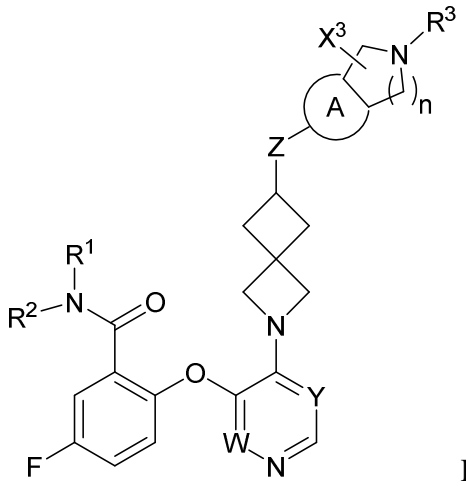
CLAIMS

What is claimed is:

1. A compound of Formula (I),



Formula (I),

a stereoisomer, or a pharmaceutically acceptable salt thereof, wherein:

W is N or CH;

Y is N or CH;

R^1 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl is optionally substituted with one or more halo, OH, oxo, CN, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or $N(R^{4a'})(R^{4b'})$;

R^2 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl is optionally substituted with one or more halo, OH, oxo, CN, or $N(R^{4a'})(R^{4b'})$;

R^1 and R^2 optionally form a 3- to 12-membered heterocyclyl, wherein the heterocyclyl is optionally substituted with one or more C_1-C_6 alkyl, halo, OH, or CN;

Z is O, CH_2, or NH;

Ring A is 6- to 10-membered aryl or 6- to 10-membered heteroaryl, wherein the 6- to 10-membered aryl or 6- to 10-membered heteroaryl is optionally substituted with one or more C_1-C_6 alkyl, halo, OH, CN, or C_1-C_6 alkoxy;

X^3 is H or C_1-C_6 alkyl, wherein the C_1-C_6 alkyl is optionally substituted with one or more halo, 3- to 12-membered heterocyclyl, $S(=O)_2R^{4a}$, OR^{4a}, oxo, CN, $C(=O)N(R^{4a})(R^{4b})$, or $N(R^{4a})(R^{4b})$;

R^3 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl is optionally substituted with one or more R^{3a}, or

R^3 forms a 3- to 12-membered heterocyclyl with the carbon atom next to the nitrogen atom to which it is connected, wherein the 3- to 12-membered heterocyclyl is optionally substituted with one or more R^{3a};

each R^{3a} is independently halo, OR^{4a}, oxo, $C(O)O(R^{4a})$, CN, $C(=O)N(R^{4a})(R^{4b})$, $OC(O)N(R^{4a})(R^{4b})$, $S(=O)_2R^{4b'}$, $N(R^{4a})(R^{4b})$, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, C_1-C_6 alkoxy, C_6-C_{10} aryl, 3- to 12-membered heterocyclyl, or 5- to 10-membered heteroaryl, wherein the C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 3- to 12-membered heterocyclyl or 5- to 10-membered heteroaryl is optionally substituted with one or more substituent independently selected from halo, $O(R^{4a'})$, oxo, CN, $C(O)OR^{4a'}$, $OC(O)N(R^{4a'})(R^{4b'})$, $N(R^{4a'})(R^{4b'})$, $N(R^{4a'})C(O)(R^{4b'})$, $N(R^{4a'})C(O)O(R^{4b'})$, C_1-C_6 alkyl that is optionally substituted with $O(R^{4a})$, and 3- to 12-membered heterocyclyl that is optionally substituted with oxo;

each R^{4a} is independently H, CN, or C_1-C_6 alkyl optionally substituted with one or more halo, C_6-C_{10} aryl or $N(R^{4a'})(R^{4b'})$;

each R^{4b} is independently H, $S(=O)_2R^{4b'}$, $C(O)OR^{4b'}$, $C(O)R^{4b'}$, $C(O)NR^{4a'}R^{4b'}$, $C(O)CH_2$-$N(R^{4a'})(R^{4b'})$, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, $C_{6\text{-}10}$ aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl, wherein the C_1-C_6 alkyl is optionally substituted with C_1-C_6 alkoxy or $C(O)N(R^{4a'})(R^{4b'})$;

each $R^{4a'}$ and $R^{4b'}$ is independently H, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, or 3- to 12-membered heterocyclyl; and

n is 1, 2, or 3.

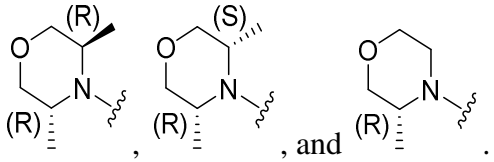
2. The compound of claim 1, wherein R^2 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl is optionally substituted with one or more halo, OH, oxo, CN, or $N(R^{4a'})(R^{4b'})$.

3. The compound of claim 1 or 2, wherein R^2 is C_1-C_6 alkyl, wherein the C_1-C_6 alkyl is optionally substituted with one or more halo, OH, oxo, CN, or $N(R^{4a'})(R^{4b'})$.

4. The compound of any one of the preceding claims, wherein R^2 is isopropyl.

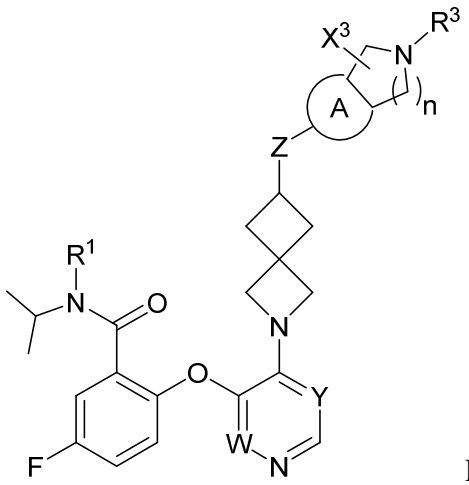
5. The compound of any one of the preceding claims, wherein R^1 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl is optionally substituted with one or more halo, OH, oxo, CN, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or $N(R^{4a'})(R^{4b'})$.

6. The compound of claim 1, wherein R^1 and R^2 form a group selected from:



, , and .

7. A compound of Formula (II),



Formula (II),

a stereoisomer, or a pharmaceutically acceptable salt thereof, wherein:

W is N or CH;

Y is N or CH;

R^1 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl, wherein the C_1-

C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl is optionally substituted with one or more halo, OH, oxo, CN, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or $N(R^{4a'})(R^{4b'})$;

Z is O, CH_2, or NH;

Ring A is 6- to 10-membered aryl or 6- to 10-membered heteroaryl, wherein the 6- to 10-membered aryl or 6- to 10-membered heteroaryl is optionally substituted with one or more C_1-C_6 alkyl, halo, OH, CN, or C_1-C_6 alkoxy;

X^3 is H or C_1-C_6 alkyl, wherein the C_1-C_6 alkyl is optionally substituted with one or more halo, 3- to 12-membered heterocyclyl, $S(=O)_2R^{4a}$, OR^{4a}, oxo, CN, $C(=O)N(R^{4a})(R^{4b})$, or $N(R^{4a})(R^{4b})$;

R^3 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl is optionally substituted with one or more R^{3a}, or

R^3 forms a 3- to 12-membered heterocyclyl with the carbon atom next to the nitrogen atom to which it is connected, wherein the 3- to 12-membered heterocyclyl is optionally substituted with one or more R^{3a};

each R^{3a} is independently halo, OR^{4a}, oxo, $C(O)O(R^{4a})$, CN, $C(=O)N(R^{4a})(R^{4b})$, $OC(O)N(R^{4a})(R^{4b})$, $S(=O)_2R^{4b'}$, $N(R^{4a})(R^{4b})$, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, C_1-C_6 alkoxy, C_6-C_{10} aryl, 3- to 12-membered heterocyclyl, or 5- to 10-membered heteroaryl, wherein the C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 3- to 12-membered heterocyclyl or 5- to 10-membered heteroaryl is optionally substituted with one or more substituent independently selected from halo, $O(R^{4a'})$, oxo, CN, $C(O)OR^{4a'}$, $OC(O)N(R^{4a'})(R^{4b'})$, $N(R^{4a'})(R^{4b'})$, $N(R^{4a'})C(O)(R^{4b'})$, $N(R^{4a'})C(O)O(R^{4b'})$, C_1-C_6 alkyl that is optionally substituted with $O(R^{4a})$, and 3- to 12-membered heterocyclyl that is optionally substituted with oxo;

each R^{4a} is independently H, CN, or C_1-C_6 alkyl optionally substituted with one or more halo, C_6-C_{10} aryl or $N(R^{4a'})(R^{4b'})$;

each R^{4b} is independently H, $S(=O)_2R^{4b'}$, $C(O)OR^{4b'}$, $C(O)R^{4b'}$, $C(O)NR^{4a'}R^{4b'}$, $C(O)CH_2$-$N(R^{4a'})(R^{4b'})$, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, $C_{6\text{-}10}$ aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl, wherein the C_1-C_6 alkyl is optionally substituted with C_1-C_6 alkoxy or $C(O)N(R^{4a'})(R^{4b'})$;

each $R^{4a'}$ and $R^{4b'}$ is independently H, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, or 3- to 12-membered heterocyclyl; and

n is 1, 2, or 3.

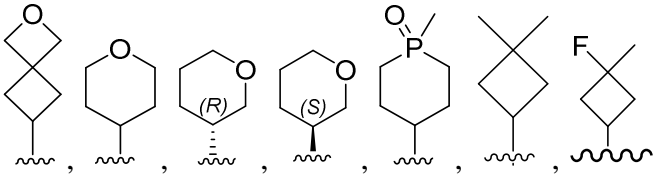
8. The compound of any one of the preceding claims, wherein W is N.

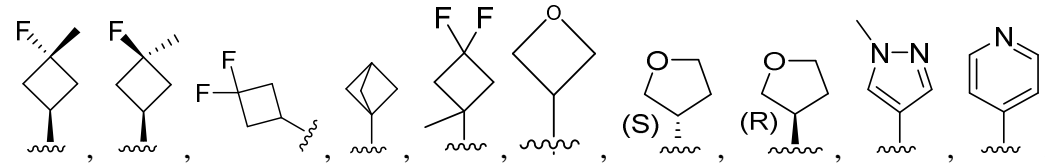
9. The compound of any one of the preceding claims, wherein W is CH.

10. The compound of any one of the preceding claims, wherein Y is N.

11. The compound of any one of the preceding claims, wherein Y is CH.

12. The compound of any one of claims 1-5 or 7-11, wherein R^1 is C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, or 3- to 12-membered heterocyclyl, wherein the C_1-C_6 alkyl, the C_3-C_{12} cycloalkyl, or the 3- to 12-membered heterocyclyl is optionally substituted with one or more halo, OH, oxo, CN, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or $N(R^{4a'})(R^{4b'})$.

13. The compound of any one of claims 1-5 or 7-12, wherein R^1 is methyl, ethyl, isopropyl, 2,2-difluoroethyl, -CH_2-CN, -CH_2-phenyl, 

, 

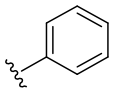
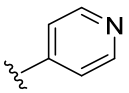
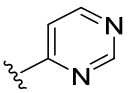
, cyclobutyl substituted by one OH and one methyl group, cyclobutyl substituted by one CN and one methyl group, cyclobutyl substituted by one methoxy group, cyclobutyl substituted by one 1H-pyrazol-1-yl group, cyclobutyl substituted by one 1H-imidazol-1-yl group, or cyclobutyl substituted by one 1H-imidazol-1-yl group and one methyl group.

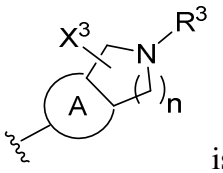
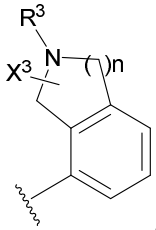
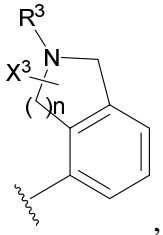
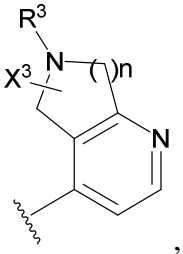
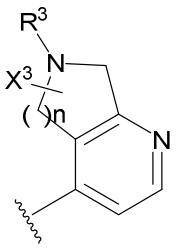
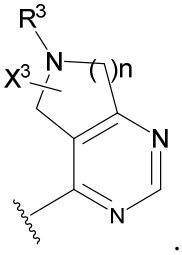
14. The compound of any one of the preceding claims, wherein Z is O.

15. The compound of any one of claims 1-13, wherein Z is CH_2.

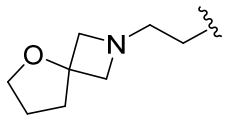
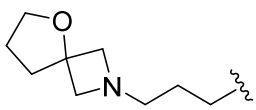
16. The compound of any one of claims 1-13, wherein Z is NH.

17. The compound of any one of the preceding claims, wherein Ring A is 6- to 10-membered aryl or 6- to 10-membered heteroaryl.

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

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

20. The compound of any one of the preceding claims, wherein X^3 is H or C_1-C_6 alkyl.

21. The compound of any one of claims 1-19, wherein X^3 is methyl, -CH_2-OCH_3, -CH_2-CH_2-OCH_3, -CH_2-CH_2-CH_2-OCH_3, -CH_2-O-CH_2-CHF_2, -CH_2-CH_2-CH_2-O-CHF_2, -CH_2-O-CH_2-CH_2-$N(CH_3)_2$, -CH_2-CH_2-S(O)$_2$-CH_3, -CH_2-CH_2-CH_2-S(O)$_2$-CH_3, -CH_2-CH_2-NH-C(O)-CH_3, -CH_2-CH_2-NH-S(O)$_2$-CH_3, , or .

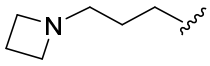
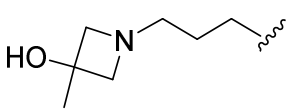
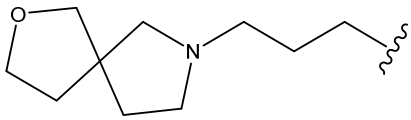
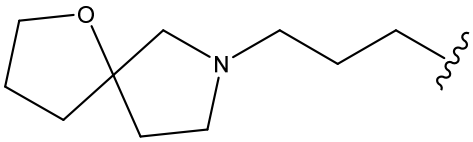
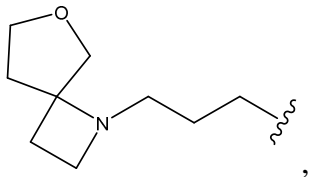
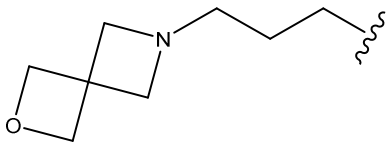
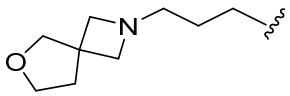
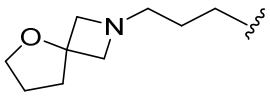
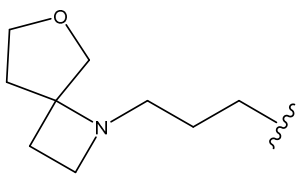
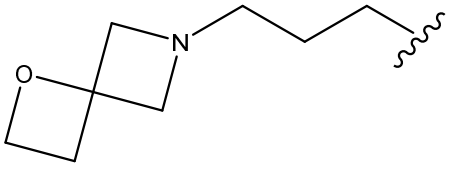
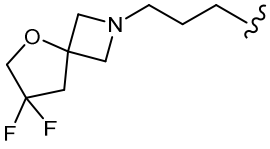
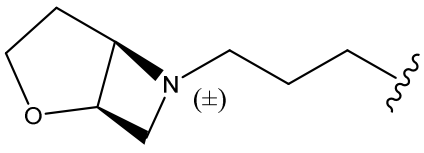
22. The compound of any one of the preceding claims, wherein R^3 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl is optionally substituted with one or more R^{3a}, wherein:

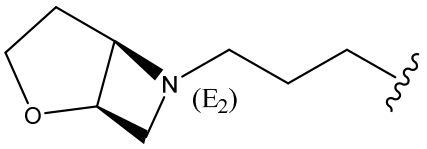
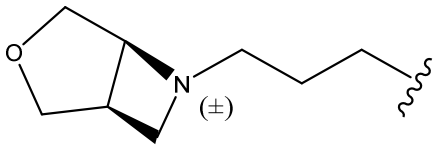
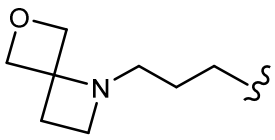
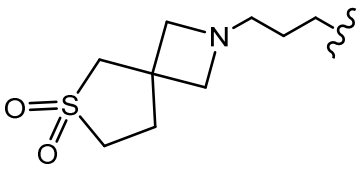
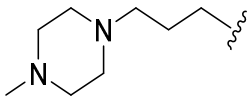
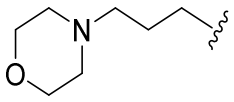
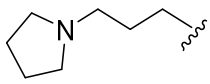
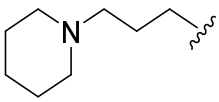
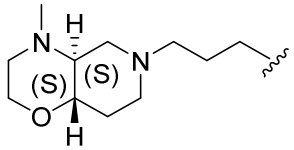
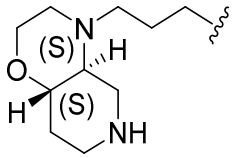
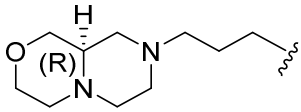
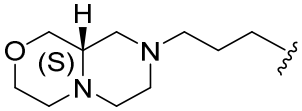
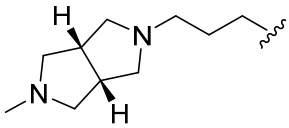
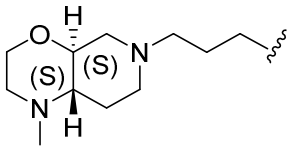
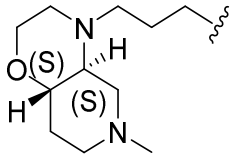
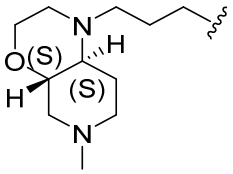
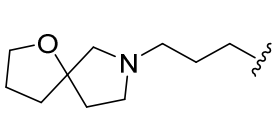
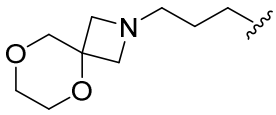
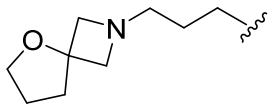
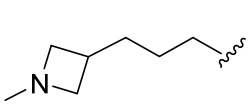
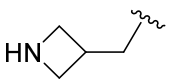
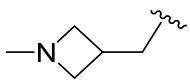
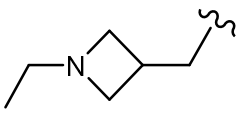
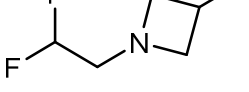
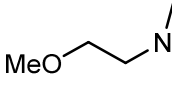
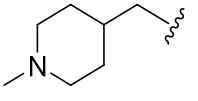
each R^{3a} is independently halo, OR^{4a}, oxo, $C(O)O(R^{4a})$, CN, $C(=O)N(R^{4a})(R^{4b})$, $OC(O)N(R^{4a})(R^{4b})$, $S(=O)_2R^{4b'}$, $N(R^{4a})(R^{4b})$, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, C_1-C_6 alkoxy, C_6-C_{10} aryl, 3- to 12-membered heterocyclyl, or 5- to 10-membered heteroaryl, wherein the C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, C_6-C_{10} aryl, 3- to 12-membered heterocyclyl or 5- to 10-membered heteroaryl is optionally substituted with one or more substituent independently selected from halo, $O(R^{4a'})$, oxo, CN, $C(O)OR^{4a'}$, $OC(O)N(R^{4a'})(R^{4b'})$, $N(R^{4a'})(R^{4b'})$, $N(R^{4a'})C(O)(R^{4b'})$, $N(R^{4a'})C(O)O(R^{4b'})$, C_1-C_6 alkyl that is optionally substituted with $O(R^{4a})$, and 3- to 12-membered heterocyclyl that is optionally substituted with oxo;

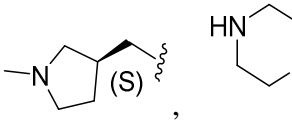
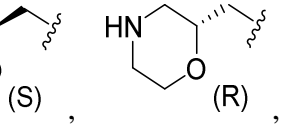
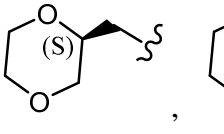
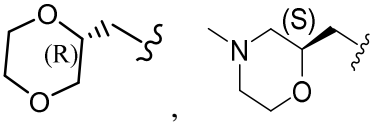
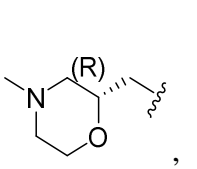
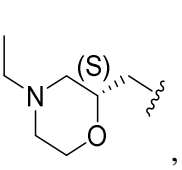
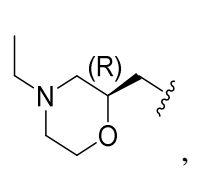
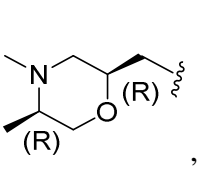
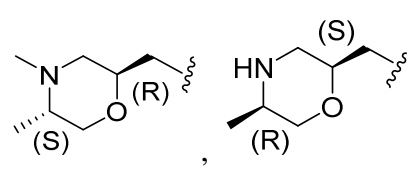
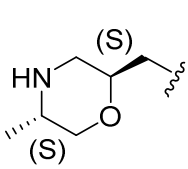
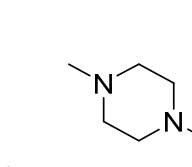
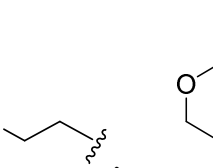
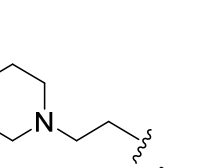
each R^{4a} is independently H, CN, or C_1-C_6 alkyl optionally substituted with one or more halo, C_6-C_{10} aryl or $N(R^{4a'})(R^{4b'})$;

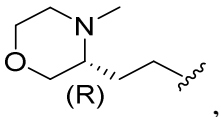
each R^{4b} is independently H, $S(=O)_2R^{4b'}$, $C(O)OR^{4b'}$, $C(O)R^{4b'}$, $C(O)NR^{4a'}R^{4b'}$, $C(O)CH_2$-$N(R^{4a'})(R^{4b'})$, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, $C_{6\text{-}10}$ aryl, 5- to 10-membered heteroaryl, or 3- to 12-membered heterocyclyl, wherein the C_1-C_6 alkyl is optionally substituted with C_1-C_6 alkoxy or $C(O)N(R^{4a'})(R^{4b'})$; and

each $R^{4a'}$ and $R^{4b'}$ is independently H, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, or 3- to 12-membered heterocyclyl.

23. The compound of any one of claims 1-22, wherein R^3 is H, methyl, ethyl, isopropyl, -CH_2-CH_2-$N(CH_3)_2$, -CH_2-CH_2-CH_2-$N(CH_3)_2$, -CH_2-CH_2-CH_2-CH_2-$N(CH_3)_2$, -CH_2-CH_2-CH_2-CH_2-$N(CH_3)_2$, -CH_2-CH_2-$S(=O)_2Me$, -CH_2-CH_2-CH_2-$S(=O)_2Me$, , , , , , , , , , , , 



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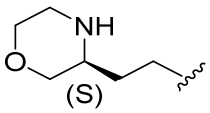

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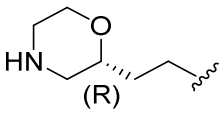

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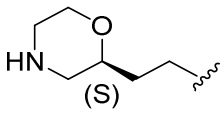

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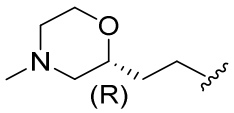

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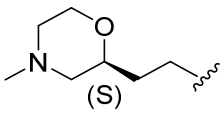

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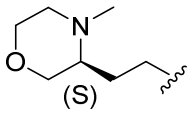

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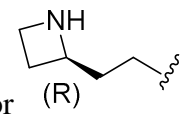

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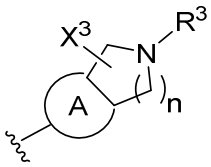
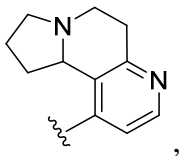
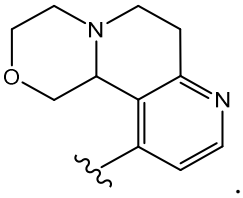
24. The compound of any one of claims 1-21, wherein R^3 forms a 3- to 12-membered heterocyclyl with the carbon atom next to the nitrogen atom to which it is connected.

25. The compound of claim 24, wherein 

is 

, or 

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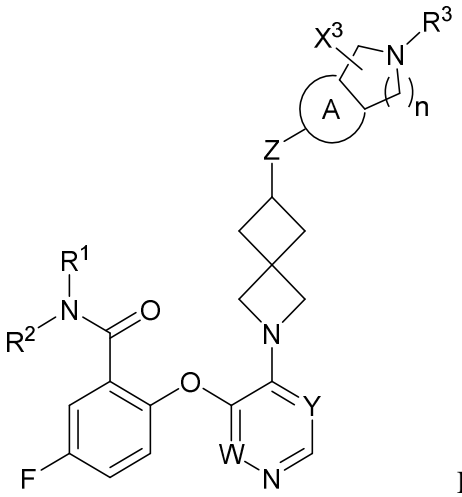
26. The compound of any one of the preceding claims, wherein n is 1.

27. The compound of any one of claims 1-25, wherein n is 2.

28. The compound of any one of claims 1-25, wherein n is 3.

29. A compound of Formula (III),



Formula (III),

a stereoisomer, or a pharmaceutically acceptable salt thereof, wherein:

W is N or CH;

Y is N or CH;

R^1 is C_1-C_6 alkyl or C_3-C_{12} cycloalkyl, wherein the C_1-C_6 alkyl or the C_3-C_{12} cycloalkyl is optionally substituted with one or more halo, C_1-C_6 alkoxy, C_6-C_{10} aryl, or 5- to 10-membered heteroaryl;

R^2 is C_1-C_6 alkyl;

Z is O, CH_2, or NH;

Ring A is 6- to 10-membered aryl or 6- to 10-membered heteroaryl;

X^3 is H or C_1-C_6 alkyl;

R^3 is H or C_1-C_6 alkyl, wherein the C_1-C_6 alkyl is optionally substituted with one or more R^{3a}, or

R^3 forms a 3- to 12-membered heterocyclyl with the carbon atom next to the nitrogen atom to which it is connected;

each R^{3a} is independently $N(R^{4a})(R^{4b})$ or 3- to 12-membered heterocyclyl, wherein the 3- to 12-membered heterocyclyl is optionally substituted with one or more substituent independently selected from C_1-C_6 alkyl and $O(R^{4a'})$;

each R^{4a} and R^{4b} is independently C_1-C_6 alkyl;

$R^{4a'}$ is H; and

n is 1 or 2.

30. A compound as shown in Table 1, or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof.

31. The compound according to any one of the preceding claims, wherein the compound is useful for the treatment of a cancer and wherein the compound minimizes hERG binding.

32. A pharmaceutical composition comprising a compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

33. The compound of any one of claims 1-31 or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 32, for use in treating or preventing cancer.

34. The compound or pharmaceutical composition for use of claim 33, wherein the cancer is a hematological cancer.

35. The compound or pharmaceutical composition for use of claim 33, wherein the cancer is a leukemia or a lymphoma.

36. The compound or pharmaceutical composition for use of claim 33, wherein the cancer is mixed lineage leukemia (MLL), MLL-related leukemia, MLL-associated leukemia, MLL-positive leukemia, MLL-induced leukemia, rearranged mixed lineage (KMT2A-rearranged) leukemia (MLL-r), leukemia associated with a MLL rearrangement or a rearrangement of the *MLL* gene, acute leukemia, chronic leukemia, indolent leukemia, lymphoblastic leukemia, lymphocytic leukemia, myeloid leukemia, myelogenous leukemia, childhood leukemia, acute lymphocytic leukemia (ALL), acute myeloid leukemia (AML), acute granulocytic leukemia, acute nonlymphocytic leukemia, chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), therapy related leukemia, myelodysplastic syndrome (MDS), myeloproliferative disease (MPD), myeloproliferative neoplasia (MPN), plasma cell neoplasm, multiple myeloma, myelodysplasia, cutaneous T-cell lymphoma, lymphoid neoplasm, AIDS-related lymphoma, thymoma, thymic carcinoma, mycosis fungoides, Alibert-Bazin syndrome, granuloma fungoides, Sézary syndrome, hairy cell leukemia, T-cell prolymphocytic leukemia (T-PLL), large granular lymphocytic leukemia, meningeal leukemia, leukemic leptomeningitis, leukemic meningitis, Hodgkin's lymphoma, non-Hodgkin's lymphoma (malignant lymphoma), or Waldenstrom's macroglobulinemia.

37. The compound or pharmaceutical composition for use of claim 33, wherein the cancer is an abstract nucleophosmin (NPM1)-mutated acute myeloid leukemia or a rearranged mixed lineage (KMT2A-rearranged) acute leukemia (MLL-r).