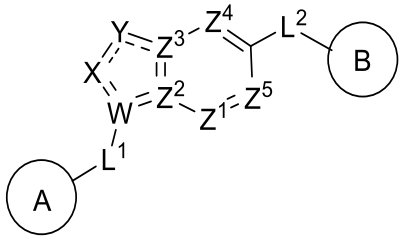
CLAIMS

1. A compound of Formula (I):



(I), or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein:

A and B are each independently cycloalkyl, heterocyclyl, aryl, or heteroaryl, each of which is optionally substituted with one or more R^1;

X is $C(R^{2a})$, O, S, N, or $N(R^{2c})$;

Y is $C(R^{2a})$, $C(R^{2a})(R^{2b})$, N, $N(R^{2c})$, O, or S, wherein at least one of X and Y is N or $N(R^{2c})$, and the bonds within the ring containing X and Y are single bonds or double bounds depending on valence;

W is C, $C(R^{2a})$, or N;

Z^1 is $C(R^{2d})$, $C(R^{2d})(R^{2e})$, or N;

Z^2 and Z^3 are each independently C or N;

Z^4 is $C(R^{2d})$ or N;

Z^5 is $C(R^{2d})$, $C(R^{2d})(R^{2e})$, N, $N(R^{2c})$, wherein the bonds within the ring containing Z^1, Z^2, Z^3, Z^4, and Z^5 are single bonds or double bounds depending on valence;

L^1 and L^2 are each absent, C_1-C_6-alkylene, C_1-C_6-heteroalkylene, -O-, -S-, -C(O)-, -$N(R^3)$-, -$N(R^3)C(O)$-, or -$C(O)N(R^3)$-, wherein each alkylene and heteroalkylene is optionally substituted with one or more R^4;

each R^1 is independently hydrogen, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, cycloalkyl, heterocyclyl, aryl, C_1-C_6 alkylene-aryl, C_1-C_6 alkenylene-aryl, C_1-C_6 alkylene-heteroaryl, heteroaryl, halo, cyano, oxo, $–OR^A$, $–NR^BR^C$, $–NR^BC(O)R^D$, $–NO_2$, $–C(O)NR^BR^C$, $–C(O)R^D$, $–C(O)OR^D$, $–S(O)_xR^D$, or $-P(O)_yR^ER^F$, wherein each alkyl, alkylene, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^5; or

two R^1 groups, together with the atoms to which they are attached, form a 3-7-membered cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^5;

R^{2a}, R^{2b}, R^{2d}, and R^{2e} are each independently hydrogen, deuterium, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, halo, cyano, cycloalkyl, heterocyclyl, aryl, heteroaryl, $–OR^A$, $–NR^BR^C$, $–NR^BC(O)R^D$, $–NO_2$, $–C(O)NR^BR^C$, $–C(O)R^D$, $–C(O)OR^D$, $–S(O)_xR^D$, or $-P(O)_yR^ER^F$, wherein each cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^5;

or R^{2d} and R^{2e} are taken together with the carbon atom to which they are attached to form a carbonyl group;

R^{2c} is hydrogen, deuterium, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, $–C(O)R^D$, $–C(O)OR^D$, or $–S(O)_xR^D$, wherein each alkyl, alkenyl, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^5;

R^3 is hydrogen, C_1-C_6-alkyl, C_1-C_6-heteroalkyl, or C_1-C_6-haloalkyl;

each R^4 is independently C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, cycloalkyl, halo, cyano, oxo, $–OR^A$, $–NR^BR^C$, $–C(O)R^D$, or $–C(O)OR^D$; wherein each C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, and cycloalkyl is optionally substituted with one or more R^9;

each R^5 is independently hydrogen, deuterium, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, halo, oxo, cyano, $–OR^A$, $–NR^BR^C$, $–NR^BC(O)R^D$, $–NO_2$, $–C(O)NR^BR^C$, $–C(O)R^D$, $–C(O)OR^D$, or $–S(O)_xR^D$, wherein each alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more R^6;

each R^6 is independently C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, halo, cyano, oxo, or $–OR^A$;

each R^A is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, aryl, heteroaryl, C_1-C_6 alkylene-aryl, C_1-C_6 alkylene-heteroaryl, cycloalkyl, heterocyclyl, $–C(O)R^D$, or $–S(O)_xR^D$; wherein each alkyl, heteroalkyl, haloalkyl, aryl, heteroaryl, cycloalkyl, and heterocyclyl is optionally substituted with one or more R^7;

each of R^B and R^C is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, or $–OR^{A1}$, wherein each alkyl, heteroalkyl, cycloalkyl, and heterocyclyl is optionally substituted with one or more R^7; or

R^B and R^C together with the atom to which they are attached form a 3-7-membered heterocyclyl ring optionally substituted with one or more R^7;

each R^D, R^E, and R^F is independently hydrogen, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, C_1-C_6 haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_6 alkylene-aryl, C_1-C_6 alkylene-heteroaryl, or $–NR^{B1}R^{C1}$, wherein each alkyl, heteroalkyl, cycloalkyl, and heterocyclyl is optionally substituted with one or more R^7;

each R^7 is independently hydrogen, deuterium, C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, halo, cyano, or oxo;

each R^9 is independently C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, halo, cyano, oxo, $–OR^A$, $–NR^BR^C$, $–C(O)R^D$, or $–C(O)OR^D$;

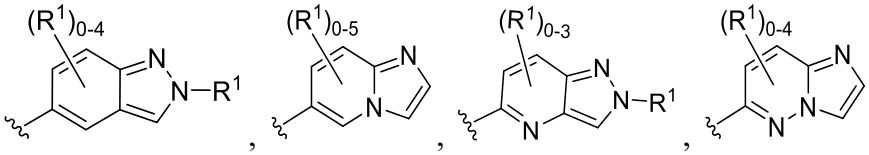
each R^{A1}, R^{B1}, and R^{C1} is hydrogen, deuterium, or C_1-C_6 alkyl;

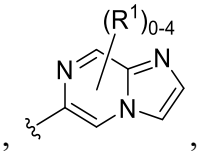
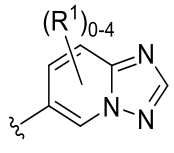
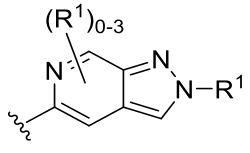
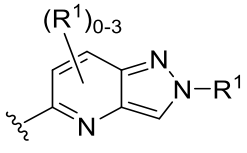
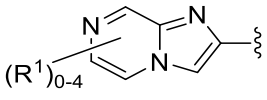
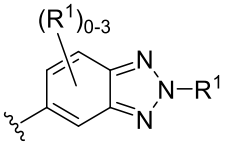
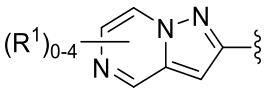
x is 0, 1, or 2; and

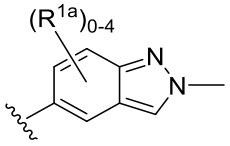
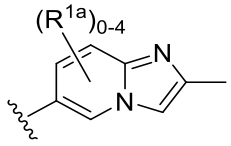
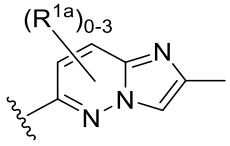
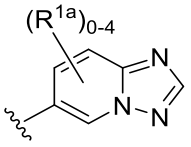
y is 1, 2, or 3.

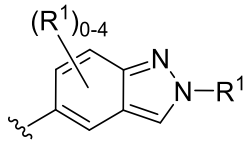
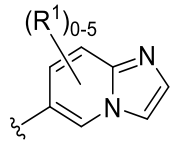
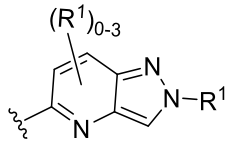
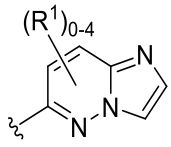
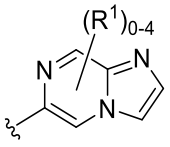
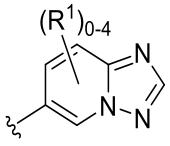
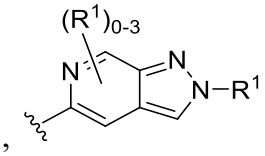
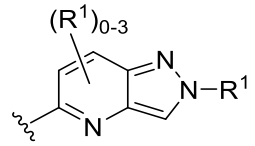
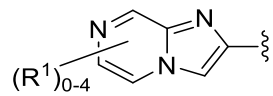
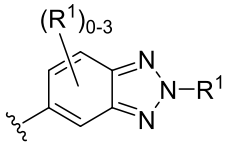
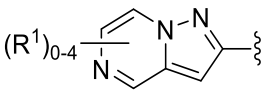
2. The compound of claim 1, wherein one of A and B is independently a bicyclic heteroaryl optionally substituted with one or more R^1.

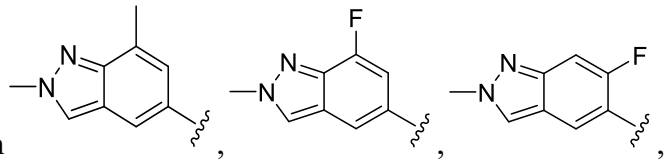
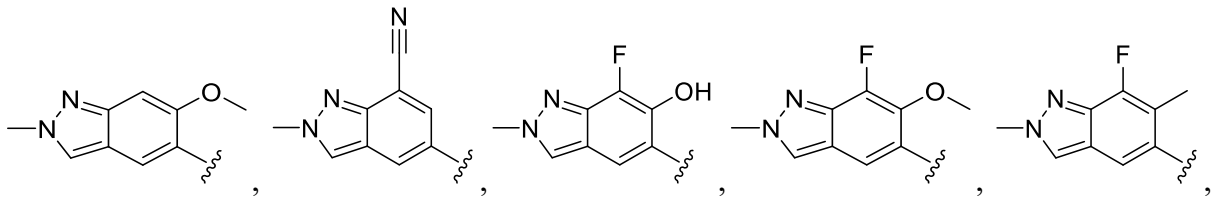
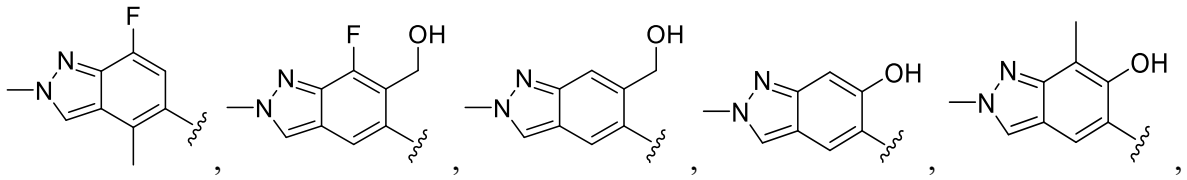
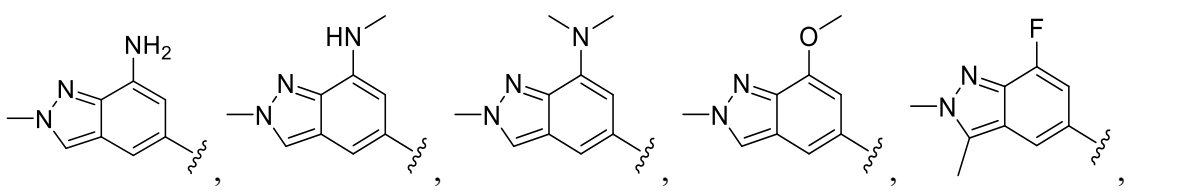
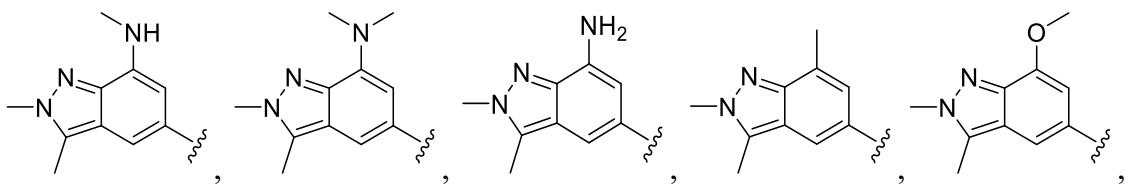
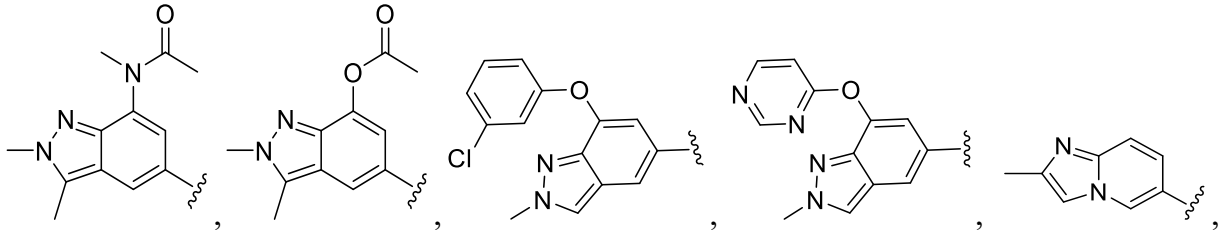
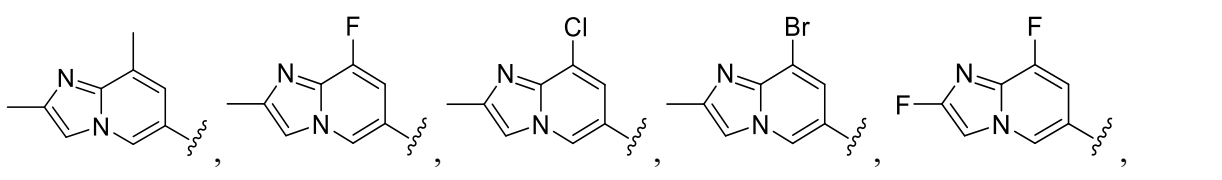
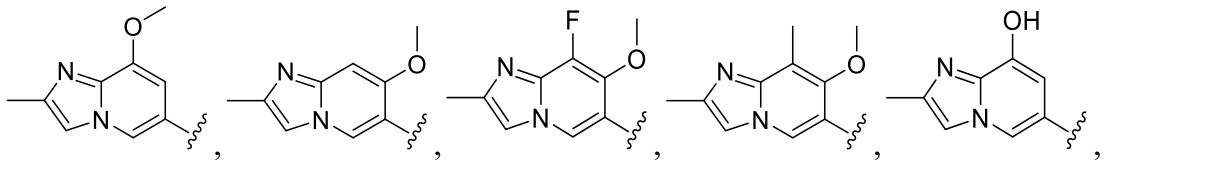
3. The compound of claim 1 or 2, wherein one of A and B is independently a nitrogen-containing heteroaryl optionally substituted with one or more R^1.

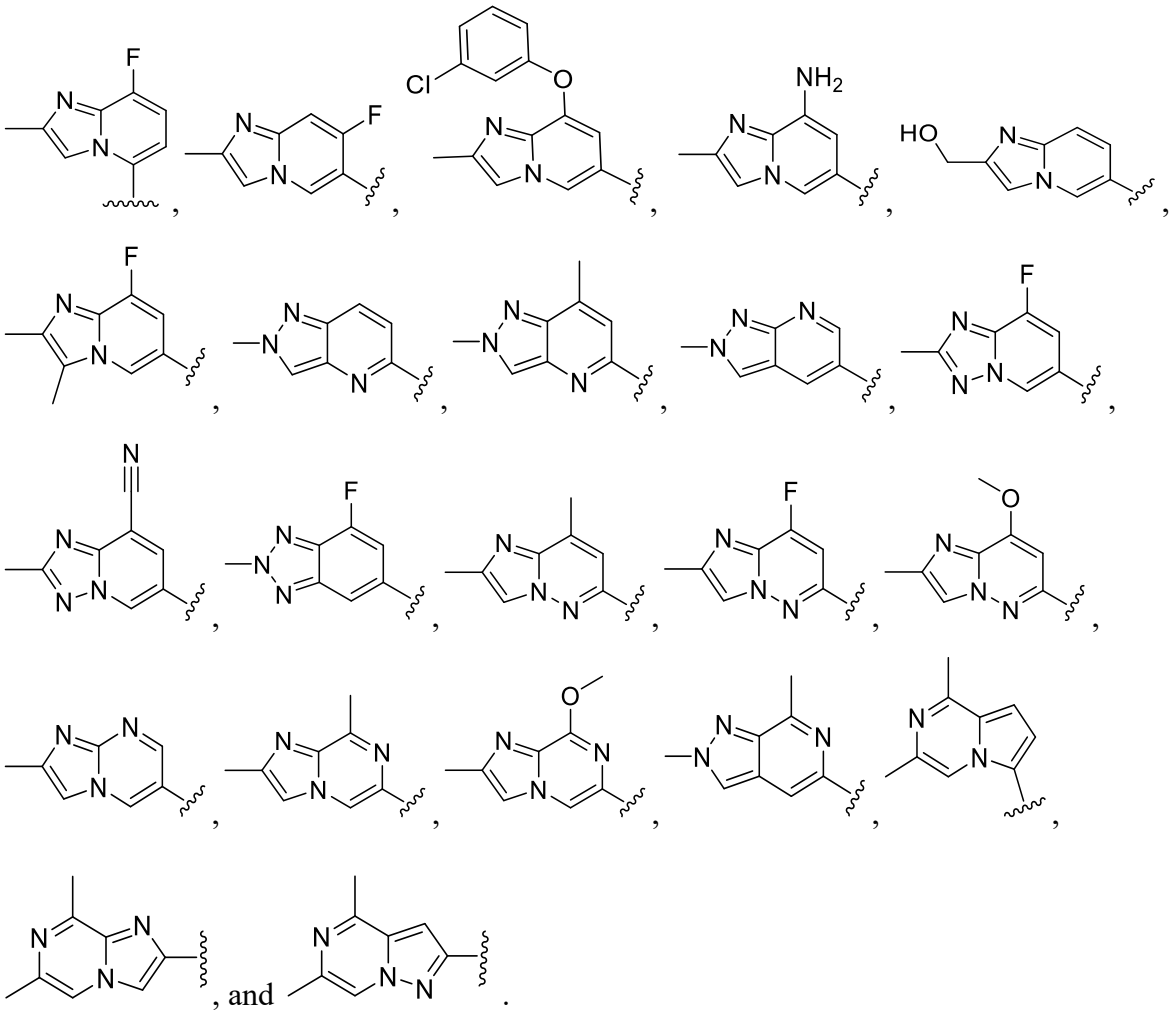
4. The compound of any one of the preceding claims, wherein one of A and B is independently selected from 

, , , , , , , and , wherein R^1 is as described in claim 1.

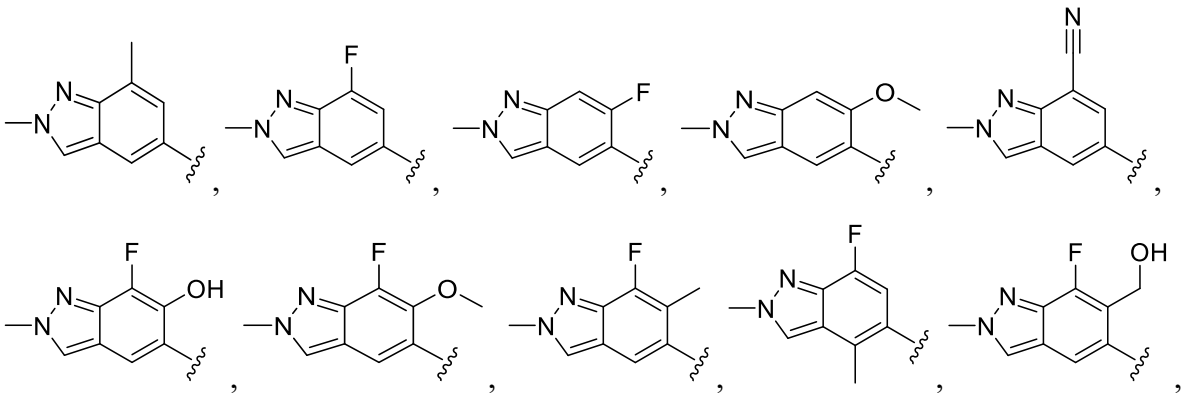
5. The compound of any one of the preceding claims, wherein one of A and B is independently selected from , , , and  wherein each R^{1a} is independently C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, halo, cyano, or $–OR^A$, and each alkyl, heteroalkyl, and haloalkyl is optionally substituted with one or more R^7.

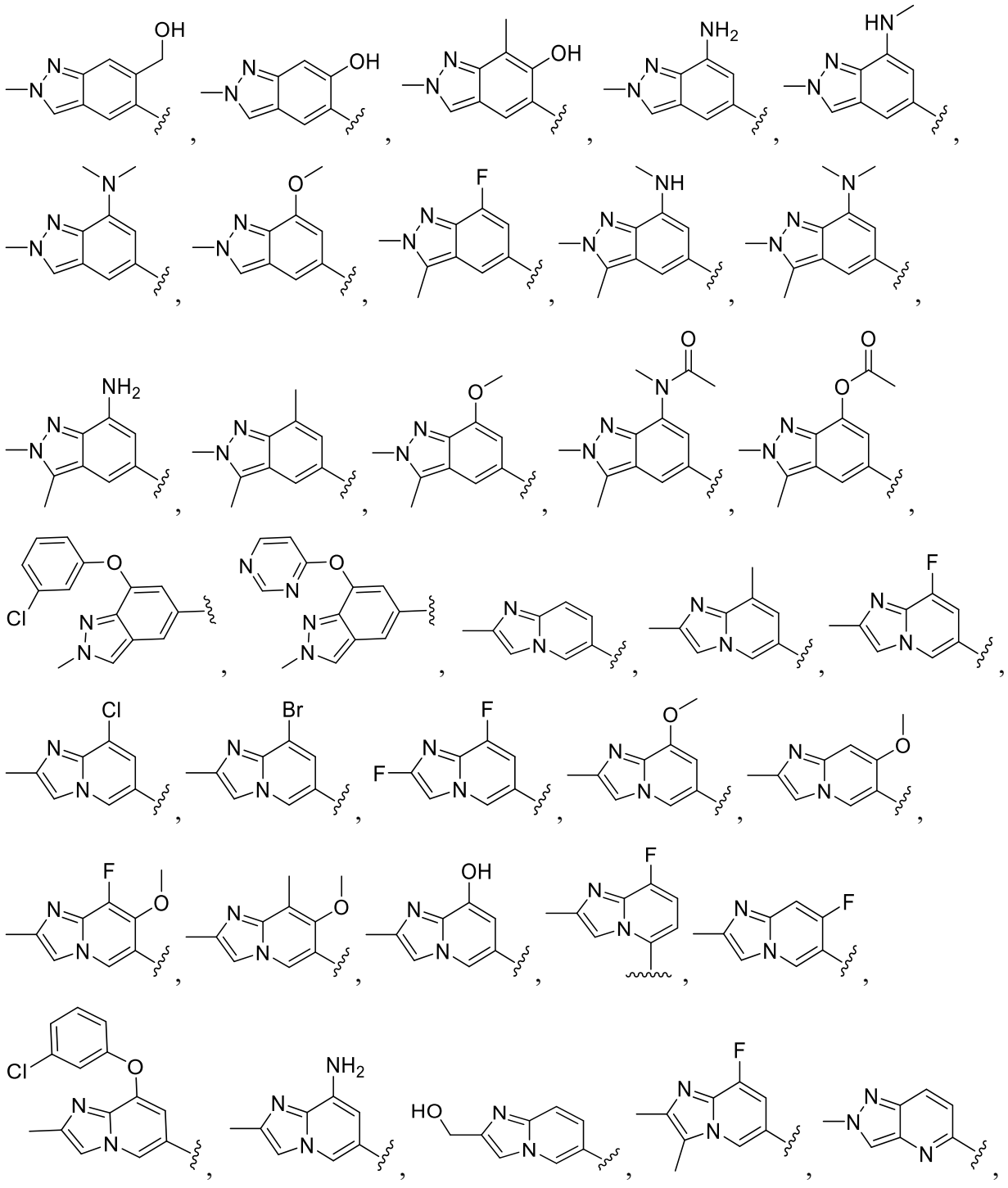
6. The compound of any one of the preceding claims, wherein A is selected from , , , , , , , , , , and , wherein R^1 is as described in claim 1.

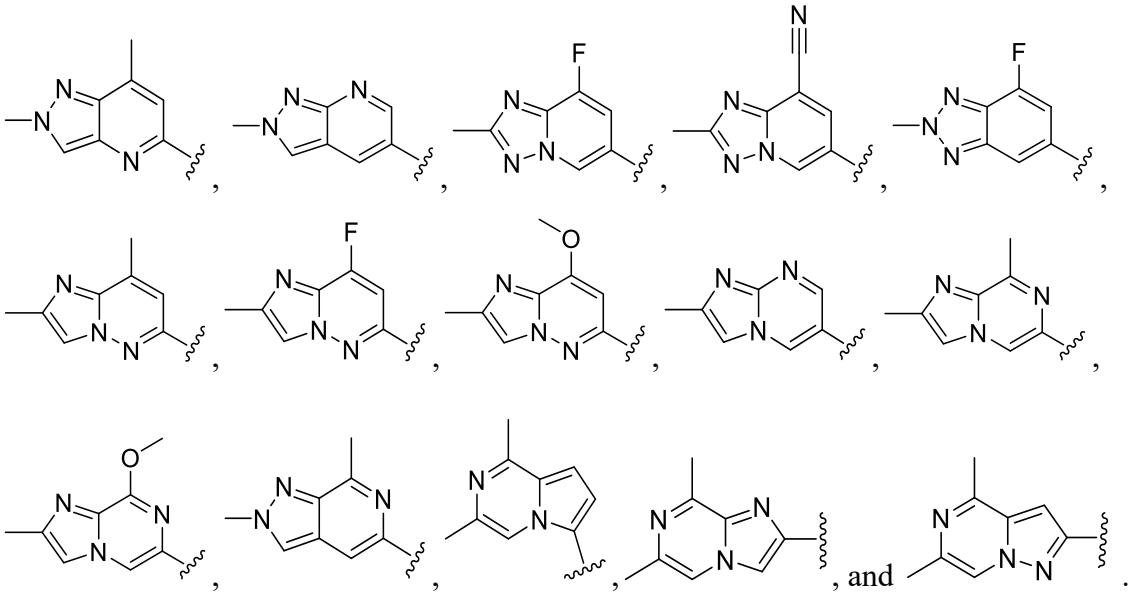
7. The compound of any one of the preceding claims, wherein one of A and B is independently selected from , , , , , , , 

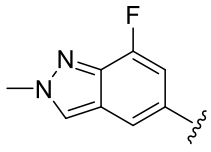
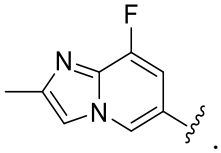


8. The compound of any one of the preceding claims, wherein A is selected from



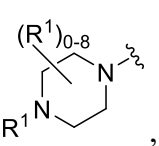
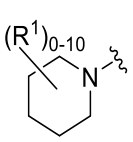
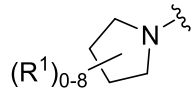
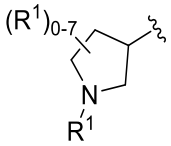
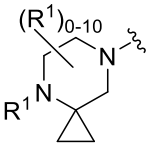
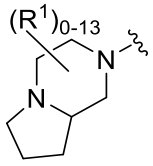
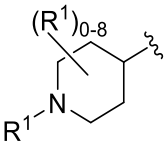


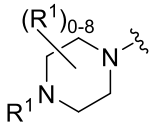
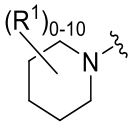
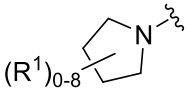
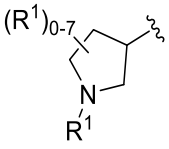
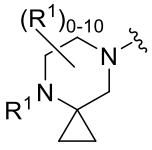
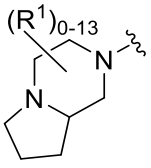
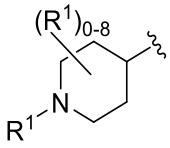


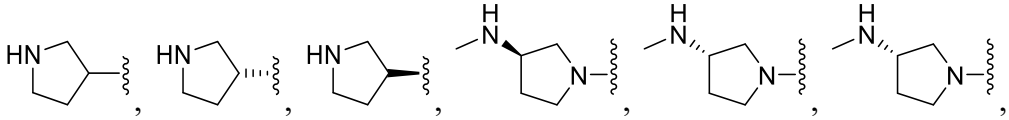
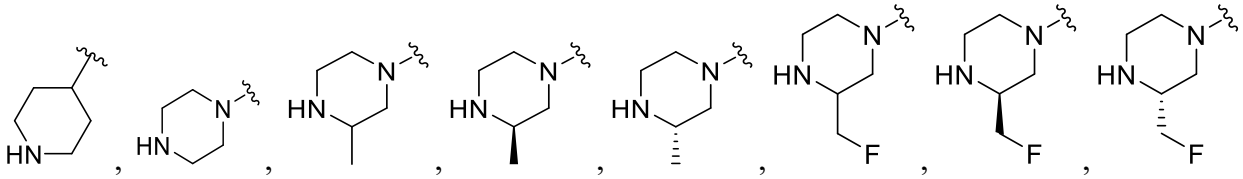
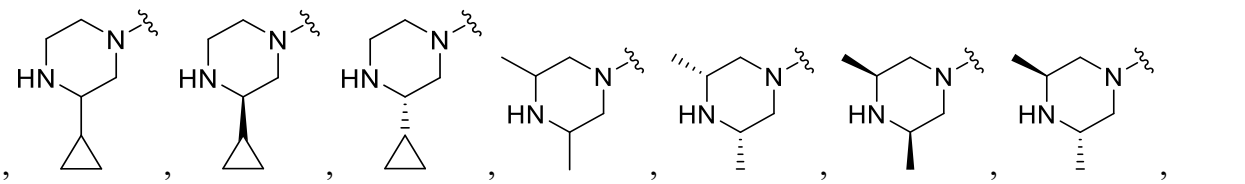
9. The compound of any one of the preceding claims, wherein A is  or .

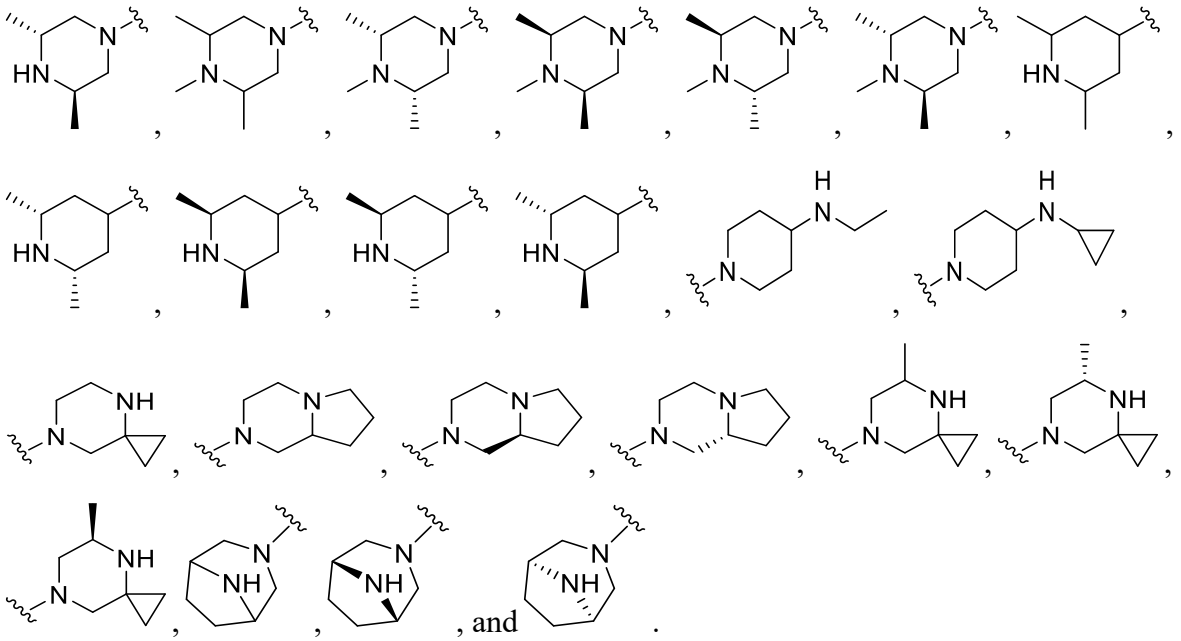
10. The compound of any one of the preceding claims, wherein one of A and B is independently a monocyclic heterocyclyl or bicyclic heterocyclyl, each of which is optionally substituted with one or more R^1.

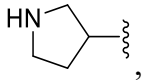
11. The compound of any one of the preceding claims, wherein one of A and B is independently a nitrogen-containing heterocyclyl optionally substituted with one or more R^1.

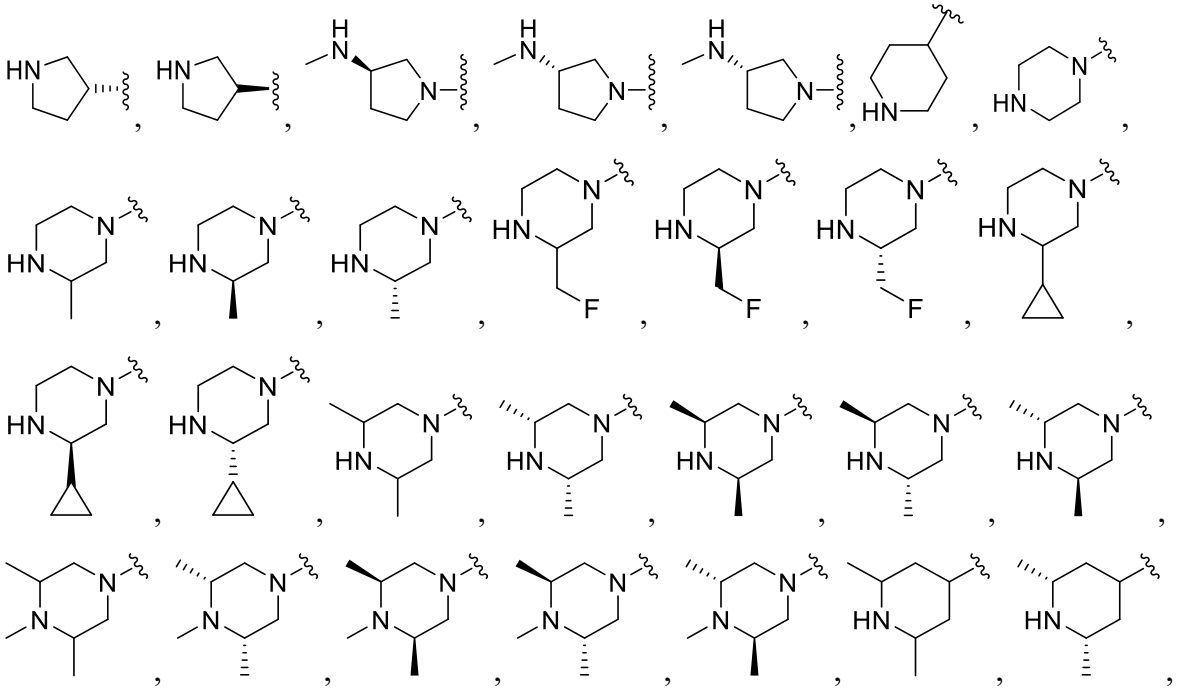
12. The compound of any one of the preceding claims, wherein one of A and B is independently selected from , , , , , , and , wherein R^1 is as described in claim 1.

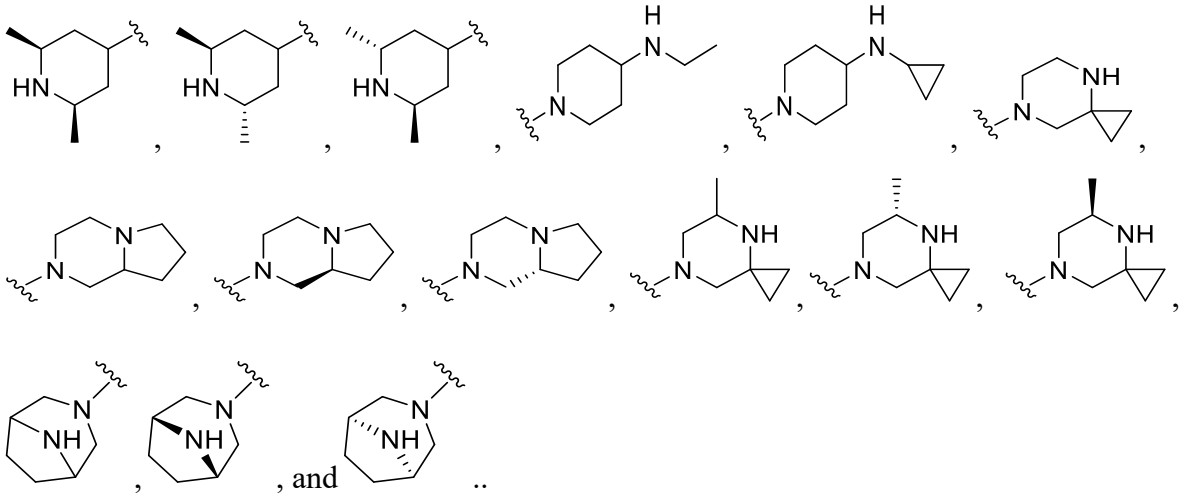
13. The compound of any one of the preceding claims, wherein B is selected from , , , , , , and , wherein R^1 is as described in claim 1.

14. The compound of any one of the preceding claims, wherein one of A and B is independently selected from , , .



15. The compound of any one of the preceding claims, wherein B is selected from ,





16. The compound of any one of the preceding claims, wherein L^1 is absent or $N(R^3)$- (e.g., -NH or $-NCH_3$).

17. The compound of any one of the preceding claims, wherein L^2 is absent, $-N(R^3)-$, or -O-,.

18. The compound of any one of the preceding claims, wherein L^1 is $-N(R^3)-$ and L^2 is absent.

19. The compound of any one of the preceding claims, wherein X is N.

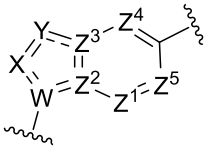
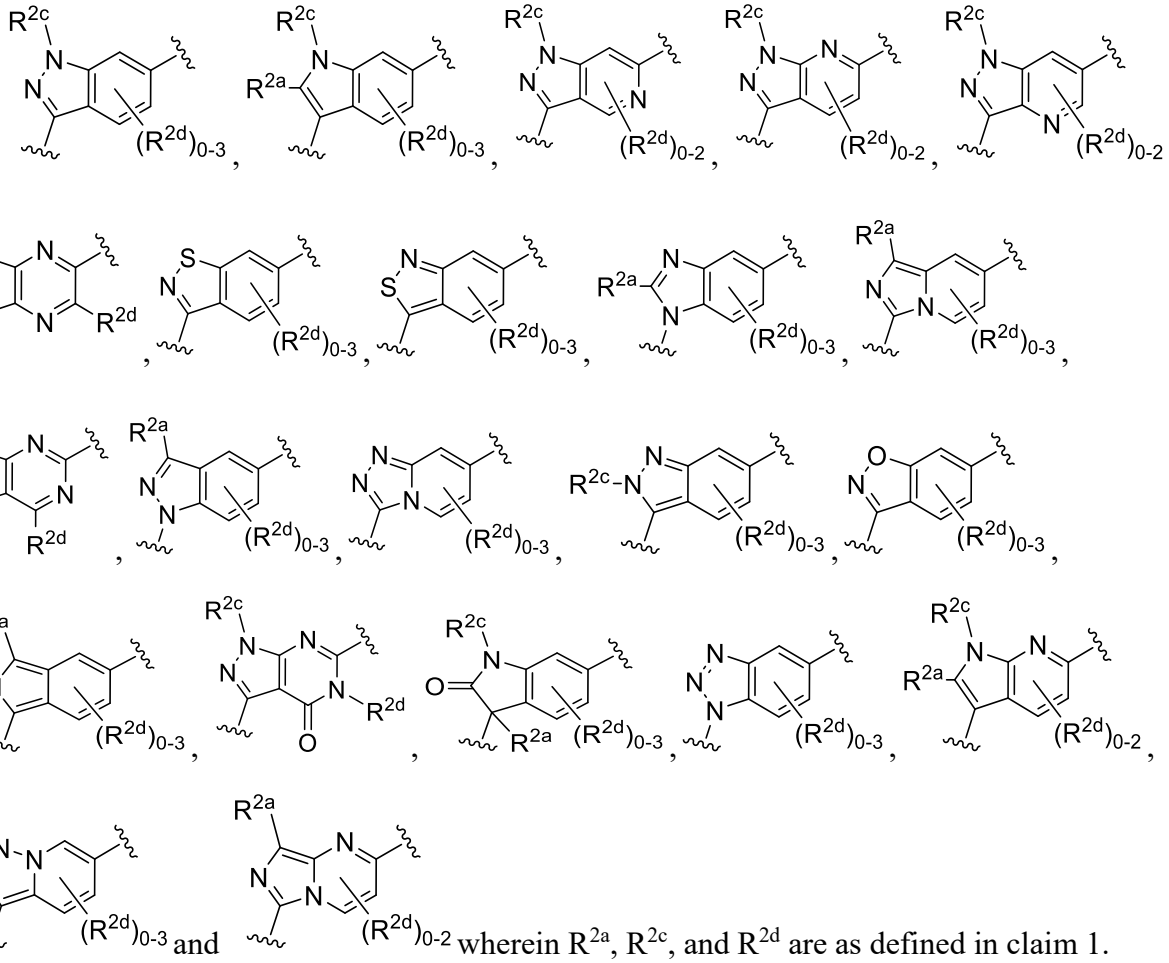
20. The compound of any one of the preceding claims, wherein Y is $C(R^{2a})$, $N(R^{2c})$, or N.

21. The compound of any one of the preceding claims, wherein W is C.

22. The compound of any one of the preceding claims, wherein at least one of Z^1, Z^2, Z^3, Z^4, and Z^5 is independently N.

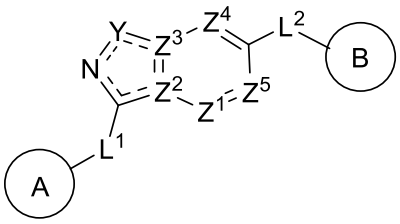
23. The compound of any one of the preceding claims, wherein Z^2 is N.

24. The compound of any one of the preceding claims, wherein Z^1, Z^2, Z^3, Z^4, and Z^5 are each independently C or C(R^{2d}).

25. The compound of any one of the preceding claims wherein  is selected from: , wherein R^{2a}, R^{2c}, and R^{2d} are as defined in claim 1.

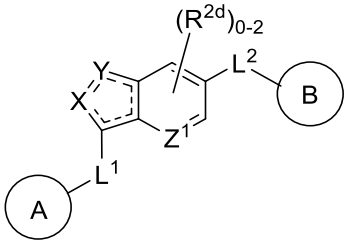
26. The compound of any one of the preceding claims, wherein the compound of Formula (I) is a compound of:

(i) Formula (I-ai):



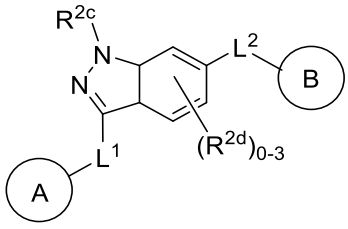
(I-ai), or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein A, B, Y, Z^1, Z^2, Z^3, Z^4, Z^5, L^1, L^2, and variables therein are as defined in claim 1;

(ii) Formula (I-b):



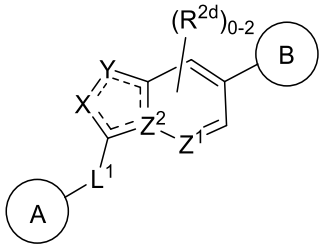
(I-b), or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein A, B, X, Y, Z^1, L^1, L^2, and variables therein are as defined in claim 1, and each R^{2d} is hydrogen, C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, halo, or $–OR^{A1}$;

(iii) Formula (I-c):



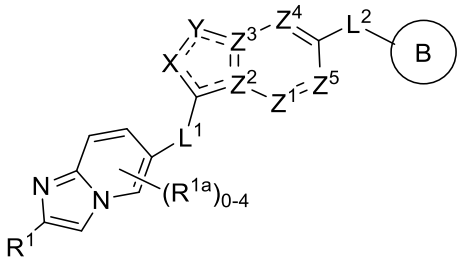
(I-c), or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein A, B, L^1, L^2, R^{2c}, R^{2d}, and variables therein are as defined in claim 1, and each R^{2d} is hydrogen, C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, halo, or $–OR^{A1}$;

(iv) Formula (I-d):



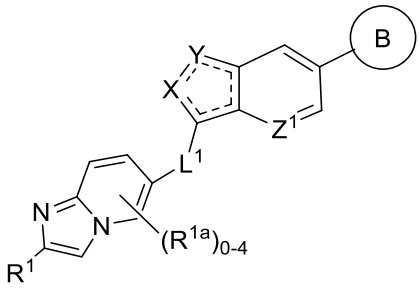
(I-d), or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein A, B, X, Y, Z^1, Z^2, L^1, and variables therein are as defined in claim 1;

(v) Formula (I-e):



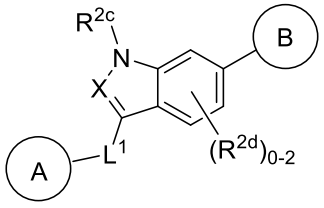
(I-e), or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein each R^{1a} is independently C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, halo, cyano, or $–OR^A$, and each alkyl, heteroalkyl, and haloalkyl is optionally substituted with one or more R^7; and wherein B, X, Y, Z^1, Z^2, Z^3, Z^4, Z^5, L^1, L^2, and variables therein are as defined in claim 1;

(vi) Formula (I-f):



(I-f), or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein each R^{1a} is independently C_1-C_6-alkyl, C_1-C_6-heteroalkyl, C_1-C_6-haloalkyl, halo, cyano, or $–OR^A$, and each alkyl, heteroalkyl, and haloalkyl is optionally substituted with one or more R^7; and wherein B, X, Y, L^1, Z^1, and variables therein are as described in claim 1; or

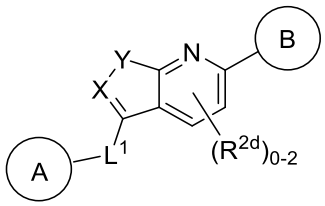
(vii) Formula (I-g):



(I-g), or a pharmaceutically acceptable salt thereof, wherein A, B, X, L^1, R^{2c}, and R^{2d} are as defined in claim 1.

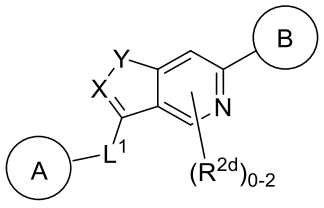
27. The compound of any one of the preceding claims, wherein the compound of Formula (I) is a compound of:

(i) Formula (I-h):



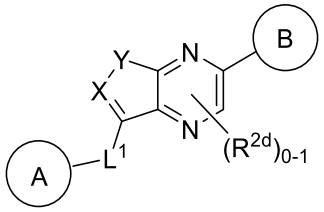
(I-h), or a pharmaceutically acceptable salt thereof, wherein each of A, B, X, Y, L^1, and R^{2d} are as defined in claim 1;

(ii) Formula (I-i):



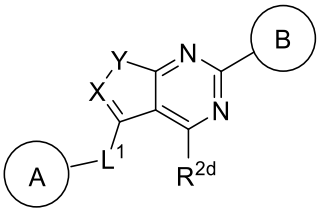
(I-i), or a pharmaceutically acceptable salt thereof, wherein each of A, B, X, Y, L^1, and R^{2d} are as defined in claim 1;

(iii) Formula (I-j):



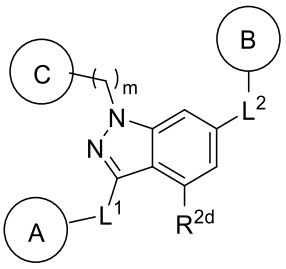
(I-j), or a pharmaceutically acceptable salt thereof, wherein each of A, B, X, Y, L^1, and R^{2d} are as defined in claim 1; or

(iv) Formula (I-k):



(I-k), or a pharmaceutically acceptable salt thereof, wherein each of A, B, X, Y, L^1, and R^{2d} are as defined in claim 1.

28. The compound of any one of the preceding claims, wherein the compound of Formula (I) is a compound of Formula (I-l):



, (I-l), or a pharmaceutically acceptable salt thereof, wherein each of A, B, X, Y, L^1, L^2, and R^{2d} are as defined in claim 1; and m is 0, 1, 2, 3, 4, 5, or 6.

29. The compound of any one of the preceding claims, wherein the compound is selected from a compound listed in Table 1 or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof.

30. A pharmaceutical composition comprising a compound of any one of claims 1-29 and a pharmaceutically acceptable excipient.

31. The compound of any one of claims 1-29 or the pharmaceutical composition of claim 30, wherein the compound alters, binds to, or stabilizes a target nucleic acid (e.g., an RNA, e.g., a pre-mRNA).

32. The compound of any one of claims 1-29 or the pharmaceutical composition of claim 30, wherein the compound increases or decreases splicing at splice site on a target nucleic acid (e.g., an RNA, e.g., a pre-mRNA), by about 0.5%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 15%,

20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or more, e.g., as determined by qPCR.

33. A method of modulating splicing of a nucleic acid (e.g., DNA, RNA, e.g., a pre-mRNA) comprising contacting the nucleic acid with a compound of Formula (I) as described in any one of claims 1-29 or the pharmaceutical composition of claim 30.

34. A method of forming a complex comprising a component of a spliceosome (e.g., a major spliceosome component or a minor spliceosome component), a nucleic acid (e.g., a DNA, RNA, e.g., a pre-mRNA), and a compound of Formula (I) as described in any one of claims 1-29, comprising contacting the nucleic acid (e.g., a DNA, RNA, e.g., a pre-mRNA) with a compound of Formula (I).

35. A method of altering the conformation of a nucleic acid (e.g., a DNA, RNA, e.g., a pre-mRNA) comprising contacting the nucleic acid with a compound of Formula (I) as described in any one of claims 1-29.

36. The method of claim 35, wherein the altering comprises:
(i) forming a bulge in the nucleic acid;
(ii) stabilizing a bulge in the nucleic acid; and/or
(iii) reducing a bulge in the nucleic acid.

37. A method of treating a disease or disorder in a subject comprising administering to the subject a compound of Formula (I) as described in any one of claims 1-29 or the pharmaceutical composition of claim 30.

38. A composition for use in treating a disease or disorder in a subject comprising a compound of Formula (I) as described in any one of claims 1-29 or the pharmaceutical composition of claim 30.

39. The composition for use of claim 38, wherein the disease or disorder comprises a proliferative disease (e.g., cancer, a benign neoplasm, or angiogenesis); or a neurological disease or disorder, autoimmune disease or disorder, immunodeficiency disease or disorder, lysosomal storage disease or disorder, cardiovascular disease or disorder, metabolic disease or disorder, respiratory disease or disorder, renal disease or disorder, or infectious disease.