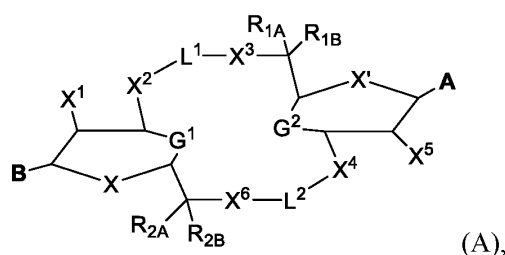


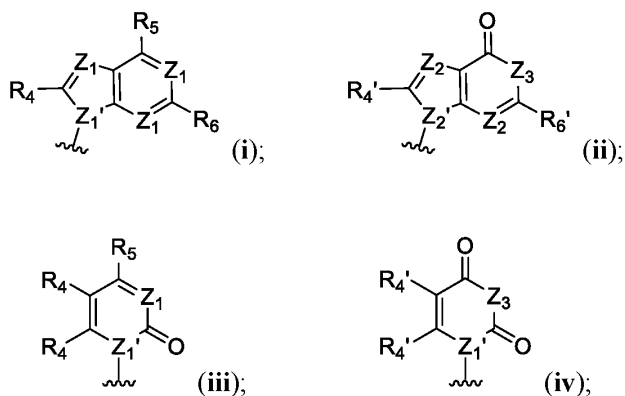
WHAT IS CLAIMED IS:

1. A compound of Formula (A):



or a pharmaceutically acceptable salt thereof, wherein:

A and **B** are each independently selected from the group consisting of Formulae (i), (ii), (iii), and (iv):



X and **X'** are each independently selected from the group consisting of O, S, S(O), SO₂, CH₂, CHF, CF₂, CH₂O, OCH₂, CH₂CH₂, CH=CH, NR³, and N(O⁻)R³;

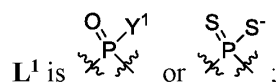
G¹ is a bond connecting (i) the carbon directly attached to **X²** and (ii) the carbon directly attached to C(R^{2A})(R^{2B})(X⁶); or is C(R^{G1A})(R^{G1B});

G^2 is a bond connecting (i) the carbon directly attached to X^4 and (ii) the carbon directly attached to $C(R^{1A})(R^{1B})(X^3)$; or is $C(R^{G2A})(R^{G2B})$;

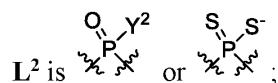
X^1 and X^5 are each independently selected from the group consisting of H, C₁₋₄ alkyl, C₁₋₄ haloalkyl, halo (e.g., F), -CN, -NO₂, -N₃, -OH, -OR^{a1}, -SH, -SR^{a1}, -C(O)H, -C(O)R^{a1}, -C(O)NR^{c1}R^{d1}, -C(O)OH, -C(O)OR^{a1}, -OC(O)H, -OC(O)R^{a1}, -OC(O)NR^{b1}R^{c1}, -C(=NR^{c1})NR^{b1}R^{c1}, -NR^{d1}C(=NR^{c1})NR^{b1}R^{c1}, -NR^{b1}R^{c1}, -⁺NR^{b1}R^{c1}R^{d1}, -NR^{d1}C(O)H, -NR^{d1}C(O)R^{a1}, -NR^{d1}C(O)OR^{a1}, -NR^{d1}C(O)NR^{b1}R^{c1}, -NR^{d1}S(O)R^{a1}, -NR^{d1}S(O)₂R^{a1}, -NR^{d1}S(O)₂NR^{b1}R^{c1}, -S(O)R^{a1}, -S(O)NR^{b1}R^{c1}, -S(O)₂R^{a1}, and -S(O)₂NR^{b1}R^{c1};

10

X^2 , X^3 , X^4 and X^6 are each independently selected from the group consisting of O, S, and N-R³;



15



Y^1 and Y^2 are each independently selected from the group consisting of -OH, -OR^{a1}, O⁻, -SH, -SR^{a1}, S⁻; and -NR^{b1}R^{c1};

R^{1A} and R^{1B} are each independently selected from the group consisting of H; halo; C₁₋₄ alkyl; C₁₋₄ haloalkyl; C₂₋₄ alkenyl; C₂₋₄ alkynyl; and C₃₋₅ cycloalkyl, which is optionally substituted with from 1-4 independently selected C₁₋₄ alkyl; or R^{1A} and R^{1B} , together with the carbon atom to which each is attached, form a C₃₋₅ cycloalkyl or heterocyclyl, including from 4-5 ring atoms, wherein from 1-2 (e.g., 1) ring atoms are independently selected from the group consisting of nitrogen and oxygen (e.g. oxetane), wherein the C₃₋₅ cycloalkyl or heterocyclyl ring can each be optionally substituted with from 1-4 independently selected C₁₋₄ alkyl;

25

R^{2A} and **R^{2B}** are each independently selected from the group consisting of H; halo; C₁₋₄ alkyl; C₁₋₄ haloalkyl; C₂₋₄ alkenyl; C₂₋₄ alkynyl; and C₃₋₅ cycloalkyl, which is optionally substituted with from 1-4 independently selected C₁₋₄ alkyl; or **R^{2A}** and **R^{2B}**, together with the carbon atom to which each is attached, form a C₃₋₅ cycloalkyl or heterocyclyl, including from 4-5 ring atoms, wherein from 1-2 (e.g., 1) ring atoms are independently selected from the group consisting of nitrogen and oxygen (e.g., oxetane), wherein the C₃₋₅ cycloalkyl or heterocyclyl ring can each be optionally substituted with from 1-4 independently selected C₁₋₄ alkyl,

Z₁ is N or C-R⁴;
Z_{1'} is N or C-H;
Z₂ is N or C-R^{4'};
Z_{2'} is N or C-H;
Z₃ is N-R³ or C-R⁴;

each occurrence of **R^{a1}** is independently selected from the group consisting of:

- C₁₋₁₀ alkyl optionally substituted with from 1-3 **R^A**;
- C₁₋₁₀ haloalkyl optionally substituted with from 1-3 **R^A**;
- C₂₋₁₀ alkenyl optionally substituted with from 1-3 **R^B**;
- C₂₋₁₀ alkynyl optionally substituted with from 1-3 **R^B**;
- C₃₋₁₀ cycloalkyl optionally substituted with from 1-5 **R^C**;
- (C₃₋₁₀ cycloalkyl)-C₁₋₆ alkylene, wherein the alkylene serves as the point of attachment, and wherein the C₃₋₁₀ cycloalkyl optionally substituted with from 1-5 **R^C**;
- heterocyclyl, including from 3-10 ring atoms, wherein from 1-3 ring atoms are independently selected from the group consisting of nitrogen, oxygen and sulfur, and which is optionally substituted with from 1-5 **R^C**;
- (heterocyclyl as defined above)-C₁₋₆ alkylene, wherein the alkylene serves as the point of attachment, and wherein the heterocyclyl is optionally substituted with from 1-5 **R^C**;

- C₆₋₁₀ aryl optionally substituted with from 1-5 R^D;
- heteroaryl including from 5-10 ring atoms, wherein from 1-4 ring atoms are independently selected from the group consisting of nitrogen, oxygen and sulfur, and which is optionally substituted with from 1-5 R^D; and
- 5 • (heteroaryl as defined above)-C₁₋₆ alkylene, wherein the alkylene serves as the point of attachment, and wherein the heteroaryl optionally substituted with from 1-5 R^D;

each occurrence of **R³**, **R^{b1}**, **R^{c1}**, **R^{d1}**, and **R^{e1}** is independently selected from the group consisting of: H; R^{a1}; -C(O)H, -C(O)R^{a1}, -C(O)NR^{c1}R^{d1}, -C(O)OR^{a1}, -OC(O)H, --
 10 C(=NR^{e1})NR^{b1}R^{c1}, -NR^{d1}C(=NR^{e1})NR^{b1}R^{c1}, -NR^{b1}R^{c1}, -S(O)R^{a1}, -S(O)NR^{b1}R^{c1}, -S(O)₂R^{a1}, and -S(O)₂NR^{b1}R^{c1}; or

R^{b1} and R^{c1} taken together with the nitrogen atom to which each is attached form a heterocyclyl, including from 3-10 ring atoms, wherein from 1-3 ring atoms are
 15 independently selected from the group consisting of nitrogen, oxygen and sulfur, and which is optionally substituted with from 1-5 R^C; (e.g., azetidiny, morpholino, piperidinyl);

each occurrence of **R^{G1A}**, **R^{G1B}**, **R^{G1A}**, **R^{G1B}**, **R⁴**, **R^{4'}**, **R⁵**, **R⁶**, and **R^{6'}** is independently selected from the group consisting of: H; R^{a1}; halo, -CN, -NO₂, -N₃, -OH, -
 20 OR^{a1}, -SH, -SR^{a1}, -C(O)H, -C(O)R^{a1}, -C(O)NR^{c1}R^{d1}, -C(O)OH, -C(O)OR^{a1}, -OC(O)H, -OC(O)R^{a1}, -OC(O)NR^{b1}R^{c1}, -C(=NR^{e1})NR^{b1}R^{c1}, -NR^{d1}C(=NR^{e1})NR^{b1}R^{c1}, -NR^{b1}R^{c1}, -N⁺R^{b1}R^{c1}R^{d1}, -NR^{d1}C(O)H, -NR^{d1}C(O)R^{a1}, -NR^{c1}C(O)OR^{a1}, -NR^{d1}C(O)NR^{b1}R^{c1}, -NR^{d1}S(O)R^{a1}, -NR^{d1}S(O)₂R^{a1}, -NR^{d1}S(O)₂NR^{b1}R^{c1}, -S(O)R^{a1}, -S(O)NR^{b1}R^{c1}, -S(O)₂R^{a1}, and -S(O)₂NR^{b1}R^{c1};

25 each occurrence of **R^A** is independently selected from the group consisting of: -CN; -OH; C₁₋₆ alkoxy; C₁₋₆ haloalkoxy; -C(O)NRR', wherein R' and R'' are each independently selected from H and C₁₋₄ alkyl; -C(O)OH; -C(O)O(C₁₋₆ alkyl); and -NR''R''', wherein R'' and R''' are each independently selected from the group consisting of H, C₁₋₄ alkyl, -SO₂(C₁₋₆ alkyl), -C(O)(C₁₋₆ alkyl), and -C(O)O(C₁₋₆ alkyl);

each occurrence of **R^B** is independently selected from the group consisting of: halo; -CN; -OH; C₁₋₆ alkoxy; C₁₋₆ haloalkoxy; -C(O)NRR', wherein R' and R'' are each independently selected from H and C₁₋₄ alkyl; -C(O)OH; -C(O)O(C₁₋₆ alkyl); and -NR''R''', wherein R'' and R''' are each independently selected from the group consisting of H, C₁₋₄ alkyl, -SO₂(C₁₋₆ alkyl), -C(O)(C₁₋₆ alkyl), and -C(O)O(C₁₋₆ alkyl);;

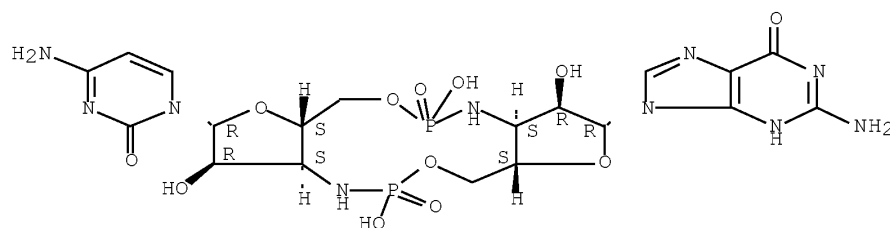
each occurrence of **R^C** is independently selected from the group consisting of: C₁₋₆ alkyl; C₁₋₄ haloalkyl; halo; -CN; -OH; oxo; C₁₋₆ alkoxy; C₁₋₆ haloalkoxy; -C(O)NRR', wherein R' and R'' are each independently selected from H and C₁₋₄ alkyl; -C(O)(C₁₋₆ alkyl); -C(O)OH; -C(O)O(C₁₋₆ alkyl); and -NR''R''', wherein R'' and R''' are each independently selected from the group consisting of H, C₁₋₄ alkyl, -SO₂(C₁₋₆ alkyl), -C(O)(C₁₋₆ alkyl), and -C(O)O(C₁₋₆ alkyl);

each occurrence of **R^D** is independently selected from the group consisting of:

- C₁₋₆ alkyl optionally substituted with from 1-2 substituents independently selected from the group consisting of: -OH, C₁₋₄ alkoxy; C₁₋₄ haloalkoxy; -NH₂, -NH(C₁₋₄ alkyl), and -N(C₁₋₄ alkyl)₂;
- C₁₋₄ haloalkyl;
- C₂₋₄ alkenyl;
- C₂₋₄ alkynyl;
- halo;
- -CN;
- -NO₂;
- -N₃;
- -OH;
- C₁₋₆ alkoxy;
- C₁₋₆ haloalkoxy;
- -C(O)NRR', wherein R' and R'' are each independently selected from H and C₁₋₄ alkyl;

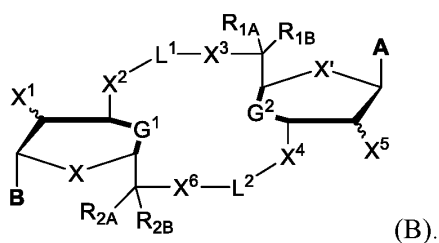
- -SO₂NRR', wherein R' and R'' are each independently selected from H and C₁₋₄ alkyl;
- -C(O)(C₁₋₆ alkyl);
- -C(O)OH;
- 5 • -C(O)O(C₁₋₆ alkyl);
- -SO₂(C₁₋₆ alkyl),
- -NR''R''', wherein R'' and R''' are each independently selected from the group consisting of H, C₁₋₄ alkyl, -SO₂(C₁₋₆ alkyl), -C(O)(C₁₋₆ alkyl), and -C(O)O(C₁₋₆ alkyl);
- 10 • (C₃₋₁₀ cycloalkyl)-(CH₂)₀₋₂, wherein the CH₂ (when present) serves as the point of attachment, and wherein the C₃₋₁₀ cycloalkyl is optionally substituted with from 1-5 independently selected C₁₋₄ alkyl;
- (heterocyclyl as defined above)-(CH₂)₀₋₂, wherein the CH₂ (when present) serves as the point of attachment, and wherein the heterocyclyl is
- 15 optionally substituted with from 1-5 independently selected C₁₋₄ alkyl;
- (phenyl)-(CH₂)₀₋₂, wherein the CH₂ (when present) serves as the point of attachment, and wherein the phenyl is optionally substituted with from 1-5 substituents independently selected from halo, C₁₋₄ alkyl, -CF₃, -OCH₃, -SCH₃, -OCF₃, -NO₂, -N₃, -NH₂, -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)₂, -
- 20 C(O)(C₁₋₄ alkyl), -C(O)OH, -C(O)O(C₁₋₄ alkyl), -SO₂(CH₃), and cyclopropyl;
- (heteroaryl as defined above)-(CH₂)₀₋₂, wherein the CH₂ (when present) serves as the point of attachment, and wherein the phenyl is optionally substituted with from 1-5 substituents independently selected from halo,
- 25 C₁₋₄ alkyl, -CF₃, -OCH₃, -SCH₃, -OCF₃, -NO₂, -N₃, -NH₂, -NH(C₁₋₄ alkyl), -N(C₁₋₄ alkyl)₂, -C(O)(C₁₋₄ alkyl), -C(O)OH, -C(O)O(C₁₋₄ alkyl), -SO₂(CH₃), and cyclopropyl; and

provided at least one of X², X³, X⁴ and X⁶ is N-R³; and further provided that the
 30 compound is not:

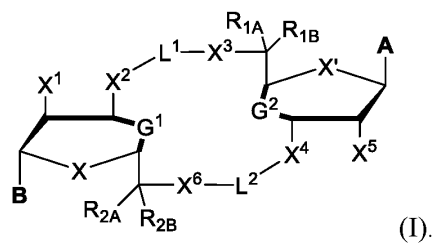


2. The compound of claim 1, wherein the compound has formula (B):

5



3. The compound of claim 1 or 2, wherein the compound has formula (I):



10

4. The compound of any one of claims 1-3, wherein the carbon directly attached to X^1 has the (*R*)-configuration.

15

5. The compound of any one of claims 1-3, wherein the carbon directly attached to X^1 has the (*S*)-configuration.

6. The compound of any one of claims 1-5, wherein the carbon directly attached to X^5 has the (*R*)-configuration.

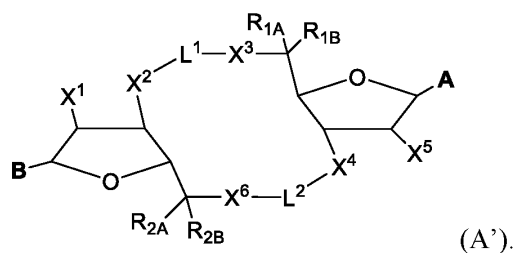
5 7. The compound of any one of claims 1-5, wherein the carbon directly attached to X^5 has the (*S*)-configuration.

8. The compound of any one of claims 1-7, wherein **X** and **X'** are each O.

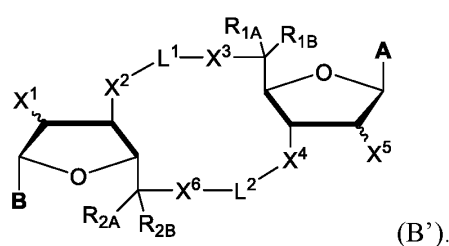
10 9. The compound of any one of claims 1-8, wherein **G**¹ is a bond connecting (i) the carbon directly attached to X^2 and (ii) the carbon directly attached to $C(R^{2A})(R^{2B})(X^6)$.

15 10. The compound of any one of claims 1-9, wherein **G**² is a bond connecting (i) the carbon directly attached to X^4 and (ii) the carbon directly attached to $C(R^{1A})(R^{1B})(X^3)$.

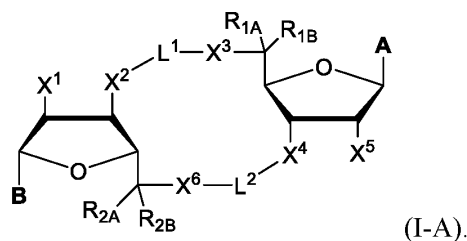
20 11. The compound of claim 1, wherein **X** and **X'** are each O, **G**¹ is a bond connecting (i) the carbon directly attached to X^2 and (ii) the carbon directly attached to $C(R^{2A})(R^{2B})(X^6)$; or is $C(R^{G1A})(R^{G1B})$; **G**² is a bond connecting (i) the carbon directly attached to X^4 and (ii) the carbon directly attached to $C(R^{1A})(R^{1B})(X^3)$, and the compound has formula (A'):



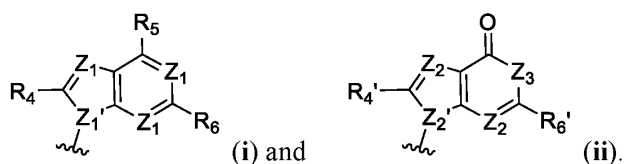
12. The compound of claim 11, wherein **X** and **X'** are each O, **G**¹ is a bond connecting (i) the carbon directly attached to **X**² and (ii) the carbon directly attached to C(**R**^{2A})(**R**^{2B})(**X**⁶); or is C(**R**^{G1A})(**R**^{G1B}); **G**² is a bond connecting (i) the carbon directly attached to **X**⁴ and (ii) the carbon directly attached to C(**R**^{1A})(**R**^{1B})(**X**³), and the compound has formula (**B'**):



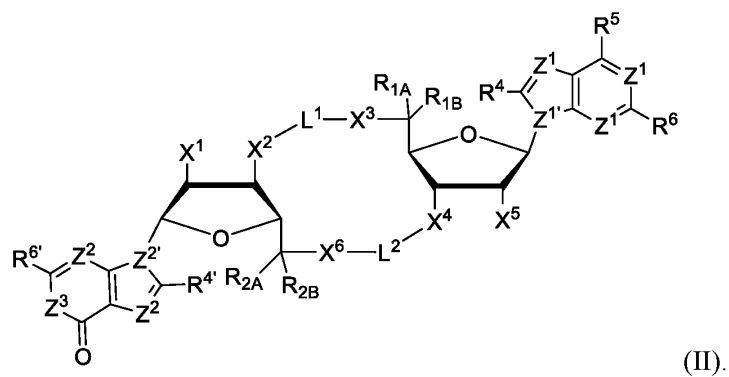
13. The compound of claim 1, wherein **X** and **X'** are each O, **G**¹ is a bond connecting (i) the carbon directly attached to **X**² and (ii) the carbon directly attached to C(**R**^{2A})(**R**^{2B})(**X**⁶); or is C(**R**^{G1A})(**R**^{G1B}); **G**² is a bond connecting (i) the carbon directly attached to **X**⁴ and (ii) the carbon directly attached to C(**R**^{1A})(**R**^{1B})(**X**³), and the compound has formula (**I-A**):



14. The compound of any one of claims 1-13, wherein **A** and **B** are each independently selected from the group consisting of:

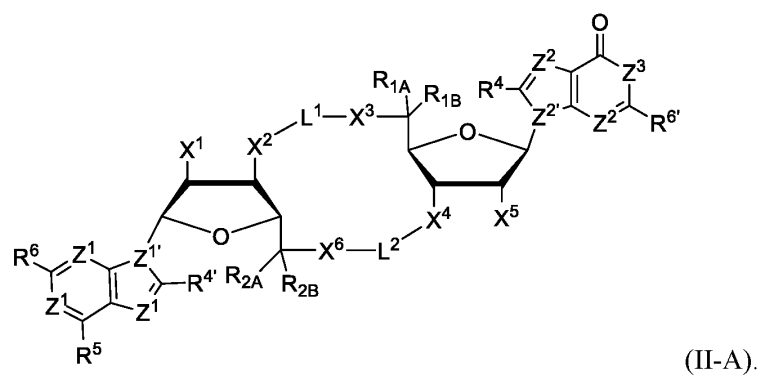


15. The compound of any one of claims 1-14, wherein the compound has the following formula:



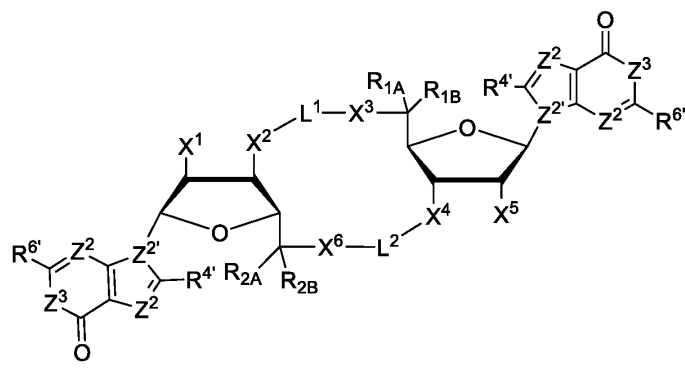
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16. The compound of any one of claims 1-14, wherein the compound has the following formula:

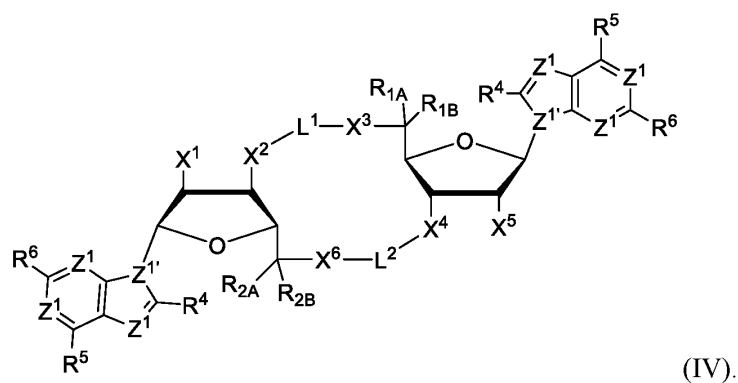


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17. The compound of any one of claims 1-14, wherein the compound has the following formula:



18. The compound of any one of claims 1-14, wherein the compound has the following formula:



5

19. The compound of any one of claims 1-16 and 18, wherein each occurrence of Z^1 is N, and $Z^{1'}$ is N.

10 20. The compound of any one of claims 1-16, 18 and 19, wherein R^5 is -
 $NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, R^4 and/or R^6 is H; or R^4 is
 other than H, and R^6 is H).

15 21. The compound of any one of claims 1-16 and 18 and 19, wherein R^5 is -
 OH.

22. The compound of claim 21, wherein R^6 is H (e.g., in certain embodiments, R^4 is H; in other embodiments, R^4 is other than H).

23. The compound of any one of claims 1-17, wherein each occurrence of Z^2 is N, $Z^{2'}$ is N, and Z^3 is N- R^3 (e.g., N-H).

24. The compound of any one of claims 1-17 and 23, wherein $R^{6'}$ is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, $R^{4'}$ is H; in other embodiments, $R^{4'}$ is other than H).

10

25. The compound of any one of claims 1-24, wherein X^1 is H, $-OH$, $-OR^{a1}$, $-SH$, $-SR^{a1}$, $-OC(O)H$, $-OC(O)R^{a1}$, $-OC(O)NR^{b1}R^{c1}$, C_{1-4} alkyl, C_{1-4} haloalkyl (e.g., CF_3), halo (e.g., F), $-CN$, $-C(O)H$, $-C(O)R^{a1}$, $-C(O)NR^{c1}R^{d1}$, $-C(O)OH$, $-C(O)OR^{a1}$, $-C(=NR^{e1})NR^{b1}R^{c1}$, $-S(O)R^{a1}$, $-S(O)NR^{b1}R^{c1}$, $-S(O)_2R^{a1}$, or $-S(O)_2NR^{b1}R^{c1}$; or X^1 is $-OH$, $-OR^{a1}$, $-SH$, $-SR^{a1}$, $-OC(O)H$, $-OC(O)R^{a1}$, $-OC(O)NR^{b1}R^{c1}$, C_{1-4} alkyl, C_{1-4} haloalkyl (e.g., CF_3), halo (e.g., F), $-CN$, $-C(O)H$, $-C(O)R^{a1}$, $-C(O)NR^{c1}R^{d1}$, $-C(O)OH$, $-C(O)OR^{a1}$, $-C(=NR^{e1})NR^{b1}R^{c1}$, $-S(O)R^{a1}$, $-S(O)NR^{b1}R^{c1}$, $-S(O)_2R^{a1}$, or $-S(O)_2NR^{b1}R^{c1}$.

15

26. The compound of any one of claims 1-25, wherein X^1 is H, $-OH$, $-OR^{a1}$, $-SH$, $-SR^{a1}$, $-OC(O)H$, $-OC(O)R^{a1}$, $-OC(O)NR^{b1}R^{c1}$, C_{1-4} alkyl, C_{1-4} haloalkyl (e.g., CF_3), halo (e.g., F), $-CN$, or $-S(O)_2R^{a1}$; or X^1 is $-OH$, $-OR^{a1}$, $-SH$, $-SR^{a1}$, $-OC(O)H$, $-OC(O)R^{a1}$, $-OC(O)NR^{b1}R^{c1}$, C_{1-4} alkyl, C_{1-4} haloalkyl (e.g., CF_3), halo (e.g., F), $-CN$, or $-S(O)_2R^{a1}$.

20

27. The compound of any one of claims 1-26, wherein X^1 is $-F$, $-OH$, $-OR^{a1}$, $-OC(O)H$, $-OC(O)R^{a1}$, or $-OC(O)NR^{b1}R^{c1}$.

25

28. The compound of any one of claims 1-27, wherein X^1 is $-F$, $-OH$, or $-OR^{a1}$.

29. The compound of any one of claims 1-28, wherein X^1 is $-F$ or $-OH$.

30

30. The compound of any one of claims 1-26, wherein X^1 is -OH, -OR^{al}, -SH, -SR^{al}, -OC(O)H, -OC(O)R^{al}, or -OC(O)NR^{b1}R^{c1}.

31. The compound of any one of claims 1-26 and 30, wherein X^1 is -OH, -OR^{al},
5 -OC(O)H, -OC(O)R^{al}, or -OC(O)NR^{b1}R^{c1}.

32. The compound of any one of claims 1-26, 30, and 31, wherein X^1 is -OH or -OR^{al} (e.g., R^{al} can be C₁₋₁₀ alkyl, e.g., C₁₋₄ alkyl).

10 33. The compound of any one of claims 1-32, wherein X^1 is -OH.

34. The compound of any one of claims 1-25, wherein X^1 is H, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, -C(O)H, -C(O)R^{al}, -C(O)NR^{c1}R^{d1}, -C(O)OH, -C(O)OR^{al}, -C(=NR^{e1})NR^{b1}R^{c1}, -S(O)R^{al}, -S(O)NR^{b1}R^{c1}, -S(O)₂R^{al}, or -S(O)₂NR^{b1}R^{c1}; or
15 X^1 is C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, -C(O)H, -C(O)R^{al}, -C(O)NR^{c1}R^{d1}, -C(O)OH, -C(O)OR^{al}, -C(=NR^{e1})NR^{b1}R^{c1}, -S(O)R^{al}, -S(O)NR^{b1}R^{c1}, -S(O)₂R^{al}, or -S(O)₂NR^{b1}R^{c1}.

35. The compound of any one of claims 1-25 and 34, wherein X^1 is H, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, or -S(O)₂R^{al}; or X^1 is C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, or -S(O)₂R^{al}; or X^1 is H, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), or halo (e.g., F); or X^1 is C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), or halo (e.g., F)).

36. The compound of any one of claims 1-25, 34 and 35, wherein X^1 is H or
25 halo (e.g., F).

37. The compound of any one of claims 1-29 and 34-36, wherein X^1 is halo (e.g., F).

38. The compound of any one of claims 1-37, wherein X^5 is H, -OH, -OR^{al}, -SH, -SR^{al}, -OC(O)H, -OC(O)R^{al}, -OC(O)NR^{b1}R^{cl}, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, -C(O)H, -C(O)R^{al}, -C(O)NR^{cl}R^{d1}, -C(O)OH, -C(O)OR^{al}, -C(=NR^{cl})NR^{b1}R^{cl}, -S(O)R^{al}, -S(O)NR^{b1}R^{cl}, -S(O)₂R^{al}, or -S(O)₂NR^{b1}R^{cl}; or X^5 is -OH, -OR^{al}, -SH, -SR^{al}, -OC(O)H, -OC(O)R^{al}, -OC(O)NR^{b1}R^{cl}, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, -C(O)H, -C(O)R^{al}, -C(O)NR^{cl}R^{d1}, -C(O)OH, -C(O)OR^{al}, -C(=NR^{cl})NR^{b1}R^{cl}, -S(O)R^{al}, -S(O)NR^{b1}R^{cl}, -S(O)₂R^{al}, or -S(O)₂NR^{b1}R^{cl}.

39. The compound of any one of claims 1-38, wherein X^5 is H, -OH, -OR^{al}, -SH, -SR^{al}, -OC(O)H, -OC(O)R^{al}, -OC(O)NR^{b1}R^{cl}, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, and -S(O)₂R^{al}; or X^5 is -OH, -OR^{al}, -SH, -SR^{al}, -OC(O)H, -OC(O)R^{al}, -OC(O)NR^{b1}R^{cl}, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, and -S(O)₂R^{al}.

40. The compound of any one of claims 1-39, wherein X^5 is -F, -OH, -OR^{al}, -OC(O)H, -OC(O)R^{al}, or -OC(O)NR^{b1}R^{cl}.

41. The compound of any one of claims 1-40, wherein X^5 is -F, -OH, or -OR^{al}.

42. The compound of any one of claims 1-41, wherein X^5 is -F or -OH.

43. The compound of any one of claims 1-39, wherein X^5 is -OH, -OR^{al}, -SH, -SR^{al}, -OC(O)H, -OC(O)R^{al}, or -OC(O)NR^{b1}R^{cl}.

44. The compound of any one of claims 1-39 and 43, wherein X^5 is -OH, -OR^{al}, -OC(O)H, -OC(O)R^{al}, or -OC(O)NR^{b1}R^{cl}.

45. The compound of any one of claims 1-39, 43, and 44, wherein X^5 is -OH or -OR^{al} (e.g., R^{al} can be C₁₋₁₀ alkyl, e.g., C₁₋₄ alkyl).

46. The compound of any one of claims 1-45, wherein X^5 is -OH.

47. The compound of any one of claims 1-38, wherein X^5 is H, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, -C(O)H, -C(O)R^{al}, -C(O)NR^{cl}R^{dl}, -C(O)OH, -C(O)OR^{al}, -C(=NR^{cl})NR^{bl}R^{cl}, -S(O)R^{al}, -S(O)NR^{bl}R^{cl}, -S(O)₂R^{al}, or -S(O)₂NR^{bl}R^{cl}; or
 5 X^5 is C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, -C(O)H, -C(O)R^{al}, -C(O)NR^{cl}R^{dl}, -C(O)OH, -C(O)OR^{al}, -C(=NR^{cl})NR^{bl}R^{cl}, -S(O)R^{al}, -S(O)NR^{bl}R^{cl}, -S(O)₂R^{al}, or -S(O)₂NR^{bl}R^{cl}.

48. The compound of any one of claims 1-38 and 47, wherein X^5 is H, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, or -S(O)₂R^{al}; or X^5 is C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, or -S(O)₂R^{al}; or X^5 is H, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), or halo (e.g., F); or X^5 is C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), or halo (e.g., F)).
 10

49. The compound of any one of claims 1-39, 47, and 48, wherein X^5 is H or
 15 halo (e.g., F).

50. The compound of any one of claims 1-42 and 46-49, wherein X^5 is halo (e.g., -F).

51. The compound of any one of claims 1-24, wherein each of X^1 and X^5 is independently selected from the group consisting of: H, -OH, -OR^{al}, -SH, -SR^{al}, -OC(O)H, -OC(O)R^{al}, -OC(O)NR^{bl}R^{cl}, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, -C(O)H, -C(O)R^{al}, -C(O)NR^{cl}R^{dl}, -C(O)OH, -C(O)OR^{al}, -C(=NR^{cl})NR^{bl}R^{cl}, -S(O)R^{al}, -S(O)NR^{bl}R^{cl}, -S(O)₂R^{al}, and -S(O)₂NR^{bl}R^{cl}; or each of X^1 and X^5 is independently
 20 selected from the group consisting of: -OH, -OR^{al}, -SH, -SR^{al}, -OC(O)H, -OC(O)R^{al}, -OC(O)NR^{bl}R^{cl}, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, -C(O)H, -C(O)R^{al}, -C(O)NR^{cl}R^{dl}, -C(O)OH, -C(O)OR^{al}, -C(=NR^{cl})NR^{bl}R^{cl}, -S(O)R^{al}, -S(O)NR^{bl}R^{cl}, -S(O)₂R^{al}, and -S(O)₂NR^{bl}R^{cl}.
 25

52. The compound of any one of claims 1-24 and 51, wherein each of X^1 and X^5 is independently selected from the group consisting of: H, -OH, -OR^{al}, -SH, -SR^{al}, -OC(O)H, -OC(O)R^{al}, -OC(O)NR^{b1}R^{c1}, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, and -S(O)₂R^{al}; or each of X^1 and X^5 is independently selected from the group consisting of: -OH, -OR^{al}, -SH, -SR^{al}, -OC(O)H, -OC(O)R^{al}, -OC(O)NR^{b1}R^{c1}, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, and -S(O)₂R^{al}.

53. The compound of any one of claims 1-24, 51, and 52, wherein each of X^1 and X^5 is independently selected from the group consisting of -F, -OH, -OR^{al}, -OC(O)H, -OC(O)R^{al}, and -OC(O)NR^{b1}R^{c1}.

54. The compound of any one of claims 1-24 and 51-53, wherein each of X^1 and X^5 is independently selected from the group consisting of -F, -OH, and -OR^{al}.

55. The compound of any one of claims 1-24 and 51-54, wherein each of X^1 and X^5 is independently selected from the group consisting of: -F and -OH.

56. The compound of any one of claims 1-24, wherein each of X^1 and X^5 is independently selected from the group consisting of: -OH, -OR^{al}, -SH, -SR^{al}, -OC(O)H, -OC(O)R^{al}, and -OC(O)NR^{b1}R^{c1}.

57. The compound of any one of claims 1-24 and 56, wherein each of X^1 and X^5 is independently selected from the group consisting of -OH, -OR^{al}, -OC(O)H, -OC(O)R^{al}, and -OC(O)NR^{b1}R^{c1}.

58. The compound of any one of claims 1-24, 56, and 57, wherein each of X^1 and X^5 is independently selected from the group consisting of -OH and -OR^{al} (e.g., R^{al} can be C₁₋₁₀ alkyl, e.g., C₁₋₄ alkyl).

59. The compound of any one of claims 1-24 and 51-57, wherein each of X^1 and X^5 is -OH.

60. The compound of any one of claims 1-24, wherein each of X^1 and X^5 is independently selected from the group consisting of: H, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, -C(O)H, -C(O)R^{al}, -C(O)NR^{cl}R^{d1}, -C(O)OH, -C(O)OR^{al}, -C(=NR^{cl})NR^{b1}R^{cl}, -S(O)R^{al}, -S(O)NR^{b1}R^{cl}, -S(O)₂R^{al}, and -S(O)₂NR^{b1}R^{cl}; or each of X^1 and X^5 is independently selected from the group consisting of: C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, -C(O)H, -C(O)R^{al}, -C(O)NR^{cl}R^{d1}, -C(O)OH, -C(O)OR^{al}, -C(=NR^{cl})NR^{b1}R^{cl}, -S(O)R^{al}, -S(O)NR^{b1}R^{cl}, -S(O)₂R^{al}, and -S(O)₂NR^{b1}R^{cl}.

61. The compound of any one of claims 1-24 and 60, wherein each of X^1 and X^5 is independently selected from the group consisting of: H, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, and -S(O)₂R^{al}; or each of X^1 and X^5 is independently selected from the group consisting of: C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, or -S(O)₂R^{al}; or each of X^1 and X^5 is independently selected from the group consisting of: H, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), or halo (e.g., F); or each of X^1 and X^5 is independently selected from the group consisting of: C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), or halo (e.g., F)).

62. The compound of any one of claims 1-24 and 59-61, wherein each of X^1 and X^5 is independently selected from the group consisting of: H and halo (e.g., F).

63. The compound of any one of claims 1-24 and 59-62, wherein each of X^1 and X^5 is an independently selected halo (e.g., -F).

64. The compound of any one of claims 1-24 and 59-63, wherein X^1 and X^5 are the same (e.g., X^1 and X^5 are both -OH; or X^1 and X^5 are both halo (e.g., X^1 and X^5 are both -F); or X^1 and X^5 are both -OR^{al}, in which R^{al} can be C₁₋₁₀ alkyl, e.g., C₁₋₄ alkyl).

65. The compound of any one of claims 1-24 and 59-63, wherein X^1 and X^5 are different (e.g., one of X^1 and X^5 can be -OH, and the other can be halo (e.g., -F); or one of X^1 and X^5 can be -OH, and the other can be -OR^{al}, in which R^{al} can be C₁₋₁₀ alkyl, e.g., C₁₋₄ alkyl; or one of X^1 and X^5 can be -OR^{al}, in which R^{al} can be C₁₋₁₀ alkyl, e.g., C₁₋₄ alkyl, and the other can be halo (e.g., -F)).

66. The compound of any one of claims 1-65, wherein two of X^2 , X^3 , X^4 and X^6 (e.g., X^2 and X^4 ; or X^3 and X^6) are N-R³ (e.g., N-H).

67. The compound of any one of claims 1-66, wherein two of X^2 , X^3 , X^4 and X^6 (e.g., X^2 and X^4 ; or X^3 and X^6) are N-R³ (e.g., N-H), and the others are O.

68. The compound of any one of claims 1-67, wherein L^1 is .

69. The compound of any one of claims 1-68, wherein Y^1 is -OH, -OR^{al}, O⁻, -SH, -SR^{al}, or S⁻.

70. The compound of any one of claims 1-69, wherein Y^1 is -OH, -OR^{al}, or O⁻.

71. The compound of any one of claims 1-69, wherein Y^1 is SH or S⁻.

72. The compound of claim 71, wherein L^1 has the R_P configuration.

73. The compound of claim 71, wherein L^1 has the S_P configuration.

74. The compound of any one of claims 1-73, wherein L^2 is .

75. The compound of any one of claims 1-74, wherein Y^2 is -OH, -OR^{al}, O⁻, -SH, -SR^{al}, or S⁻.

76. The compound of any one of claims 1-75, wherein Y^2 is -OH, -OR^{al}, or O⁻.

77. The compound of any one of claims 1-75, wherein Y^2 is SH or S⁻.

78. The compound of claim 77, wherein L^2 has the R_P configuration.

79. The compound of claim 77, wherein L^2 has the S_P configuration.

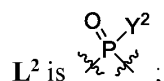
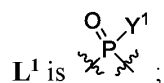
80. The compound of any one of claims 1-79, wherein R^{1A} and R^{1B} are each H and/or R^{2A} and R^{2B} are each H.

81. The compound of any one of claims 1-80, wherein each occurrence of R^3 , R^{b1} , R^{c1} , R^{d1} , and R^{e1} (or each occurrence of R^{b1} and R^{c1} ; or each occurrence of R^{c1} and R^{d1} ; or each occurrence of R^3 ; or each occurrence of R^{e1}) is independently selected from the group consisting of: H; R^{al}; -C(O)H, -C(O)R^{al}, --C(O)NRR', wherein R and R' are each independently selected from H and C₁₋₄ alkyl optionally substituted with from 1-3 R^A; -C(O)OR^{al}, -OC(O)H, -S(O)R^{al}, and -S(O)₂R^{al}; or

R^{b1} and R^{c1} taken together with the nitrogen atom to which each is attached form a heterocyclyl, including from 3-10 (e.g., 3-6, 4-6, 5-6) ring atoms, wherein from 1-3 ring atoms are independently selected from the group consisting of nitrogen, oxygen and sulfur, and which is optionally substituted with from 1-5 R^C; (e.g., azetidiny, morpholino, piperidiny).

82. The compound of claim 1, wherein X^1 and X^5 are each independently selected from the group consisting of -OH, -OR^{al}, -OC(O)H, -OC(O)R^{al}, and -OC(O)NR^{b1}R^{c1}.

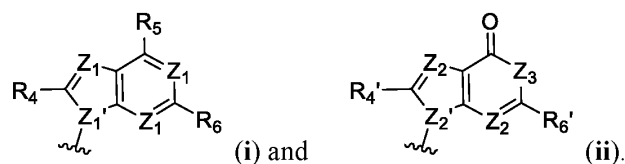
two of X^2 , X^3 , X^4 and X^6 are $N-R^3$ (e.g., $N-H$);



Y^1 and Y^2 are each independently selected from $-OH$, $-OR^{al}$, O^- , $-SH$, $-SR^{al}$, or S ;

5 and

A and **B** are each independently selected from the group consisting of:



10 83. The compound of claim 43, wherein **A** has formula (i), and **B** has formula (ii); or **A** has formula (ii), and **B** has formula (ii); or **A** has formula (i), and **B** has formula (i); or **A** has formula (ii), and **B** has formula (i).

15 84. The compound of claim 82 or 83, wherein each occurrence of Z^1 is N , and $Z^{1'}$ is N .

20 85. The compound of any one of claims 82-84, wherein R^5 is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, R^4 and/or R^6 is H ; or R^4 is other than H , and R^6 is H).

25 86. The compound of any one of claims 82-84, wherein R^5 is $-OH$, and R^6 is H (e.g., in certain embodiments, R^4 is H ; in other embodiments, R^4 is other than H).

87. The compound of any one of claims 82-86, wherein each occurrence of Z^2 is N , $Z^{2'}$ is N , and Z^3 is $N-R^3$ (e.g., $N-H$).

88. The compound of any one of claims 82-87, wherein $R^{6'}$ is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, $R^{4'}$ is H; in other embodiments, $R^{4'}$ is other than H).

5

89. The compound of any one of claims 82-88, wherein X^1 and X^5 are each independently selected from the group consisting of $-OH$, or $-OR^{a1}$ (e.g., R^{a1} can be C_{1-10} alkyl, e.g., C_{1-4} alkyl).

10

90. The compound of any one of claims 82-89, wherein X^1 and X^5 are each $-OH$.

91. The compound of any one of claims 82-90, wherein two of X^2 , X^3 , X^4 and X^6 are $N-R^3$ (e.g., $N-H$), and the others are O.

15

92. The compound of any one of claims 82-91, wherein Y^1 and Y^2 are each O $^-$.

93. The compound of any one of claims 82-91, wherein Y^1 and Y^2 are each SH or S $^-$.

20

94. The compound of claim 93, wherein L^1 and L^2 both have the R_P configuration or both have the S_P configuration.

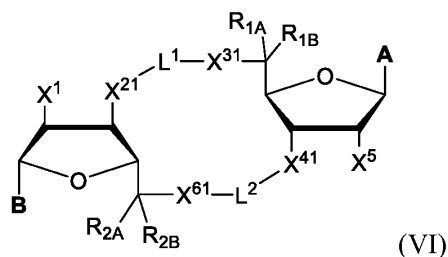
95. The compound of claim 93, wherein one of L^1 and L^2 has the R_P configuration, and the other has the S_P configuration.

25

96. The compound of any one of claims 82-95, wherein R^{1A} and R^{1B} are each H, and R^{2A} and R^{2B} are each H.

30

97. The compound of claim 1, wherein the compound has formula (VI):

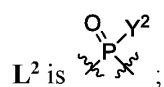
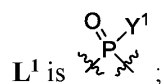


wherein,

X^1 and X^5 are each independently selected from the group consisting of -OH, -OR^{a1}, -OC(O)H, -OC(O)R^{a1}, or -OC(O)NR^{b1}R^{c1};

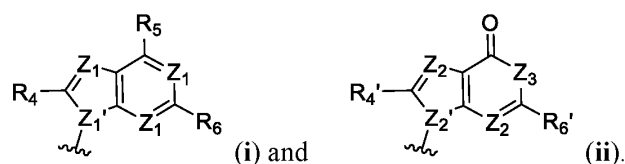
X^{21} and X^{41} are each an independently selected N-R³ (e.g., N-H);

X^{31} and X^{61} are O;



Y^1 and Y^2 are each independently selected from -OH, -OR^{a1}, O⁻, -SH, -SR^{a1}, or S;
and

A and **B** are each independently selected from the group consisting of:



15

98. The compound of claim 97, wherein **A** has formula (i), and **B** has formula (ii); or **A** has formula (ii), and **B** has formula (ii); or **A** has formula (i), and **B** has formula (i); or **A** has formula (ii), and **B** has formula (i).

99. The compound of claim 97 or 98, wherein each occurrence of Z¹ is N, and Z^{1'} is N.

100. The compound of any one of claims 97-99, wherein R^5 is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, R^4 and/or R^6 is H; or R^4 is other than H, and R^6 is H).

5

101. The compound of any one of claims 97-99, wherein R^5 is $-OH$, and R^6 is H (e.g., in certain embodiments, R^4 is H; in other embodiments, R^4 is other than H).

102. The compound of any one of claims 97-101, wherein each occurrence of Z^2 is N, $Z^{2'}$ is N, and Z^3 is $N-R^3$ (e.g., N-H).

10

103. The compound of any one of claims 97-102, wherein $R^{6'}$ is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, $R^{4'}$ is H; in other embodiments, $R^{4'}$ is other than H).

15

104. The compound of any one of claims 97-103, wherein X^1 and X^5 are each independently selected from the group consisting of $-OH$, $-OR^{a1}$, $-OC(O)H$, $-OC(O)R^{a1}$, or $-OC(O)NR^{b1}R^{c1}$.

20

105. The compound of any one of claims 97-104, wherein X^1 and X^5 are each independently selected from the group consisting of $-OH$ and $-OR^{a1}$ (e.g., R^{a1} can be C_{1-10} alkyl, e.g., C_{1-4} alkyl).

25

106. The compound of any one of claims 97-105, wherein X^1 and X^5 are each $-OH$.

107. The compound of any one of claims 97-106, wherein Y^1 and Y^2 are each O^- .

108. The compound of any one of claims 97-106, wherein $\mathbf{Y}^1$ and $\mathbf{Y}^2$ are each $\mathbf{S}^-$.

109. The compound of claim 108, wherein $\mathbf{L}^1$ and $\mathbf{L}^2$ both have the $\mathbf{R}_P$ configuration or both have the $\mathbf{S}_P$ configuration.

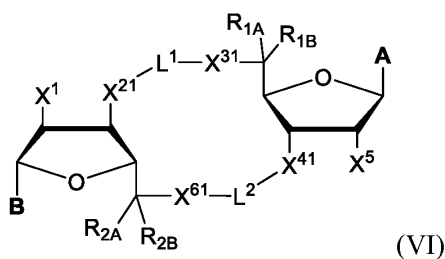
5

110. The compound of claim 108, wherein one of $\mathbf{L}^1$ and $\mathbf{L}^2$ has the $\mathbf{R}_P$ configuration, and the other has the $\mathbf{S}_P$ configuration.

111. The compound of any one of claims 97-110, wherein $\mathbf{R}^{1A}$ and $\mathbf{R}^{1B}$ are each H, and $\mathbf{R}^{2A}$ and $\mathbf{R}^{2B}$ are each H.

10

112. The compound of claim 1, wherein the compound has formula (VI):

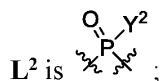
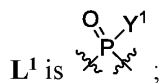


wherein,

15 $\mathbf{X}^1$ and $\mathbf{X}^5$ are each independently selected from the group consisting of -OH, -OR^{al}, -OC(O)H, -OC(O)R^{al}, or -OC(O)NR^{b1}R^{c1};

$\mathbf{X}^{31}$ and $\mathbf{X}^{61}$ are each an independently selected N-R³ (e.g., N-H);

$\mathbf{X}^{21}$ and $\mathbf{X}^{41}$ are O;

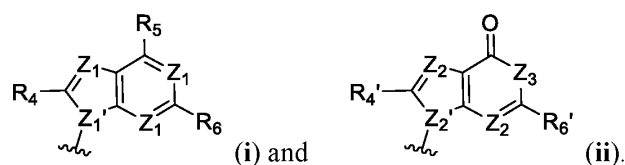


20

$\mathbf{Y}^1$ and $\mathbf{Y}^2$ are each independently selected from -OH, -OR^{al}, O⁻, -SH, -SR^{al}, or S;

and

$\mathbf{A}$ and $\mathbf{B}$ are each independently selected from the group consisting of:



113. The compound of claim 112, wherein **A** has formula (i), and **B** has
 5 formula (ii); or **A** has formula (ii), and **B** has formula (ii); or **A** has formula (i), and **B** has
 formula (i); or **A** has formula (ii), and **B** has formula (i).

114. The compound of claim 112 or 113, wherein each occurrence of Z^1 is N,
 and $Z^{1'}$ is N.
 10

115. The compound of any one of claims 112-114, wherein R^5 is $-NR^{b1}R^{c1}$ (e.g.,
 $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, R^4 and/or R^6 is H; or R^4 is other than H, and
 R^6 is H).

116. The compound of any one of claims 112-114, wherein R^5 is $-OH$, and R^6 is
 H (e.g., in certain embodiments, R^4 is H; in other embodiments, R^4 is other than H).
 15

117. The compound of any one of claims 112-116, wherein each occurrence of
 Z^2 is N, $Z^{2'}$ is N, and Z^3 is $N-R^3$ (e.g., N-H).
 20

118. The compound of any one of claims 112-117, wherein $R^{6'}$ is $-NR^{b1}R^{c1}$ (e.g.,
 $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, $R^{4'}$ is H; in other embodiments, $R^{4'}$ is other
 than H).

119. The compound of any one of claims 112-118, wherein X^1 and X^5 are each
 independently selected from the group consisting of $-OH$, $-OR^{a1}$, $-OC(O)H$, $-OC(O)R^{a1}$, or
 $-OC(O)NR^{b1}R^{c1}$.
 25

120. The compound of any one of claims 112-119, wherein X^1 and X^5 are each independently selected from the group consisting of $-OH$ and $-OR^{al}$ (e.g., R^{al} can be C_{1-10} alkyl, e.g., C_{1-4} alkyl).

5

121. The compound of any one of claims 112-120, wherein X^1 and X^5 are each $-OH$.

10

122. The compound of any one of claims 112-121, wherein Y^1 and Y^2 are each O^- .

123. The compound of any one of claims 112-121, wherein Y^1 and Y^2 are each S^- .

15

124. The compound of claim 123, wherein L^1 and L^2 both have the R_P configuration or both have the S_P configuration.

125. The compound of claim 123, wherein one of L^1 and L^2 has the R_P configuration, and the other has the S_P configuration.

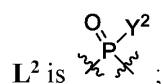
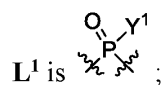
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126. The compound of any one of claims 112-125, wherein R^{1A} and R^{1B} are each H, and R^{2A} and R^{2B} are each H.

25

127. The compound of claim 1, wherein X^1 and X^5 are each independently selected from the group consisting of H, C_{1-4} alkyl, C_{1-4} haloalkyl (e.g., CF_3), halo (e.g., F), $-CN$, $-C(O)H$, $-C(O)R^{al}$, $-C(O)NR^{cl}R^{dl}$, $-C(O)OH$, $-C(O)OR^{al}$, $-C(=NR^{cl})NR^{bl}R^{cl}$, $-S(O)R^{al}$, $-S(O)NR^{bl}R^{cl}$, $-S(O)_2R^{al}$, and $-S(O)_2NR^{bl}R^{cl}$;

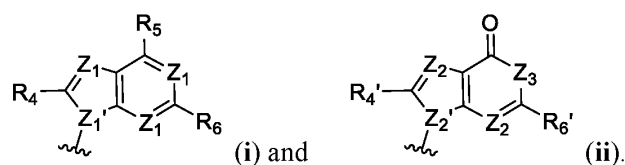
two of X^2 , X^3 , X^4 and X^6 are $N-R^3$ (e.g., $N-H$);



Y^1 and Y^2 are each independently selected from $-\text{OH}$, $-\text{OR}^{\text{al}}$, O^- , $-\text{SH}$, $-\text{SR}^{\text{al}}$, or S ;

and

5 **A** and **B** are each independently selected from the group consisting of:



128. The compound of claim 85, wherein **A** has formula (i), and **B** has formula
 10 (ii); or **A** has formula (ii), and **B** has formula (ii); or **A** has formula (i), and **B** has formula
 (i); or **A** has formula (ii), and **B** has formula (i).

129. The compound of claim 127 or 128, wherein each occurrence of Z^1 is N ,
 and $\text{Z}^{1'}$ is N .

15

130. The compound of any one of claims 127-129, wherein R^5 is $-\text{NR}^{\text{bl}}\text{R}^{\text{cl}}$
 (e.g., $-\text{NH}_2$ or $-\text{NHR}^{\text{cl}}$; e.g., in certain embodiments, R^4 and/or R^6 is H ; or R^4 is other than
 H , and R^6 is H).

20 131. The compound of any one of claims 127-129, wherein R^5 is $-\text{OH}$, and R^6
 is H (e.g., in certain embodiments, R^4 is H ; in other embodiments, R^4 is other than H).

132. The compound of any one of claims 127-131, wherein each occurrence of
 Z^2 is N , $\text{Z}^{2'}$ is N , and Z^3 is N-R^3 (e.g., N-H).

25

133. The compound of any one of claims 127-132, wherein $R^{6'}$ is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, $R^{4'}$ is H; in other embodiments, $R^{4'}$ is other than H).

5 134. The compound of any one of claims 127-133, wherein X^1 and X^5 are each independently selected from the group consisting of H, C_{1-4} alkyl, C_{1-4} haloalkyl (e.g., CF_3), halo (e.g., F), $-CN$, and $-S(O)_2R^{a1}$ (in certain embodiments, each of X^1 and X^5 is other than H).

10 135. The compound of any one of claims 127-134, wherein X^1 and X^5 are each independently selected from the group consisting of H, C_{1-4} alkyl, C_{1-4} haloalkyl (e.g., CF_3), and halo (e.g., F) (in certain embodiments, each of X^1 and X^5 is other than H).

15 136. The compound of any one of claims 127-135, wherein X^1 and X^5 are each independently selected from the group consisting of H and halo (e.g., F).

 137. The compound of any one of claims 127-136, wherein X^1 and X^5 are each an independently selected halo (e.g., F).

20 138. The compound of any one of claims 127-137, wherein two of X^2 , X^3 , X^4 and X^6 are $N-R^3$ (e.g., N-H), and the others are O.

 139. The compound of any one of claims 127-138, wherein Y^1 and Y^2 are each O.

25 140. The compound of any one of claims 127-138, wherein Y^1 and Y^2 are each SH or S.

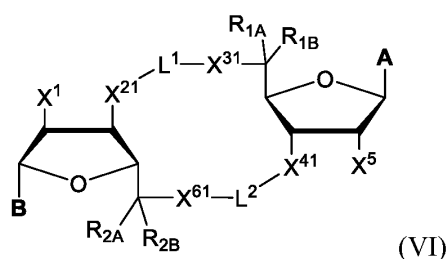
 141. The compound of claim 140, wherein L^1 and L^2 both have the R_P configuration or both have the S_P configuration.

30

142. The compound of claim 140, wherein one of L^1 and L^2 has the R_P configuration, and the other has the S_P configuration.

5 143. The compound of any one of claims 127-142, wherein R^{1A} and R^{1B} are each H, and R^{2A} and R^{2B} are each H.

144. The compound of claim 1, wherein the compound has formula (VI):

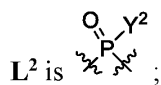
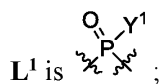


10 wherein,

X^1 and X^5 are each independently selected from the group consisting of H, C_{1-4} alkyl, C_{1-4} haloalkyl (e.g., CF_3), halo (e.g., F), -CN, -C(O)H, -C(O) R^{a1} , -C(O)NR c1 R d1 , -C(O)OH, -C(O)OR a1 , -C(=NR c1)NR b1 R c1 , -S(O)R a1 , -S(O)NR b1 R c1 , -S(O) $_2$ R a1 , and -S(O) $_2$ NR b1 R c1 ;

15 X^{21} and X^{41} are each an independently selected N-R 3 (e.g., N-H);

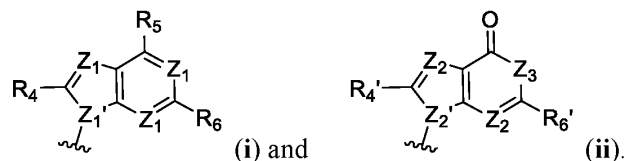
X^{31} and X^{61} are O;



Y^1 and Y^2 are each independently selected from -OH, -OR a1 , O $^-$, -SH, -SR a1 , or S;

20 and

A and **B** are each independently selected from the group consisting of:



145. The compound of claim 144, wherein **A** has formula (i), and **B** has formula (ii); or **A** has formula (ii), and **B** has formula (ii); or **A** has formula (i), and **B** has formula (i).; or **A** has formula (ii), and **B** has formula (i).

146. The compound of claim 144 or 145, wherein each occurrence of Z^1 is N, and $Z^{1'}$ is N.

147. The compound of any one of claims 144-146, wherein R^5 is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, R^4 and/or R^6 is H; or R^4 is other than H, and R^6 is H).

148. The compound of any one of claims 144-146, wherein R^5 is $-OH$, and R^6 is H (e.g., in certain embodiments, R^4 is H; in other embodiments, R^4 is other than H).

149. The compound of any one of claims 144-148, wherein each occurrence of Z^2 is N, $Z^{2'}$ is N, and Z^3 is $N-R^3$ (e.g., $N-H$).

150. The compound of any one of claims 144-149, wherein $R^{6'}$ is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, $R^{4'}$ is H; in other embodiments, $R^{4'}$ is other than H).

151. The compound of any one of claims 144-150, wherein X^1 and X^5 are each independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} haloalkyl (e.g., CF_3), halo (e.g., F), $-CN$, and $-S(O)_2R^{a1}$ (in certain embodiments, each of X^1 and X^5 is other than H).

152. The compound of any one of claims 144-151, wherein X^1 and X^5 are each independently selected from the group consisting of H, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), and halo (e.g., F) (in certain embodiments, each of X^1 and X^5 is other than H).

5

153. The compound of any one of claims 144-152, wherein X^1 and X^5 are each independently selected from the group consisting of H and halo (e.g., F).

154. The compound of any one of claims 144-153, wherein X^1 and X^5 are each an independently selected halo (e.g., F).

10

155. The compound of any one of claims 144-154, wherein Y^1 and Y^2 are each O⁻.

156. The compound of any one of claims 144-154, wherein Y^1 and Y^2 are each S⁻.

15

157. The compound of claim 156, wherein L^1 and L^2 both have the R_P configuration or both have the S_P configuration.

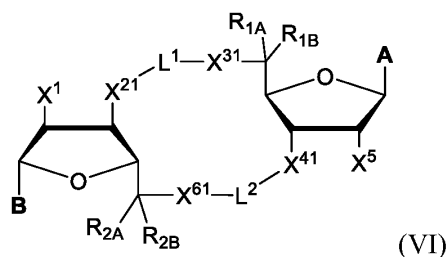
20

158. The compound of claim 156, wherein one of L^1 and L^2 has the R_P configuration, and the other has the S_P configuration.

159. The compound of any one of claims 144-158, wherein R^{1A} and R^{1B} are each H, and R^{2A} and R^{2B} are each H.

25

160. The compound of claim 1, wherein the compound has formula (VI):

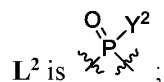
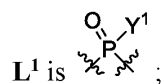


wherein,

X^1 and X^5 are each independently selected from the group consisting of H, C₁₋₄ alkyl, C₁₋₄ haloalkyl (e.g., CF₃), halo (e.g., F), -CN, -C(O)H, -C(O)R^{al}, -C(O)NR^{cl}R^{dl}, -C(O)OH, -C(O)OR^{al}, -C(=NR^{cl})NR^{bl}R^{cl}, -S(O)R^{al}, -S(O)NR^{bl}R^{cl}, -S(O)₂R^{al}, and -S(O)₂NR^{bl}R^{cl};

X^{31} and X^{61} are each an independently selected N-R³ (e.g., N-H);

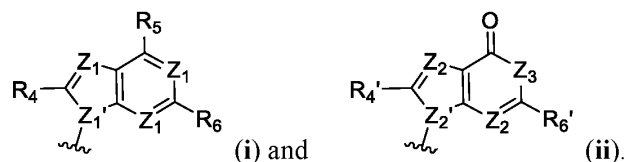
X^{21} and X^{41} are O;



Y^1 and Y^2 are each independently selected from -OH, -OR^{al}, O⁻, -SH, -SR^{al}, or S;

and

A and **B** are each independently selected from the group consisting of:



161. The compound of claim 160, wherein **A** has formula (i), and **B** has formula (ii); or **A** has formula (ii), and **B** has formula (ii); or **A** has formula (i), and **B** has formula (i); or **A** has formula (ii), and **B** has formula (i).

162. The compound of claim 160 or 161, wherein each occurrence of Z^1 is N, and $Z^{1'}$ is N.

163. The compound of any one of claims 160-162, wherein R^5 is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, R^4 and/or R^6 is H; or R^4 is other than H, and R^6 is H).

164. The compound of any one of claims 160-162, wherein R^5 is $-OH$, and R^6 is H (e.g., in certain embodiments, R^4 is H; in other embodiments, R^4 is other than H).

10

165. The compound of any one of claims 160-164, wherein each occurrence of Z^2 is N, $Z^{2'}$ is N, and Z^3 is $N-R^3$ (e.g., N-H).

166. The compound of any one of claims 160-165, wherein $R^{6'}$ is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, $R^{4'}$ is H; in other embodiments, $R^{4'}$ is other than H).

15

167. The compound of any one of claims 160-166, wherein X^1 and X^5 are each independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} haloalkyl (e.g., CF_3), halo (e.g., F), $-CN$, and $-S(O)_2R^{a1}$ (in certain embodiments, each of X^1 and X^5 is other than H).

20

168. The compound of any one of claims 160-167, wherein X^1 and X^5 are each independently selected from the group consisting of H, C_{1-4} alkyl, C_{1-4} haloalkyl (e.g., CF_3), and halo (e.g., F) (in certain embodiments, each of X^1 and X^5 is other than H).

25

169. The compound of any one of claims 160-168, wherein X^1 and X^5 are each independently selected from the group consisting of H and halo (e.g., F).

170. The compound of any one of claims 160-169, wherein X^1 and X^5 are each halo (e.g., F).

171. The compound of any one of claims 160-170, wherein Y^1 and Y^2 are each O^- .

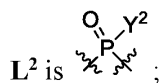
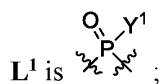
172. The compound of any one of claims 160-171, wherein Y^1 and Y^2 are each S^- .

173. The compound of claim 172, wherein L^1 and L^2 both have the R_P configuration or both have the S_P configuration.

174. The compound of claim 172, wherein one of L^1 and L^2 has the R_P configuration, and the other has the S_P configuration.

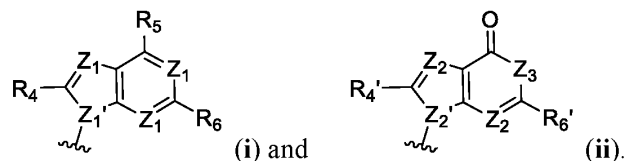
175. The compound of any one of claims 160-174, wherein R^{1A} and R^{1B} are each H, and R^{2A} and R^{2B} are each H.

176. The compound of claim 1, wherein X^1 and X^5 are each independently selected from the group consisting of halo (e.g., -F), -OH, -OR^{a1}, -OC(O)H, -OC(O)R^{a1}, or -OC(O)NR^{b1}R^{c1}; two of X^2 , X^3 , X^4 and X^6 are N-R³ (e.g., N-H);



Y^1 and Y^2 are each independently selected from -OH, -OR^{a1}, O^- , -SH, -SR^{a1}, or S; and

A and **B** are each independently selected from the group consisting of:



177. The compound of claim 176, wherein **A** has formula (i), and **B** has formula (ii); or **A** has formula (ii), and **B** has formula (ii); or **A** has formula (i), and **B** has formula (i); or **A** has formula (ii), and **B** has formula (i).

178. The compound of claim 176 or 177, wherein each occurrence of Z^1 is N, and $Z^{1'}$ is N.

179. The compound of any one of claims 176-178, wherein R^5 is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, R^4 and/or R^6 is H; or R^4 is other than H, and R^6 is H).

180. The compound of any one of claims 176-178, wherein R^5 is $-OH$, and R^6 is H (e.g., in certain embodiments, R^4 is H; in other embodiments, R^4 is other than H).

181. The compound of any one of claims 176-180, wherein each occurrence of Z^2 is N, $Z^{2'}$ is N, and Z^3 is $N-R^3$ (e.g., N-H).

182. The compound of any one of claims 176-181, wherein $R^{6'}$ is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, $R^{4'}$ is H; in other embodiments, $R^{4'}$ is other than H).

183. The compound of any one of claims 176-182, wherein each of X^1 and X^5 is independently selected from the group consisting of halo (e.g., -F), -OH, and $-OR^{a1}$ (e.g., R^{a1} can be C_{1-10} alkyl, e.g., C_{1-4} alkyl).

184. The compound of any one of claims 176-183, wherein each of X^1 and X^5 is independently selected from the group consisting of: halo (e.g., -F) and -OH (in certain embodiments, one of X^1 and X^5 is halo (e.g., -F), and the other is -OH).

5 185. The compound of any one of claims 176-184, wherein two of X^2 , X^3 , X^4 and X^6 are N- R^3 (e.g., N-H), and the others are O.

186. The compound of any one of claims 176-185, wherein Y^1 and Y^2 are each O^- .

10

187. The compound of any one of claims 176-185, wherein Y^1 and Y^2 are each SH or S^- .

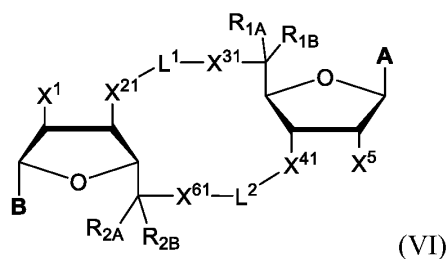
188. The compound of claim 187, wherein L^1 and L^2 both have the R_P configuration or both have the S_P configuration.

15

189. The compound of claim 187, wherein one of L^1 and L^2 has the R_P configuration, and the other has the S_P configuration.

20 190. The compound of any one of claims 176-189, wherein R^{1A} and R^{1B} are each H, and R^{2A} and R^{2B} are each H.

191. The compound of claim 1, wherein the compound has formula (VI):



25

wherein,

X^1 and X^5 are each independently selected from the group consisting of halo (e.g., -F), -OH, -OR^{a1}, -OC(O)H, -OC(O)R^{a1}, or -OC(O)NR^{b1}R^{c1};

X^{21} and X^{41} are each an independently selected N-R³ (e.g., N-H);

X^{31} and X^{61} are O;

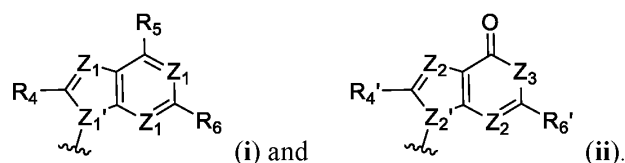
5 L^1 is ;

L^2 is ;

Y^1 and Y^2 are each independently selected from -OH, -OR^{a1}, O⁻, -SH, -SR^{a1}, or S;
and

A and **B** are each independently selected from the group consisting of:

10



192. The compound of claim 191, wherein **A** has formula (i), and **B** has formula (ii); or **A** has formula (ii), and **B** has formula (ii); or **A** has formula (i), and **B** has formula (i); or **A** has formula (ii), and **B** has formula (i).

15

193. The compound of claim 191 or 192, wherein each occurrence of Z^1 is N, and $Z^{1'}$ is N.

20 194. The compound of any one of claims 191-193, wherein R^5 is -NR^{b1}R^{c1} (e.g., -NH₂ or -NHR^{c1}; e.g., in certain embodiments, R^4 and/or R^6 is H; or R^4 is other than H, and R^6 is H).

25 195. The compound of any one of claims 191-193, wherein R^5 is -OH, and R^6 is H (e.g., in certain embodiments, R^4 is H; in other embodiments, R^4 is other than H).

196. The compound of any one of claims 191-195, wherein each occurrence of Z^2 is N, $Z^{2'}$ is N, and Z^3 is N- R^3 (e.g., N-H).

5 197. The compound of any one of claims 191-196, wherein $R^{6'}$ is - $NR^{b1}R^{c1}$ (e.g., - NH_2 or - NHR^{c1} ; e.g., in certain embodiments, $R^{4'}$ is H; in other embodiments, $R^{4'}$ is other than H).

10 198. The compound of any one of claims 191-197, wherein each of X^1 and X^5 is independently selected from the group consisting of halo (e.g., -F), -OH, and - OR^{a1} (e.g., R^{a1} can be C_{1-10} alkyl, e.g., C_{1-4} alkyl).

15 199. The compound of any one of claims 191-198, wherein each of X^1 and X^5 is independently selected from the group consisting of: halo (e.g., -F) and -OH (in certain embodiments, one of X^1 and X^5 is halo (e.g., -F), and the other is -OH).

200. The compound of any one of claims 191-199, wherein Y^1 and Y^2 are each O^- .

20 201. The compound of any one of claims 191-200, wherein Y^1 and Y^2 are each S^- .

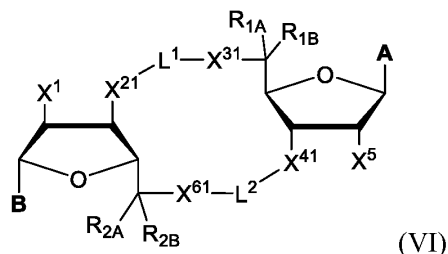
202. The compound of claim 201, wherein L^1 and L^2 both have the R_P configuration or both have the S_P configuration.

25

203. The compound of claim 201, wherein one of L^1 and L^2 has the R_P configuration, and the other has the S_P configuration.

30 204. The compound of any one of claims 97-110, wherein R^{1A} and R^{1B} are each H, and R^{2A} and R^{2B} are each H.

205. The compound of claim 1, wherein the compound has formula (VI):

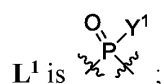


wherein,

5 X^1 and X^5 are each independently selected from the group consisting of halo (e.g., -F), -OH, -OR^{a1}, -OC(O)H, -OC(O)R^{a1}, or -OC(O)NR^{b1}R^{c1};

X^{31} and X^{61} are each an independently selected N-R³ (e.g., N-H);

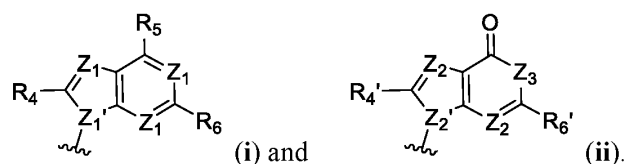
X^{21} and X^{41} are O;



Y^1 and Y^2 are each independently selected from -OH, -OR^{a1}, O⁻, -SH, -SR^{a1}, or S;

and

A and **B** are each independently selected from the group consisting of:



206. The compound of claim 205, wherein **A** has formula (i), and **B** has formula (ii); or **A** has formula (ii), and **B** has formula (ii); or **A** has formula (i), and **B** has formula (i); or **A** has formula (ii), and **B** has formula (i).

20

207. The compound of claim 205 or 206, wherein each occurrence of Z^1 is N, and $Z^{1'}$ is N.

208. The compound of any one of claims 205-207, wherein R^5 is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, R^4 and/or R^6 is H; or R^4 is other than H, and R^6 is H).

209. The compound of any one of claims 205-207, wherein R^5 is $-OH$, and R^6 is H (e.g., in certain embodiments, R^4 is H; in other embodiments, R^4 is other than H).

10

210. The compound of any one of claims 205-209, wherein each occurrence of Z^2 is N, $Z^{2'}$ is N, and Z^3 is $N-R^3$ (e.g., N-H).

211. The compound of any one of claims 205-210, wherein $R^{6'}$ is $-NR^{b1}R^{c1}$ (e.g., $-NH_2$ or $-NHR^{c1}$; e.g., in certain embodiments, $R^{4'}$ is H; in other embodiments, $R^{4'}$ is other than H).

15

212. The compound of any one of claims 205-211, wherein each of X^1 and X^5 is independently selected from the group consisting of halo (e.g., -F), -OH, and $-OR^{a1}$ (e.g., R^{a1} can be C_{1-10} alkyl, e.g., C_{1-4} alkyl).

20

213. The compound of any one of claims 205-212, wherein each of X^1 and X^5 is independently selected from the group consisting of: halo (e.g., -F) and -OH (in certain embodiments, one of X^1 and X^5 is halo (e.g., -F), and the other is -OH).

25

214. The compound of any one of claims 205-213, wherein Y^1 and Y^2 are each O $^-$.

215. The compound of any one of claims 205-213, wherein Y^1 and Y^2 are each S $^-$.

30

216. The compound of claim 215, wherein L^1 and L^2 both have the R_P configuration or both have the S_P configuration.

5 217. The compound of claim 215, wherein one of L^1 and L^2 has the R_P configuration, and the other has the S_P configuration.

218. The compound of any one of claims 205-217, wherein R^{1A} and R^{1B} are each H, and R^{2A} and R^{2B} are each H.

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219. The compound of claim 1, wherein the compound is a compound delineated in Table 1.

220. A pharmaceutical composition comprising a compound or salt as claimed
15 in any one of claims 1-219 and one or more pharmaceutically acceptable excipients.

221. A method for modulating STING activity, the method comprising contacting STING with a compound as claimed in any one of claims 1-219.

20 222. The method of claim 221, wherein the modulating comprises agonizing STING.

223. The method of any one of claims 221 or 222, which is carried out *in vitro*.

25 224. The method of claim 223, wherein the method comprises contacting a sample comprising one or more cells comprising STING with the compound.

225. The method of claim 224, wherein at least one of the one or more cells is an innate immune cell (e.g., mast cells, macrophages, dendritic cells (DCs), and natural
30 killer cells).

226. The method of claim 225, wherein said contacting induces an immune response sufficient to kill at least one of the one or more cancer cells.

5 227. The method of claim 226, wherein the sample further comprises one or more cancer cells (e.g., wherein the cancer is selected from the group consisting of melanoma, cervical cancer, breast cancer, ovarian cancer, prostate cancer, testicular cancer, urothelial carcinoma, bladder cancer, non-small cell lung cancer, small cell lung cancer, sarcoma, colorectal adenocarcinoma, gastrointestinal stromal tumors, gastroesophageal carcinoma,
10 colorectal cancer, pancreatic cancer, kidney cancer, hepatocellular cancer, malignant mesothelioma, leukemia, lymphoma, myelodysplasia syndrome, multiple myeloma, transitional cell carcinoma, neuroblastoma, plasma cell neoplasms, Wilm's tumor, or hepatocellular carcinoma).

15 228. The method of claim 221, which is carried out *in vivo*.

229. The method of claim 228, wherein the method comprises administering the compound to a subject having a disease in which repressed or impaired STING signaling contributes to the pathology and/or symptoms and/or progression of the disease.

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230. The method of claim 229, wherein the subject is a human.

231. The method of claim 229, wherein the disease is cancer.

25 232. The method of claim 231, wherein the cancer is selected from the group consisting of melanoma, cervical cancer, breast cancer, ovarian cancer, prostate cancer, testicular cancer, urothelial carcinoma, bladder cancer, non-small cell lung cancer, small cell lung cancer, sarcoma, colorectal adenocarcinoma, gastrointestinal stromal tumors, gastroesophageal carcinoma, colorectal cancer, pancreatic cancer, kidney cancer,
30 hepatocellular cancer, malignant mesothelioma, leukemia, lymphoma, myelodysplasia

syndrome, multiple myeloma, transitional cell carcinoma, neuroblastoma, plasma cell neoplasms, Wilm's tumor, or hepatocellular carcinoma.

233. The method of claim 231 or 232, wherein the cancer is a refractory cancer.

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234. The method of claim 229, wherein the compound is administered in combination with one or more additional cancer therapies.

235. The method of claim 234, wherein the one or more additional cancer therapies comprises surgery, radiotherapy, chemotherapy, toxin therapy, immunotherapy, cryotherapy or gene therapy, or a combination thereof.

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236. The method of claim 235, wherein chemotherapy comprises administering one or more additional chemotherapeutic agents.

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237. The method of claim 236, wherein the one or more additional chemotherapeutic agents is selected from an alkylating agent (e.g., cisplatin, carboplatin, mechlorethamine, cyclophosphamide, chlorambucil, ifosfamide and/or oxaliplatin); an anti-metabolite (e.g., azathioprine and/or mercaptopurine); a terpenoid (e.g., a vinca alkaloid and/or a taxane; e.g., Vincristine, Vinblastine, Vinorelbine and/or Vindesine Taxol, Paclitaxel and/or Docetaxel); a topoisomerase (e.g., a type I topoisomerase and/or a type 2 topoisomerase; e.g., camptothecins, such as irinotecan and/or topotecan; amsacrine, etoposide, etoposide phosphate and/or teniposide); a cytotoxic antibiotic (e.g., actinomycin, anthracyclines, doxorubicin, daunorubicin, valrubicin, idarubicin, epirubicin, bleomycin, plicamycin and/or mitomycin); a hormone (e.g., a lutenizing hormone releasing hormone agonist; e.g., leuprolidine, goserelin, triptorelin, histrelin, bicalutamide, flutamide and/or nilutamide); an antibody (e.g., Abciximab, Adalimumab, Alemtuzumab, Atlizumab, Basiliximab, Belimumab, Bevacizumab, Bretuximab vedotin, Canakinumab, Cetuximab, Ceertolizumab pegol, Daclizumab, Denosumab, Eculizumab, Efalizumab, Gemtuzumab, Golimumab, Golimumab, Ibritumomab tiuxetan, Infliximab, Ipilimumab,

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Muromonab-CD3, Natalizumab, Ofatumumab, Omalizumab, Palivizumab, Panitumumab, Ranibizumab, Rituximab, Tocilizumab, Tositumomab and/or Trastuzumab); an anti-angiogenic agent; a cytokine; a thrombotic agent; a growth inhibitory agent; an anti-helminthic agent; and an immune checkpoint inhibitor that targets an immune checkpoint receptor selected from the group consisting of CTLA-4, PD-1, PD-L1, PD-1 – PD-L1, PD-1 – PD-L2, interleukin-2 (IL-2), indoleamine 2,3-dioxygenase (IDO), IL-10, transforming growth factor- β (TGF β), T cell immunoglobulin and mucin 3 (TIM3 or HAVCR2), Galectin 9 – TIM3, Phosphatidylserine – TIM3, lymphocyte activation gene 3 protein (LAG3), MHC class II – LAG3, 4-1BB–4-1BB ligand, OX40–OX40 ligand, GITR, GITR ligand – GITR, CD27, CD70-CD27, TNFRSF25, TNFRSF25–TL1A, CD40L, CD40–CD40 ligand, HVEM–LIGHT–LTA, HVEM, HVEM – BTLA, HVEM – CD160, HVEM – LIGHT, HVEM–BTLA–CD160, CD80, CD80 – PDL-1, PDL2 – CD80, CD244, CD48 – CD244, CD244, ICOS, ICOS–ICOS ligand, B7-H3, B7-H4, VISTA, TMIGD2, HHLA2–TMIGD2, Butyrophilins, including BTNL2, Siglec family, TIGIT and PVR family members, KIRs, ILTs and LIRs, NKG2D and NKG2A, MICA and MICB, CD244, CD28, CD86 – CD28, CD86 – CTLA, CD80 – CD28, CD39, CD73 Adenosine–CD39–CD73, CXCR4–CXCL12, Phosphatidylserine, TIM3, Phosphatidylserine – TIM3, SIRPA–CD47, VEGF, Neuropilin, CD160, CD30, and CD155 (e.g., CTLA-4 or PD1 or PD-L1).

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238. The method of any one of claims 229-237, wherein the compound is administered intratumorally.

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239. A method of treating cancer, comprising administering to a subject in need of such treatment an effective amount of a compound as claimed in any one of claims 1-219, or a pharmaceutical composition as claimed in claim 220.

240. The method of claim 239, wherein the cancer is selected from the group consisting of melanoma, cervical cancer, breast cancer, ovarian cancer, prostate cancer, testicular cancer, urothelial carcinoma, bladder cancer, non-small cell lung cancer, small cell lung cancer, sarcoma, colorectal adenocarcinoma, gastrointestinal stromal tumors, gastroesophageal carcinoma, colorectal cancer, pancreatic cancer, kidney cancer, hepatocellular cancer, malignant mesothelioma, leukemia, lymphoma, myelodysplasia syndrome, multiple myeloma, transitional cell carcinoma, neuroblastoma, plasma cell neoplasms, Wilm's tumor, or hepatocellular carcinoma.

241. The method of claim 239 or 240, wherein the cancer is a refractory cancer.

242. The method of claim 239, wherein the compound is administered in combination with one or more additional cancer therapies.

243. The method of claim 242, wherein the one or more additional cancer therapies comprises surgery, radiotherapy, chemotherapy, toxin therapy, immunotherapy, cryotherapy or gene therapy, or a combination thereof.

244. The method of claim 243, wherein chemotherapy comprises administering one or more additional chemotherapeutic agents.

245. The method of claim 244, wherein the one or more additional chemotherapeutic agents is selected from an alkylating agent (e.g., cisplatin, carboplatin, mechlorethamine, cyclophosphamide, chlorambucil, ifosfamide and/or oxaliplatin); an anti-metabolite (e.g., azathioprine and/or mercaptopurine); a terpenoid (e.g., a vinca alkaloid and/or a taxane; e.g., Vincristine, Vinblastine, Vinorelbine and/or Vindesine Taxol, Paclitaxel and/or Docetaxel); a topoisomerase (e.g., a type I topoisomerase and/or a type 2 topoisomerase; e.g., camptothecins, such as irinotecan and/or topotecan; amsacrine, etoposide, etoposide phosphate and/or teniposide); a cytotoxic antibiotic (e.g., actinomycin, anthracyclines, doxorubicin, daunorubicin, valrubicin, idarubicin, epirubicin,

bleomycin, plicamycin and/or mitomycin); a hormone (e.g., a lutenizing hormone releasing hormone agonist; e.g., leuprolidine, goserelin, triptorelin, histrelin, bicalutamide, flutamide and/or nilutamide); an antibody (e.g., Abciximab, Adalimumab, Alemtuzumab, Atlizumab, Basiliximab, Belimumab, Bevacizumab, Bretuximab vedotin, Canakinumab, Cetuximab, Ceertolizumab pegol, Daclizumab, Denosumab, Eculizumab, Efalizumab, Gemtuzumab, Golimumab, Golimumab, Ibritumomab tiuxetan, Infliximab, Ipilimumab, Muromonab-CD3, Natalizumab, Ofatumumab, Omalizumab, Palivizumab, Panitumuab, Ranibizumab, Rituximab, Tocilizumab, Tositumomab and/or Trastuzumab); an anti-angiogenic agent; a cytokine; a thrombotic agent; a growth inhibitory agent; an anti-helminthic agent; and an immune checkpoint inhibitor that targets an immune checkpoint receptor selected from the group consisting of CTLA-4, PD-1, PD-L1, PD-1 – PD-L1, PD-1 – PD-L2, interleukin-2 (IL-2), indoleamine 2,3-dioxygenase (IDO), IL-10, transforming growth factor- β (TGF β), T cell immunoglobulin and mucin 3 (TIM3 or HAVCR2), Galectin 9 – TIM3, Phosphatidylserine – TIM3, lymphocyte activation gene 3 protein (LAG3), MHC class II – LAG3, 4-1BB–4-1BB ligand, OX40–OX40 ligand, GITR, GITR ligand – GITR, CD27, CD70–CD27, TNFRSF25, TNFRSF25–TL1A, CD40L, CD40–CD40 ligand, HVEM–LIGHT–LTA, HVEM, HVEM – BTLA, HVEM – CD160, HVEM – LIGHT, HVEM–BTLA–CD160, CD80, CD80 – PDL-1, PDL2 – CD80, CD244, CD48 – CD244, CD244, ICOS, ICOS–ICOS ligand, B7-H3, B7-H4, VISTA, TMIGD2, HHLA2–TMIGD2, Butyrophilins, including BTNL2, Siglec family, TIGIT and PVR family members, KIRs, ILTs and LIRs, NKG2D and NKG2A, MICA and MICB, CD244, CD28, CD86 – CD28, CD86 – CTLA, CD80 – CD28, CD39, CD73 Adenosine–CD39–CD73, CXCR4–CXCL12, Phosphatidylserine, TIM3, Phosphatidylserine – TIM3, SIRPA–CD47, VEGF, Neuropilin, CD160, CD30, and CD155 (e.g., CTLA-4 or PD1 or PD-L1).

246. The method of any one of claims 239-245, wherein the compound is administered intratumorally.

247. A method of inducing an immune response in a subject in need thereof, the method comprising administering to the subject an effective amount of a compound as claimed in any one of claims 1-219, or a pharmaceutical composition as claimed in claim 220.

248. The method of claim 247, wherein the subject has cancer.

249. The method of claim 248, wherein the subject has undergone and/or is undergoing and/or will undergo one or more cancer therapies.

250. The method of claim 248, wherein the cancer selected from the group consisting of melanoma, cervical cancer, breast cancer, ovarian cancer, prostate cancer, testicular cancer, urothelial carcinoma, bladder cancer, non-small cell lung cancer, small cell lung cancer, sarcoma, colorectal adenocarcinoma, gastrointestinal stromal tumors, gastroesophageal carcinoma, colorectal cancer, pancreatic cancer, kidney cancer, hepatocellular cancer, malignant mesothelioma, leukemia, lymphoma, myelodysplasia syndrome, multiple myeloma, transitional cell carcinoma, neuroblastoma, plasma cell neoplasms, Wilm's tumor, or hepatocellular carcinoma .

251. The method of claim 250, wherein the cancer is a refractory cancer.

252. The method of claim 247, wherein the immune response is an innate immune response.

253. The method of claim 252, wherein the at least one or more cancer therapies comprises surgery, radiotherapy, chemotherapy, toxin therapy, immunotherapy, cryotherapy or gene therapy, or a combination thereof.

254. The method of claim 253, wherein chemotherapy comprises administering one or more additional chemotherapeutic agents.

255. The method of claim 254, wherein the one or more additional
 5 chemotherapeutic agents is selected from alkylating agent (e.g., cisplatin, carboplatin, mechlorethamine, cyclophosphamide, chlorambucil, ifosfamide and/or oxaliplatin); an anti-metabolite (e.g., azathioprine and/or mercaptopurine); a terpenoid (e.g., a vinca alkaloid and/or a taxane; e.g., Vincristine, Vinblastine, Vinorelbine and/or Vindesine Taxol, Paclitaxel and/or Docetaxel); a topoisomerase (e.g., a type I topoisomerase and/or
 10 a type 2 topoisomerase; e.g., camptothecins, such as irinotecan and/or topotecan; amsacrine, etoposide, etoposide phosphate and/or teniposide); a cytotoxic antibiotic (e.g., actinomycin, anthracyclines, doxorubicin, daunorubicin, valrubicin, idarubicin, epirubicin, bleomycin, plicamycin and/or mitomycin); a hormone (e.g., a lutenizing hormone releasing hormone agonist; e.g., leuprolidine, goserelin, triptorelin, histrelin, bicalutamide,
 15 flutamide and/or nilutamide); an antibody (e.g., Abciximab, Adalimumab, Alemtuzumab, Atlizumab, Basiliximab, Belimumab, Bevacizumab, Bretuximab vedotin, Canakinumab, Cetuximab, Ceertolizumab pegol, Daclizumab, Denosumab, Eculizumab, Efalizumab, Gemtuzumab, Golimumab, Golimumab, Ibritumomab tiuxetan, Infliximab, Ipilimumab, Muromonab-CD3, Natalizumab, Ofatumumab, Omalizumab, Palivizumab, Panitumuab,
 20 Ranibizumab, Rituximab, Tocilizumab, Tositumomab and/or Trastuzumab); an anti-angiogenic agent; a cytokine; a thrombotic agent; a growth inhibitory agent; an anti-helminthic agent; and an immune checkpoint inhibitor that targets an immune checkpoint receptor selected from the group consisting of CTLA-4, PD-1, PD-L1, PD-1 – PD-L1, PD-1 – PD-L2, interleukin-2 (IL-2), indoleamine 2,3-dioxygenase (IDO), IL-10, transforming
 25 growth factor- β (TGF β), T cell immunoglobulin and mucin 3 (TIM3 or HAVCR2), Galectin 9 – TIM3, Phosphatidylserine – TIM3, lymphocyte activation gene 3 protein (LAG3), MHC class II – LAG3, 4-1BB–4-1BB ligand, OX40–OX40 ligand, GITR, GITR ligand – GITR, CD27, CD70-CD27, TNFRSF25, TNFRSF25–TL1A, CD40L, CD40–CD40 ligand, HVEM–LIGHT–LTA, HVEM, HVEM – BTLA, HVEM – CD160, HVEM

– LIGHT, HVEM–BTLA–CD160, CD80, CD80 – PDL-1, PDL2 – CD80, CD244, CD48
– CD244, CD244, ICOS, ICOS–ICOS ligand, B7-H3, B7-H4, VISTA, TMIGD2,
HHLA2–TMIGD2, Butyrophilins, including BTNL2, Siglec family, TIGIT and PVR
family members, KIRs, ILTs and LIRs, NKG2D and NKG2A, MICA and MICB, CD244,
5 CD28, CD86 – CD28, CD86 – CTLA, CD80 – CD28, CD39, CD73 Adenosine–CD39–
CD73, CXCR4–CXCL12, Phosphatidylserine, TIM3, Phosphatidylserine – TIM3,
SIRPA–CD47, VEGF, Neuropilin, CD160, CD30, and CD155 (e.g., CTLA-4 or PD1 or
PD-L1).

10 256. A method of inducing STING-dependent type I interferon production in a
subject in need thereof, the method comprising administering to the subject an effective
amount of a compound as claimed in any one of claims 1-219, or a pharmaceutical
composition as claimed in claim 220.

15 257. The method of claim 256, wherein the subject has cancer.

258. The method of claim 257, wherein the wherein the subject has undergone
and/or is undergoing and/or will undergo one or more additional cancer therapies.

20 259. The method of claim 257, wherein the cancer selected from the group
consisting of melanoma, cervical cancer, breast cancer, ovarian cancer, prostate cancer,
testicular cancer, urothelial carcinoma, bladder cancer, non-small cell lung cancer, small
cell lung cancer, sarcoma, colorectal adenocarcinoma, gastrointestinal stromal tumors,
gastroesophageal carcinoma, colorectal cancer, pancreatic cancer, kidney cancer,
25 hepatocellular cancer, malignant mesothelioma, leukemia, lymphoma, myelodysplasia
syndrome, multiple myeloma, transitional cell carcinoma, neuroblastoma, plasma cell
neoplasms, Wilm's tumor, or hepatocellular carcinoma.

260. The method of claim 259, wherein the cancer is a refractory cancer.

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261. The method of claim 258, wherein the one or more additional cancer therapies comprises surgery, radiotherapy, chemotherapy, toxin therapy, immunotherapy, cryotherapy or gene therapy, or a combination thereof.

5 262. The method of claim 261, wherein at least one of the one or more additional cancer therapies is chemotherapy.

263. The method of claim 262, wherein chemotherapy comprises administering one or more additional chemotherapeutic agents.

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264. The method of claim 263, wherein the one or more additional chemotherapeutic agents is selected from alkylating agent (e.g., cisplatin, carboplatin, mechlorethamine, cyclophosphamide, chlorambucil, ifosfamide and/or oxaliplatin); an anti-metabolite (e.g., azathioprine and/or mercaptopurine); a terpenoid (e.g., a vinca alkaloid and/or a taxane; e.g., Vincristine, Vinblastine, Vinorelbine and/or Vindesine Taxol, Paclitaxel and/or Docetaxel); a topoisomerase (e.g., a type I topoisomerase and/or a type 2 topoisomerase; e.g., camptothecins, such as irinotecan and/or topotecan; amsacrine, etoposide, etoposide phosphate and/or teniposide); a cytotoxic antibiotic (e.g., actinomycin, anthracyclines, doxorubicin, daunorubicin, valrubicin, idarubicin, epirubicin, bleomycin, plicamycin and/or mitomycin); a hormone (e.g., a lutenizing hormone releasing hormone agonist; e.g., leuprolidine, goserelin, triptorelin, histrelin, bicalutamide, flutamide and/or nilutamide); an antibody (e.g., Abciximab, Adalimumab, Alemtuzumab, Atlizumab, Basiliximab, Belimumab, Bevacizumab, Bretuximab vedotin, Canakinumab, Cetuximab, Ceertolizumab pegol, Daclizumab, Denosumab, Eculizumab, Efalizumab, Gemtuzumab, Golimumab, Golimumab, Ibritumomab tiuxetan, Infliximab, Ipilimumab, Muromonab-CD3, Natalizumab, Ofatumumab, Omalizumab, Palivizumab, Panitumuab, Ranibizumab, Rituximab, Tocilizumab, Tositumomab and/or Trastuzumab); an anti-angiogenic agent; a cytokine; a thrombotic agent; a growth inhibitory agent; an anti-helminthic agent; and an immune checkpoint inhibitor that targets an immune
20
25
30 checkpoint receptor selected from the group consisting of CTLA-4, PD-1, PD-L1, PD-1 –

PD-L1, PD-1 – PD-L2, interleukin-2 (IL-2), indoleamine 2,3-dioxygenase (IDO), IL-10, transforming growth factor- β (TGF β), T cell immunoglobulin and mucin 3 (TIM3 or HAVCR2), Galectin 9 – TIM3, Phosphatidylserine – TIM3, lymphocyte activation gene 3 protein (LAG3), MHC class II – LAG3, 4-1BB–4-1BB ligand, OX40–OX40 ligand,

5 GITR, GITR ligand – GITR, CD27, CD70–CD27, TNFRSF25, TNFRSF25–TL1A, CD40L, CD40–CD40 ligand, HVEM–LIGHT–LTA, HVEM, HVEM – BTLA, HVEM – CD160, HVEM – LIGHT, HVEM–BTLA–CD160, CD80, CD80 – PDL-1, PDL2 – CD80, CD244, CD48 – CD244, CD244, ICOS, ICOS–ICOS ligand, B7-H3, B7-H4, VISTA, TMIGD2, HHLA2–TMIGD2, Butyrophilins, including BTNL2, Siglec family,

10 TIGIT and PVR family members, KIRs, ILTs and LIRs, NKG2D and NKG2A, MICA and MICB, CD244, CD28, CD86 – CD28, CD86 – CTLA, CD80 – CD28, CD39, CD73 Adenosine–CD39–CD73, CXCR4–CXCL12, Phosphatidylserine, TIM3, Phosphatidylserine – TIM3, SIRPA–CD47, VEGF, Neuropilin, CD160, CD30, and CD155 (e.g., CTLA-4 or PD1 or PD-L1) .

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265. A method of treatment of a disease in which repressed or impaired STING signaling contributes to the pathology and/or symptoms and/or progression of the disease, comprising administering to a subject in need of such treatment an effective amount of a compound as claimed in any one of claims 1-219, or a pharmaceutical composition as

20 claimed in claim 220.

266. A method of treatment comprising administering to a subject having a disease in which repressed or impaired STING signaling contributes to the pathology and/or symptoms and/or progression of the disease an effective amount of a compound as

25 claimed in any one of claims 1-219, or a pharmaceutical composition as claimed in claim 220.

267. A method of treatment comprising administering to a subject a compound as claimed in any one of claims 1-219, or a pharmaceutical composition as claimed in claim 220, wherein the compound or composition is administered in an amount effective to treat a disease in which repressed or impaired STING signaling contributes to the pathology and/or symptoms and/or progression of the disease, thereby treating the disease.

268. The method of any one of claims 265-267, wherein the disease is cancer.

269. The method of claim 268, wherein the cancer is selected from the group consisting of melanoma, cervical cancer, breast cancer, ovarian cancer, prostate cancer, testicular cancer, urothelial carcinoma, bladder cancer, non-small cell lung cancer, small cell lung cancer, sarcoma, colorectal adenocarcinoma, gastrointestinal stromal tumors, gastroesophageal carcinoma, colorectal cancer, pancreatic cancer, kidney cancer, hepatocellular cancer, malignant mesothelioma, leukemia, lymphoma, myelodysplasia syndrome, multiple myeloma, transitional cell carcinoma, neuroblastoma, plasma cell neoplasms, Wilm's tumor, or hepatocellular carcinoma.

270. The method of claim 268 or 269, wherein the cancer is a refractory cancer.

271. The method of any one of claims 265-270, wherein the compound is administered in combination with one or more additional cancer therapies.

272. The method of claim 271, wherein the one or more additional cancer therapies comprises surgery, radiotherapy, chemotherapy, toxin therapy, immunotherapy, cryotherapy or gene therapy, or a combination thereof.

273. The method of claim 272, wherein chemotherapy comprises administering one or more additional chemotherapeutic agents.

274. The method of claim 273, wherein the one or more additional chemotherapeutic agents is selected from an alkylating agent (e.g., cisplatin, carboplatin, mechlorethamine, cyclophosphamide, chlorambucil, ifosfamide and/or oxaliplatin); an anti-metabolite (e.g., azathioprine and/or mercaptopurine); a terpenoid (e.g., a vinca alkaloid and/or a taxane; e.g., Vincristine, Vinblastine, Vinorelbine and/or Vindesine
5 Taxol, Paclitaxel and/or Docetaxel); a topoisomerase (e.g., a type I topoisomerase and/or a type 2 topoisomerase; e.g., camptothecins, such as irinotecan and/or topotecan; amsacrine, etoposide, etoposide phosphate and/or teniposide); a cytotoxic antibiotic (e.g., actinomycin, anthracyclines, doxorubicin, daunorubicin, valrubicin, idarubicin, epirubicin,
10 bleomycin, plicamycin and/or mitomycin); a hormone (e.g., a lutenizing hormone releasing hormone agonist; e.g., leuprolidine, goserelin, triptorelin, histrelin, bicalutamide, flutamide and/or nilutamide); an antibody (e.g., Abciximab, Adalimumab, Alemtuzumab, Atlizumab, Basiliximab, Belimumab, Bevacizumab, Bretuximab vedotin, Canakinumab, Cetuximab, Ceertolizumab pegol, Daclizumab, Denosumab, Eculizumab, Efalizumab,
15 Gemtuzumab, Golimumab, Golimumab, Ibritumomab tiuxetan, Infliximab, Ipilimumab, Muromonab-CD3, Natalizumab, Ofatumumab, Omalizumab, Palivizumab, Panitumab, Ranibizumab, Rituximab, Tocilizumab, Tositumomab and/or Trastuzumab); an anti-angiogenic agent; a cytokine; a thrombotic agent; a growth inhibitory agent; an anti-helminthic agent; and an immune checkpoint inhibitor that targets an immune checkpoint
20 receptor selected from the group consisting of CTLA-4, PD-1, PD-L1, PD-1 – PD-L1, PD-1 – PD-L2, interleukin-2 (IL-2), indoleamine 2,3-dioxygenase (IDO), IL-10, transforming growth factor- β (TGF β), T cell immunoglobulin and mucin 3 (TIM3 or HAVCR2), Galectin 9 – TIM3, Phosphatidylserine – TIM3, lymphocyte activation gene 3 protein (LAG3), MHC class II – LAG3, 4-1BB–4-1BB ligand, OX40–OX40 ligand, GITR, GITR
25 ligand – GITR, CD27, CD70-CD27, TNFRSF25, TNFRSF25–TL1A, CD40L, CD40–CD40 ligand, HVEM–LIGHT–LTA, HVEM, HVEM – BTLA, HVEM – CD160, HVEM – LIGHT, HVEM–BTLA–CD160, CD80, CD80 – PDL-1, PDL2 – CD80, CD244, CD48 – CD244, CD244, ICOS, ICOS–ICOS ligand, B7-H3, B7-H4, VISTA, TMIGD2,

5 HHLA2–TMIGD2, Butyrophilins, including BTNL2, Siglec family, TIGIT and PVR family members, KIRs, ILTs and LIRs, NKG2D and NKG2A, MICA and MICB, CD244, CD28, CD86 – CD28, CD86 – CTLA, CD80 – CD28, CD39, CD73 Adenosine–CD39–CD73, CXCR4–CXCL12, Phosphatidylserine, TIM3, Phosphatidylserine – TIM3, SIRPA–CD47, VEGF, Neuropilin, CD160, CD30, and CD155 (e.g., CTLA-4 or PD1 or PD-L1).

10 275. The method of any one of claims 265-274, wherein the compound is administered intratumorally.

276. The method of any one of claims 229-275, wherein the method further comprises identifying the subject.