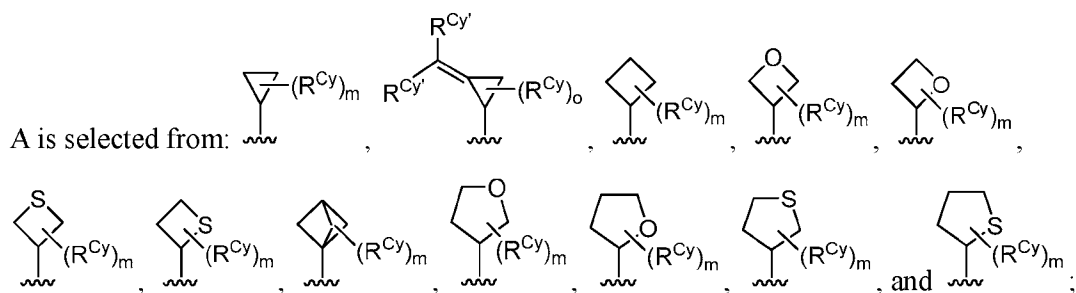
(i)



(j)



(k);



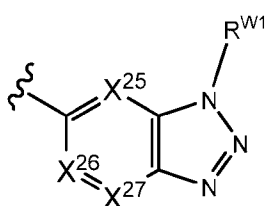
wherein

each  $R^{Cy'}$  is selected from from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ,

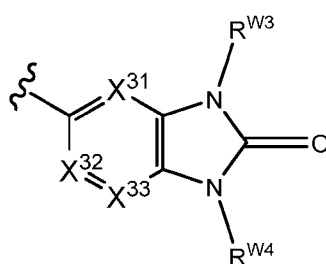
$m$  is an integer selected from 0, 1, 2, 3, 4, and 5; and

$o$  is an integer selected from 0, 1, 2, and 3.

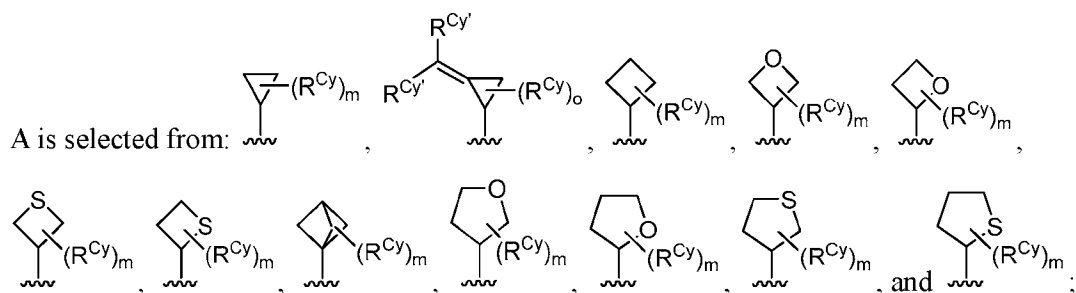
97. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein B is of formula (i) or formula (k):



(i)



(k);



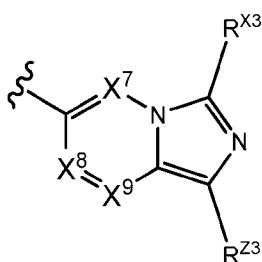
wherein

each  $R^{Cy'}$  is selected from from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ,

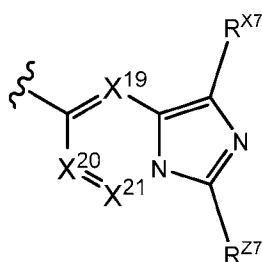
m is an integer selected from 0, 1, 2, 3, 4, and 5; and

o is an integer selected from 0, 1, 2, and 3.

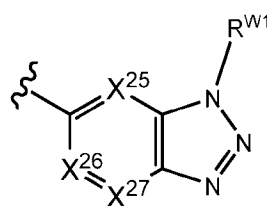
98. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein B is of formula (c), formula (g), formula (i), formula (j), or formula (k):



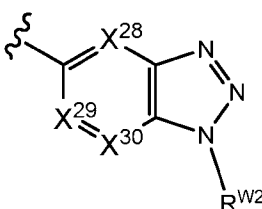
(c)



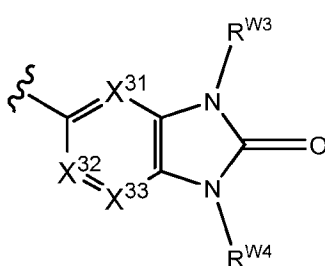
(g)



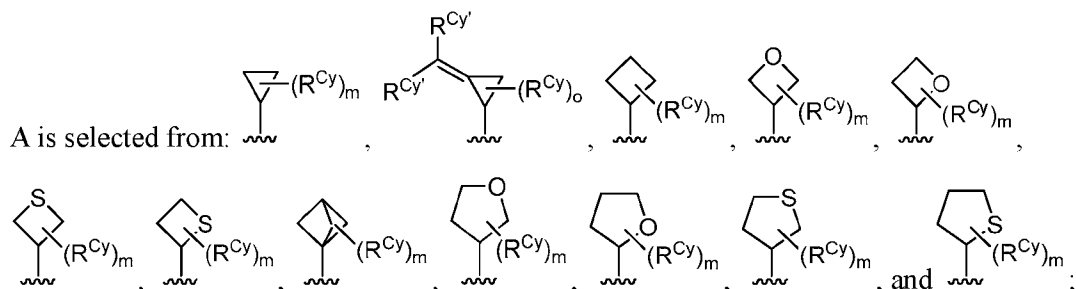
(i)



(j)



(k);



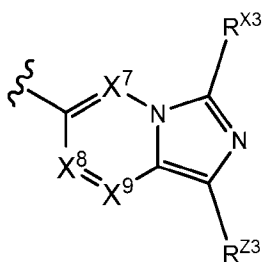
wherein

each  $R^{Cy'}$  is selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>;

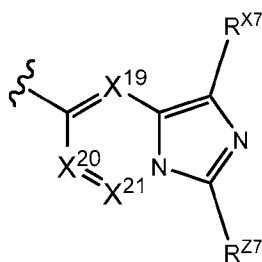
m is an integer selected from 0, 1, 2, 3, 4, and 5; and

o is an integer selected from 0, 1, 2, and 3.

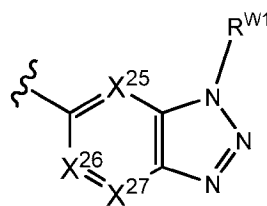
99. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein B is of formula (c), formula (g), formula (i), formula (j), or formula (k):



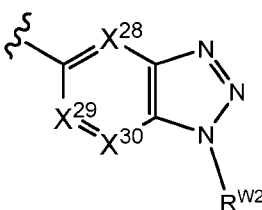
(c)



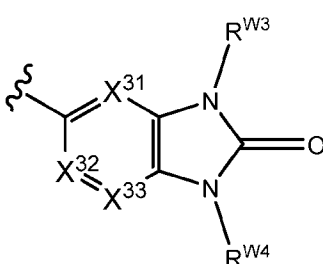
(g)



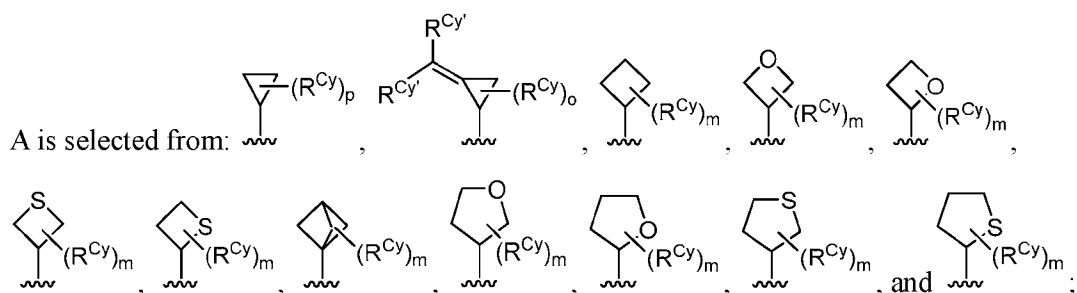
(i)



(j)



(k);



wherein

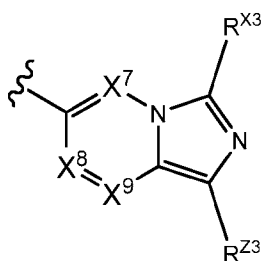
each  $R^{Cy'}$  is selected from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ .

m is an integer selected from 0, 1, 2, 3, 4, and 5;

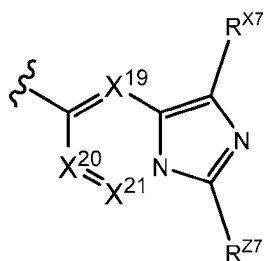
o is an integer selected from 0, 1, 2, and 3; and

p is an integer selected from 0, 2, 3, 4, and 5.

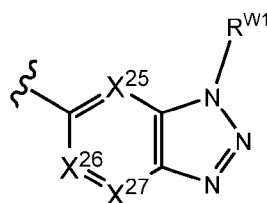
100. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein B is of formula (c), formula (g), formula (i), or formula (k):



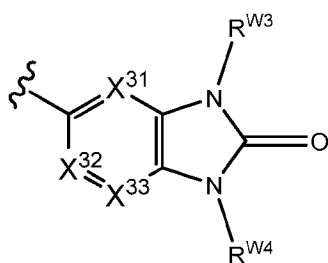
(c)



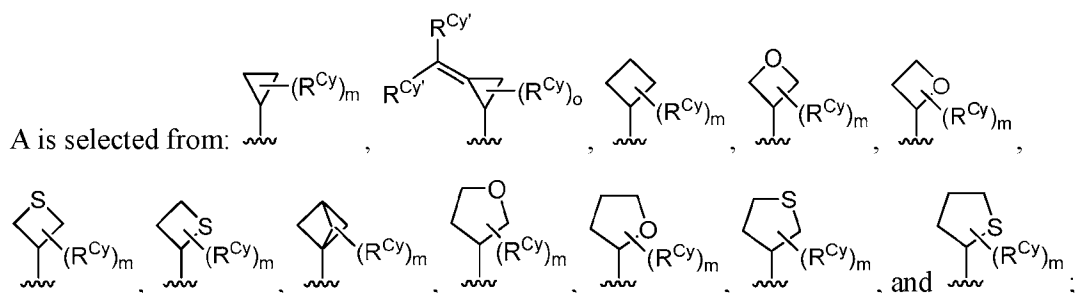
(g)



(i)



(k);



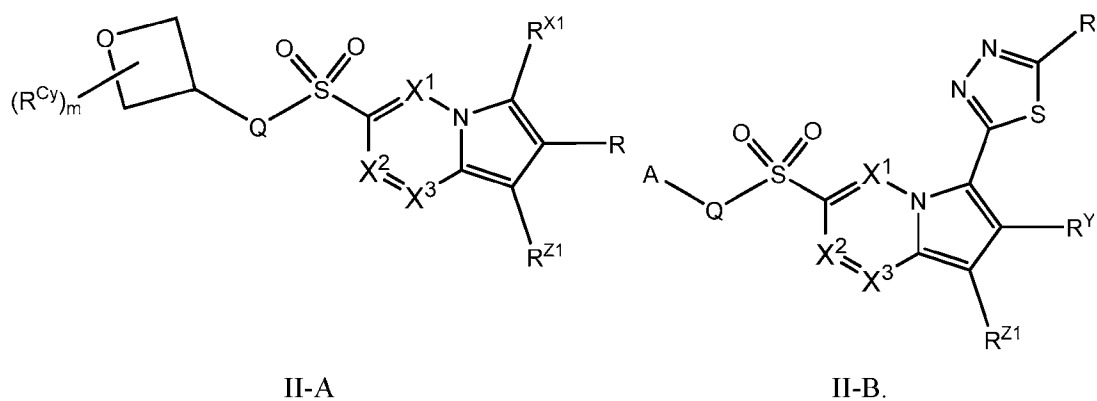
wherein

each  $R^{Cy'}$  is selected from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ .

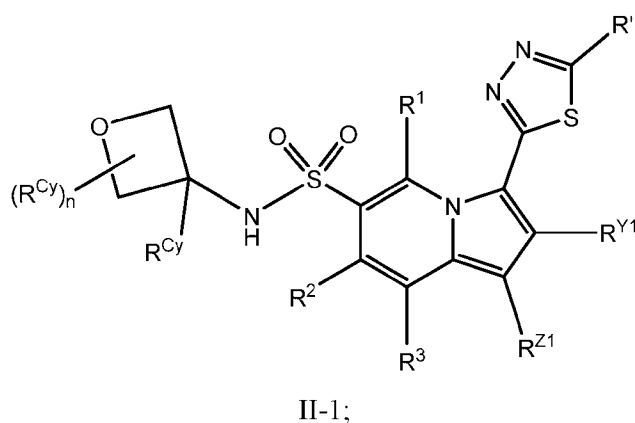
$m$  is an integer selected from 0, 1, 2, 3, 4, and 5; and

$o$  is an integer selected from 0, 1, 2, and 3.

101. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula II-A or II-B:

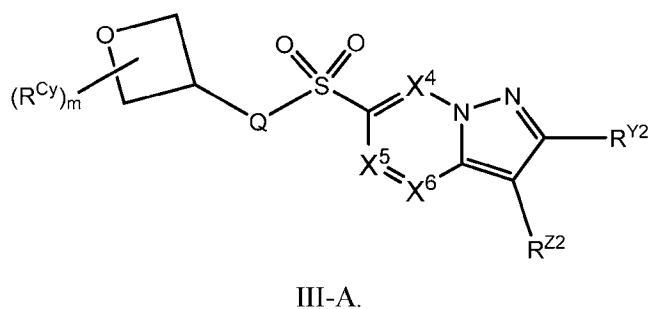


102. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula II-1:

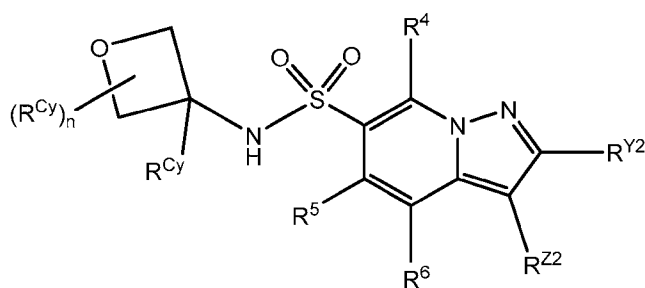


wherein n is an integer selected from 0, 1, 2, 3, and 4.

103. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula III-A:



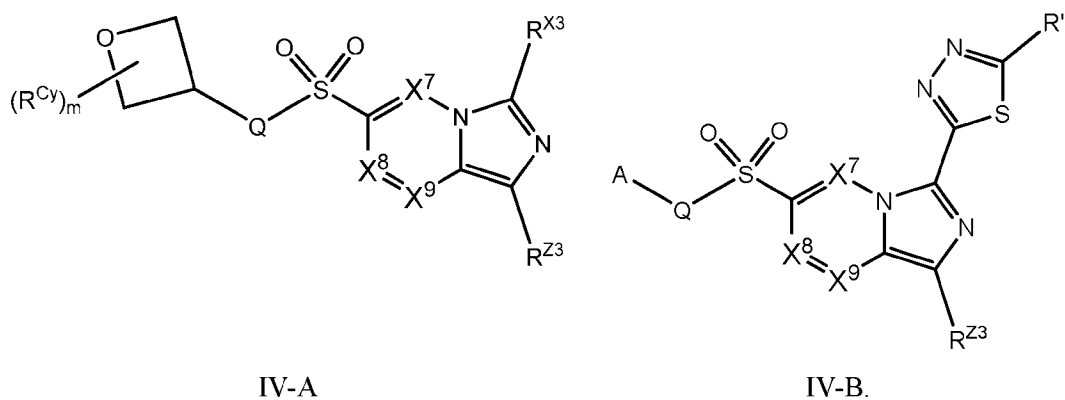
104. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula III-1:



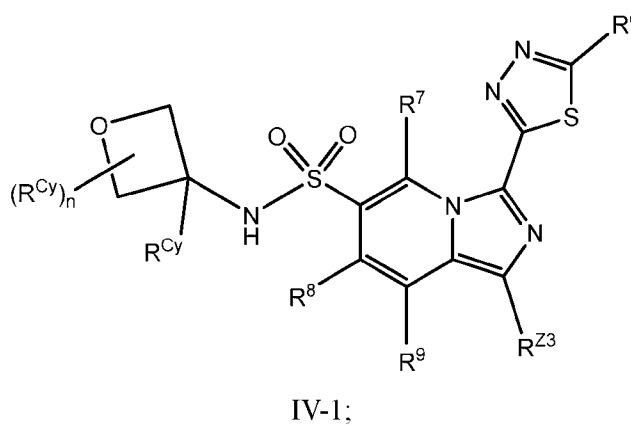
III-1;

wherein n is an integer selected from 0, 1, 2, 3, and 4.

105. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula IV-A or IV-B:



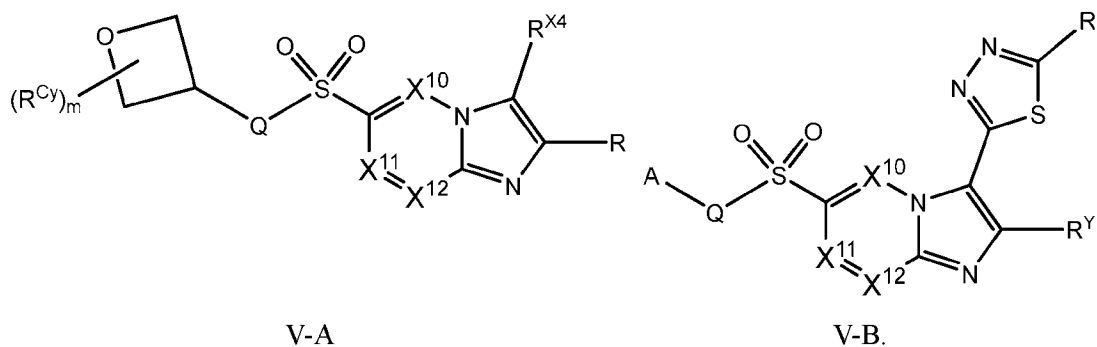
106. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula IV-1:



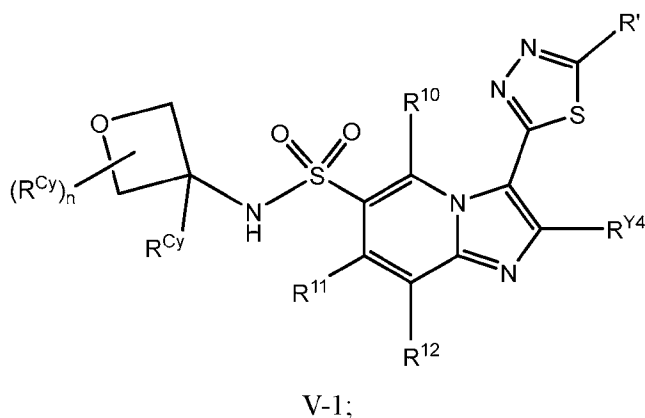
IV-1;

wherein n is an integer selected from 0, 1, 2, 3, and 4.

107. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula V-A or V-B:

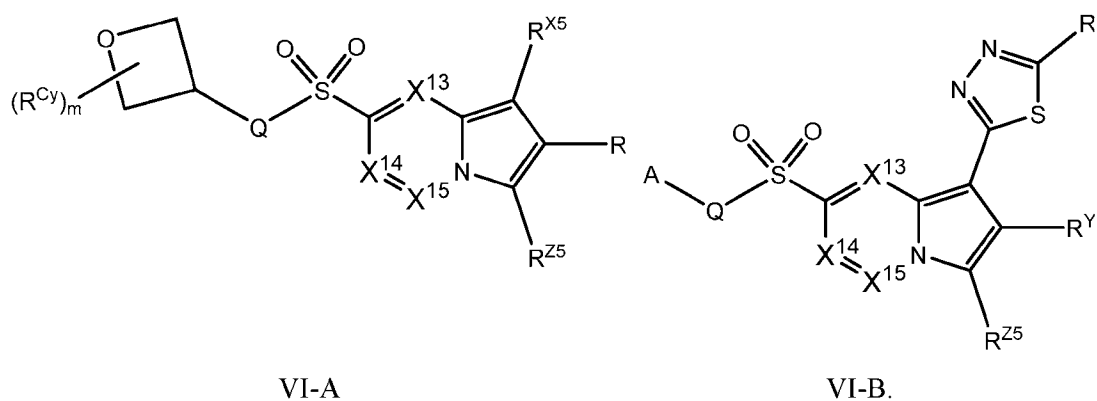


108. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula V-1:



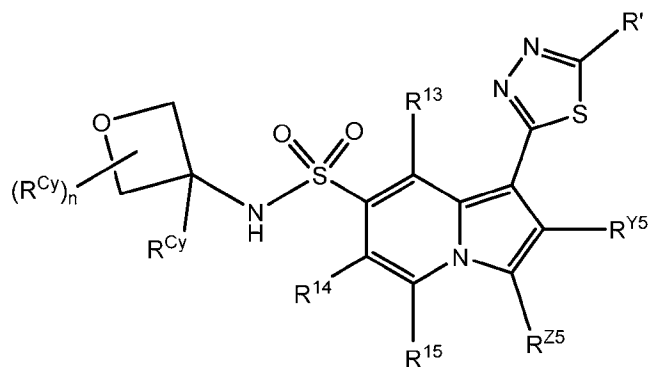
wherein n is an integer selected from 0, 1, 2, 3, and 4.

109. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula VI-A or VI-B:





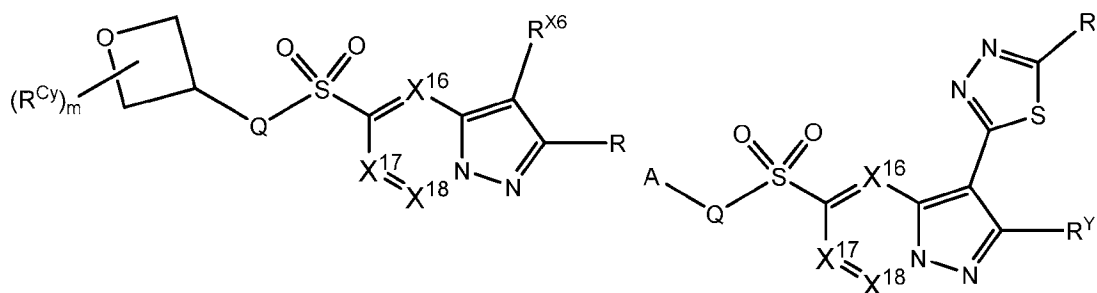
110. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula II-1:



VI-1;

wherein n is an integer selected from 0, 1, 2, 3, and 4.

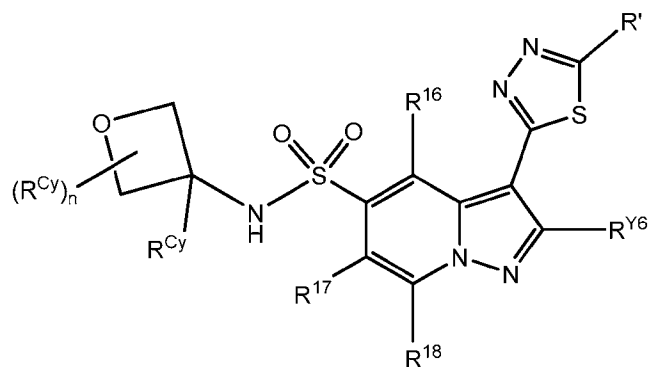
111. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula VII-A or VII-B:



VII-A

VII-B.

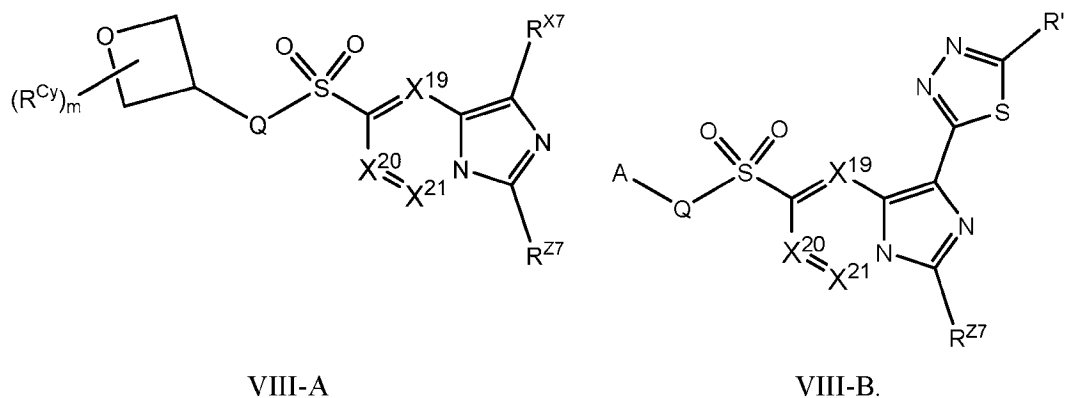
112. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula VII-1:



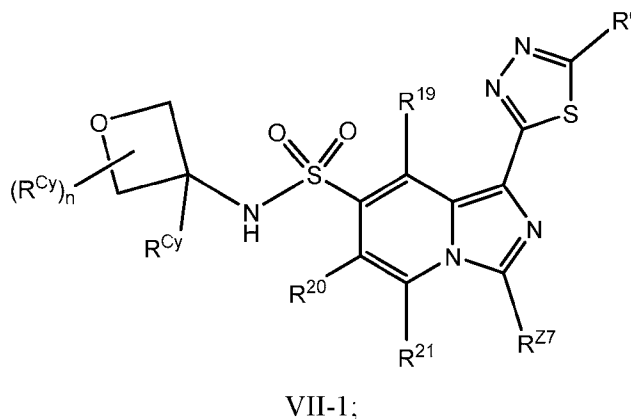
VII-1;

wherein n is an integer selected from 0, 1, 2, 3, and 4.

113. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula VIII-A or VIII-B:

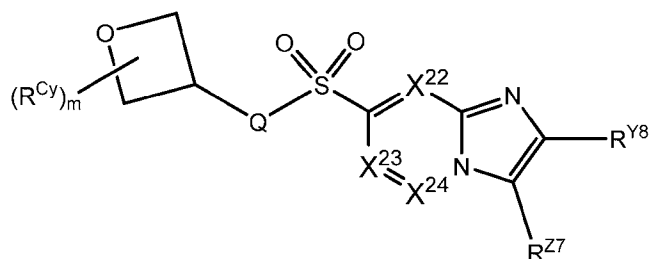


114. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula VIII-1:



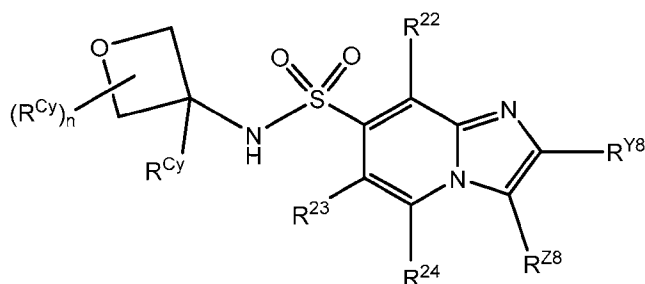
wherein n is an integer selected from 0, 1, 2, 3, and 4.

115. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula IX-A or IX-B:



## IX-A.

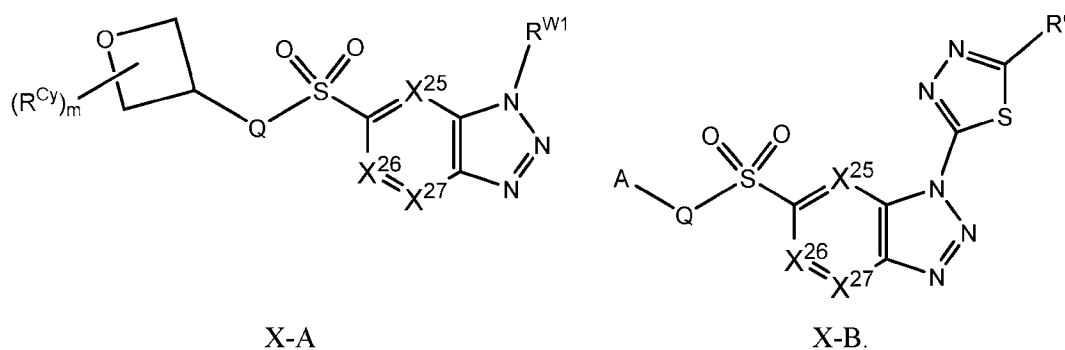
116. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula IX-1:



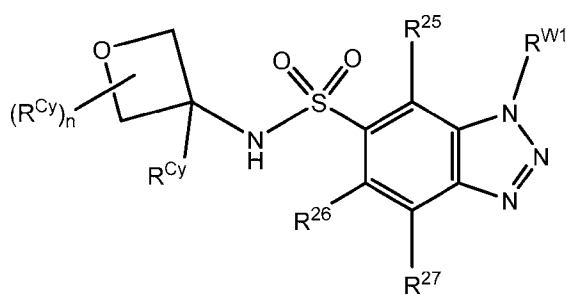
IX-1;

wherein n is an integer selected from 0, 1, 2, 3, and 4.

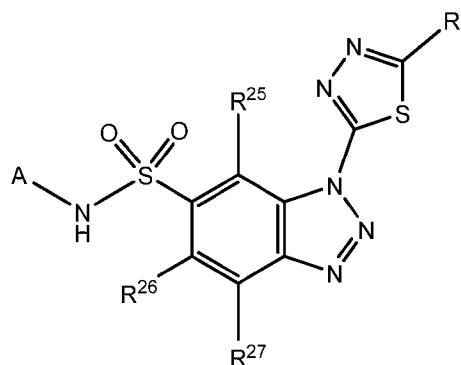
117. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula X-A or X-B:



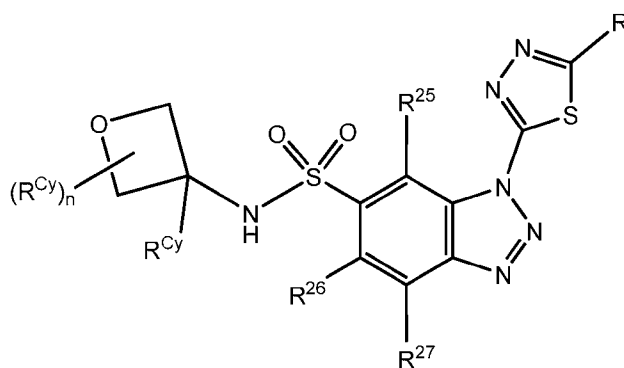
118. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula X-1, X-2, or X-3:



X-1



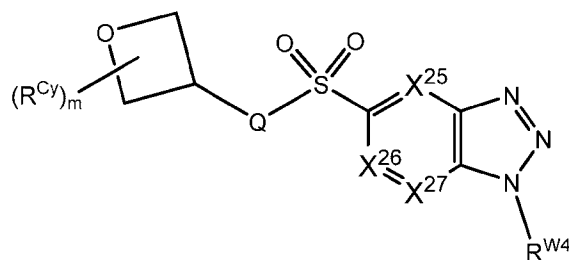
X-2



X-3;

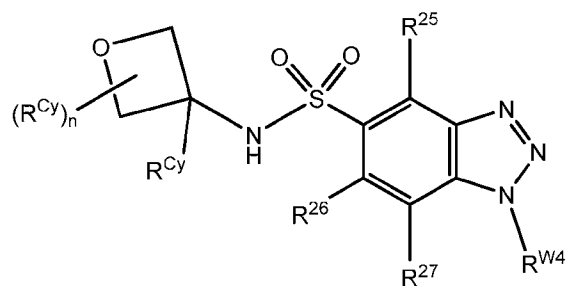
wherein n is an integer selected from 0, 1, 2, 3, and 4.

119. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula XI-A or XI-B:



XI-A.

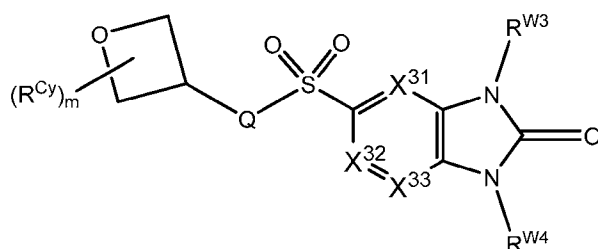
120. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula XI-1:



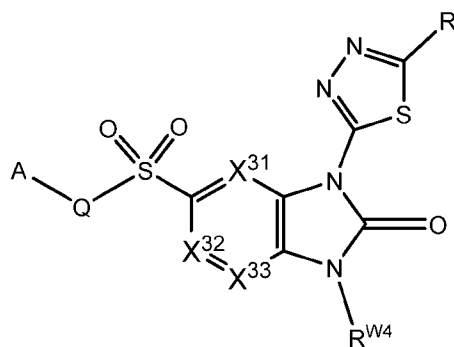
XI-1;

wherein n is an integer selected from 0, 1, 2, 3, and 4.

121. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula XII-A or XII-B:

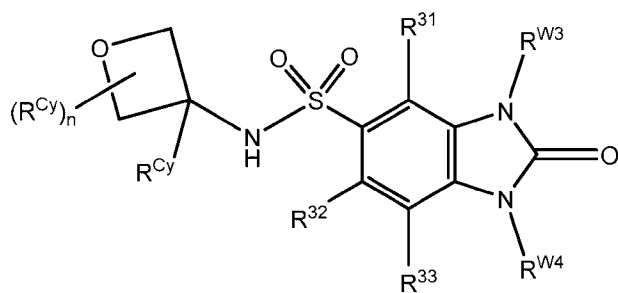


XII-A

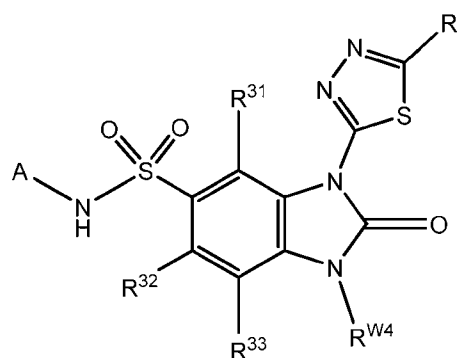


XII-B.

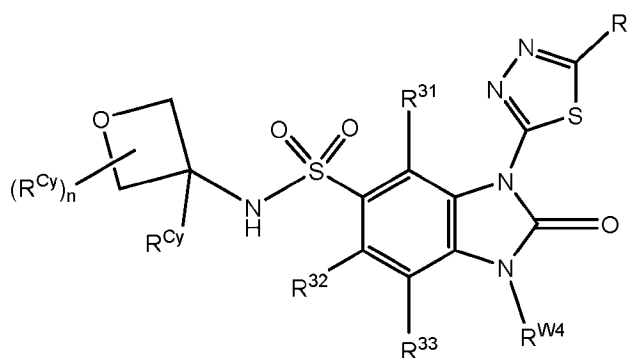
122. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein the compound is of Formula XII-1, XII-2, or XII-3:



XII-1



XII-2



XII-3;

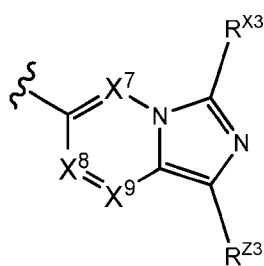
wherein n is an integer selected from 0, 1, 2, 3, and 4.

123. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

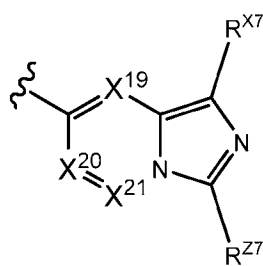
Q is NH or CH<sub>2</sub>;

A is Cy or Cy-C<sub>1-4</sub> alkyl-;

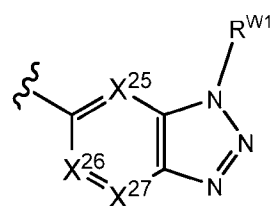
B is of formula (c), formula (g), formula (i), formula (j), or formula (k):



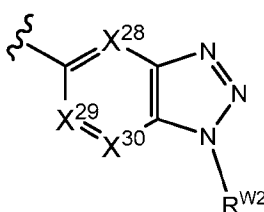
(c)



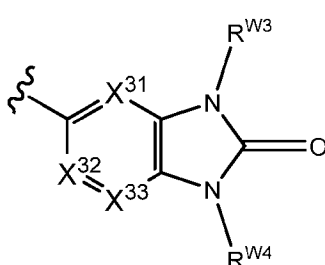
(g)



(i)



(j)



(k);

X<sup>7</sup> is N or CR<sup>7</sup>;

X<sup>8</sup> is N or CR<sup>8</sup>;

X<sup>9</sup> is N or CR<sup>9</sup>;

X<sup>19</sup> is N or CR<sup>19</sup>;

X<sup>20</sup> is N or CR<sup>20</sup>;

$X^{21}$  is N or  $CR^{21}$ ;

$X^{25}$  is N or  $CR^{25}$ ;

$X^{26}$  is N or  $CR^{26}$ ;

$X^{27}$  is N or  $CR^{27}$ ;

$X^{28}$  is N or  $CR^{28}$ ;

$X^{29}$  is N or  $CR^{29}$ ;

$X^{30}$  is N or  $CR^{30}$ ;

$X^{31}$  is N or  $CR^{31}$ ;

$X^{32}$  is N or  $CR^{32}$ ;

$X^{33}$  is N or  $CR^{33}$ ;

wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;

wherein no more than two of  $X^{19}$ ,  $X^{20}$ , and  $X^{21}$  are simultaneously N;

wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

wherein no more than two of  $X^{28}$ ,  $X^{29}$ , and  $X^{30}$  are simultaneously N;

wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each Cy is independently selected from  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from  $R^{Cy}$ ;

each  $R^{Cy}$  is independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ , wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl of  $R^{Cy}$  is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

$R^7$ ,  $R^8$ ,  $R^{19}$ ,  $R^{20}$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{28}$ ,  $R^{29}$ ,  $R^{31}$ , and  $R^{32}$  are each independently selected from H, halo, and  $C_{1-4}$  alkyl;

$R^9$ ,  $R^{21}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each independently selected from H, halo,  $OR^{a2}$ ,  $NR^{c2}R^{d2}$ ,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $R^9$ ,  $R^{21}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $(CH_2)_qOR^{a2}$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ .

$R^{X3}$ ,  $R^{X7}$ ,  $R^{Z3}$ , and  $R^{Z7}$  are each independently selected from H, halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl, and 5-membered heteroaryl, wherein said  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl, and 5-membered heteroaryl of  $R^{X3}$ ,  $R^{X7}$ ,  $R^{Z3}$ , and  $R^{Z7}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ .

$R^{W1}$ ,  $R^{W2}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from H,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{3-7}$  cycloalkyl, and 5-membered heteroaryl, wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{3-7}$  cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4  $R'$ ;

each  $R'$  is independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a3}$ ,  $SR^{a3}$ ,  $C(O)R^{b3}$ ,  $C(O)NR^{c3}R^{d3}$ ,  $C(O)OR^{a3}$ ,  $OC(O)R^{b3}$ ,  $OC(O)NR^{c3}R^{d3}$ ,  $C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}R^{d3}$ ,  $NR^{c3}C(O)R^{b3}$ ,  $NR^{c3}C(O)OR^{a3}$ ,  $NR^{c3}C(O)NR^{c3}R^{d3}$ ,  $NR^{c3}S(O)R^{b3}$ ,  $NR^{c3}S(O)_2R^{b3}$ ,  $NR^{c3}S(O)_2NR^{c3}R^{d3}$ ,  $S(O)R^{b3}$ ,  $S(O)NR^{c3}R^{d3}$ ,  $S(O)_2R^{b3}$ , and  $S(O)_2NR^{c3}R^{d3}$ , wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$



7 cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R' is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, SR<sup>a3</sup>, C(O)R<sup>b3</sup>, C(O)NR<sup>c3</sup>R<sup>d3</sup>, C(O)OR<sup>a3</sup>, OC(O)R<sup>b3</sup>, OC(O)NR<sup>c3</sup>R<sup>d3</sup>, C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(=NR<sup>e3</sup>)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>C(O)R<sup>b3</sup>, NR<sup>c3</sup>C(O)OR<sup>a3</sup>, NR<sup>c3</sup>C(O)NR<sup>c3</sup>R<sup>d3</sup>, NR<sup>c3</sup>S(O)R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>R<sup>b3</sup>, NR<sup>c3</sup>S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>, S(O)R<sup>b3</sup>, S(O)NR<sup>c3</sup>R<sup>d3</sup>, S(O)<sub>2</sub>R<sup>b3</sup>, and S(O)<sub>2</sub>NR<sup>c3</sup>R<sup>d3</sup>;

each R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>a1</sup>, R<sup>b1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>b3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, R<sup>d</sup>, R<sup>a1</sup>, R<sup>b1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>b3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>;

or R<sup>c</sup> and R<sup>d</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>;

or R<sup>c1</sup> and R<sup>d1</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>;

or R<sup>c2</sup> and R<sup>d2</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents

independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

or R<sup>c3</sup> and R<sup>d3</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

or R<sup>c4</sup> and R<sup>d4</sup>, together with the N atom to which they are attached, form a 4-7 membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>e4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

each R<sup>a4</sup>, R<sup>b4</sup>, R<sup>c4</sup>, and R<sup>d4</sup> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl are each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, NHC<sub>1-4</sub> alkyl, N(C<sub>1-4</sub> alkyl)<sub>2</sub>, halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkyl, and C<sub>1-6</sub> haloalkoxy;

each R<sup>e</sup>, R<sup>e1</sup>, R<sup>e2</sup>, R<sup>e3</sup>, and R<sup>e4</sup> is independently selected from H, C<sub>1-4</sub> alkyl, and CN; and

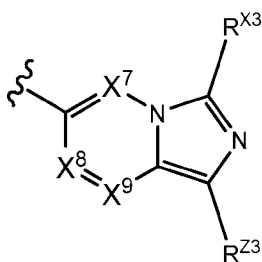
q is an integer selected from 1, 2, 3, 4, 5, and 6;

wherein when B is formula (c), formula (g), or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

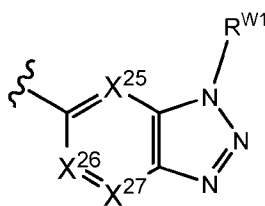
124. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:  
Q is NH or CH<sub>2</sub>;

A is Cy or Cy-C<sub>1-4</sub> alkyl-;

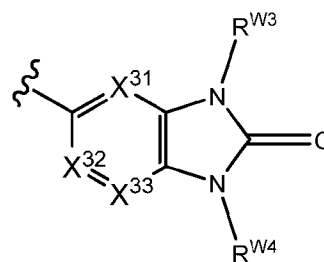
B is of formula (c), formula (i), or formula (k):



(c)



(i)



(k);

X<sup>7</sup> is N or CR<sup>7</sup>;

X<sup>8</sup> is N or CR<sup>8</sup>;

X<sup>9</sup> is N or CR<sup>9</sup>;

X<sup>25</sup> is N or CR<sup>25</sup>;

X<sup>26</sup> is N or CR<sup>26</sup>;

X<sup>27</sup> is N or CR<sup>27</sup>;

X<sup>31</sup> is N or CR<sup>31</sup>;

X<sup>32</sup> is N or CR<sup>32</sup>;

X<sup>33</sup> is N or CR<sup>33</sup>;

wherein no more than two of X<sup>7</sup>, X<sup>8</sup>, and X<sup>9</sup> are simultaneously N;

wherein no more than two of X<sup>25</sup>, X<sup>26</sup>, and X<sup>27</sup> are simultaneously N;

wherein no more than two of X<sup>31</sup>, X<sup>32</sup>, and X<sup>33</sup> are simultaneously N;

each Cy is independently selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>;

each R<sup>Cy</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, and NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of R<sup>Cy</sup> is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, and NR<sup>c1</sup>R<sup>d1</sup>;

R<sup>7</sup>, R<sup>8</sup>, R<sup>25</sup>, R<sup>26</sup>, R<sup>31</sup>, and R<sup>32</sup> are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;

R<sup>9</sup>, R<sup>27</sup>, and R<sup>33</sup> are each independently selected from H, halo, OR<sup>a2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of R<sup>9</sup>, R<sup>27</sup>, and R<sup>33</sup> are each optionally substituted with 1, 2, 3, or 4

substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>q</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, and C(O)OR<sup>a2</sup>;

R<sup>X3</sup> and R<sup>Z3</sup> are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of R<sup>X3</sup> and R<sup>Z3</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>c2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>c2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>;

R<sup>W1</sup>, R<sup>W2</sup>, R<sup>W3</sup>, and R<sup>W4</sup> are each independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4 R<sup>•</sup>;

each R<sup>•</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, and NR<sup>c3</sup>R<sup>d3</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, and C<sub>6-10</sub> aryl of R<sup>•</sup> is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, and NR<sup>c3</sup>R<sup>d3</sup>;

each R<sup>a1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>3-7</sub> cycloalkyl, and 4-10 membered heterocycloalkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, and 4-10 membered heterocycloalkyl of R<sup>a1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-6</sub> haloalkyl, CN, and OR<sup>a4</sup>;

each R<sup>a4</sup> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, amino, NHC<sub>1-4</sub> alkyl, and N(C<sub>1-4</sub> alkyl)<sub>2</sub>;

q is an integer selected from 1, 2, 3, 4, 5, and 6;

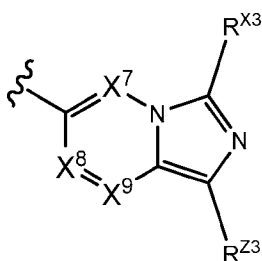
wherein when B is formula (c) or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

125. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

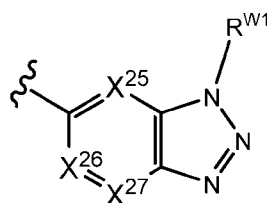
Q is NH;

A is Cy;

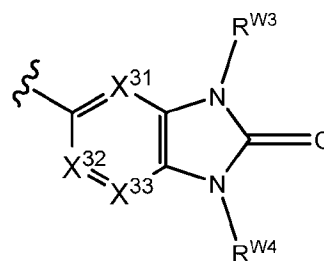
B is of formula (c), formula (i), or formula (k):



(c)



(i)



(k);

$X^7$  is  $CR^7$ ;

$X^8$  is  $CR^8$ ;

$X^9$  is  $CR^9$ ;

$X^{25}$  is  $CR^{25}$ ;

$X^{26}$  is  $CR^{26}$ ;

$X^{27}$  is  $CR^{27}$ ;

$X^{31}$  is  $CR^{31}$ ;

$X^{32}$  is  $CR^{32}$ ;

$X^{33}$  is  $CR^{33}$ ;

each Cy is independently selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>;

each R<sup>Cy</sup> is independently selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, and CN;

R<sup>7</sup>, R<sup>8</sup>, R<sup>25</sup>, R<sup>26</sup>, R<sup>31</sup>, and R<sup>32</sup> are each independently selected from H and halo;

R<sup>9</sup>, R<sup>27</sup>, and R<sup>33</sup> are each independently selected from H, halo, and 4-10 membered heterocycloalkyl, wherein 4-10 membered heterocycloalkyl of R<sup>9</sup>, R<sup>27</sup>, and R<sup>33</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> alkyl, (CH<sub>2</sub>)<sub>q</sub>OR<sup>a2</sup>, C(O)R<sup>b2</sup>, and C(O)NR<sup>c2</sup>R<sup>d2</sup>;

R<sup>X3</sup> and R<sup>Z3</sup> are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of R<sup>X3</sup> and R<sup>Z3</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> haloalkyl;

R<sup>W1</sup>, R<sup>W2</sup>, R<sup>W3</sup>, and R<sup>W4</sup> are each independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkynyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkynyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4 R<sup>\*</sup>;

each R<sup>\*</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkynyl, and C<sub>1-6</sub> haloalkyl, wherein the C<sub>1-6</sub> alkyl of R<sup>\*</sup> is optionally substituted with 1, 2, or 3 groups independently selected from OR<sup>a3</sup>;

each  $R^{a1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{c3}$ , and  $R^{d3}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>3-7</sub> cycloalkyl, and 4-10 membered heterocycloalkyl, wherein said C<sub>1-6</sub> alkyl, C<sub>3-7</sub> cycloalkyl, and 4-10 membered heterocycloalkyl of  $R^{a1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{c3}$ , and  $R^{d3}$  is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from C<sub>1-6</sub> haloalkyl and  $OR^{a4}$ ;

each  $R^{a4}$  is independently selected from H, C<sub>1-6</sub> alkyl, and N(C<sub>1-4</sub> alkyl)<sub>2</sub>;

q is 1;

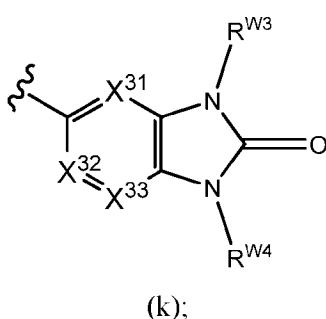
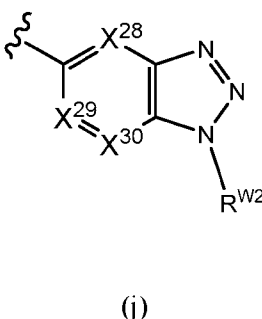
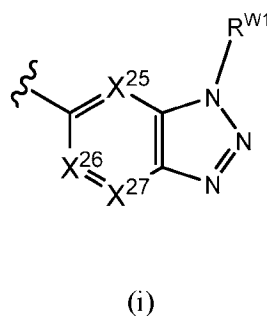
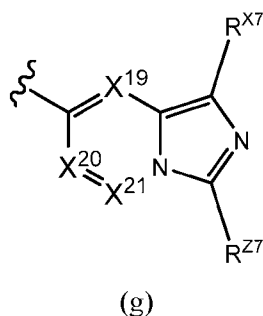
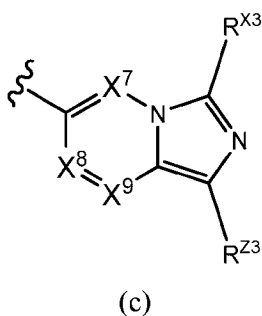
wherein when B is formula (c) or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

126. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

Q is NH;

A is Cy or Cy-C<sub>1-4</sub> alkyl-;

B is of formula (c), formula (g), formula (i), formula (j), or formula (k):



$X^7$  is N or CR<sup>7</sup>;

$X^8$  is N or CR<sup>8</sup>;

$X^9$  is N or CR<sup>9</sup>;

$X^{19}$  is N or CR<sup>19</sup>;

$X^{20}$  is N or CR<sup>20</sup>;

$X^{21}$  is N or  $CR^{21}$ ;

$X^{25}$  is N or  $CR^{25}$ ;

$X^{26}$  is N or  $CR^{26}$ ;

$X^{27}$  is N or  $CR^{27}$ ;

$X^{28}$  is N or  $CR^{28}$ ;

$X^{29}$  is N or  $CR^{29}$ ;

$X^{30}$  is N or  $CR^{30}$ ;

$X^{31}$  is N or  $CR^{31}$ ;

$X^{32}$  is N or  $CR^{32}$ ;

$X^{33}$  is N or  $CR^{33}$ ;

wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;

wherein no more than two of  $X^{19}$ ,  $X^{20}$ , and  $X^{21}$  are simultaneously N;

wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

wherein no more than two of  $X^{28}$ ,  $X^{29}$ , and  $X^{30}$  are simultaneously N;

wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each  $Cy$  is independently selected from  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from  $R^{Cy}$ ;

each  $R^{Cy}$  is independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl, CN,  $NO_2$ ,  $OR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ , wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, and 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl of  $R^{Cy}$  is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN,  $NO_2$ ,  $OR^{a1}$ ,  $SR^{a1}$ ,  $C(O)R^{b1}$ ,  $C(O)NR^{c1}R^{d1}$ ,  $C(O)OR^{a1}$ ,  $OC(O)R^{b1}$ ,  $OC(O)NR^{c1}R^{d1}$ ,  $C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}C(=NR^{e1})NR^{c1}R^{d1}$ ,  $NR^{c1}R^{d1}$ ,  $NR^{c1}C(O)R^{b1}$ ,  $NR^{c1}C(O)OR^{a1}$ ,  $NR^{c1}C(O)NR^{c1}R^{d1}$ ,  $NR^{c1}S(O)R^{b1}$ ,  $NR^{c1}S(O)_2R^{b1}$ ,  $NR^{c1}S(O)_2NR^{c1}R^{d1}$ ,  $S(O)R^{b1}$ ,  $S(O)NR^{c1}R^{d1}$ ,  $S(O)_2R^{b1}$ , and  $S(O)_2NR^{c1}R^{d1}$ ;

$R^7$ ,  $R^8$ ,  $R^{19}$ ,  $R^{20}$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{28}$ ,  $R^{29}$ ,  $R^{31}$ , and  $R^{32}$  are each independently selected from H, halo, and  $C_{1-4}$  alkyl;

$R^9$ ,  $R^{21}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each independently selected from H, halo,  $OR^{a2}$ ,  $NR^{c2}R^{d2}$ ,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, and 4-

10 membered heterocycloalkyl of  $R^9$ ,  $R^{21}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl, CN,  $NO_2$ ,  $(CH_2)_mOR^{a2}$ ,  $OR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ .

$R^{X3}$ ,  $R^{X7}$ ,  $R^{Z3}$ , and  $R^{Z7}$  are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of  $R^{X3}$ ,  $R^{X7}$ ,  $R^{Z3}$ , and  $R^{Z7}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl,  $C_{6-10}$  aryl,  $C_{3-7}$  cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl,  $C_{6-10}$  aryl- $C_{1-4}$  alkyl,  $C_{3-7}$  cycloalkyl- $C_{1-4}$  alkyl, 5-10 membered heteroaryl- $C_{1-4}$  alkyl, 4-10 membered heterocycloalkyl- $C_{1-4}$  alkyl, CN,  $NO_2$ ,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ .

$R^{W1}$ ,  $R^{W2}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from H,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{3-7}$  cycloalkyl, and 5-membered heteroaryl, wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{3-7}$  cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4  $R'$ ;

each  $R'$  is independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl, CN,  $NO_2$ ,  $OR^{a3}$ ,  $SR^{a3}$ ,  $C(O)R^{b3}$ ,  $C(O)NR^{c3}R^{d3}$ ,  $C(O)OR^{a3}$ ,  $OC(O)R^{b3}$ ,  $OC(O)NR^{c3}R^{d3}$ ,  $C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}R^{d3}$ ,  $NR^{c3}C(O)R^{b3}$ ,  $NR^{c3}C(O)OR^{a3}$ ,  $NR^{c3}C(O)NR^{c3}R^{d3}$ ,  $NR^{c3}S(O)R^{b3}$ ,  $NR^{c3}S(O)_2R^{b3}$ ,  $NR^{c3}S(O)_2NR^{c3}R^{d3}$ ,  $S(O)R^{b3}$ ,  $S(O)NR^{c3}R^{d3}$ ,  $S(O)_2R^{b3}$ , and  $S(O)_2NR^{c3}R^{d3}$ , wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{1-6}$  haloalkyl, and  $C_{6-10}$  aryl of  $R'$  is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN,  $NO_2$ ,  $OR^{a3}$ ,  $SR^{a3}$ ,  $C(O)R^{b3}$ ,  $C(O)NR^{c3}R^{d3}$ ,  $C(O)OR^{a3}$ ,  $OC(O)R^{b3}$ ,  $OC(O)NR^{c3}R^{d3}$ ,  $C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}R^{d3}$ ,  $NR^{c3}C(O)R^{b3}$ ,  $NR^{c3}C(O)OR^{a3}$ ,  $NR^{c3}C(O)NR^{c3}R^{d3}$ ,  $NR^{c3}S(O)R^{b3}$ ,  $NR^{c3}S(O)_2R^{b3}$ ,  $NR^{c3}S(O)_2NR^{c3}R^{d3}$ ,  $S(O)R^{b3}$ ,  $S(O)NR^{c3}R^{d3}$ ,  $S(O)_2R^{b3}$ , and  $S(O)_2NR^{c3}R^{d3}$ .

each  $R^{a1}$ ,  $R^{b1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{b3}$ ,  $R^{c3}$ , and  $R^{d3}$  is independently selected from H,  $C_{1-6}$  alkyl,  $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, , wherein said  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl, and  $C_{2-6}$  alkynyl of  $R^{a1}$ ,  $R^{b1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{b3}$ ,  $R^{c3}$ , and  $R^{d3}$  is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo,  $C_{1-4}$  alkyl,  $C_{1-4}$  haloalkyl,  $C_{1-6}$  haloalkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, CN,  $OR^{a4}$ ,  $SR^{a4}$ ,



$C(O)R^{b4}$ ,  $C(O)NR^{c4}R^{d4}$ ,  $C(O)OR^{a4}$ ,  $OC(O)R^{b4}$ ,  $OC(O)NR^{c4}R^{d4}$ ,  $NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)R^{b4}$ ,  $NR^{c4}C(O)NR^{c4}R^{d4}$ ,  $NR^{c4}C(O)OR^{a4}$ ,  $C(=NR^{e4})NR^{c4}R^{d4}$ ,  $NR^{c4}C(=NR^{e4})NR^{c4}R^{d4}$ ,  $S(O)R^{b4}$ ,  $S(O)NR^{c4}R^{d4}$ ,  $S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2R^{b4}$ ,  $NR^{c4}S(O)_2NR^{c4}R^{d4}$ , and  $S(O)_2NR^{c4}R^{d4}$ ;

each  $R^{a4}$ ,  $R^{b4}$ ,  $R^{c4}$ , and  $R^{d4}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl, wherein said C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl are each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkyl, and C<sub>1-6</sub> haloalkoxy; and

each  $R^e$ ,  $R^{e1}$ ,  $R^{e2}$ ,  $R^{e3}$ , and  $R^{e4}$  is independently selected from H, C<sub>1-4</sub> alkyl, and CN;

and

q is an integer selected from 1, 2, 3, 4, 5, and 6;

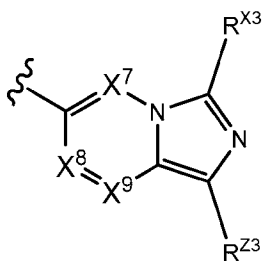
wherein when B is formula (c), formula (g), or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

127. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

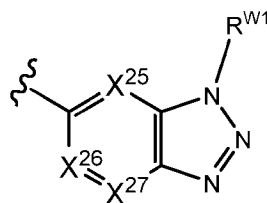
Q is NH;

A is Cy or Cy-C<sub>1-4</sub> alkyl-;

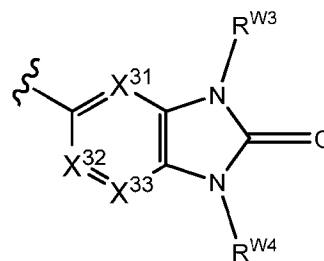
B is a group of formula (c), formula (i) or formula (k):



(c)



(i)



(k);

$X^7$  is N or CR<sup>7</sup>;

$X^8$  is N or CR<sup>8</sup>;

$X^9$  is N or CR<sup>9</sup>;

$X^{25}$  is N or CR<sup>25</sup>;

$X^{26}$  is N or CR<sup>26</sup>;

$X^{27}$  is N or CR<sup>27</sup>;

$X^{31}$  is N or CR<sup>31</sup>;

$X^{32}$  is N or CR<sup>32</sup>;

$X^{33}$  is N or CR<sup>33</sup>;

wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N; wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each Cy is independently selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from  $R^{Cy}$ ;

each  $R^{Cy}$  is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, and NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of  $R^{Cy}$  is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, and NR<sup>c1</sup>R<sup>d1</sup>;

$R^7$ ,  $R^8$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{31}$ , and  $R^{32}$  are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;

$R^9$ ,  $R^{27}$ , and  $R^{33}$  are each independently selected from H, halo, OR<sup>a2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $R^9$ ,  $R^{27}$ , and  $R^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, (CH<sub>2</sub>)<sub>m</sub>OR<sup>a2</sup>, OR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, and C(O)OR<sup>a2</sup>;

$R^{X3}$  and  $R^{Z3}$  are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of  $R^{X3}$  and  $R^{Z3}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>c2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>c2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>;

$R^{W1}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-7</sub> cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4 R<sup>'</sup>;

each R<sup>'</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, and NR<sup>c3</sup>R<sup>d3</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, and C<sub>6-10</sub> aryl of R<sup>'</sup> is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, and NR<sup>c3</sup>R<sup>d3</sup>;

each R<sup>a1</sup>, R<sup>c1</sup>, R<sup>d1</sup>, R<sup>a2</sup>, R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, R<sup>a3</sup>, R<sup>c3</sup>, and R<sup>d3</sup> is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl; and

q is an integer selected from 1, 2, 3, 4, 5, and 6;

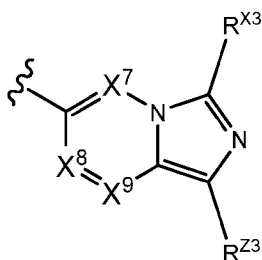
wherein when B is formula (c) or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

128. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

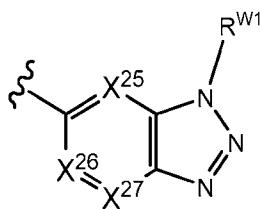
Q is NH;

A is Cy;

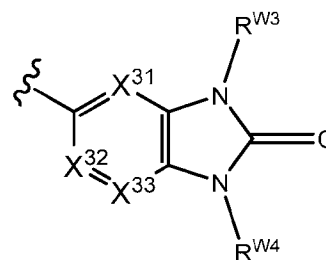
B is a group of formula (c), formula (i), or formula (k):



(c)



(i)



(k);

$X^7$  is  $CR^7$ ;

$X^8$  is  $CR^8$ ;

$X^9$  is  $CR^9$ ;

$X^{25}$  is  $CR^{25}$ ;

$X^{26}$  is  $CR^{26}$ ;

$X^{27}$  is  $CR^{27}$ ;

$X^{31}$  is  $CR^{31}$ ;

$X^{32}$  is  $CR^{32}$ ;

$X^{33}$  is  $CR^{33}$ ;

each Cy is independently selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>;

each R<sup>Cy</sup> is independently selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, and CN;

R<sup>7</sup>, R<sup>8</sup>, R<sup>25</sup>, R<sup>26</sup>, R<sup>31</sup>, and R<sup>32</sup> are each independently selected from H and halo;

R<sup>9</sup>, R<sup>27</sup>, and R<sup>33</sup> are each independently selected from H, halo, and 4-10 membered heterocycloalkyl, wherein said 4-10 membered heterocycloalkyl of R<sup>9</sup>, R<sup>27</sup>, and R<sup>33</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> alkyl, C(O)NR<sup>d2</sup>, (CH<sub>2</sub>)<sub>m</sub>OR<sup>a2</sup>, and C(O)R<sup>b2</sup>;

$R^{X3}$  and  $R^{Z3}$  are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of  $R^{X3}$  and  $R^{Z3}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from  $C_{1-6}$  haloalkyl;

$R^{W1}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from H,  $C_{1-6}$  alkyl,  $C_{3-7}$  cycloalkyl, and 5-membered heteroaryl, wherein the  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{3-7}$  cycloalkyl, and 5-membered heteroaryl are optionally substituted with 1, 2, 3, or 4  $R'$ ;

each  $R'$  is independently selected from halo,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkynyl, and  $C_{1-6}$  haloalkyl, wherein the  $C_{1-6}$  alkyl of  $R'$  is optionally substituted with 1, 2, or 3 groups independently selected from  $OR^{a3}$ ;

each  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ , and  $R^{a3}$  is independently selected from H and  $C_{1-6}$  alkyl; and  $q$  is 1;

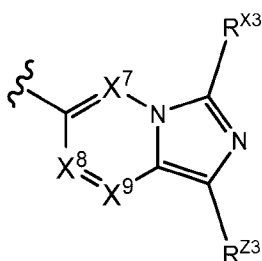
wherein when  $B$  is formula (c) or formula (k), then  $A$  is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

129. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein:

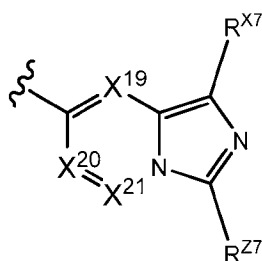
$Q$  is NH;

$A$  is Cy or Cy- $C_{1-4}$  alkyl-;

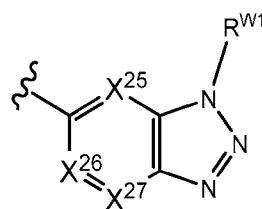
$B$  is of formula (c), formula (g), formula (i), formula (j), or formula (k):



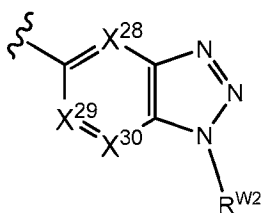
(c)



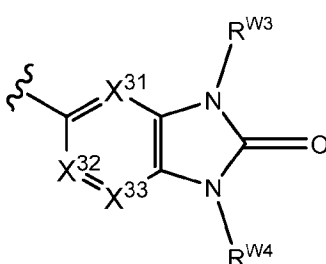
(g)



(i)



(j)



(k);

$X^7$  is N or CR<sup>7</sup>;

$X^8$  is N or CR<sup>8</sup>;

$X^9$  is N or CR<sup>9</sup>;

$X^{19}$  is N or CR<sup>19</sup>;

$X^{20}$  is N or CR<sup>20</sup>;

$X^{21}$  is N or CR<sup>21</sup>;

$X^{25}$  is N or CR<sup>25</sup>;

$X^{26}$  is N or CR<sup>26</sup>;

$X^{27}$  is N or CR<sup>27</sup>;

$X^{28}$  is N or CR<sup>28</sup>;

$X^{29}$  is N or CR<sup>29</sup>;

$X^{30}$  is N or CR<sup>30</sup>;

$X^{31}$  is N or CR<sup>31</sup>;

$X^{32}$  is N or CR<sup>32</sup>;

$X^{33}$  is N or CR<sup>33</sup>;

wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N;

wherein no more than two of  $X^{19}$ ,  $X^{20}$ , and  $X^{21}$  are simultaneously N;

wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

wherein no more than two of  $X^{28}$ ,  $X^{29}$ , and  $X^{30}$  are simultaneously N;

wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each Cy is independently selected from C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>;

each R<sup>Cy</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, and 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl of R<sup>Cy</sup> is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, SR<sup>a1</sup>, C(O)R<sup>b1</sup>, C(O)NR<sup>c1</sup>R<sup>d1</sup>, C(O)OR<sup>a1</sup>, OC(O)R<sup>b1</sup>, OC(O)NR<sup>c1</sup>R<sup>d1</sup>, C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(=NR<sup>e1</sup>)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>C(O)R<sup>b1</sup>, NR<sup>c1</sup>C(O)OR<sup>a1</sup>, NR<sup>c1</sup>C(O)NR<sup>c1</sup>R<sup>d1</sup>, NR<sup>c1</sup>S(O)R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>R<sup>b1</sup>, NR<sup>c1</sup>S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>, S(O)R<sup>b1</sup>, S(O)NR<sup>c1</sup>R<sup>d1</sup>, S(O)<sub>2</sub>R<sup>b1</sup>, and S(O)<sub>2</sub>NR<sup>c1</sup>R<sup>d1</sup>.

$R^7$ ,  $R^8$ ,  $R^{19}$ ,  $R^{20}$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{28}$ ,  $R^{29}$ ,  $R^{31}$ , and  $R^{32}$  are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;

$R^9$ ,  $R^{21}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each independently selected from H, halo,  $OR^{a2}$ ,  $NR^{c2}R^{d2}$ , C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $R^9$ ,  $R^{21}$ ,  $R^{27}$ ,  $R^{30}$ , and  $R^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>,  $OR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^cC(O)OR^{a2}$ ,  $NR^cC(O)NR^{c2}R^{d2}$ ,  $NR^cS(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ ;

$R^{X3}$ ,  $R^{X7}$ ,  $R^{Z3}$ , and  $R^{Z7}$  are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of  $R^{X3}$ ,  $R^{X7}$ ,  $R^{Z3}$ , and  $R^{Z7}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C<sub>6-10</sub> aryl-C<sub>1-4</sub> alkyl, C<sub>3-7</sub> cycloalkyl-C<sub>1-4</sub> alkyl, 5-10 membered heteroaryl-C<sub>1-4</sub> alkyl, 4-10 membered heterocycloalkyl-C<sub>1-4</sub> alkyl, CN, NO<sub>2</sub>,  $OR^{a2}$ ,  $SR^{a2}$ ,  $C(O)R^{b2}$ ,  $C(O)NR^{c2}R^{d2}$ ,  $C(O)OR^{a2}$ ,  $OC(O)R^{b2}$ ,  $OC(O)NR^{c2}R^{d2}$ ,  $C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}C(=NR^{e2})NR^{c2}R^{d2}$ ,  $NR^{c2}R^{d2}$ ,  $NR^{c2}C(O)R^{b2}$ ,  $NR^{c2}C(O)OR^{a2}$ ,  $NR^{c2}C(O)NR^{c2}R^{d2}$ ,  $NR^{c2}S(O)R^{b2}$ ,  $NR^{c2}S(O)_2R^{b2}$ ,  $NR^{c2}S(O)_2NR^{c2}R^{d2}$ ,  $S(O)R^{b2}$ ,  $S(O)NR^{c2}R^{d2}$ ,  $S(O)_2R^{b2}$ , and  $S(O)_2NR^{c2}R^{d2}$ ;

$R^{W1}$ ,  $R^{W2}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4  $R^*$ ;

each  $R^*$  is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>,  $OR^{a3}$ ,  $SR^{a3}$ ,  $C(O)R^{b3}$ ,  $C(O)NR^{c3}R^{d3}$ ,  $C(O)OR^{a3}$ ,  $OC(O)R^{b3}$ ,  $OC(O)NR^{c3}R^{d3}$ ,  $C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}R^{d3}$ ,  $NR^{c3}C(O)R^{b3}$ ,  $NR^{c3}C(O)OR^{a3}$ ,  $NR^{c3}C(O)NR^{c3}R^{d3}$ ,  $NR^{c3}S(O)R^{b3}$ ,  $NR^{c3}S(O)_2R^{b3}$ ,  $NR^{c3}S(O)_2NR^{c3}R^{d3}$ ,  $S(O)R^{b3}$ ,  $S(O)NR^{c3}R^{d3}$ ,  $S(O)_2R^{b3}$ , and  $S(O)_2NR^{c3}R^{d3}$ , wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, and C<sub>6-10</sub> aryl of  $R^*$  is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>,  $OR^{a3}$ ,  $SR^{a3}$ ,  $C(O)R^{b3}$ ,  $C(O)NR^{c3}R^{d3}$ ,  $C(O)OR^{a3}$ ,  $OC(O)R^{b3}$ ,  $OC(O)NR^{c3}R^{d3}$ ,  $C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}C(=NR^{e3})NR^{c3}R^{d3}$ ,  $NR^{c3}R^{d3}$ ,  $NR^{c3}C(O)R^{b3}$ ,  $NR^{c3}C(O)OR^{a3}$ ,  $NR^{c3}C(O)NR^{c3}R^{d3}$ ,  $NR^{c3}S(O)R^{b3}$ ,  $NR^{c3}S(O)_2R^{b3}$ ,  $NR^{c3}S(O)_2NR^{c3}R^{d3}$ ,  $S(O)R^{b3}$ ,  $S(O)NR^{c3}R^{d3}$ ,  $S(O)_2R^{b3}$ , and  $S(O)_2NR^{c3}R^{d3}$ ;

each  $R^{a1}$ ,  $R^{b1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{b3}$ ,  $R^{c3}$ , and  $R^{d3}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, , wherein said C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of  $R^{a1}$ ,  $R^{b1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{b3}$ ,  $R^{c3}$ , and  $R^{d3}$  is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, CN, OR<sup>a4</sup>, SR<sup>a4</sup>, C(O)R<sup>b4</sup>, C(O)NR<sup>c4</sup>R<sup>d4</sup>, C(O)OR<sup>a4</sup>, OC(O)R<sup>b4</sup>, OC(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)R<sup>b4</sup>, NR<sup>c4</sup>C(O)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(O)OR<sup>a4</sup>, C(=NR<sup>c4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, NR<sup>c4</sup>C(=NR<sup>c4</sup>)NR<sup>c4</sup>R<sup>d4</sup>, S(O)R<sup>b4</sup>, S(O)NR<sup>c4</sup>R<sup>d4</sup>, S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>R<sup>b4</sup>, NR<sup>c4</sup>S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>, and S(O)<sub>2</sub>NR<sup>c4</sup>R<sup>d4</sup>,

each  $R^{a4}$ ,  $R^{b4}$ ,  $R^{c4}$ , and  $R^{d4}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl, wherein said C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl are each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> haloalkyl, and C<sub>1-6</sub> haloalkoxy; and

each  $R^e$ ,  $R^{e1}$ ,  $R^{e2}$ ,  $R^{e3}$ , and  $R^{e4}$  is independently selected from H, C<sub>1-4</sub> alkyl, and CN;

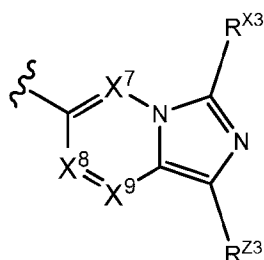
wherein when B is formula (c), formula (g), or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

130. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein:

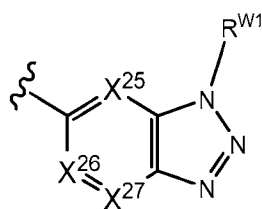
Q is NH;

A is Cy or Cy-C<sub>1-4</sub> alkyl-;

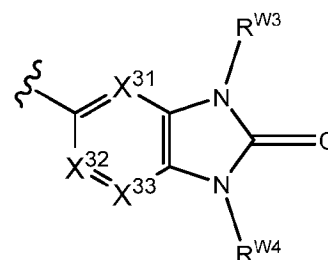
B is a group of formula (c), formula (i) or formula (k):



(c)



(i)



(k);

$X^7$  is N or CR<sup>7</sup>;

$X^8$  is N or CR<sup>8</sup>;

$X^9$  is N or CR<sup>9</sup>;

$X^{25}$  is N or CR<sup>25</sup>;

$X^{26}$  is N or CR<sup>26</sup>;

$X^{27}$  is N or CR<sup>27</sup>;

$X^{31}$  is N or  $CR^{31}$ ;

$X^{32}$  is N or  $CR^{32}$ ;

$X^{33}$  is N or  $CR^{33}$ ;

wherein no more than two of  $X^7$ ,  $X^8$ , and  $X^9$  are simultaneously N; wherein no more than two of  $X^{25}$ ,  $X^{26}$ , and  $X^{27}$  are simultaneously N;

wherein no more than two of  $X^{31}$ ,  $X^{32}$ , and  $X^{33}$  are simultaneously N;

each Cy is independently selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from  $R^{Cy}$ ;

each  $R^{Cy}$  is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a1</sup>, and NR<sup>c1</sup>R<sup>d1</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and C<sub>2-6</sub> alkynyl of  $R^{Cy}$  is optionally substituted by 1, 2, or 3 substituents independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a1</sup>, and NR<sup>c1</sup>R<sup>d1</sup>;

$R^7$ ,  $R^8$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{31}$ , and  $R^{32}$  are each independently selected from H, halo, and C<sub>1-4</sub> alkyl;

$R^9$ ,  $R^{27}$ , and  $R^{33}$  are each independently selected from H, halo, OR<sup>a2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl, wherein said C<sub>6-10</sub> aryl, C<sub>3-7</sub> cycloalkyl, 5-10 membered heteroaryl, and 4-10 membered heterocycloalkyl of  $R^9$ ,  $R^{27}$ , and  $R^{33}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, and C(O)OR<sup>a2</sup>;

$R^{X3}$  and  $R^{Z3}$  are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of  $R^{X3}$  and  $R^{Z3}$  are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a2</sup>, SR<sup>a2</sup>, C(O)R<sup>b2</sup>, C(O)NR<sup>c2</sup>R<sup>d2</sup>, C(O)OR<sup>a2</sup>, OC(O)R<sup>b2</sup>, OC(O)NR<sup>c2</sup>R<sup>d2</sup>, C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(=NR<sup>e2</sup>)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>C(O)R<sup>b2</sup>, NR<sup>c2</sup>C(O)OR<sup>a2</sup>, NR<sup>c2</sup>C(O)NR<sup>c2</sup>R<sup>d2</sup>, NR<sup>c2</sup>S(O)R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>R<sup>b2</sup>, NR<sup>c2</sup>S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>, S(O)R<sup>b2</sup>, S(O)NR<sup>c2</sup>R<sup>d2</sup>, S(O)<sub>2</sub>R<sup>b2</sup>, and S(O)<sub>2</sub>NR<sup>c2</sup>R<sup>d2</sup>;

$R^{W1}$ ,  $R^{W3}$ , and  $R^{W4}$  are each independently selected from C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4 R<sup>'</sup>;

each R<sup>'</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, CN, NO<sub>2</sub>, OR<sup>a3</sup>, and NR<sup>c3</sup>R<sup>d3</sup>, wherein the C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>1-6</sub> haloalkyl, and C<sub>6-10</sub> aryl of R<sup>'</sup> is optionally substituted with 1, 2, or 3 groups independently selected from halo, CN, NO<sub>2</sub>, OR<sup>a3</sup>, and NR<sup>c3</sup>R<sup>d3</sup>;



each  $R^{a1}$ ,  $R^{c1}$ ,  $R^{d1}$ ,  $R^{a2}$ ,  $R^{b2}$ ,  $R^{c2}$ ,  $R^{d2}$ ,  $R^{a3}$ ,  $R^{c3}$ , and  $R^{d3}$  is independently selected from H, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl;

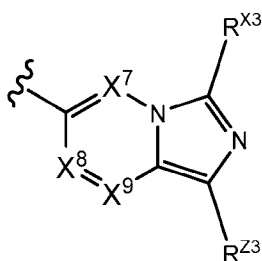
wherein when B is formula (c) or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

131. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein:

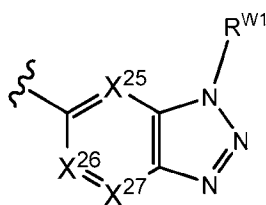
Q is NH;

A is Cy;

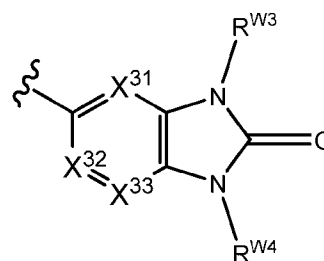
B is a group of formula (c), formula (i), or formula (k):



(c)



(i)



(k);

$X^7$  is CR<sup>7</sup>;

$X^8$  is CR<sup>8</sup>;

$X^9$  is CR<sup>9</sup>;

$X^{25}$  is CR<sup>25</sup>;

$X^{26}$  is CR<sup>26</sup>;

$X^{27}$  is CR<sup>27</sup>;

$X^{31}$  is CR<sup>31</sup>;

$X^{32}$  is CR<sup>32</sup>;

$X^{33}$  is CR<sup>33</sup>;

each Cy is independently selected from C<sub>3-7</sub> cycloalkyl and 4-10 membered heterocycloalkyl, each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>;

each R<sup>Cy</sup> is independently selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> haloalkyl, and CN;

$R^7$ ,  $R^8$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{31}$ , and  $R^{32}$  are each independently selected from H and halo;

$R^9$ ,  $R^{27}$ , and  $R^{33}$  are each independently selected from H, halo, and 4-10 membered heterocycloalkyl, wherein said 4-10 membered heterocycloalkyl of  $R^9$ ,  $R^{27}$ , and  $R^{33}$  are each

optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> alkyl, C(O)NR<sup>c2</sup>R<sup>d2</sup>, and C(O)R<sup>b2</sup>;

R<sup>X3</sup> and R<sup>Z3</sup> are each independently selected from H, halo, and 5-membered heteroaryl, wherein said 5-membered heteroaryl of R<sup>X3</sup> and R<sup>Z3</sup> are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from C<sub>1-6</sub> haloalkyl;

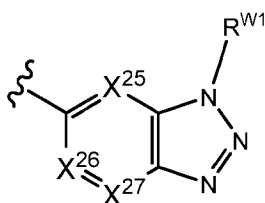
R<sup>W1</sup>, R<sup>W3</sup>, and R<sup>W4</sup> are each independently selected from C<sub>1-6</sub> alkyl and 5-membered heteroaryl, each optionally substituted with 1, 2, 3, or 4 R<sup>'</sup>;

each R<sup>'</sup> is independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkynyl, and C<sub>1-6</sub> haloalkyl, wherein the C<sub>1-6</sub> alkyl of R<sup>'</sup> is optionally substituted with 1, 2, or 3 groups independently selected from OR<sup>a3</sup>;

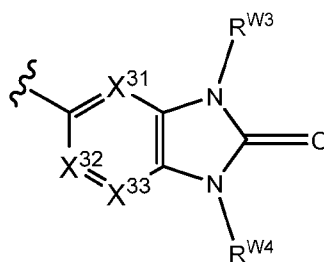
each R<sup>b2</sup>, R<sup>c2</sup>, R<sup>d2</sup>, and R<sup>a3</sup> is independently selected from H and C<sub>1-6</sub> alkyl;

wherein when B is formula (c) or formula (k), then A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

132. The compound of any one of claims 123-131, or a pharmaceutically acceptable salt thereof, wherein B is a group of formula (i) or formula (k):

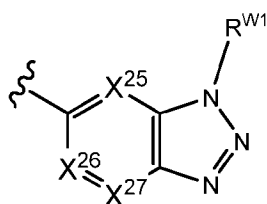


(i)



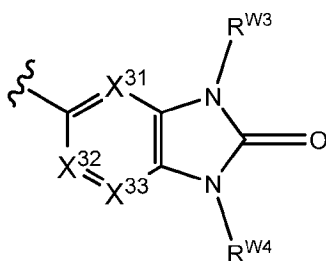
(k).

133. The compound of any one of claims 123-131, or a pharmaceutically acceptable salt thereof, wherein B is a group of formula (i):



(i).

134. The compound of any one of claims 123-131, or a pharmaceutically acceptable salt thereof, wherein B is a group of formula (k):



(k).

135. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein:

when B is formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (k); A is Cy; and Cy is C<sub>3-7</sub> cycloalkyl,

then Cy is substituted with 0, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>.

136. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein:

when B is formula (a), formula (c), formula (d), formula (e), formula (f), formula (g), or formula (k); and A is Cy;

then Cy is C<sub>4-7</sub> cycloalkyl substituted with 1, 2, 3, 4, or 5 substituents independently selected from R<sup>Cy</sup>.

137. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, wherein A is not 1-methylcyclopropyl, 1-cyanocyclopropyl, or 1-(fluoromethyl)cyclopropyl.

138. The compound of claim 1, selected from:

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-(2-methoxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-(2-methoxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1-(2-propynyl)-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

3-{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-6-fluoro-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonylamino}-3-oxetanecarbonitrile;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-fluoro-2-oxo-1-(2-propynyl)-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{7-bromo-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-(4-isobutyryl-1-piperazinyl)-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-(4-isobutyryl-1-piperazinyl)-1,3-dihydro-1,3-benzimidazol-2-one;

1-(4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1H-1,2,3-benzotriazol-4-yl}-1-piperazinyl)-2-methyl-1-propanone;

1-(4-{1-[5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1H-1,2,3-benzotriazol-4-yl}-1-piperazinyl)-2-methyl-1-propanone;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-3-(2,2,2-trifluoroethyl)-1,3-dihydro-1,3-benzimidazol-2-one; and

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-8-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-methyloxetan-3-yl)imidazo[1,5-a]pyridine-6-sulfonamide;

or a pharmaceutically acceptable salt of any of the aforementioned.

139. The compound of claim 1, selected from:

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

{7-[(R)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{7-(2,5-diazabicyclo[4.1.0]hept-2-yl)-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-1-cyclopropyl-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

N-(1-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-(3-methyl-3-oxetanylaminosulfonyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl}-3-azepanyl)2-methylpropionamide;

{7-[(3S,5S)-3,5-dimethyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

{7-[(R)-4-(N,N-dimethylcarbamoyl)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{7-[1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

N,N-dimethyl-4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-(2-hydroxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl}-1-piperazinecarboxamide;

{7-[1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl)amine;

N,N-dimethyl-4-{1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-(2-hydroxyethyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-4-yl}-1,2,3,6-tetrahydro-1-pyridinecarboxamide;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{1-[(1-methoxycyclopropyl)carbonyl]-1,2,3,6-tetrahydro-4-pyridyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]-1,3-dihydro-1,3-benzimidazol-2-one;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-(2-oxa-7-aza-7-spiro[3.5]nonyl)-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-3-azetidyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-1,3-benzimidazol-2-one;

4-{(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl}-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-1,3-benzimidazol-2-one;

{7-[(R)-4-(N,N-dimethylcarbamoyl)-3-methyl-1-piperazinyl]-3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-2-oxo-1,3-dihydro-1,3-benzimidazol-5-ylsulfonyl}(3-methyl-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(R)-3-(methoxymethyl)-1-piperazinyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(S)-3-(methoxymethyl)-1-piperazinyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-3-azetidiny)carbonyl]-1-piperazinyl}-3-methyl-1-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-1,3-dihydro-2H-1,3-benzimidazol-2-one;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-7-[(2S,6S)-2,6-dimethyl-1,2,3,6-tetrahydro-4-pyridyl]-1-methyl-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-[(R)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-7-[2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-[(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl]-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-[(S)-4-isobutyryl-3-methyl-1-piperazinyl]-3-methyl-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

3-(2-aminoethyl)-1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-4-(4-isobutyryl-1-piperazinyl)-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-3-methyl-4-(N,N-dimethylcarbamoyl)-1-piperazinyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-[(1-methoxycyclopropyl)carbonyl]-3-methyl-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[(R)-4-[(3-methoxy-1-methyl-3-azetidiny)carbonyl]-3-methyl-1-piperazinyl]-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{1-[(1-methoxycyclopropyl)carbonyl]-1,2,3,6-tetrahydro-4-pyridyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-6-(3-methyl-3-oxetanylaminosulfonyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclopropyl)carbonyl]-1-piperazinyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-3-ethyl-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(3-methoxy-1-methyl-3-azetidiny)carbonyl]-1-piperazinyl}-1,3-dihydro-2H-1,3-benzimidazol-2-one;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-methyl-2-oxo-7-(1,2,3,6-tetrahydro-4-pyridyl)-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(S)-6-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(R)-3-methyl-4-(N-methylcarbamoyl)-1-piperazinyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;

{3-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-1-ethyl-7-[(S)-2-methyl-1-(N,N-dimethylcarbamoyl)-1,2,3,6-tetrahydro-4-pyridyl]-2-oxo-2,3-dihydro-1H-1,3-benzimidazol-5-ylsulfonyl}[3-(fluoromethyl)-3-oxetanyl]amine;



1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-(1-isobutyryl-1,2,3,6-tetrahydro-4-pyridyl)-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-{4-[(1-methoxycyclobutyl)carbonyl]-1-piperazinyl}-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-3-methyl-4-(4-{[(R)-1-methyl-2-azetidiny]carbonyl}-1-piperazinyl)-1,3-dihydro-2H-1,3-benzimidazol-2-one;

and

1-[5-(difluoromethyl)-1,3,4-thiadiazol-2-yl]-6-[3-(fluoromethyl)-3-oxetanylaminosulfonyl]-4-[4-(2-methoxy-2-methylpropionyl)-1-piperazinyl]-3-methyl-1,3-dihydro-2H-1,3-benzimidazol-2-one;

or a pharmaceutically acceptable salt of any of the aforementioned.

140. The compound of claim 1, selected from:

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(1-(1-(2-hydroxyethoxy)cyclopropane-1-carbonyl)-1,2,3,6-tetrahydropyridin-4-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-(4-(1-ethoxycyclopropane-1-carbonyl)piperazin-1-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-4-((3S,5S)-3,5-dimethylpiperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1H-benzo[d][1,2,3]triazole-6-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-((3R,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-7-(4-(1-(2-fluoroethyl)-3-methoxyazetidine-3-carbonyl)piperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-((3S,5R)-3,5-dimethylpiperazin-1-yl)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

(S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-methoxycyclopropane-1-carbonyl)-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-((2S,6S)-2,6-dimethylmorpholino)-N-(3-(fluoromethyl)oxetan-3-yl)-1-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

(S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-methoxycyclobutane-1-carbonyl)-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(3-methoxyoxetane-3-carbonyl)piperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

(S)-3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(2-methoxy-2-methylpropanoyl)-3-methylpiperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-7-(4-(1-(2-(dimethylamino)ethoxy)cyclopropane-1-carbonyl)piperazin-1-yl)-1-methyl-N-(3-methyloxetan-3-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

3-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-1-ethyl-N-(3-(fluoromethyl)oxetan-3-yl)-7-(4-(1-(methoxy-d3)cyclopropane-1-carbonyl)piperazin-1-yl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazole-5-sulfonamide;

4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N-dimethyl-3,6-dihydropyridine-1(2H)-carboxamide;

4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,2-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide; and

4-(1-(5-(difluoromethyl)-1,3,4-thiadiazol-2-yl)-3-ethyl-6-(N-(3-(fluoromethyl)oxetan-3-yl)sulfamoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)-N,N,6-trimethyl-3,6-dihydropyridine-1(2H)-carboxamide;

or a pharmaceutically acceptable salt of any of the aforementioned.

141. A pharmaceutical composition comprising a compound of any one of claims 1-140, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.
142. A method of inhibiting the activity of PARG comprising contacting a compound of any one of claims 1-140, or a pharmaceutically acceptable salt thereof, with said PARG.
143. The method of claim 142, wherein the contacting is contacting *in vitro*.
144. A method of treating a disease or disorder in a patient in need of treatment comprising administering to said patient a therapeutically effective amount of a compound of any one of claims 1-140, or a pharmaceutically acceptable salt thereof, or a composition of claim 141.
145. The method of claim 144, wherein the disease or disorder is cancer.
146. The method of claim 145, wherein the cancer is a cellular stress-dependent cancer.
147. The method of claim 145, wherein said cancer is selected from lung cancer, colon cancer, breast cancer, ovarian cancer, gastric cancer, prostate cancer, liver cancer, pancreatic cancer, brain cancer, skin cancer, bladder cancer, esophageal cancer, head and neck cancer, kidney cancer, rectal cancer, stomach cancer, thyroid cancer, uterine cancer, mantle cell lymphoma, and renal cell carcinoma.