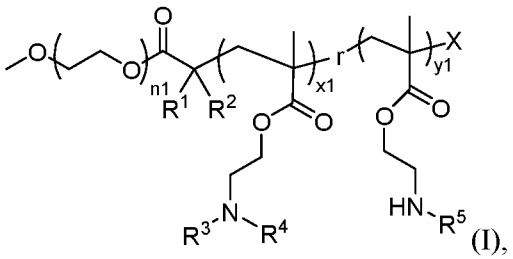
WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising:

(i) a block copolymer of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:



(I),

wherein:

n_1 is an integer from 10-200;

x_1 is an integer from 20-300;

y_1 is an integer from 0-10;

X is a halogen, -OH, or -C(O)OH;

r denotes randomness in the order of x_1 and y_1 blocks in the block copolymer;

R^1 and R^2 are each independently hydrogen or optionally substituted C_1-C_6 alkyl;

R^3 and R^4 are each independently an optionally substituted C_1-C_6 alkyl, C_3-C_{10} cycloalkyl or aryl;

or R^3 and R^4 are taken together with the corresponding nitrogen to which they are attached form an optionally substituted 5 to 7-membered ring;

R^5 is hydrogen or -C(O)CH_3; and

(ii) a non-peptide STING agonist.

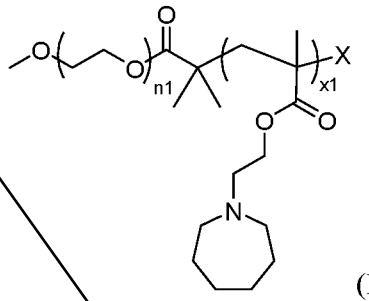
2. The pharmaceutical composition of claim 1, wherein R^1 and R^2 are each independently an optionally substituted C_1-C_6 alkyl.

3. The pharmaceutical composition of claim 1 or 2, wherein, R^1 and R^2 are each independently -CH_3.

4. The pharmaceutical composition of any one of claims 1-3, wherein, wherein R^3 and R^4 are each independently an optionally substituted C_1-C_6 alkyl.

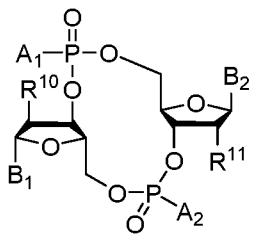
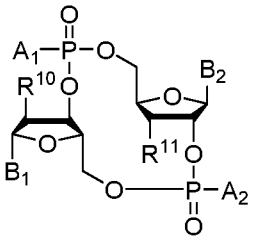
5. The pharmaceutical composition of any one of claims 1-4, wherein R^3 and R^4 are each independently -CH_2CH_3, -$CH_2CH_2CH_3$, or -$CH_2CH_2CH_2CH_3$.

6. The pharmaceutical composition of any one of claims 1-3, wherein R^3 and R^4 are taken together with the corresponding nitrogen to which they are attached form an optionally substituted 5 to 7-membered ring.
7. The pharmaceutical composition of any one of claims 1-3 or 6, wherein R^3 and R^4 taken together are $-CH_2(CH_2)_2CH_2-$, $-CH_2(CH_2)_3CH_2-$, or $-CH_2(CH_2)_4CH_2-$.
8. The pharmaceutical composition of any one of claim 1-7, wherein y_1 is 0.
9. The pharmaceutical composition of any one of claims 1-8, wherein the block copolymer of Formula (I) has the structure of Formula (Ia), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:



(Ia).

10. The pharmaceutical composition of any one of claims 1-9, wherein n_1 is an integer from 60-150 or 100-140
11. The pharmaceutical composition of claim 10, wherein n_1 is 100-140.
12. The pharmaceutical composition of any one of claims 1-11, wherein x_1 is an integer from 50-200, 60-160, or 90-140.
13. The pharmaceutical composition of claim 12, wherein x_1 is an integer from 90-140.
14. The pharmaceutical composition of any one of claims 1-13, wherein X is a halogen.
15. The pharmaceutical composition of claim 14, wherein X is -Br.
16. The pharmaceutical composition of any one of claims 1-15, wherein the non-peptide STING agonist is a cyclic dinucleotide.
17. The pharmaceutical composition of claim 16, wherein the cyclic dinucleotide is cGAMP.
18. The pharmaceutical composition of claim 16, wherein the cyclic dinucleotide is a compound having the structure of Formula (IIa) or Formula (IIb), or a pharmaceutically acceptable salt, solvate or hydrate thereof:


(IIa) or

(IIb),

wherein

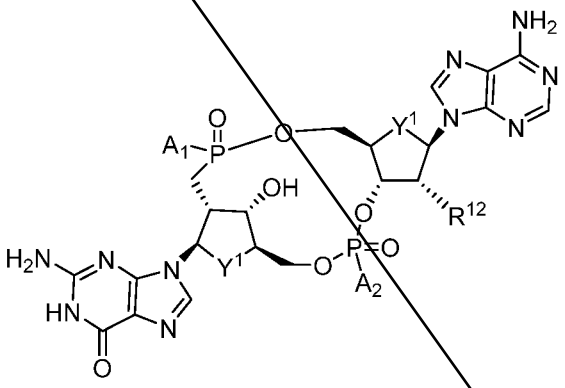
A^1 and A^2 are each independently OH or SH;

B^1 and B^2 are each independently guanine or adenine;

R^{10} is H, halogen, OH, OCH_3; and

R^{11} is halogen or OH.

19. The pharmaceutical composition of claim 16, wherein the cyclic dinucleotide is a compound having the structure of Formulas (III), or a pharmaceutically acceptable salt, solvate or hydrate thereof:

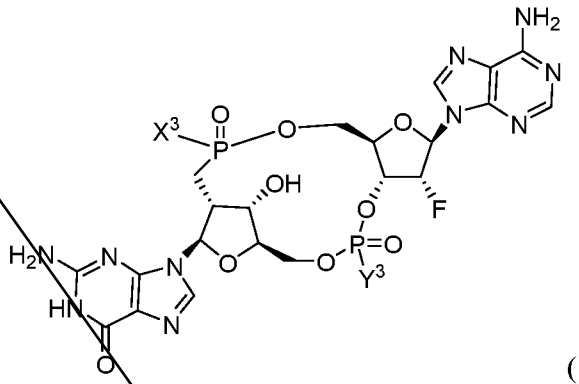

(III),

wherein

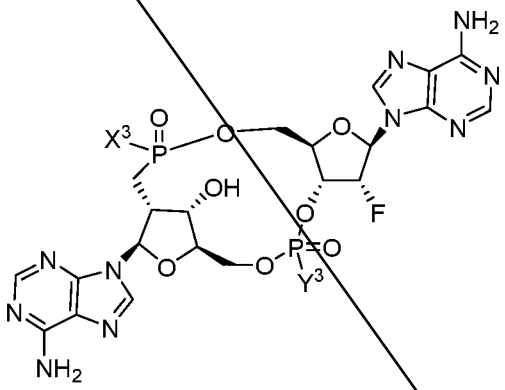
A^1 and A^2 are each independently OH or SH; and

Y^1 and Y^2 are each independently -CH- or -O-.

20. The pharmaceutical composition of claim 16, wherein the cyclic dinucleotide is a compound selected from:

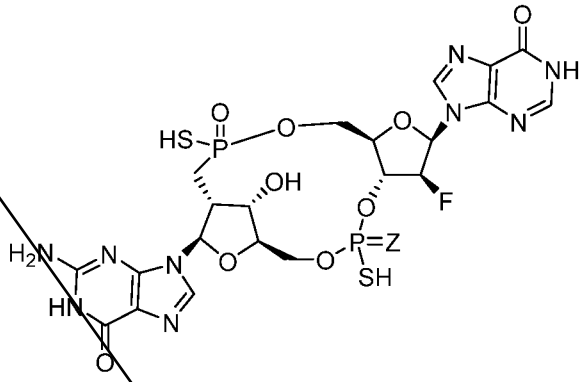


(1), and

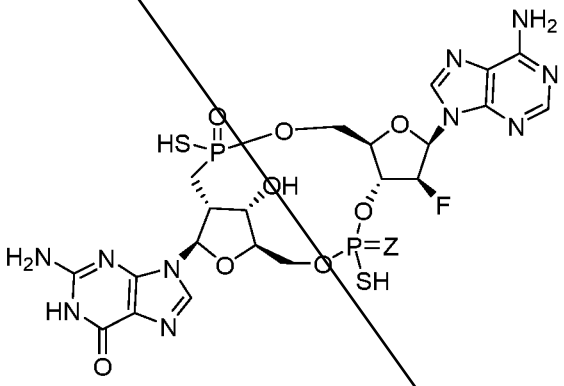


(2), wherein X^3 and Y^3 are each independently O or S; or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

21. The pharmaceutical composition of claim 16, wherein the cyclic dinucleotide is a compound selected from:

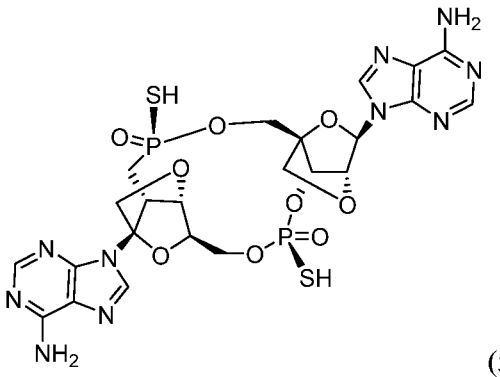


(3), and

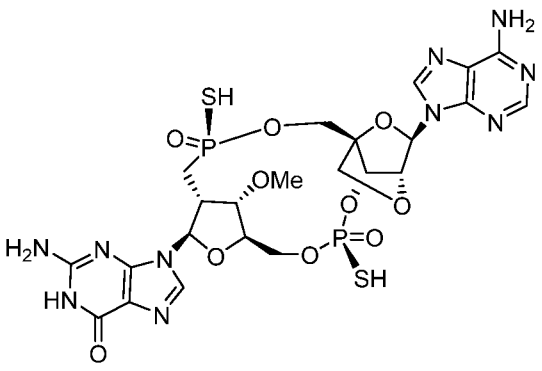


(4) wherein Z is O or S; or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

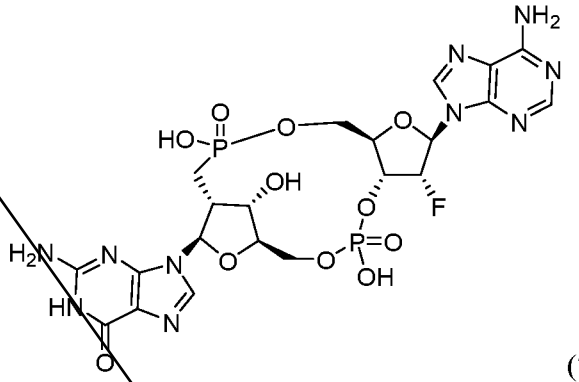
22. The pharmaceutical composition of claim 16, wherein the cyclic dinucleotide is a compound selected from:



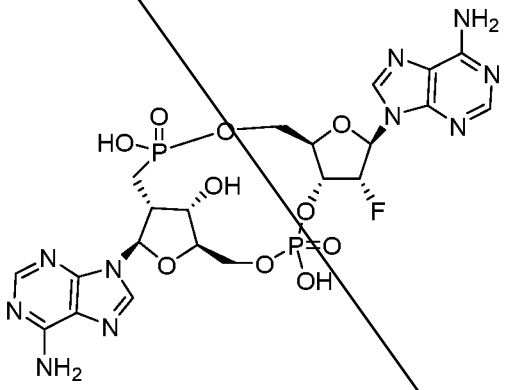
(5),



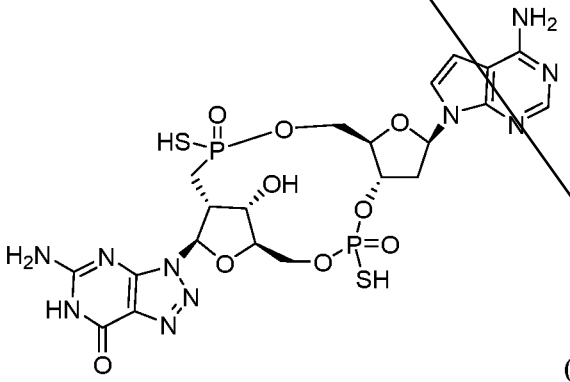
(6),



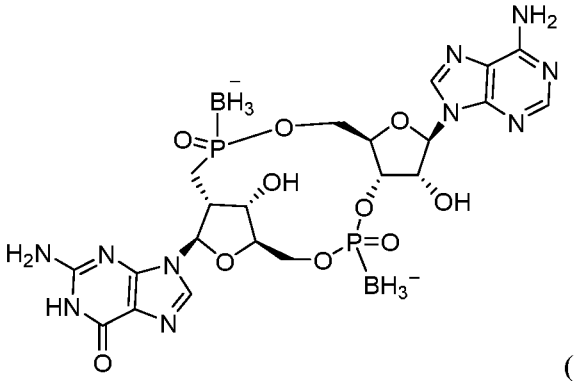
(7) ,



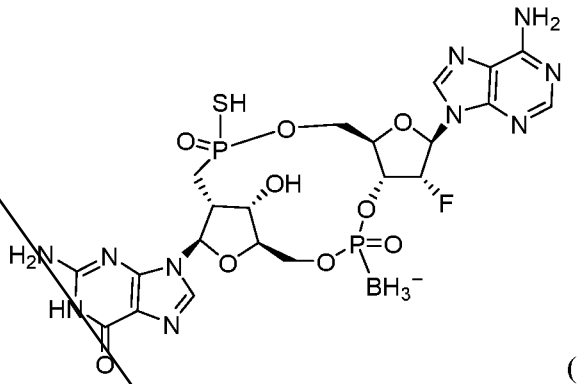
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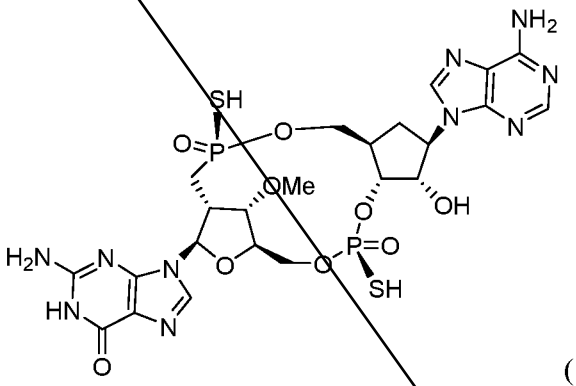
(9),



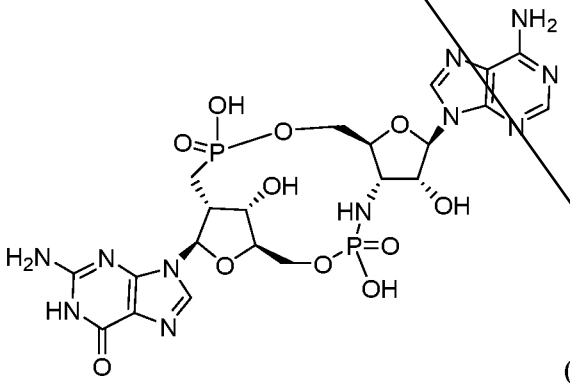
(10),



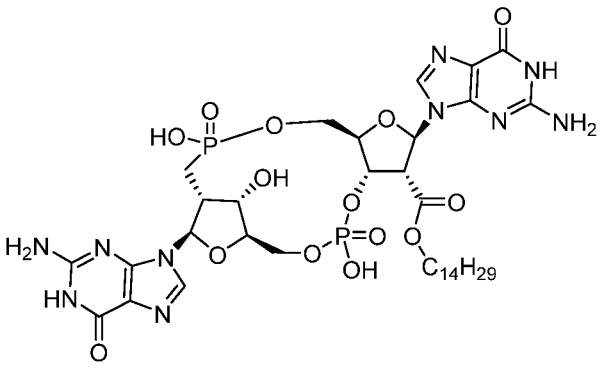
(11),



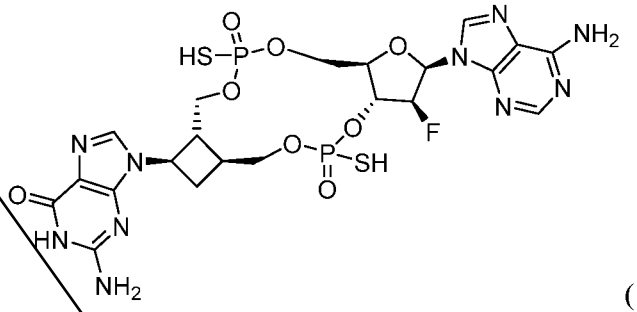
(12),



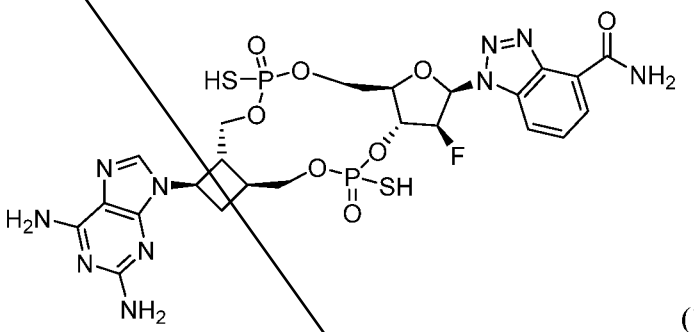
(13),



(14),

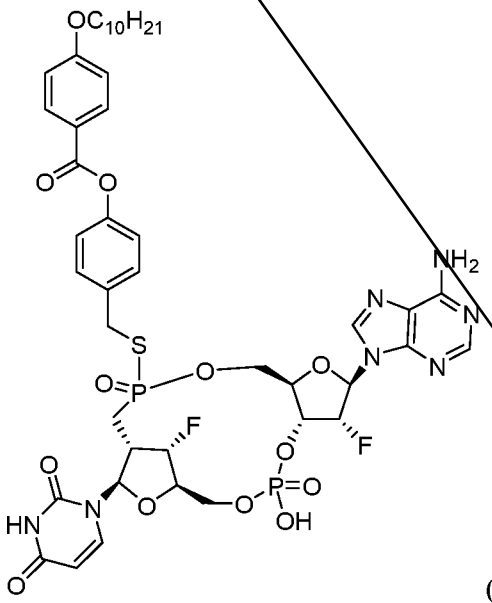


(15), and

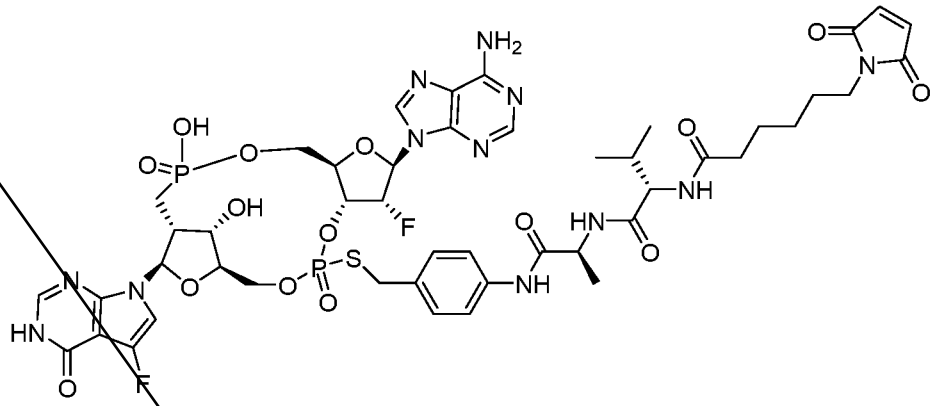


(16); or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

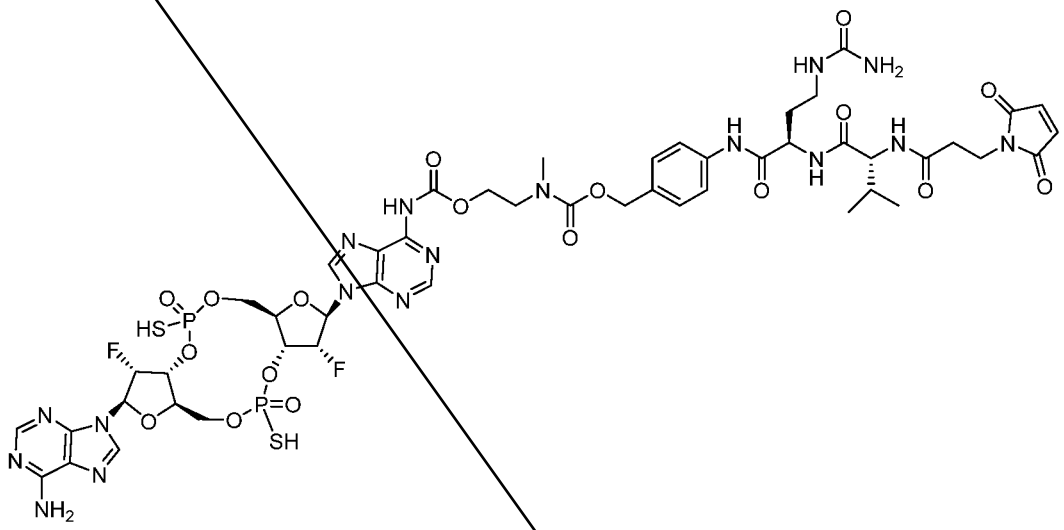
23. The pharmaceutical composition of claim 16, wherein the cyclic dinucleotide is selected from:



(17),

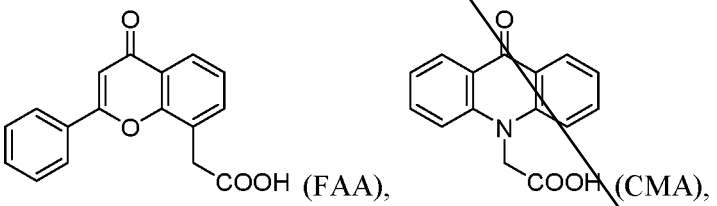


(18), or



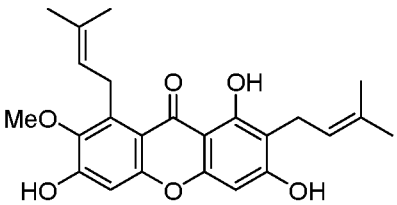
(19); or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

24. The pharmaceutical composition of any one of claims 1-15, wherein the non-peptide STING agonist is selected from:

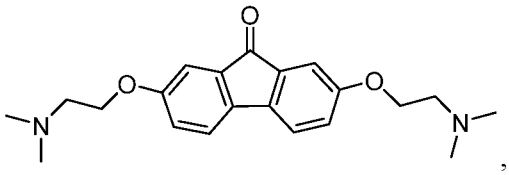


(FAA),

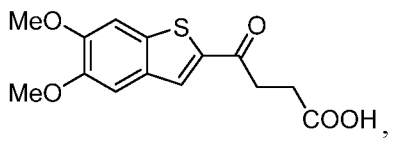
(CMA),



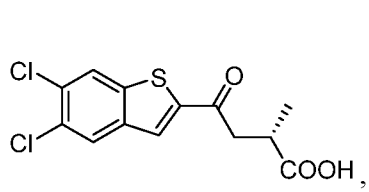
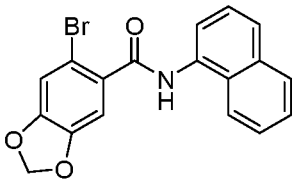
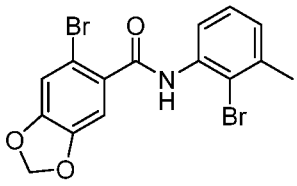
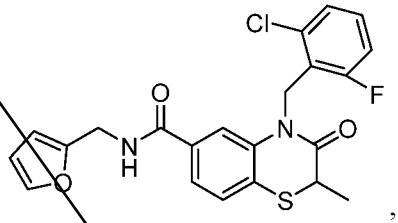
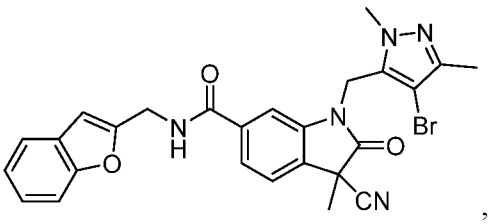
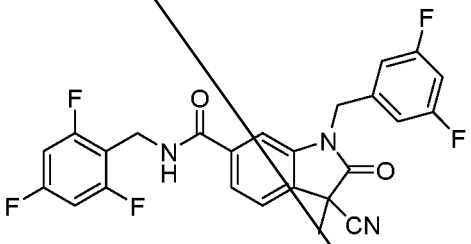
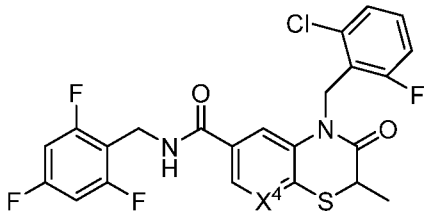
(α-Mangostin),

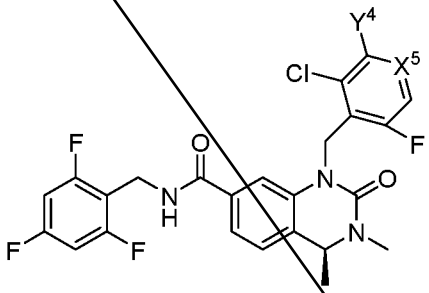


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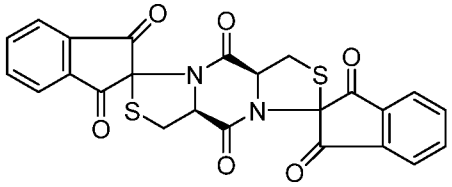
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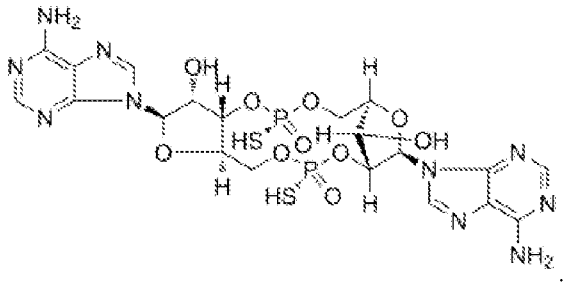

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,

,

wherein


X^4 is CH or N; and wherein X^5 is CH or N and Y^4 is NH_2 or CH_3;

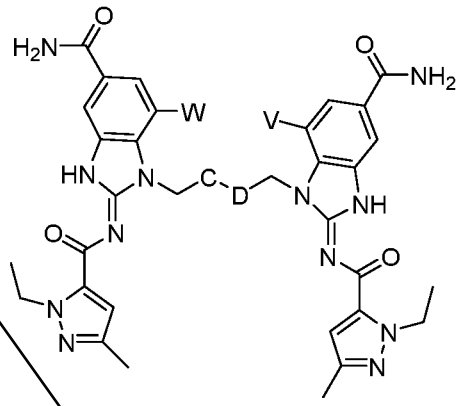
or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

25. The pharmaceutical composition of any one of claims 1-15, wherein the non-peptide STING agonist is selected from:


and


.

26. The pharmaceutical composition of any one of claims 1-15, wherein the non-peptide STING agonist is a compound having the structure of Formula (IV), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:



(IV),

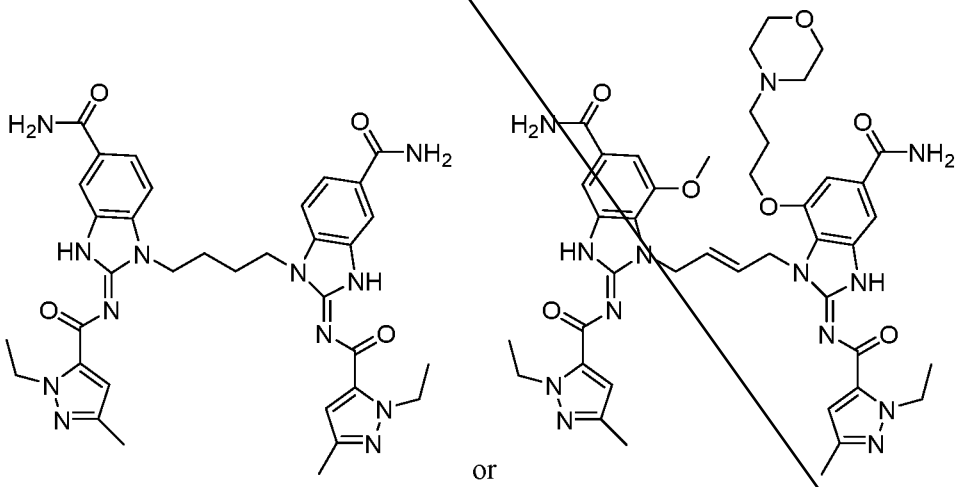
wherein:

C-D is an alkylene or alkenylene;

W is H or -OCH_3; and

V is H or -O-(C_1-C_3)alkyl-(C_3-C_6)heterocycle.

27. The pharmaceutical composition of any one of claims 1-15, wherein the non-peptide STING agonist is:



or

.

28. The pharmaceutical composition of any one of claims 1-27, wherein one or more non-peptide STING agonists is encapsulated by the block copolymer within one or more micelles.

29. The pharmaceutical composition of claim 28, wherein the micelle has a diameter of about 25 to about 50 nm.

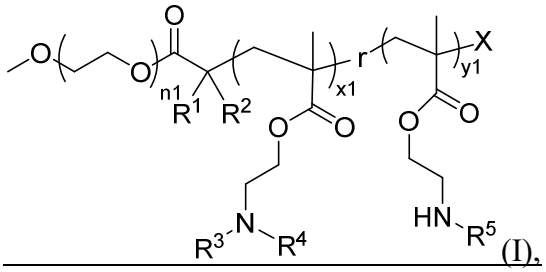
30. The pharmaceutical composition of claim 28, wherein the micelle has a diameter no more than 1 μm.
31. The pharmaceutical composition of any one of claims 28-30, wherein the micelle has a pH transition point.
32. The pharmaceutical composition of claim 31, wherein the pH transition point is between 4-8, 6-7.5, or 4.5-6.5.
33. The pharmaceutical composition of claim 31, wherein the composition has a pH response of less than 0.25 or 0.15 pH units.
34. The pharmaceutical composition of any one of claims 28-33, comprising one, two, or three different non-peptide STING agonists.
35. The pharmaceutical composition of any one of claims 1-27, wherein one or more non-peptide STING agonists is not encapsulated by the block copolymer within a micelle.
36. The pharmaceutical composition of any one of claims 1-27, wherein the block copolymer and the non-peptide STING agonist are present as a mixture.
37. The pharmaceutical composition of any one of claims 1-27, wherein the block copolymer and the non-peptide STING agonist are present in a 1:2 or 1:1 molar ratio.
38. The pharmaceutical composition of any one of claims 35-37, comprising one, two, or three different non-peptide STING agonists.
39. The pharmaceutical composition of any one of claims 35-38, further comprising a saccharide solution.
40. The pharmaceutical composition of claim 39, wherein the saccharide solution is a glucose solution.
41. A method for treating cancer in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition of any one of claims 1-40.
42. The method of claim 41, wherein the cancer is a solid tumor.
43. The method of claim 41, wherein the solid tumor is reduced in size by about 50%, about 60%, about 70%, about 80%, about 90%, or about 95%.
44. The method of claim 41, wherein the cancer is a carcinoma, sarcoma, lymphoma, leukemia, melanoma, mesothelioma, multiple myeloma, or seminoma.
45. The method of any one of claims 41-44, wherein the cancer is breast cancer, head and neck squamous cell carcinoma (HNSCC), peritoneal metastasis, lung cancer, ovarian cancer, prostate cancer, bladder cancer, urethral cancer, esophageal cancer, colorectal cancer, brain cancer, skin, or renal cancer.

46. The method of any one of claims 41-45 wherein the pharmaceutical composition of any one of claims 1-40 is administered with one of more additional therapies.
47. The method of claim 46, wherein the one of more additional therapies is a checkpoint therapy, chemotherapy, or radiation therapy.
48. The method of claim 46, wherein the one of more additional therapies is surgery.
49. A method of activating the STING pathway in a subject comprising administering to the subject in need thereof a pharmaceutical composition of any one of claims 1-38.
50. The method of claim 41, wherein the pharmaceutical composition is administered subcutaneously or intratumorally.
51. The method of claim 41, wherein the tumor is a solid tumor and the pharmaceutical composition is administered by intratumoral injection.

WHAT IS CLAIMED IS:

1. A pharmaceutical composition comprising:

(i) a block copolymer of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:



(I),

wherein:

n_1 is an integer from 10-200;

x_1 is an integer from 20-300;

y_1 is an integer from 0-10;

X is a halogen, -OH, or -C(O)OH;

r denotes randomness in the order of x_1 and y_1 blocks in the block copolymer;

R^1 and R^2 are each independently hydrogen or optionally substituted C_1-C_6 alkyl;

R^3 and R^4 are each independently an optionally substituted C_1-C_6 alkyl, C_3-C_{10} cycloalkyl or aryl;

or R^3 and R^4 are taken together with the corresponding nitrogen to which they are attached form an optionally substituted 5 to 7-membered ring;

R^5 is hydrogen or -C(O)CH_3; and

(ii) a non-peptide STING agonist.

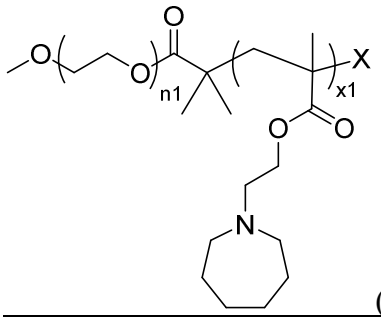
2. The pharmaceutical composition of claim 1, wherein R^1 and R^2 are each independently an optionally substituted C_1-C_6 alkyl.

3. The pharmaceutical composition of claim 1 or claim 2, wherein, wherein R^3 and R^4 are each independently an optionally substituted C_1-C_6 alkyl.

4. The pharmaceutical composition of claim 1 or claim 2, wherein R^3 and R^4 are taken together with the corresponding nitrogen to which they are attached form an optionally substituted 5 to 7-membered ring.

5. The pharmaceutical composition of any one of claims 1-4, wherein y_1 is 0.

6. The pharmaceutical composition of any one of claims 1-5, wherein the block copolymer of Formula (I) has the structure of Formula (Ia), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:

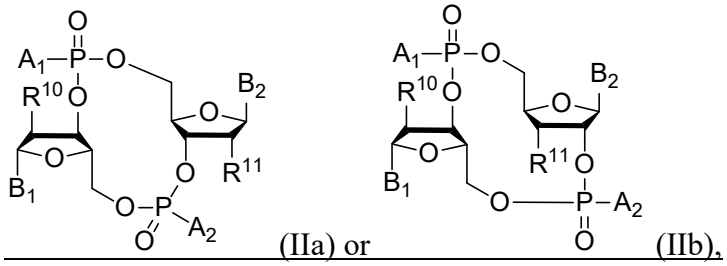


(Ia).

7. The pharmaceutical composition of any one of claims 1-6, wherein the non-peptide STING agonist is a cyclic dinucleotide.

8. The pharmaceutical composition of claim 7, wherein the cyclic dinucleotide is cGAMP.

9. The pharmaceutical composition of claim 7, wherein the cyclic dinucleotide is a compound having the structure of Formula (IIa) or Formula (IIb), or a pharmaceutically acceptable salt, solvate or hydrate thereof:



(IIa) or (IIb),

wherein

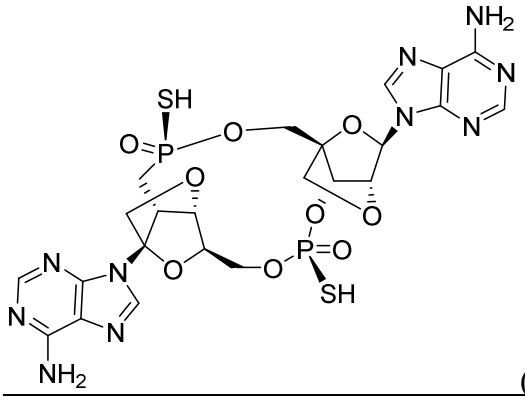
A^1 and A^2 are each independently OH or SH;

B^1 and B^2 are each independently guanine or adenine;

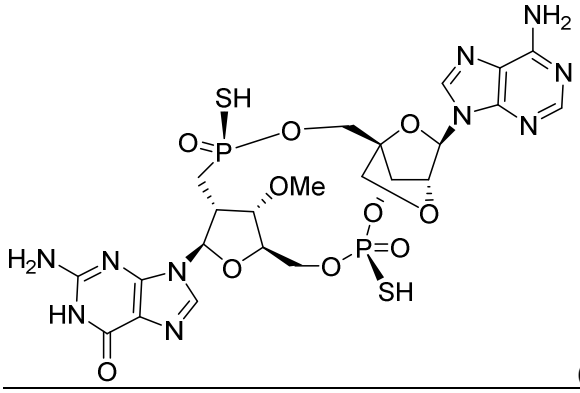
R^{10} is H, halogen, OH, OCH_3; and

R^{11} is halogen or OH.

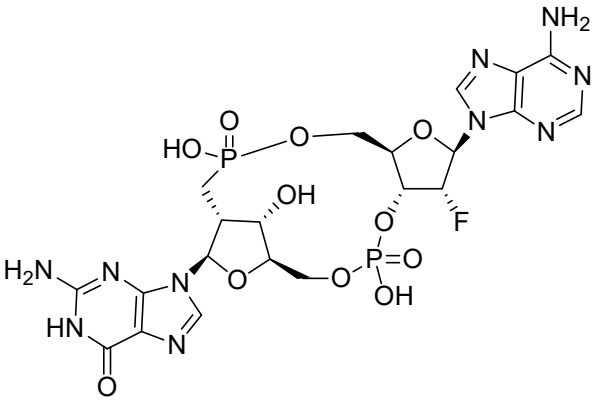
10. The pharmaceutical composition of claim 7, wherein the cyclic dinucleotide is a compound selected from:



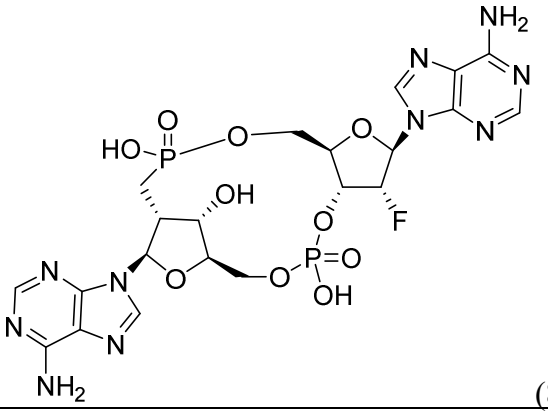
(5),



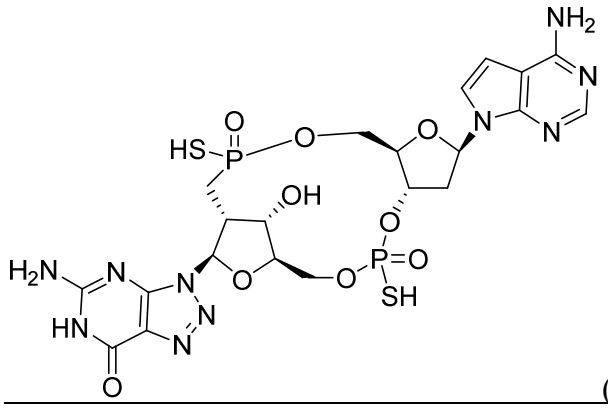
(6),



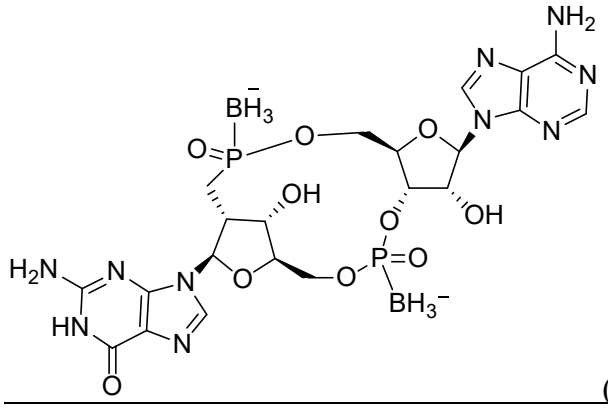
(7),



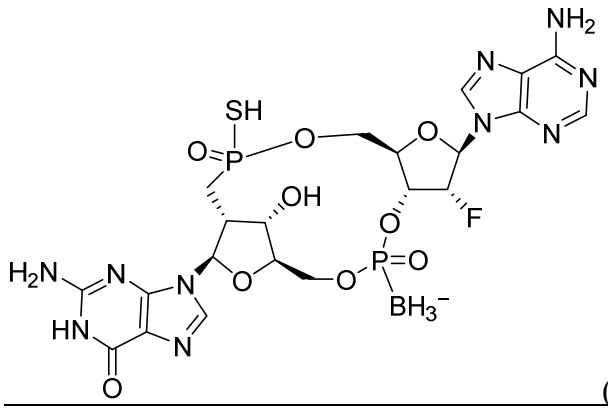
(8),



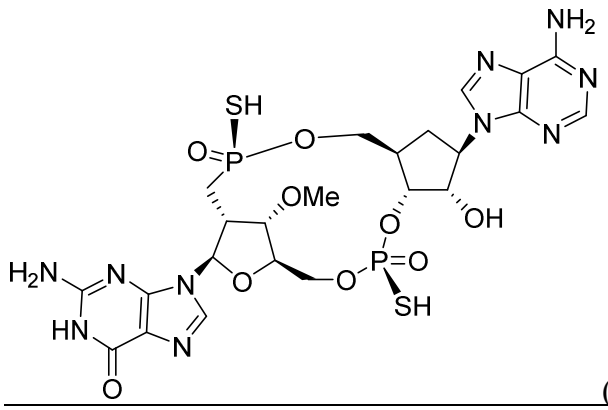
(9),



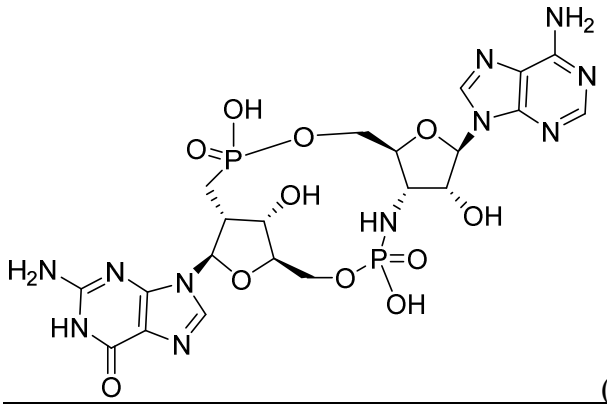
(10),



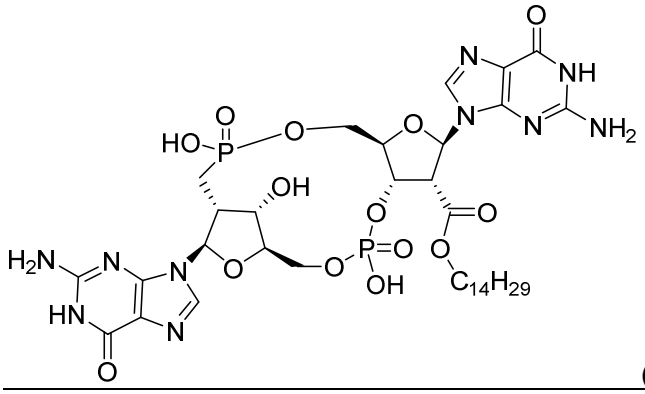
(11),



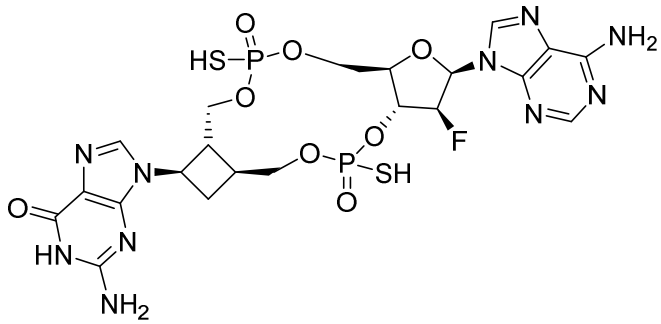
(12),



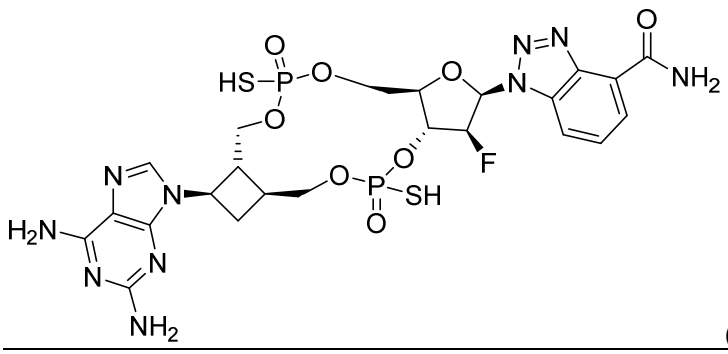
(13),



(14),

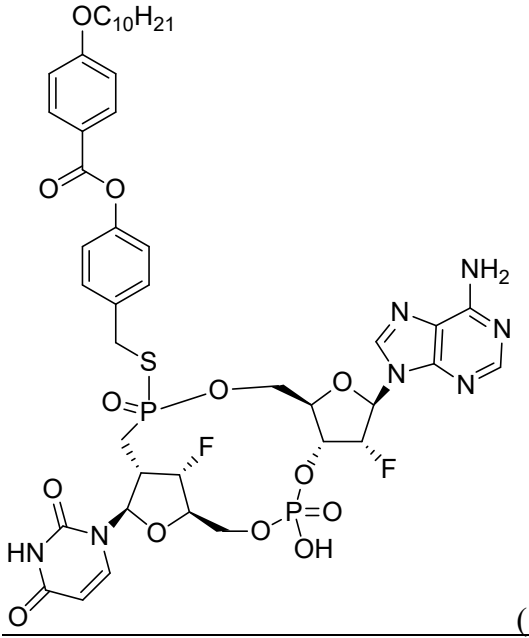


(15), and

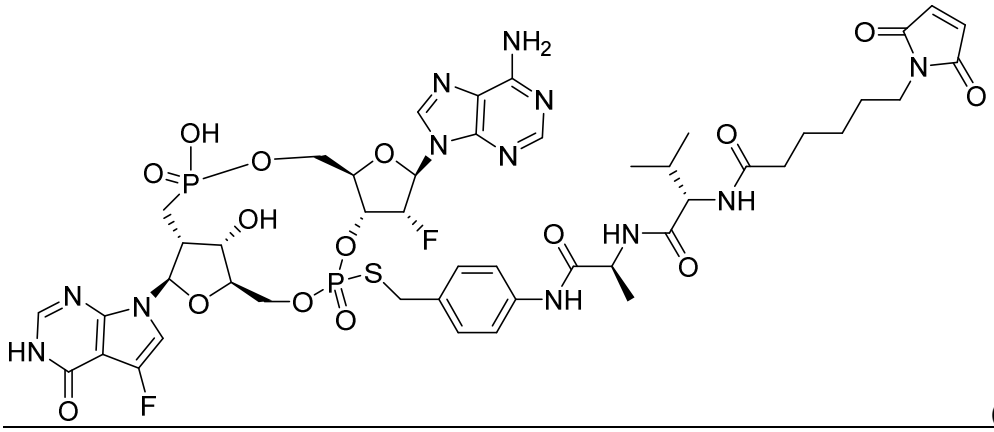


(16); or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

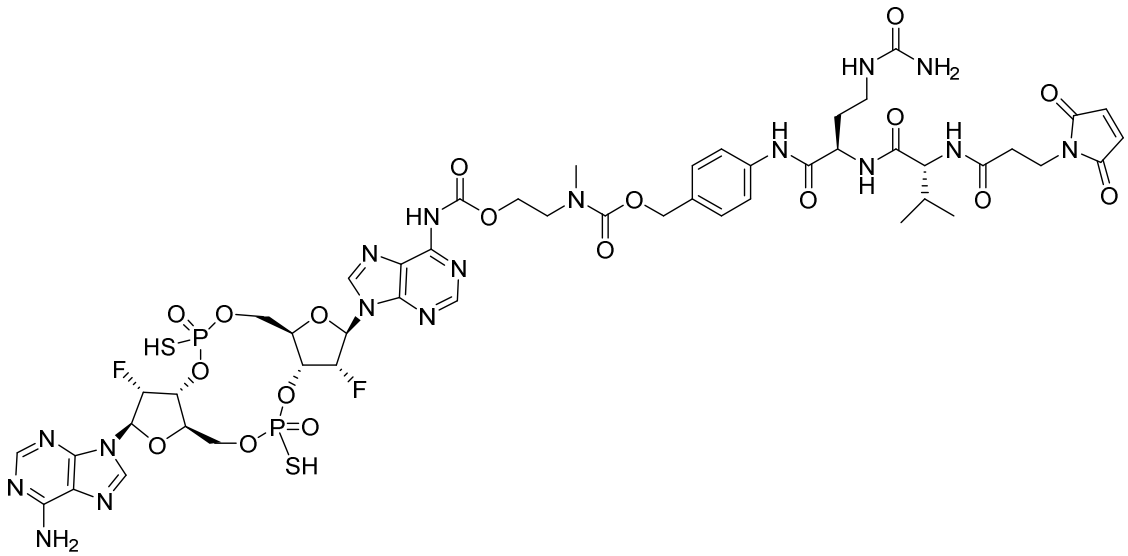
11. The pharmaceutical composition of claim 7, wherein the cyclic dinucleotide is selected from:



(17),

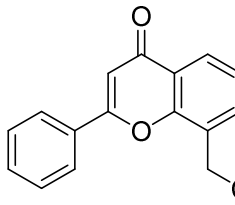
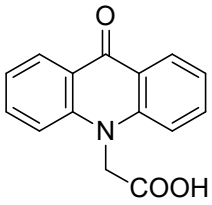
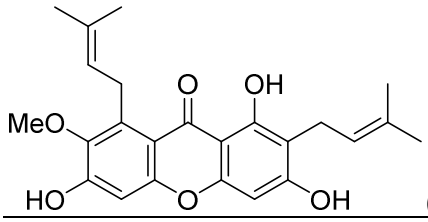
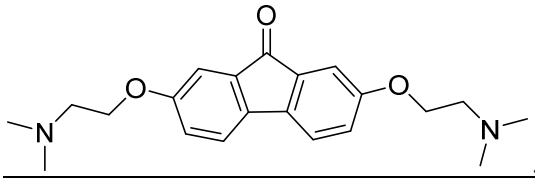
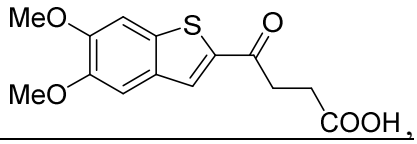
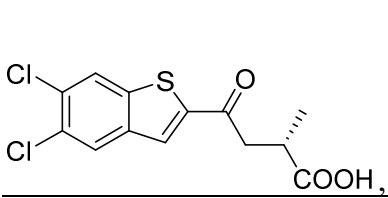
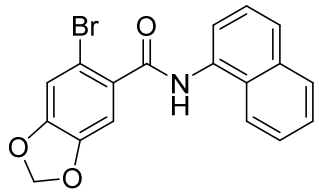
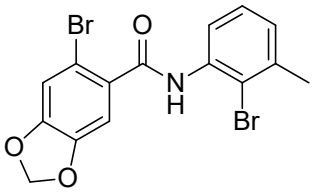
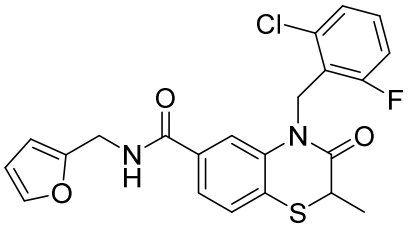
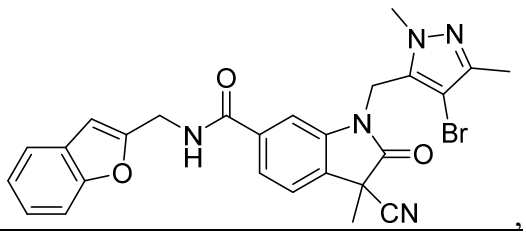
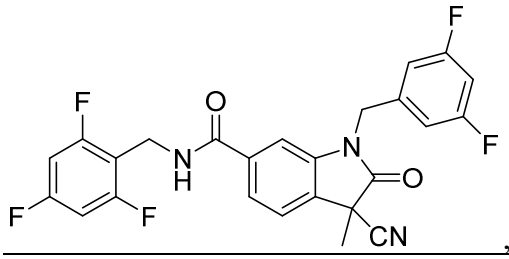
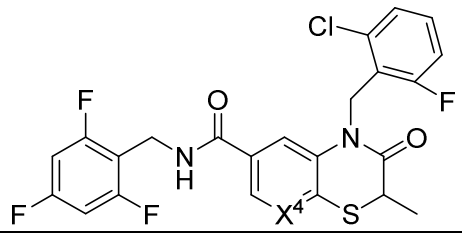
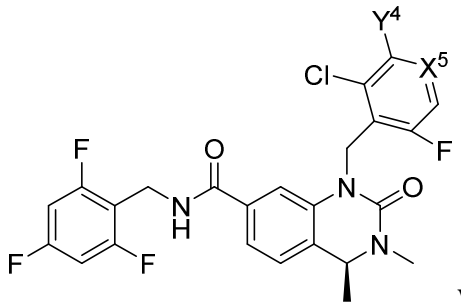


(18), or



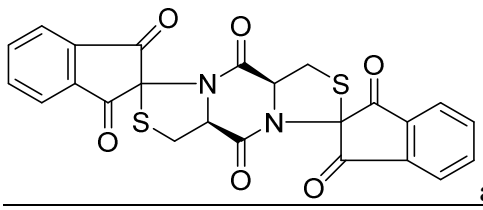
(19); or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

12. The pharmaceutical composition of any one of claims 1-6, wherein the non-peptide STING agonist is selected from:

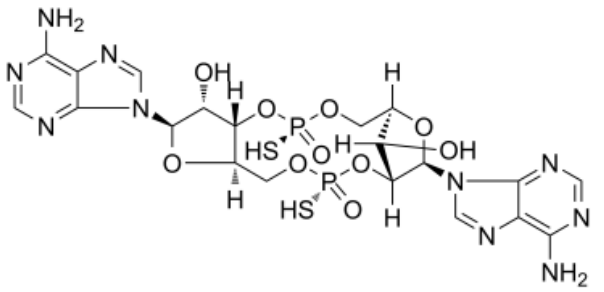

(FAA),

(CMA),

(α-Mangostin),

,

,

,

,

,

,

,

,

wherein

X^4 is CH or N; and wherein X^5 is CH or N and Y^4 is NH_2 or CH_3;

or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

13. The pharmaceutical composition of any one of claims 1-6, wherein the non-peptide STING agonist is selected from:

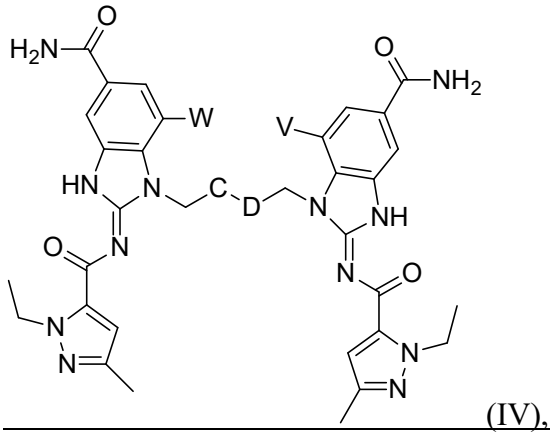


and



.

14. The pharmaceutical composition of any one of claims 1-6, wherein the non-peptide STING agonist is a compound having the structure of Formula (IV), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:



(IV),

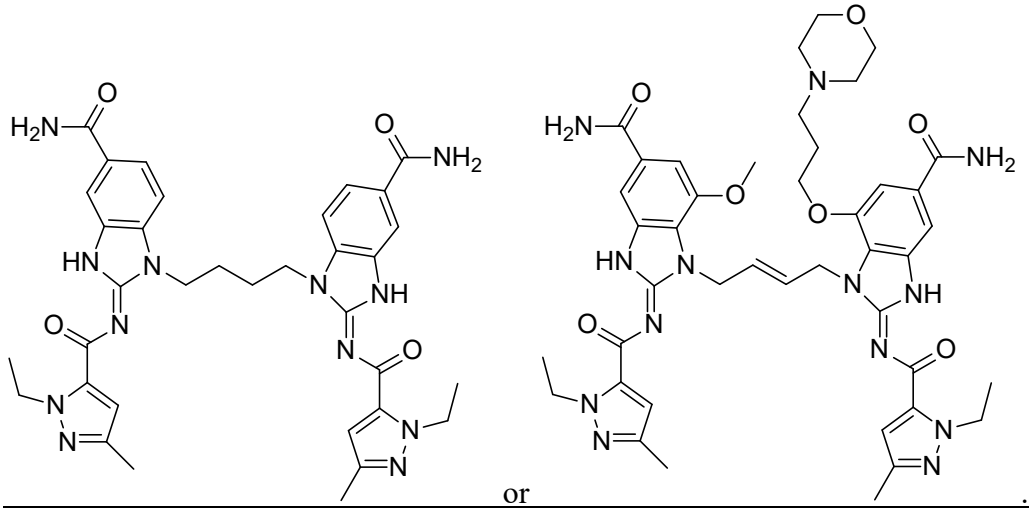
wherein:

C-D is an alkylene or alkenylene;

W is H or -OCH_3; and

V is H or -O-(C_1-C_3)alkyl-(C_3-C_6)heterocycle.

15. The pharmaceutical composition of any one of claims 1-6, wherein the non-peptide STING agonist is:



or

16. The pharmaceutical composition of any one of claims 1-15, wherein one or more non-peptide STING agonists is encapsulated by the block copolymer within one or more micelles.

17. The pharmaceutical composition of any one of claims 1-15, wherein one or more non-peptide STING agonists is not encapsulated by the block copolymer within a micelle.

18. The pharmaceutical composition of claim 17, further comprising a saccharide solution.

19. Use of a therapeutically effective amount of a pharmaceutical composition of any one of claims 1-18 in the manufacture of a medicament for treating cancer in a subject in need thereof.

20. Use of a pharmaceutical composition of any one of claims 1-18 in the manufacture of a medicament for activating the STING pathway in a subject in need thereof.