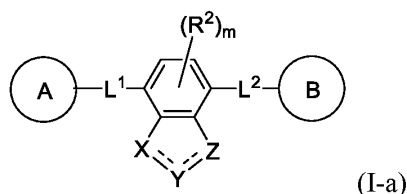


## CLAIMS

1. A compound of Formula (I-a):



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, Y, and Z are each independently  $C(R^{3a})$ ,  $C(R^{3a})(R^{3b})$ , N,  $N(R^{3c})$ , or O, wherein at least one of X, Y, and Z is N,  $N(R^{3c})$ , or O, and the bonds in the ring comprising X, Y, and Z may be single or double bonds as valency permits;

each of  $L^1$  and  $L^2$  is independently absent,  $C_1$ - $C_6$ -alkylene,  $C_1$ - $C_6$ -heteroalkylene, -O-, -C(O)-, - $N(R^4)$ -, - $N(R^4)C(O)$ -, or -C(O) $N(R^4)$ -, wherein each alkylene and heteroalkylene is optionally substituted with one or more  $R^5$ ;

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<sup>A</sup>, -NR<sup>B</sup>R<sup>C</sup>, -NR<sup>B</sup>C(O)R<sup>D</sup>, -NO<sub>2</sub>, -C(O)NR<sup>B</sup>R<sup>C</sup>, -C(O)R<sup>D</sup>, -C(O)OR<sup>D</sup>, -SR<sup>E</sup>, or -S(O)<sub>x</sub>R<sup>D</sup>, wherein each alkyl, alkylene, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more  $R^6$ ; 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  $R^6$ ;

each  $R^2$  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, halo, cyano, or -OR<sup>A</sup>;

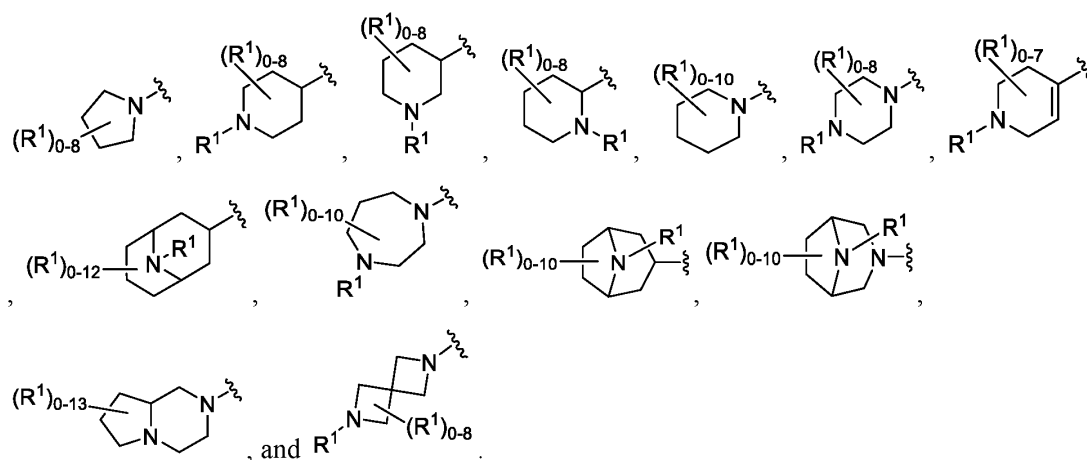
$R^{3a}$  and  $R^{3b}$  are each independently hydrogen,  $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -heteroalkyl,  $C_1$ - $C_6$ -haloalkyl, halo, cyano, -OR<sup>A</sup>, -NR<sup>B</sup>R<sup>C</sup>, -C(O)R<sup>D</sup>, or -C(O)OR<sup>D</sup>; or

each of  $R^{3a}$  and  $R^{3b}$ , together with the carbon atom to which they are attached, form an oxo group;

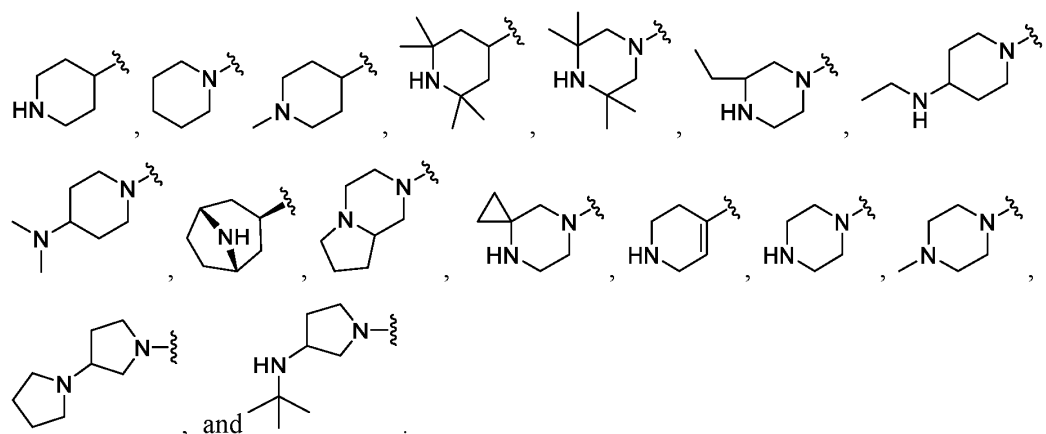
$R^{3c}$  is hydrogen or C<sub>1</sub>-C<sub>6</sub>-alkyl;  
 each  $R^4$  is independently hydrogen, C<sub>1</sub>-C<sub>6</sub>-alkyl, or C<sub>1</sub>-C<sub>6</sub>-haloalkyl;  
 each  $R^5$  is independently hydrogen, C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-heteroalkyl, C<sub>1</sub>-C<sub>6</sub>-haloalkyl, cycloalkyl, halo, cyano, oxo,  $-OR^A$ ,  $-NR^B R^C$ ,  $-C(O)R^D$ , or  $-C(O)OR^D$ ;  
 each  $R^6$  is independently C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>2</sub>-C<sub>6</sub>-alkenyl, C<sub>2</sub>-C<sub>6</sub>-alkynyl, C<sub>1</sub>-C<sub>6</sub>-heteroalkyl, C<sub>1</sub>-C<sub>6</sub>-haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, halo, cyano, oxo,  $-OR^A$ ,  $-NR^B R^C$ ,  $-NR^B C(O)R^D$ ,  $-NO_2$ ,  $-C(O)NR^B R^C$ ,  $-C(O)R^D$ ,  $-C(O)OR^D$ ,  $-SR^E$ , or  $-S(O)_x R^D$ , wherein each alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more  $R^{11}$ ;  
 each  $R^7$  is C<sub>1</sub>-C<sub>6</sub>-alkyl, halo, cyano, oxo, or  $-OR^{A1}$ ;  
 each  $R^{11}$  is independently C<sub>1</sub>-C<sub>6</sub>-alkyl, C<sub>1</sub>-C<sub>6</sub>-heteroalkyl, C<sub>1</sub>-C<sub>6</sub>-haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, halo, cyano, oxo, or  $-OR^A$ ;  
 each  $R^A$  is independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, aryl, heteroaryl, C<sub>1</sub>-C<sub>6</sub> alkylene-aryl, C<sub>1</sub>-C<sub>6</sub> alkylene-heteroaryl,  $-C(O)R^D$ , or  $-S(O)_x R^D$ ;  
 each of  $R^B$  and  $R^C$  is independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> heteroalkyl, cycloalkyl, heterocyclyl, or  $-OR^A$ ; 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  $R^D$  and  $R^E$  is independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> heteroalkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, C<sub>1</sub>-C<sub>6</sub> alkylene-aryl, or C<sub>1</sub>-C<sub>6</sub> alkylene-heteroaryl;  
 each  $R^{A1}$  is hydrogen or C<sub>1</sub>-C<sub>6</sub>-alkyl;  
 m is 0, 1, or 2; and  
 x is 0, 1, or 2.

2. The compound of claim 1, wherein A is a monocyclic or bicyclic heterocyclyl.
3. The compound of any one of the preceding claims, wherein A is a nitrogen-containing heterocyclyl.

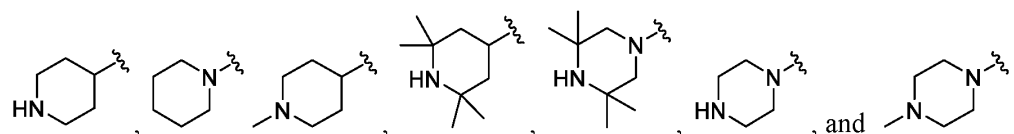
4. The compound of any one of the preceding claims, wherein A is selected from



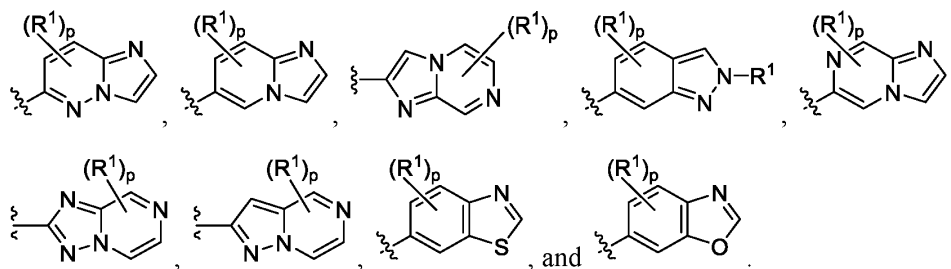
5. The compound of any one of the preceding claims, wherein A is selected from



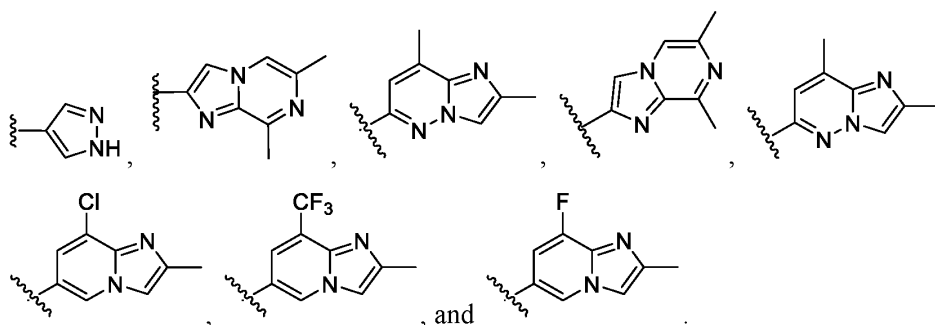
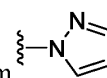
6. The compound of any one of the preceding claims, wherein A is selected from



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



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



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

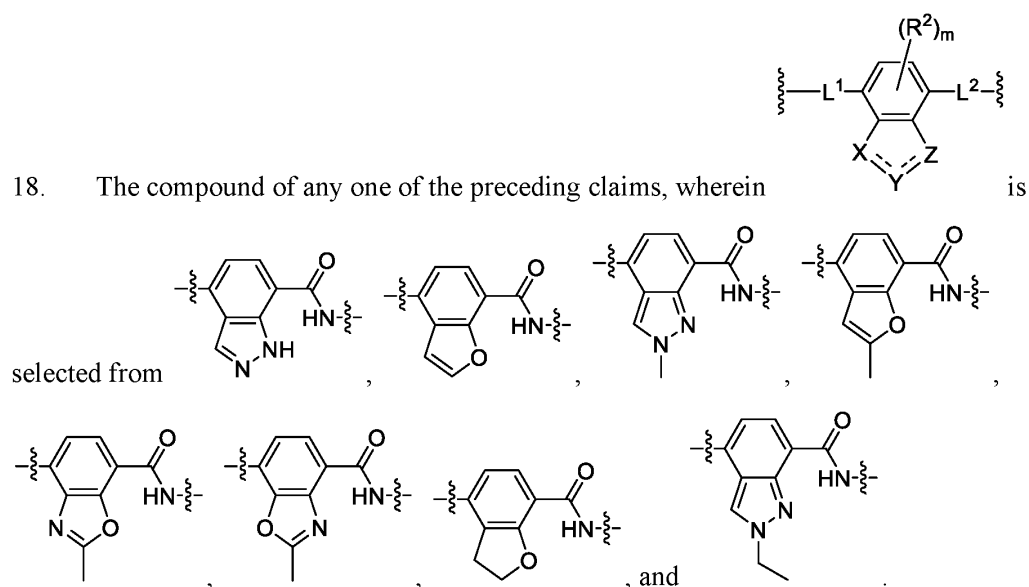


10. The compound of any one of the preceding claims, wherein  $L^1$  and  $L^2$  are each independently absent, -O-, -N(R<sup>4</sup>)-, -N(R<sup>4</sup>)C(O)-, or -C(O)N(R<sup>4</sup>)-.

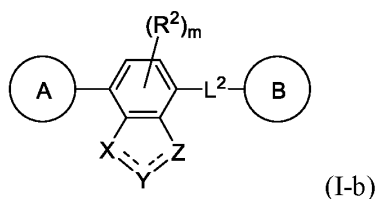
11. The compound of any one of the preceding claims, wherein  $L^1$  is absent and  $L^2$  is -C(O)N(R<sup>4</sup>)-.

12. The compound of any one of the preceding claims, wherein at least one of X, Y, and Z is N or N(R<sup>3c</sup>).

13. The compound of any one of the preceding claims, wherein one of X, Y, and Z is C(R<sup>3a</sup>) (e.g., CH), and the others of X, Y, and Z are each independently O, N or N(R<sup>3c</sup>).
14. The compound of any one of the preceding claims, wherein at least one of X, Y, and Z is O.
15. The compound of any one of the preceding claims, wherein Z and Y are each independently N or N(R<sup>3c</sup>), and X is C(R<sup>3a</sup>) (e.g., CH).
16. The compound of any one of the preceding claims, wherein X is C(R<sup>3a</sup>) (e.g., CH), and Y and Z are each independently N or N(R<sup>3c</sup>).
17. The compound of any one of the preceding claims, wherein X is C(R<sup>3a</sup>), Y is C(R<sup>3a</sup>), and Z is O.



19. The compound of any one of the preceding claims, wherein the compound of Formula (I) is Formula (I-b):



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, Y, and Z are each independently  $C(R^{3a})$ ,  $C(R^{3a})(R^{3b})$ , N,  $N(R^{3c})$ , or O, wherein at least one of X, Y, and Z is N,  $N(R^{3c})$ , or O, and the bonds in the ring comprising X, Y, and Z may be single or double bonds as valency permits;

$L^2$  is absent,  $C_1$ - $C_6$ -alkylene,  $C_1$ - $C_6$ -heteroalkylene, -O-, -C(O)-, - $N(R^4)$ -, - $N(R^4)C(O)$ -, or -C(O) $N(R^4)$ -, wherein each alkylene and heteroalkylene is optionally substituted with one or more  $R^5$ ;

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, - $OR^A$ , - $NR^B R^C$ , - $NR^B C(O)R^D$ , - $NO_2$ , -C(O) $NR^B R^C$ , -C(O) $R^D$ , -C(O) $OR^D$ , - $SR^E$ , or -S(O) $_x R^D$ , wherein each alkyl, alkylene, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more  $R^6$ ; 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  $R^6$ ;

each  $R^2$  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, halo, cyano, or - $OR^A$ ;

$R^{3a}$  and  $R^{3b}$  are each independently hydrogen,  $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -heteroalkyl,  $C_1$ - $C_6$ -haloalkyl, halo, cyano, - $OR^A$ , - $NR^B R^C$ , -C(O) $R^D$ , or -C(O) $OR^D$ ; or

each of  $R^{3a}$  and  $R^{3b}$ , together with the carbon atom to which they are attached, form an oxo group;

$R^{3c}$  is hydrogen or  $C_1$ - $C_6$ -alkyl;

each  $R^4$  is independently hydrogen,  $C_1$ - $C_6$ -alkyl, or  $C_1$ - $C_6$ -haloalkyl;

each  $R^5$  is independently hydrogen,  $C_1$ - $C_6$ -alkyl,  $C_1$ - $C_6$ -heteroalkyl,  $C_1$ - $C_6$ -haloalkyl, cycloalkyl, halo, cyano, oxo,  $-OR^A$ ,  $-NR^B R^C$ ,  $-C(O)R^D$ , or  $-C(O)OR^D$ ;

each  $R^6$  is independently  $C_1$ - $C_6$ -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, cyano, oxo,  $-OR^A$ ,  $-NR^B R^C$ ,  $-NR^B C(O)R^D$ ,  $-NO_2$ ,  $-C(O)NR^B R^C$ ,  $-C(O)R^D$ ,  $-C(O)OR^D$ ,  $-SR^E$ , or  $-S(O)_x R^D$ , wherein each alkyl, alkenyl, alkynyl, heteroalkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with one or more  $R^{11}$ ;

each  $R^7$  is  $C_1$ - $C_6$ -alkyl, halo, cyano, oxo, or  $-OR^{A1}$ ;

each  $R^{11}$  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,  $C_1$ - $C_6$  haloalkyl, aryl, heteroaryl,  $C_1$ - $C_6$  alkylene-aryl,  $C_1$ - $C_6$  alkylene-heteroaryl,  $-C(O)R^D$ , or  $-S(O)_x R^D$ ;

each of  $R^B$  and  $R^C$  is independently hydrogen,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  heteroalkyl, cycloalkyl, heterocyclyl, or  $-OR^A$ ; 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  $R^7$ ;

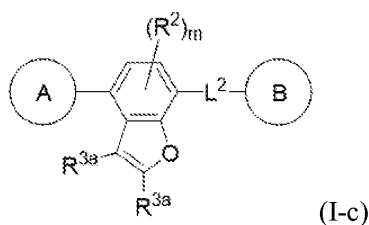
each  $R^D$  and  $R^E$  is independently hydrogen,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $C_1$ - $C_6$  heteroalkyl,  $C_1$ - $C_6$  haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl,  $C_1$ - $C_6$  alkylene-aryl, or  $C_1$ - $C_6$  alkylene-heteroaryl;

each  $R^{A1}$  is hydrogen or  $C_1$ - $C_6$ -alkyl;

m is 0, 1, or 2; and

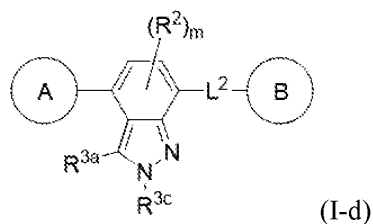
x is 0, 1, or 2.

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



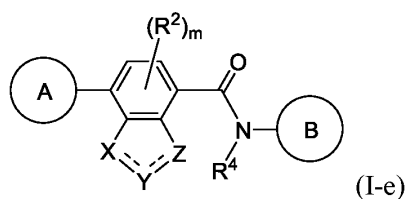
or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein each of A, B,  $L^2$ ,  $R^2$ ,  $R^{3a}$ , m, and subvariables thereof are defined as in claim 1.

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



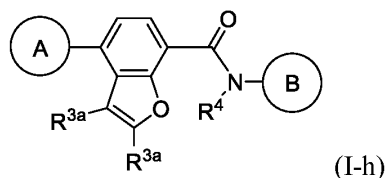
or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein each of A, B,  $L^2$ ,  $R^2$ ,  $R^{3a}$ ,  $R^{3c}$ , m, and subvariables thereof are defined as in claim 1.

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



or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein each of A, B, X, Y, Z,  $L^2$ ,  $R^2$ ,  $R^4$ , m, and subvariables thereof are defined as in claim 1.

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



or a pharmaceutically acceptable salt, solvate, hydrate, tautomer, or stereoisomer thereof, wherein each of A, B,  $L^2$ ,  $R^{3a}$ ,  $R^4$ , m, and subvariables thereof are defined as in claim 1.

24. 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.
25. A pharmaceutical composition comprising a compound of any one of the preceding claims and a pharmaceutically acceptable excipient.
26. The compound of any one of claims 1-24, or the pharmaceutical composition of claim 25, wherein the compound alters a target nucleic acid (e.g., an RNA, e.g., a pre-mRNA).
27. The compound of any one of claims 1-24, or the pharmaceutical composition of claim 25, wherein the compound binds to a target nucleic acid (e.g., an RNA, e.g., a pre-mRNA).
28. The compound of any one of claims 1-24, or the pharmaceutical composition of claim 25, wherein the compound stabilizes a target nucleic acid (e.g., an RNA, e.g., a pre-mRNA).
29. The compound of any one of claims 1-24, or the pharmaceutical composition of claim 25, wherein the compound increases 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.
30. The compound of any one of claims 1-24, or the pharmaceutical composition of claim 25, wherein the compound 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 %.
31. 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) or a composition thereof according to any one of claims 1-25:

comprising contacting the nucleic acid (e.g., a DNA, RNA, e.g., a pre-mRNA) with a compound of Formula (I).

32. The method of claim 31, wherein the component of a spliceosome is recruited to the nucleic acid in the presence of the compound of Formula (I).

33. 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) according to any one of claims 1-24, or the pharmaceutical composition of claim 25.

34. The method of claim 33, wherein the altering comprises forming a bulge in the nucleic acid.

35. The method of claim 33, wherein the altering comprises stabilizing a bulge in the nucleic acid.

36. The method of claim 33, wherein the altering comprises reducing a bulge in the nucleic acid.

37. The method of any one of any one of claims 33-36, wherein the nucleic acid comprises a splice site.

38. A composition for use in treating a disease or disorder in a subject comprising administering to the subject a compound of Formula (I) according to any one of claims 1-24 or the pharmaceutical composition of claim 25.

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).

40. The composition for use of claim 38, wherein the disease or disorder comprises 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.

41. The composition for use of claim 38, wherein the disease or disorder comprises neurological disease or disorder.

42. The composition for use of claim 38, wherein the disease or disorder comprises Huntington's disease.