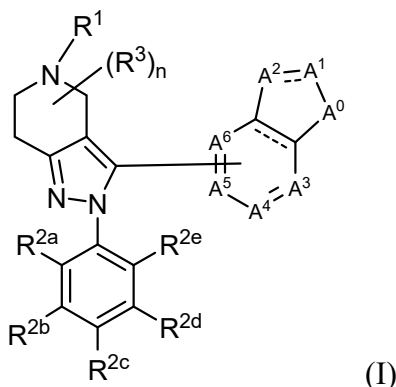


CLAIMS

1. A compound of Formula (I)



(I)

or a pharmaceutically acceptable salt thereof, wherein,

ring vertex A⁰ is NH or C(O);

each of ring vertices A¹ and A³ are independently selected from the group consisting of N, NH, CH, C(O) and C(R⁴);

each of ring vertices A², A⁵ and A⁶ is independently selected from the group consisting of N, CH, and C(R⁴);

ring vertex A⁴ is selected from the group consisting of N, N(C₁₋₄ alkyl), CH, and C(R⁴);

and no more than two of A³, A⁴, A⁵ and A⁶ are N;

each of the dashed bonds independently is a single or double bond;

R¹ is selected from the group consisting of heteroaryl, C₆₋₁₀ aryl, -C₁₋₈ alkylene-heteroaryl, -C₁₋₈ alkylene-C₆₋₁₀ aryl, C₃₋₈ cycloalkyl, four to eight membered heterocycloalkyl, C₁₋₈ alkyl, C₁₋₈ haloalkyl, -C(O)NR^{1a}R^{1b}, and -CO₂R^{1a}; wherein the heterocycloalkyl group is a 4 to 8 membered ring having from 1 to 3 heteroatoms as ring vertices selected from N, O and S; the heteroaryl group is a 5 to 10 membered aromatic ring having from 1 to 3 heteroatoms as ring vertices selected from N, O and S;

wherein R^{1a} and R^{1b} are each independently selected from the group consisting of hydrogen, C₁₋₈ alkyl, C₆₋₁₀ aryl, and -C₁₋₆ alkylene-C₆₋₁₀ aryl;

wherein R¹ is optionally substituted with 1 to 5 R⁵ substituents;

R^{2a} and R^{2e} are each independently selected from the group consisting of C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, -O-C₁₋₆ haloalkyl, -S-C₁₋₆ alkyl, -C₁₋₆ alkyl-O-C₁₋₆ alkyl, -C₁₋₆ alkyl-S-C₁₋₆ alkyl, CN, and halogen;

R^{2b} , R^{2c} , and R^{2d} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, $-O-C_{1-6}$ haloalkyl, $-S-C_{1-6}$ alkyl, $-C_{1-6}$ alkyl- $O-C_{1-6}$ alkyl, $-C_{1-6}$ alkyl- $S-C_{1-6}$ alkyl, cyano, and halogen;

each R^3 is independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} haloalkyl and hydroxyl, and optionally two R^3 groups on the same carbon atom are combined to form oxo ($=O$);

each R^4 is independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} hydroxyalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, $-O-C_{1-6}$ haloalkyl, halogen, cyano, hydroxyl, $-S-C_{1-6}$ alkyl, $-C_{1-6}$ alkyl- $O-C_{1-6}$ alkyl, $-C_{1-6}$ alkyl- $S-C_{1-6}$ alkyl, $-NR^{4a}R^{4b}$, $-CONR^{4a}R^{4b}$, $-CO_2R^{4a}$, $-COR^{4a}$, $-OC(O)NR^{4a}R^{4b}$, $-NR^{4a}C(O)R^{4b}$, $-NR^{4a}C(O)_2R^{4b}$, and $-NR^{4a}-C(O)NR^{4a}R^{4b}$;

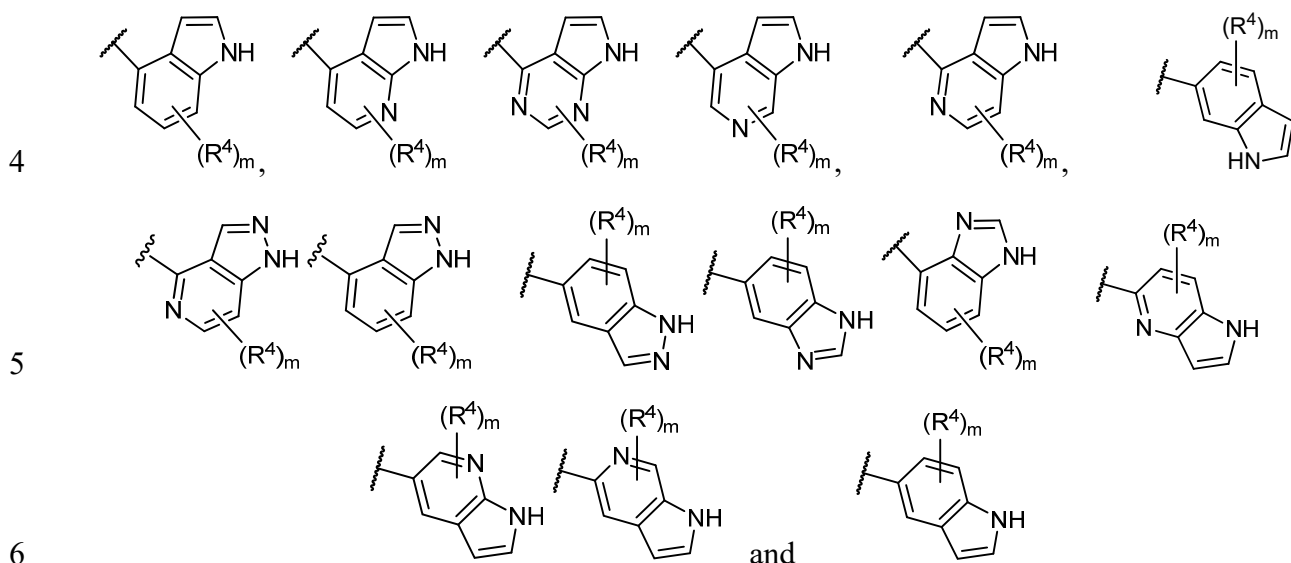
each R^{4a} and R^{4b} is independently selected from the group consisting of hydrogen, C_{1-4} alkyl, and C_{1-4} haloalkyl;

each R^5 is independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} haloalkyl, C_{1-8} haloalkoxy, C_{1-8} hydroxyalkyl, $-C_{1-8}$ alkyl-heterocycloalkyl, $-C_{1-8}$ alkyl- C_{3-8} cycloalkyl, C_{3-6} cycloalkyl, heterocycloalkyl, halogen, OH, C_{2-8} alkenyl, C_{2-8} alkynyl, CN, $C(O)R^{5a}$, $-NR^{5b}C(O)R^{5a}$, $-CONR^{5a}R^{5b}$, $-NR^{5a}R^{5b}$, $-C_{1-8}$ alkylene- $NR^{5a}R^{5b}$, $-S-C_{1-6}$ alkyl, $-C_{1-6}$ alkyl- $O-C_{1-6}$ alkyl, $-C_{1-6}$ alkyl- $S-C_{1-6}$ alkyl, $-OC(O)NR^{5a}R^{5b}$, $-NR^{5a}C(O)_2R^{5b}$, $-NR^{5a}-C(O)NR^{5b}R^{5b}$ and CO_2R^{5a} ; wherein wherein the heterocycloalkyl group is a 4 to 8 membered ring having from 1 to 3 heteroatoms as ring vertices selected from N, O and S;

wherein each R^{5a} and R^{5b} is independently selected from the group consisting of hydrogen, C_{1-4} alkyl, and C_{1-4} haloalkyl, or when attached to the same nitrogen atom R^{5a} and R^{5b} are combined with the nitrogen atom to form a five or six-membered ring having from 0 to 1 additional heteroatoms as ring vertices selected from N, O, or S; and

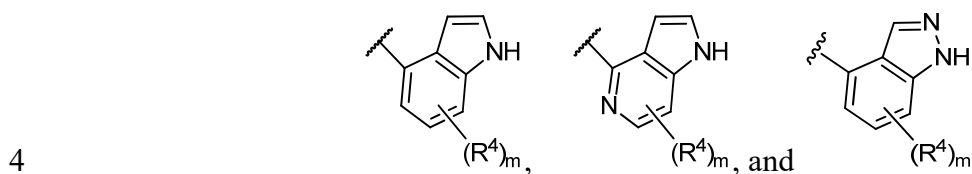
the subscript n is 0, 1, 2 or 3.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the ring portion having A^0 , A^1 , A^2 , A^3 , A^4 , A^5 , and A^6 as ring vertices is a bicyclic heteroaryl selected from the group consisting of



7 wherein m is 0, 1, 2 or 3; and wherein the R^4 substituents, when present, are attached to any
 8 suitable carbon ring vertex of the bicyclic heteroaryl.

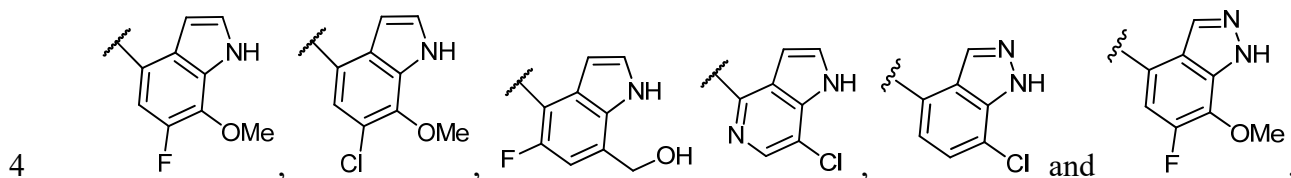
1 **3.** The compound of claim 1, or a pharmaceutically acceptable salt thereof,
 2 wherein the ring portion having A^0 , A^1 , A^2 , A^3 , A^4 , A^5 , and A^6 as ring vertices is selected from
 3 the group consisting of



wherein m is 0, 1, 2, or 3.

1 **4.** The compound of claim 1, or a pharmaceutically acceptable salt thereof,
 2 wherein each R^4 is independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy,
 3 C_{1-6} hydroxyalkyl, C_{1-4} haloalkyl, halogen, cyano, hydroxyl, $-NH_2$, $-CONR^{4a}R^{4b}$, and $-CO_2R^{4a}$;
 4 and wherein the R^4 substituents, when present, are attached to any suitable carbon ring vertex of
 5 the bicyclic heteroaryl.

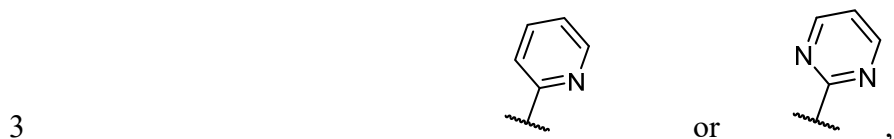
1 **5.** The compound of claim 1, or a pharmaceutically acceptable salt thereof,
 2 wherein the ring portion having A^0 , A^1 , A^2 , A^3 , A^4 , A^5 , and A^6 as ring vertices is selected from
 3 the group consisting of:



1 6. The compound of claim 1, or a pharmaceutically acceptable salt thereof,
2 wherein R^1 is selected from the group consisting of heteroaryl, C_{6-10} aryl, $-C_{1-6}$ alkylene–
3 heteroaryl, $-C_{1-6}$ alkylene– C_{6-10} aryl, four to eight membered heterocycloalkyl, C_{3-8} cycloalkyl,
4 C_{1-8} alkyl, $-C(O)NR^{1a}R^{1b}$, and $-CO_2R^{1a}$, wherein the heteroaryl group is a 5 or 6 membered
5 aromatic ring having from 1 to 3 heteroatoms as ring vertices selected from N, O and S, and R^1 is
6 optionally substituted with 1 to 3 R^5 substituents.

1 7. The compound of claim 1, or a pharmaceutically acceptable salt thereof,
2 wherein R^1 is selected from the group consisting of pyridyl, pyrimidyl, pyrazinyl, thiadiazolyl,
3 phenyl, benzyl, cyclopentyl, tetrahydropyranyl,
4 $-C(O)NR^{1a}R^{1b}$, $-CO_2R^{1a}$, and C_{1-8} alkyl, wherein R^1 is optionally substituted with 1 to 3 R^5
5 substituents.

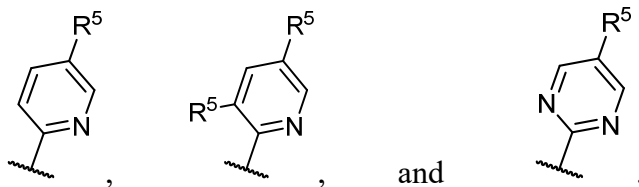
1 8. The compound of claim 1, or a pharmaceutically acceptable salt thereof,
2 wherein R^1 is



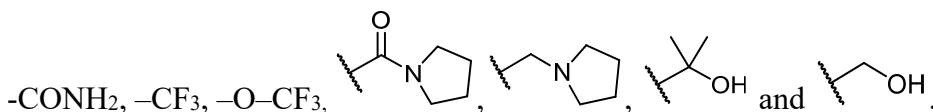
4 each of which is optionally substituted with 1 or 2 R^5 substituents.

1 9. The compound of claim 8, wherein each R^5 is independently selected from
2 the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} haloalkyl, C_{1-8} haloalkoxy, C_{1-8} hydroxyalkyl,
3 $-C_{1-8}$ alkyl-heterocycloalkyl, C_{3-6} cycloalkyl, halogen, $-CONR^{5a}R^{5b}$, $-NR^{5a}R^{5b}$, $-C_{1-8}$ alkylene–
4 $NR^{5a}R^{5b}$, and $-CO_2R^{5a}$, each R^{5a} and R^{5b} is independently selected from the group consisting of
5 hydrogen and C_{1-4} alkyl, or when attached to the same nitrogen atom can be combined with the
6 nitrogen atom to form a 5 or 6-membered ring; and the heterocycloalkyl group is a 4 to 6
7 membered ring having from 1 to 3 heteroatoms as ring vertices selected from N, O and S.

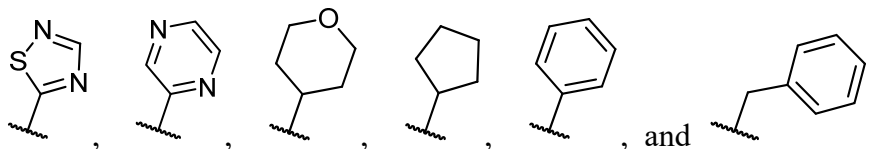
1 **10.** The compound of claim **1**, or a pharmaceutically acceptable salt thereof,
2 wherein R¹ is selected from the group consisting of



1 **11.** The compound of claim **10**, wherein each R⁵ is independently selected
2 from the group consisting of cyclopropyl, isopropyl, isopropoxy, OMe, Me, Cl, F,



1 **12.** The compound of claim **1**, or a pharmaceutically acceptable salt thereof,
2 wherein R¹ is selected from the group consisting of:

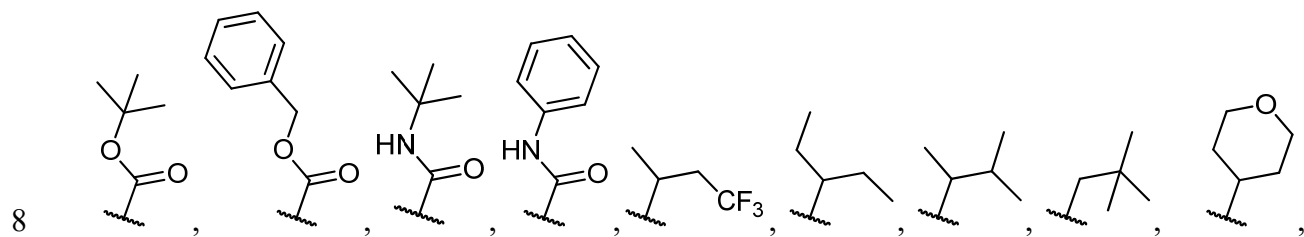
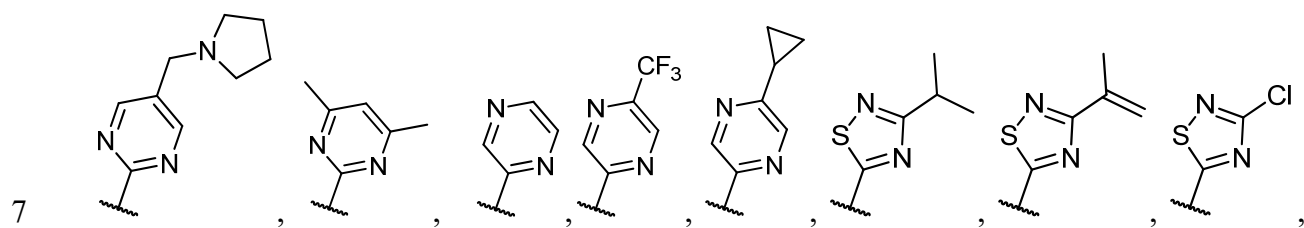
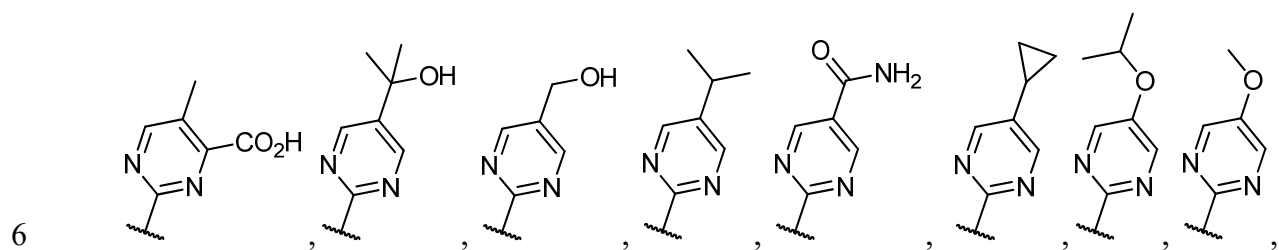
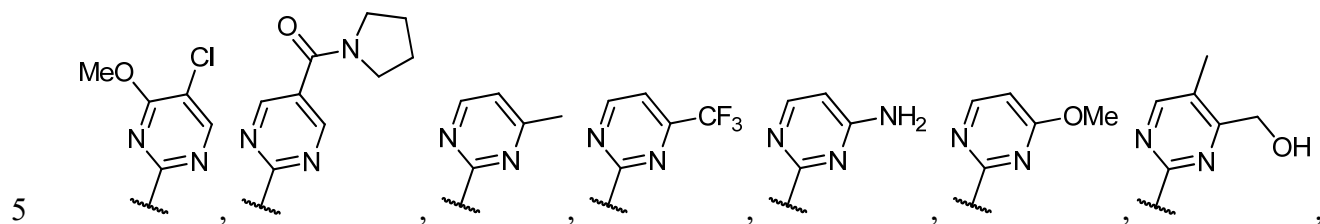
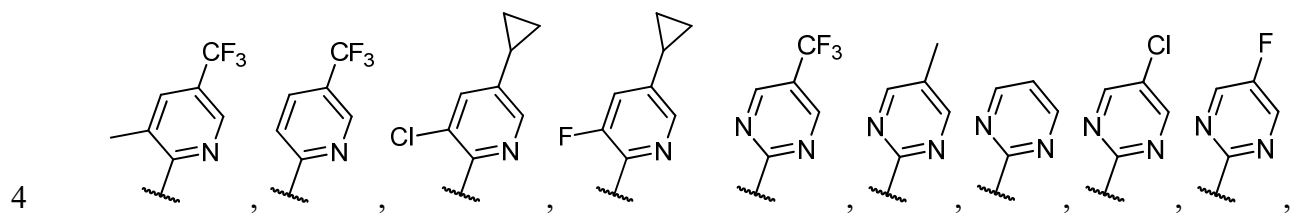
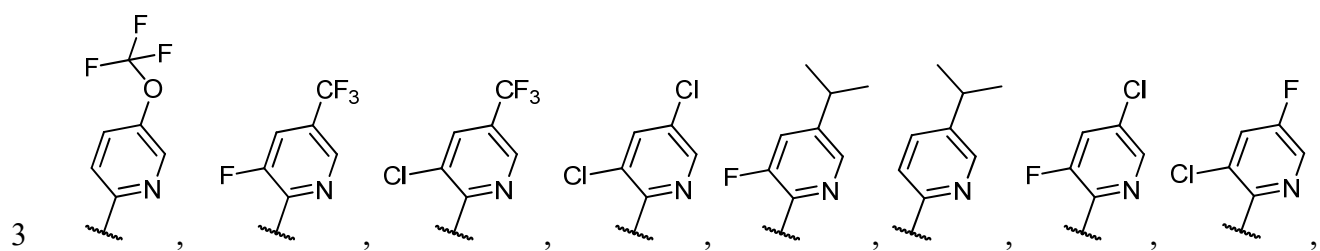


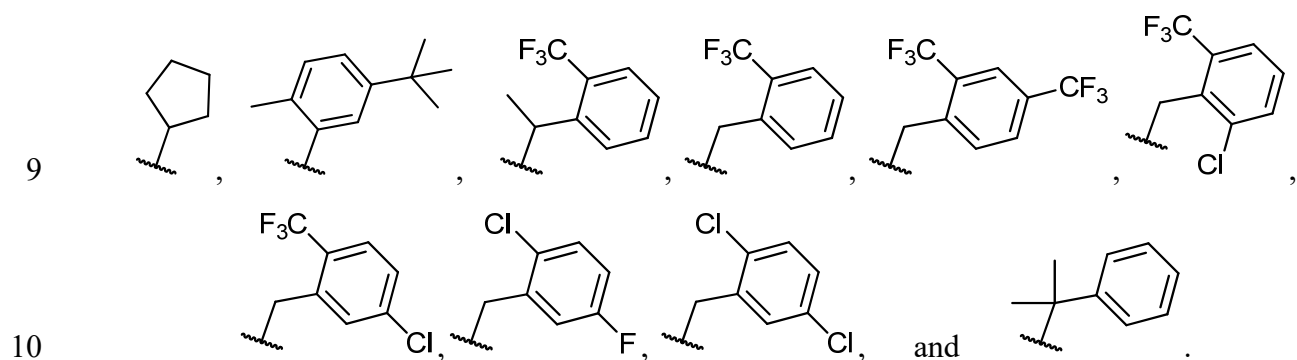
4 each of which is optionally substituted with 1 to 2 R⁵ substituents.

1 **13.** The compound of claim **12**, wherein each R⁵ is independently selected
2 from the group consisting of halogen, C₁₋₈ alkyl, C₁₋₈ haloalkyl, C₃₋₆ cycloalkyl, and C₂₋₈ alkenyl.

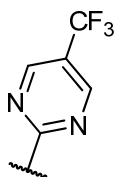
1 **14.** The compound of claim **13**, wherein each R⁵ is independently selected
2 from the group consisting of Cl, F, Me, isopropyl, -CF₃, cyclopropyl, and isopropenyl.

1 **15.** The compound of claim **1**, or a pharmaceutically acceptable salt thereof,
2 wherein R¹ is selected from the group consisting of





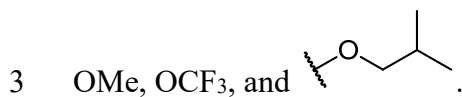
1 **16.** The compound of claim 1, or a pharmaceutically acceptable salt thereof,
 2 wherein R¹ is



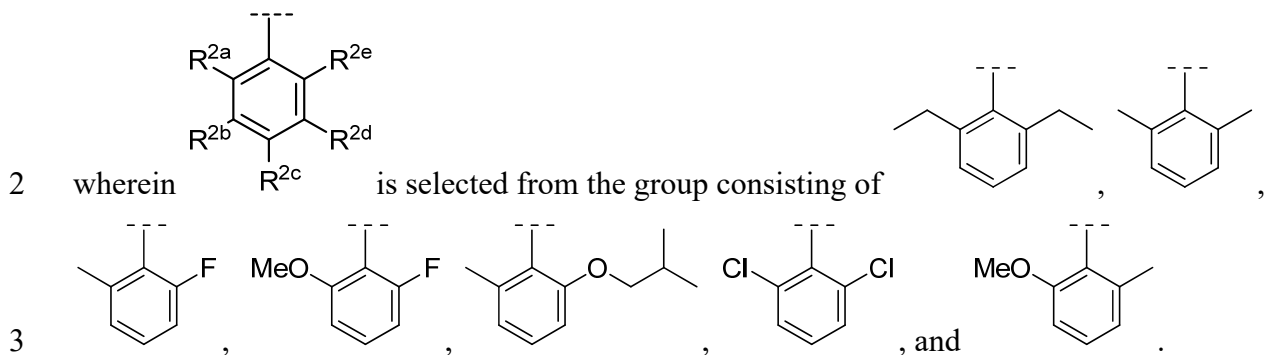
1 **17.** The compound of claim 1, or a pharmaceutically acceptable salt thereof,
 2 wherein R^{2b}, R^{2c}, and R^{2d} are each H.

1 **18.** The compound of claim 1, or a pharmaceutically acceptable salt thereof,
 2 wherein R^{2a} and R^{2e} are each independently selected from the group consisting of C₁₋₆ alkyl, C₁₋₆
 3 alkoxy, C₁₋₆ haloalkyl, -O-C₁₋₆ haloalkyl, and halogen.

1 **19.** The compound of claim 1, or a pharmaceutically acceptable salt thereof,
 2 wherein R^{2a} and R^{2e} are each independently selected from the group consisting of Me, Et, F, Cl,



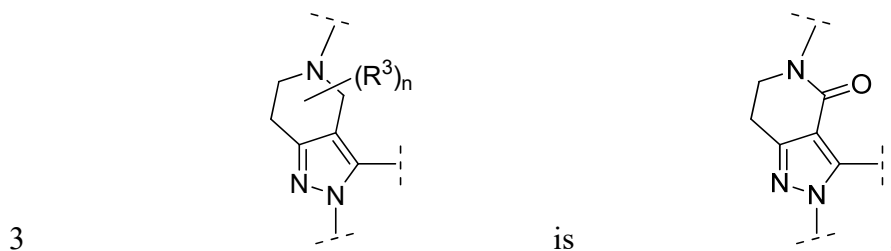
1 **20.** The compound of claim 1, or a pharmaceutically acceptable salt thereof,



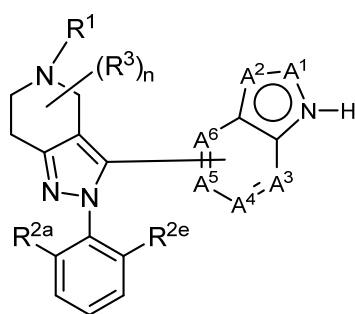
1 **21.** The compound of claim 1, or a pharmaceutically acceptable salt thereof,
2 wherein n is 0.

1 **22.** The compound of claim 1, or a pharmaceutically acceptable salt thereof,
2 wherein n is 2 and the two R³ groups are on the same carbon atom and are combined to form oxo
3 (=O).

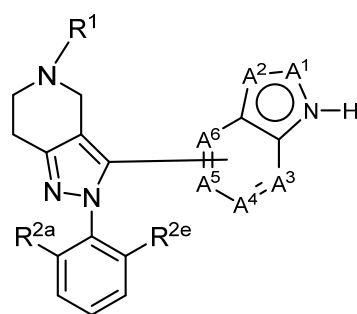
1 **23.** The compound of claim 1, or a pharmaceutically acceptable salt thereof,
2 wherein



1 **24.** The compound of claim 1, or a pharmaceutically acceptable salt thereof,
2 having a structure represented by Formula (Ia), or (Ib):
3

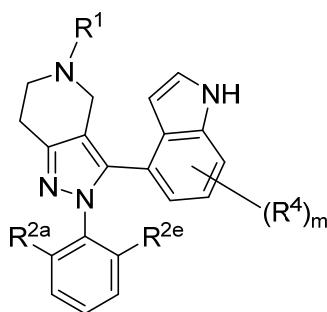


(Ia)

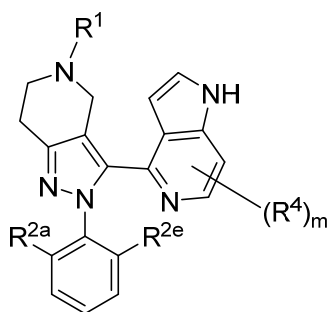


(Ib).

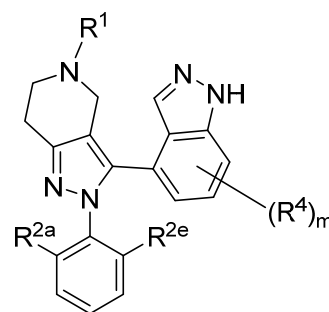
25. The compound of claim 2, or a pharmaceutically acceptable salt thereof, having a structure represented by Formula (Ic), (Id), or (Ie):



(Ic)



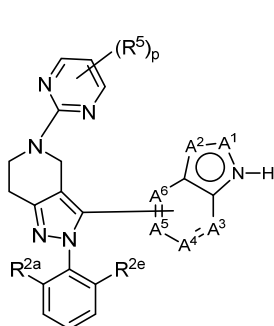
(Id)



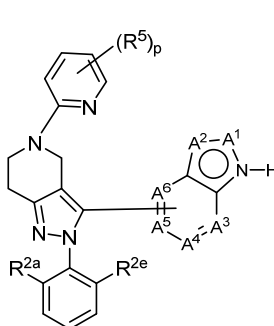
(Ie)

wherein m is 0, 1 or 2 and wherein the R⁴ substituents may be attached to any suitable carbon ring vertex of the bicyclic heteroaryl.

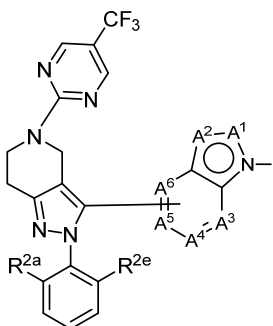
26. The compound of claim 1, or a pharmaceutically acceptable salt thereof, having a structure represented by Formula (If), (Ig), (Ih), and (Ii):



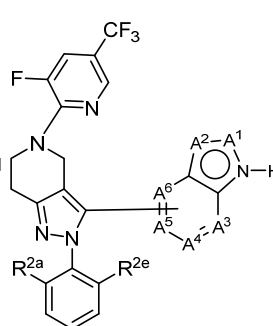
(If)



(Ig)



(Ih)

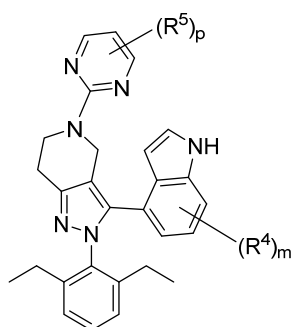


(Ii)

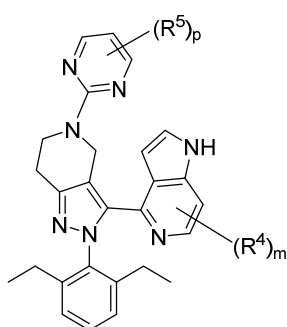
wherein p is 0, 1 or 2.

1 **27.** The compound of claim **24**, or a pharmaceutically acceptable salt thereof,
2 wherein R^{2a} and R^{2e} are both ethyl.

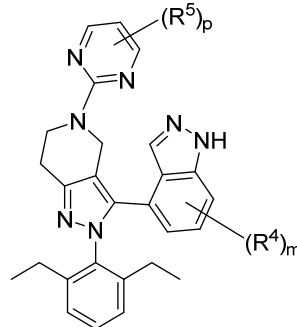
1 **28.** The compound of claim **2**, or a pharmaceutically acceptable salt thereof,
2 having a structure represented by Formula (Ik), (Il), or (Im) :



(Ik)



(Il)



(Im)

3 wherein p is 0, 1 or 2, m is 0, 1 or 2 and wherein the R⁴ substituents may be
4 attached to any suitable carbon ring vertex of the bicyclic heteroaryl.
5

1 **29.** The compound of claim **28**, or a pharmaceutically acceptable salt thereof,
2 wherein

3 p is 1 or 2;

4 m is 1 or 2;

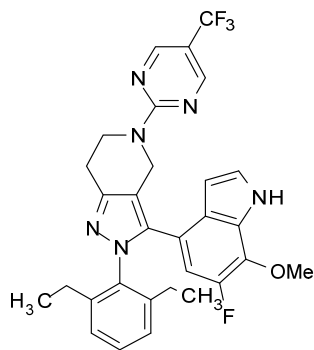
5 each R⁵ is independently selected from the group consisting of C₁₋₈ alkyl, C₁₋₈
6 alkoxy, C₁₋₈ haloalkyl, C₁₋₈ haloalkoxy, C₁₋₈ hydroxyalkyl, -C₁₋₈ alkyl-heterocycloalkyl, C₃₋₆
7 cycloalkyl, halogen, -CONR^{5a}R^{5b}, -NR^{5a}R^{5b}, and -C₁₋₈ alkylene-NR^{5a}R^{5b}, wherein each R^{5a} and
8 R^{5b} is independently selected from the group consisting of hydrogen and C₁₋₄ alkyl, or when
9 attached to the same nitrogen atom can be combined with the nitrogen atom to form a 5 or 6-
10 membered ring, wherein the heterocycloalkyl group is a 4 to 6 membered ring having from 1 to 3
11 heteroatoms as ring vertices selected from N, O, and S; and

12 each R⁴ is independently selected from the group consisting of C₁₋₄ alkyl, C₁₋₄
13 alkoxy, C₁₋₆ hydroxyalkyl, C₁₋₄ haloalkyl, halogen, cyano, hydroxyl, -NH₂, -CONR^{4a}R^{4b}, and -
14 CO₂R^{4a}.

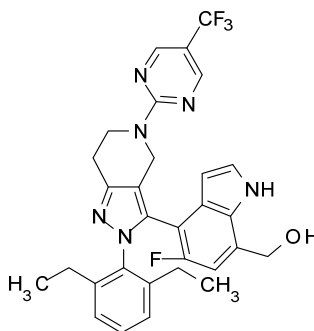
1 **30.** The compound of claim **1**, or a pharmaceutically acceptable salt thereof,
2 wherein said compound is selected from the group in **Table 3** having ++ or +++ activity.

1 **31.** A pharmaceutical composition comprising a compound of claim **1** or a
2 pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

1 **32.** The compound of claim **1**, having the structure

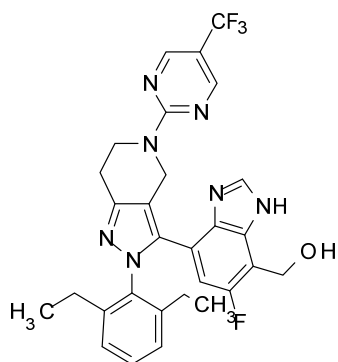


1 **33.** The compound of claim **1**, having the structure



1 **34.** The compound of claim **1**, having the structure

2



35. The compound of claim 1, having the structure

