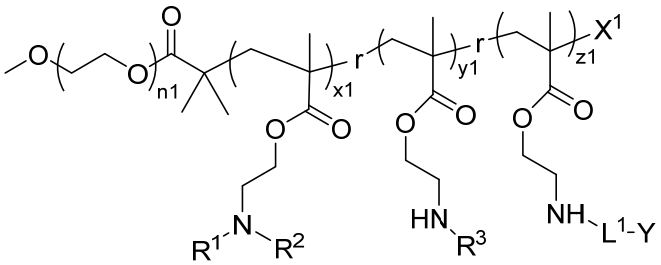
CLAIMS

~~**WHAT IS CLAIMED IS:**~~

1. A block copolymer having the structure of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:



Formula (I),

wherein:

n_1 is an integer from 10-200;

x_1 is an integer from 40-300;

y_1 is an integer from 0-6;

z_1 is an integer from 0-10;

X^1 is a halogen, -OH, or -C(O)OH;

R^1 and R^2 are each independently an optionally substituted C_1-C_6 alkyl, C_3-C_{10} cycloalkyl or aryl;

or R^1 and R^2 are taken together with the corresponding nitrogen to which they are attached to form an optionally substituted 5 to 7-membered ring;

each R^3 is independently hydrogen, acyl, or ICG;

L^1 is a bond or -C(O)-, or optionally substituted C_1-C_{10} alkylene linker or PEG linker; and

Y is a therapeutic agent.

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

3. The block copolymer of claim 1 or 2, wherein R^1 and R^2 are each independently -CH_2CH_3, -$CH_2CH_2CH_3$, or -$CH_2CH_2CH_2CH_3$.

4. The block copolymer of any one of claims 1-3, wherein R^1 and R^2 are each -$CH_2CH_2CH_2CH_3$.

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

6. The block copolymer of claim 1 or 5, wherein R^1 and R^2 taken together are -$CH_2(CH_2)_2CH_2$-, -$CH_2(CH_2)_3CH_2$-, or -$CH_2(CH_2)_4CH_2$-.

7. The block copolymer of any one of claims 1-6, wherein x_1 is an integer from 50-200, 60-160, or 90-140.

8. The block copolymer of claim 7, wherein x_1 is 90-140.

9. The block copolymer of any one of claims 1-8, wherein y_1 is an integer from 1-6, 1-5, 1-4, or 1-3.

10. The block copolymer of any one of claims 1-8, wherein y_1 is 0.

11. The block copolymer of any one of claims 1-10, wherein z_1 is an integer from 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, or 1-3.

12. The block copolymer of any one of claims 1-10, wherein z_1 is 0.

13. The block copolymer of any one of claims 1-12, wherein n_1 is an integer from 60-150 or 100-140.

14. The block copolymer of any one of claims 1-12, wherein n_1 is 100-140.

15. The block copolymer of any one of claims 1-14, wherein X^1 is a halogen.

16. The block copolymer of claim 15, wherein X^1 is -Br.

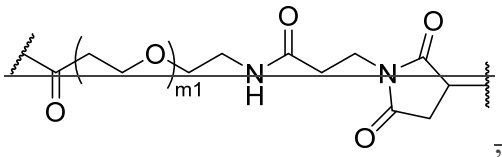
17. The block copolymer of any one of claims 1-16, wherein each R^3 is independently acyl or ICG.

18. The block copolymer of any one of claims 1-16, wherein each R^3 is independently hydrogen.

19. The block copolymer of any one of claims 1-18, wherein L^1 is an optionally substituted C_1-C_{10} alkylene linker, optionally substituted with a maleimide residual.

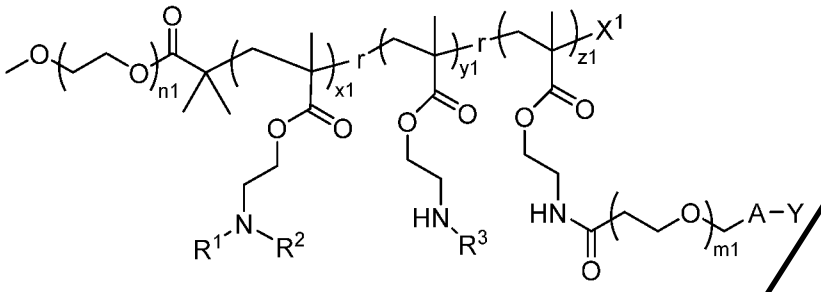
20. The block copolymer of any one of claims 1-18, wherein L^1 is an optionally substituted PEG linker, optionally substituted with a maleimide residual.

~~21. The block copolymer of any one of claims 1-18, wherein L^+ is:~~



~~, wherein m_1 is 2-200.~~

~~22. The block copolymer of claim 1, wherein the block copolymer of Formula (I) has the structure of Formula (I-a), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:~~



Formula (I-a),

wherein:

m_1 is an integer from 10-200; and

A is a bond or -C(O)- optionally substituted with a maleimide residual.

23. The block copolymer of any one of claims 1-22, wherein the therapeutic agent is a cytokine or a fragment thereof, an engineered antibody fragment, or a small molecule having a molecular weight less than 900 Daltons.

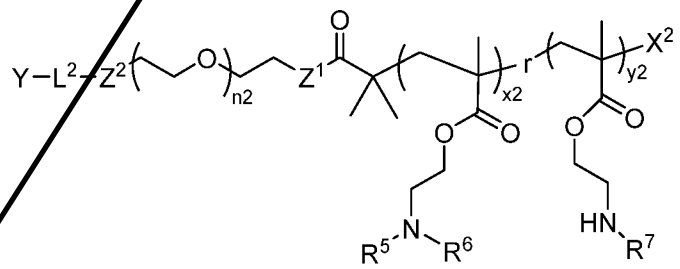
24. The block copolymer of claim 23, wherein the cytokine is IL-2, IL-12, or IL-15 or a fragment thereof.

25. The block copolymer of claim 23, wherein the cytokine is IL-2 or a fragment thereof.

26. The block copolymer of claim 23, wherein the engineered antibody fragment is a bispecific T cell engager.

27. The block copolymer of claim 23, wherein the small molecule is maytansine or a derivative thereof.

28. A block copolymer having the structure of Formula (II), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:



Formula (II),

wherein:

n_2 is an integer from 2-200;

x_2 is an integer from 40-300;

y_2 is an integer from 0-6;

X^2 is a halogen, -OH, or -C(O)OH;

R^5 and R^6 are each independently an optionally substituted C_1-C_6 alkyl, C_3-C_{10} cycloalkyl or aryl;

or R^5 and R^6 are taken together with the corresponding nitrogen to which they are attached to form an optionally substituted 5 to 7-membered ring;

each R^7 is independently hydrogen, acyl, or ICG;

Z^1 is -NH- or -O-;

Z^2 is -NH-, -O-, or a substituted triazole;

L^2 is a bond or -C(O)-, or optionally substituted C_1-C_{10} alkylene linker or PEG linker; and

Y is a therapeutic agent.

29. The block copolymer of claim 28, wherein R^5 and R^6 are each independently an optionally substituted C_1-C_6 alkyl.

30. The block copolymer of claim 28 or 29, wherein R^5 and R^6 are each independently -CH_2CH_3, -$CH_2CH_2CH_3$, or -$CH_2CH_2CH_2CH_3$.

31. The block copolymer of any one of claims 28-30, wherein R^5 and R^6 are each -$CH_2CH_2CH_2CH_3$.

32. The block copolymer of claim 28, wherein R^5 and R^6 are taken together with the corresponding nitrogen to which they are attached to form an optionally substituted 5 to 7-membered ring.

33. The block copolymer of claim 28 or 32, wherein R^5 and R^6 taken together are -$CH_2(CH_2)_2CH_2$-, -$CH_2(CH_2)_3CH_2$-, or -$CH_2(CH_2)_4CH_2$-.

34. The block copolymer of any one of claims 28-33, wherein x_2 is an integer from 50-200, 60-160, or 90-140.

35. The block copolymer of claim 34, wherein x_2 is 90-140.

36. The block copolymer of any one of claims 28-35, wherein y_2 is an integer from 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, or 1-3.

37. The block copolymer of any one of claims 28-36, wherein y_2 is 0.

38. The block copolymer of any one of claims 28 to 37, wherein n_2 is an integer from 60-150 or 100-140.

39. The block copolymer of claim 38, wherein n_2 is 100-140.

40. The block copolymer of any one of claims 28-39, wherein X^2 is a halogen.

41. The block copolymer of claim 40, wherein X^2 is -Br.

42. The block copolymer of any one of claims 28-41, wherein each R^7 is independently acyl or ICG.

43. The block copolymer of any one of claims 28-41, wherein each R^7 is independently hydrogen.

44. The block copolymer of any one of claims 28-43, wherein Z^1 is -O-.

45. The block copolymer of any one of claims 28-43, wherein Z^1 is -NH-.

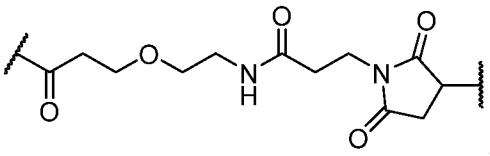
46. The block copolymer of any one of claims 28-45, wherein Z^2 is -O- or -NH-.

47. The block copolymer of any one of claims 28-46, wherein Z^2 is an optionally substituted triazole residual.

48. The block copolymer of any one of claims 28-47, wherein L^2 is an optionally substituted C_1-C_{10} alkylene linker, optionally substituted with a maleimide residual.

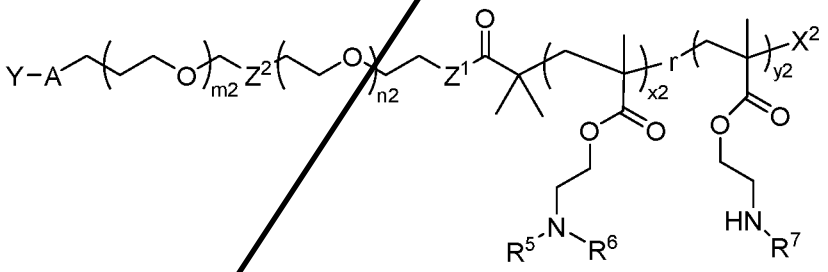
49. The block copolymer of any one of claims 28-48, wherein L^2 is an optionally substituted PEG linker, optionally substituted with a maleimide residual.

50. The block copolymer of any one of claims 28-48, wherein L^2 is



, wherein m_2 is 2-200.

51. The block copolymer of claim 28, wherein the block copolymer of Formula (II) has the structure of Formula (II-a), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:



Formula (II-a),

wherein:

m_2 is 2-200; and

A is a bond or -C(O)- optionally substituted with a maleimide residual.

52. The block copolymer of any one of claims 28-51, wherein the therapeutic agent is a cytokine or a fragment thereof, an engineered antibody fragment, or a small molecule having a molecular weight less than 900 Daltons.

53. The block copolymer of claim 52, wherein the cytokine is IL-2, IL-12, or IL-15 or a fragment thereof.

54. The block copolymer of claim 52, wherein the cytokine is IL-2 or a fragment thereof.

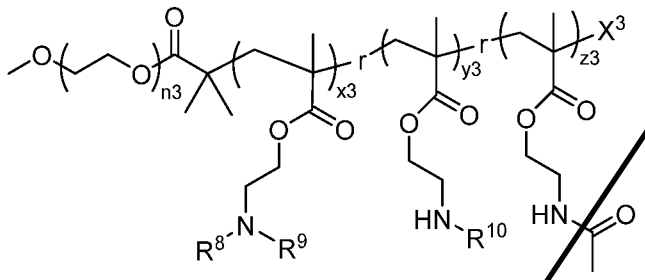
55. The block copolymer of claim 52, wherein the engineered antibody fragment is a bispecific T cell engager.

56. The block copolymer of claim 52, wherein the small molecule is maytansine or a derivative thereof.

57. The block copolymer of any one of claims 1-56, wherein the block copolymer is in the form of a micelle.

58. A micelle comprising:

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



Formula (III),

wherein:

n_3 is an integer from 10-200;

x_3 is an integer from 40-300;

y_3 is an integer from 0-6;

z_3 is an integer from 0-10;

X^3 is a halogen, -OH, or -C(O)OH;

each R^{10} is independently hydrogen or ICG;

R^8 and R^9 are each independently an optionally substituted C_1-C_6 alkyl, C_3-C_{10} cycloalkyl or aryl;

or R^8 and R^9 are taken together with the corresponding nitrogen to which they are attached to form an optionally substituted 5 to 7-membered ring; and

(ii) a therapeutic agent encapsulated by the block copolymer.

59. The micelle of claim 58, wherein R^8 and R^9 are each independently an optionally substituted C_1-C_6 alkyl.

60. The micelle of claim 58 or 59, wherein R^8 and R^9 are each independently $-CH_2CH_3$, $-CH_2CH_2CH_3$, or $-CH_2CH_2CH_2CH_3$.

61. The micelle of any one of claims 58-60, wherein R^8 and R^9 are each $-CH_2CH_2CH_2CH_3$.

62. The micelle of claim 58, wherein R^8 and R^8 are taken together with the corresponding nitrogen to which they are attached to form an optionally substituted 5 to 7-membered ring.

63. The micelle of claim 58 or 62, wherein R^8 and R^9 taken together are $-CH_2(CH_2)_2CH_2-$, $-CH_2(CH_2)_3CH_2-$, or $-CH_2(CH_2)_4CH_2-$.

64. The micelle of any one of claims 58-63, wherein x_3 is an integer from 50-200, 60-160, or 90-140.

65. The micelle of claim 64, wherein x_3 is 90-140.

66. The micelle of any one of claims 58-65, wherein y_3 is an integer from 1-6, 1-5, 1-4, or 1-3.

67. The micelle of any one of claims 58-65, wherein y_3 is 0.

68. The micelle of any one of claims 58-66, wherein z_3 is an integer from 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, or 1-3.

69. The micelle of any one of claims 58-66, wherein z_3 is 0.

70. The micelle of any one of claims 58-69, wherein n_3 is an integer from 60-150 or 100-140.

71. The micelle of claim 66, wherein n_3 is 100-140.

72. The micelle of any one of claims 58-71, wherein X^3 is a halogen.

73. The micelle of claim 72, wherein X^3 is -Br.

74. The micelle of any one of claims 58-73, wherein the therapeutic agent is a cytokine or a fragment thereof, an engineered antibody fragment, or a small molecule having a molecular weight less than 900 Daltons.

75. The micelle of claim 74, wherein the therapeutic agent is a cytokine or a fragment thereof.

76. The micelle of claim 75, wherein the cytokine is IL-2, IL-12, or IL-15 or a fragment thereof.

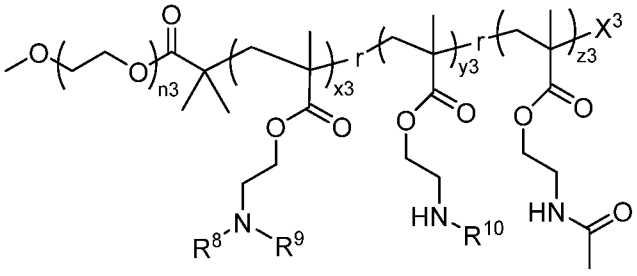
77. The micelle of claim 75, wherein the cytokine is IL-2 or a fragment thereof.

78. The micelle of claim 74, wherein the engineered antibody fragment is a bispecific T cell engager or a fragment thereof.

79. The micelle of claim 74, wherein the small molecule is maytansine or a derivative thereof.

80. A micelle comprising:

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



Formula (III),

wherein:

n_3 is an integer from 10-200;

x_3 is an integer from 40-300;

y_3 is an integer from 0-6;

z_3 is an integer from 0-10;

X^3 is a halogen, -OH, or -C(O)OH;

R^8 and R^9 are each independently an optionally substituted C_1-C_6 alkyl, C_3-C_{10} cycloalkyl or aryl;

or R^8 and R^9 are taken together with the corresponding nitrogen to which they are attached to form an optionally substituted 5 to 7-membered ring; and

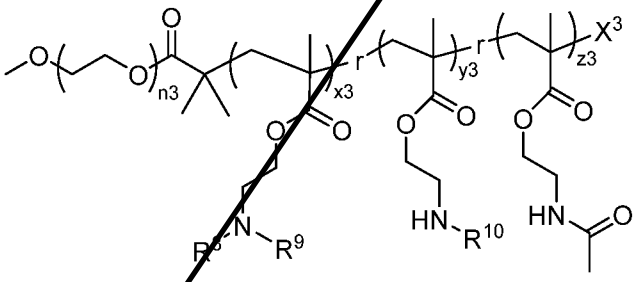
each R^{10} is independently hydrogen or ICG; and

(ii) a block copolymer of any one or claims 1-27; or

a block copolymer of any of claims 28-56.

81. A micelle comprising:

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



Formula (III),

wherein:

n_3 is an integer from 10-200;

x_3 is an integer from 40-300;

y_3 is an integer from 0-6;

z_3 is an integer from 0-10;

X^3 is a halogen, -OH, or -C(O)OH;

each R^{10} is independently hydrogen or ICG;

R^8 and R^9 are each independently an optionally substituted C_1-C_6 alkyl, C_3-C_{10} cycloalkyl or aryl;

or R^8 and R^9 are taken together with the corresponding nitrogen to which they are attached to form an optionally substituted 5 to 7-membered ring;

(ii) a block copolymer of any one or claims 1-27; and

(iii) a block copolymer of any of claims 28-56.

82. The micelle of claim 80 or 81, wherein the ratio of the block copolymer of Formula (III) to the block copolymer of any one of claims 1-27 or any one of claims 28-56 is from 1:99 to 99:1 or any ratio therein.

83. A pH response composition of any one of claim 58-78, wherein the composition has a pH transition point and optionally an emission spectrum.

84. A pH response composition of any one of claims 79-82, wherein the composition has a pH transition point and optionally an emission spectrum.

85. The pH responsive composition of claim 83 or 84, wherein the pH transition point is between 4-8, 6-7.5, or 4.5-5.5.

86. The pH responsive composition of claim 83 or 84, wherein composition has a pH response of less than 0.25 or 0.15 pH units.

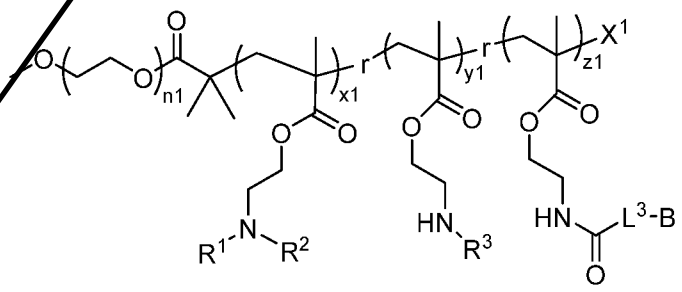
87. The pH responsive composition of claim 83 to 84, wherein the emission spectrum is between 700-900 nm.

88. A method for treating cancer in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a micelle of any one of claims 58-78.

89. The method of claim 88, wherein the cancer is a solid tumor.

90. The method of claim 88 or 89, wherein the cancer is breast cancer, cervical cancer, head and neck squamous cell carcinoma (NHSCC), peritoneal metastasis, lung cancer, ovarian cancer, pancreatic cancer, prostate cancer, bladder cancer, kidney cancer, urethral cancer, esophageal cancer, colorectal cancer, brain cancer, or skin cancer.

91. A block copolymer having the structure of Formula (I-b), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:



Formula (I-b),

wherein:

n_1 is an integer from 10-200;

x_1 is an integer from 40-300;

y_1 is an integer from 0-6;

z_1 is an integer from 0-10;

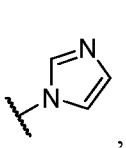
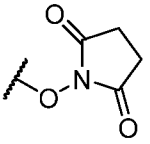
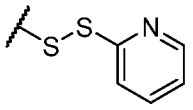
X^1 is a halogen, -OH, or -C(O)OH;

R^1 and R^2 are each independently substituted or unsubstituted C_1-C_6 alkyl, C_3-C_{10} cycloalkyl or aryl;

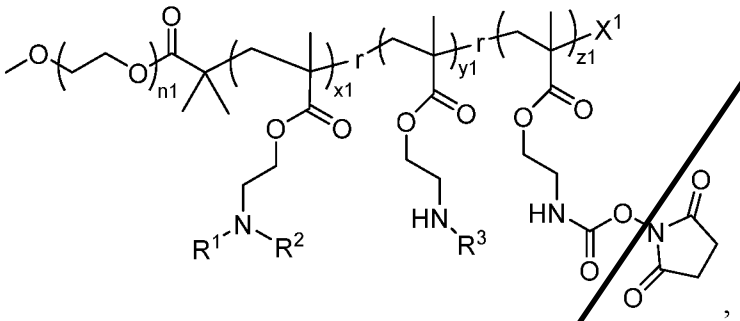
or R^1 and R^2 are taken together with the corresponding nitrogen to which they are attached to form an optionally substituted 5 to 7-membered ring;

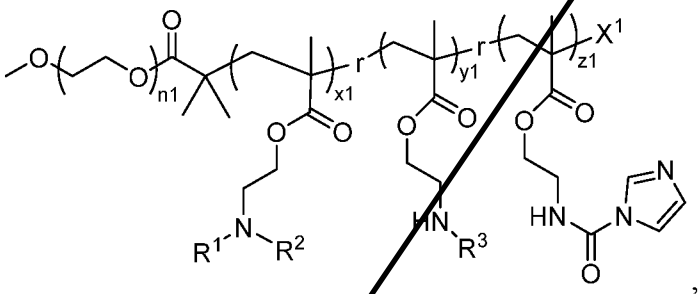
each R^3 is independently hydrogen, acyl, or ICG;

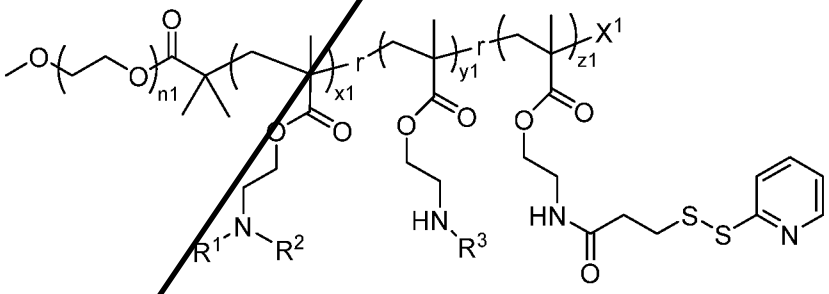
L^3 is a bond, C_1-C_{10} alkylene linker, or PEG linker; and

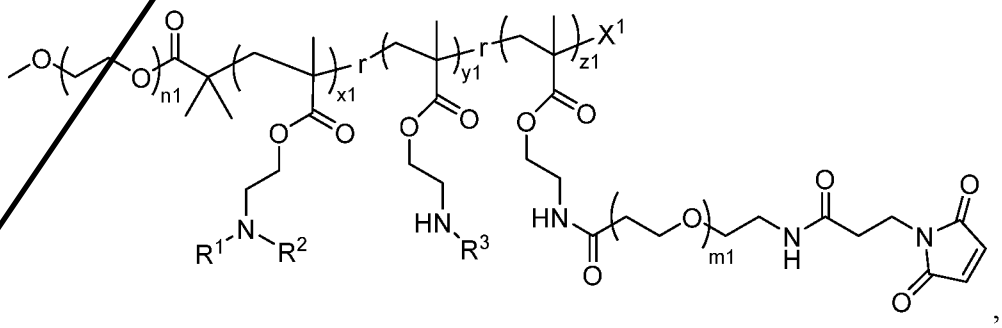
B is maleimide, , , or .

92. The block copolymer of claim 91, wherein the block copolymer is:

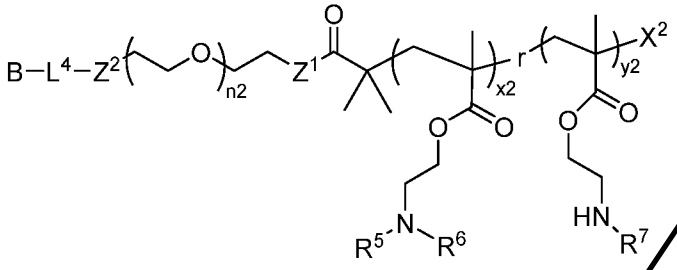
,

,

, or

, wherein m_1 is 2-200; or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

93. A block copolymer having the structure of Formula (II-b), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:



Formula (II-b),

wherein:

n_2 is an integer from 2-200;

x_2 is an integer from 40-300;

y_2 is an integer from 0-6;

X^2 is a halogen, -OH, or -C(O)OH;

R^5 and R^6 are each independently substituted or unsubstituted C_1-C_6 alkyl, C_3-C_{10} cycloalkyl or aryl;

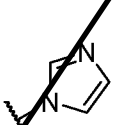
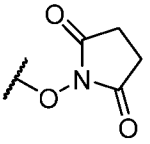
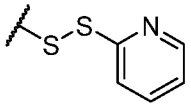
or R^5 and R^6 are taken together with the corresponding nitrogen to which they are attached to form an optionally substituted 5 to 7-membered ring;

each R^7 is independently hydrogen, acyl, or ICG;

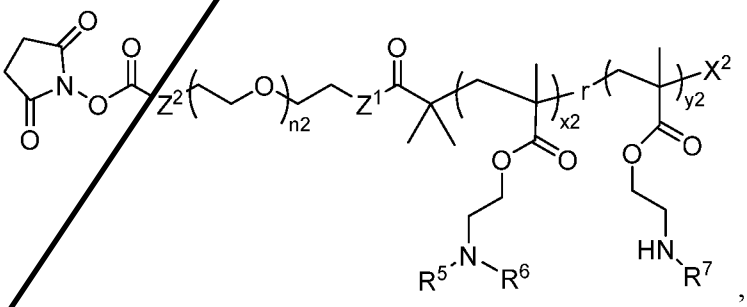
Z^1 is -NH- or -O-;

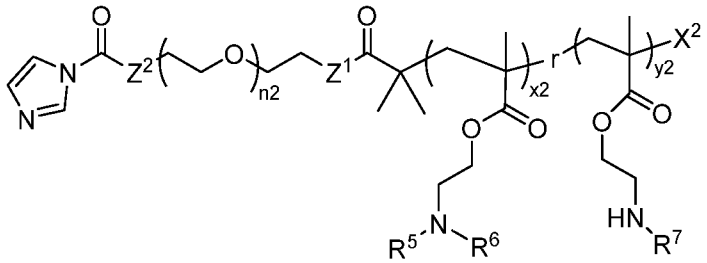
Z^2 is -NH-, -O-, or a substituted triazole;

L^4 is a bond, C_1-C_{10} alkylene linker, or PEG linker; and

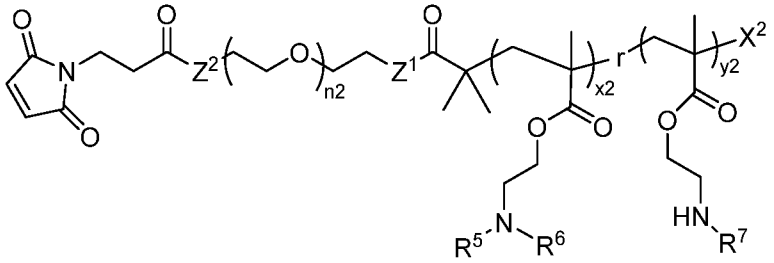
B is maleimide, , , or .

94. The block copolymer of claim 93, wherein the block copolymer is:

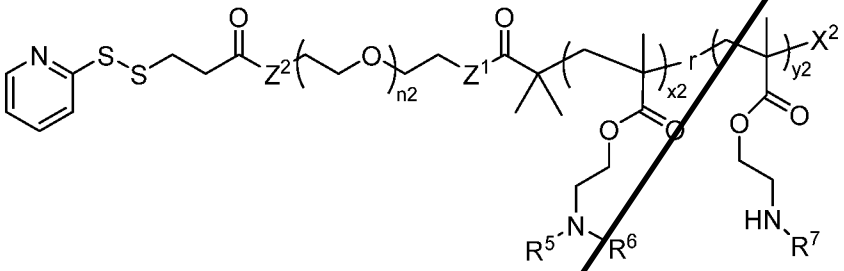
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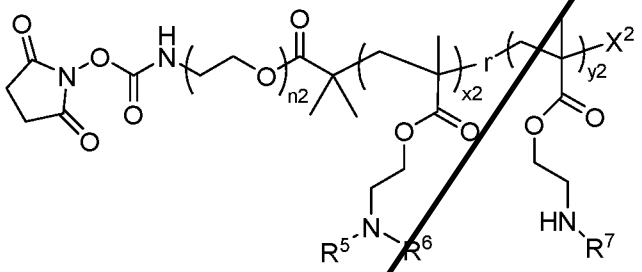
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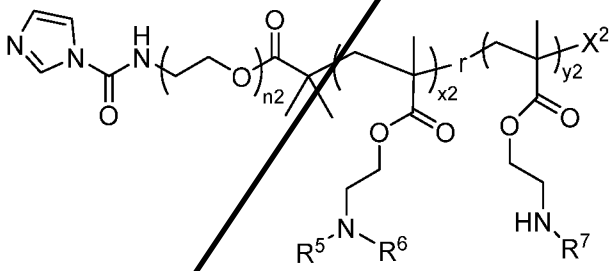
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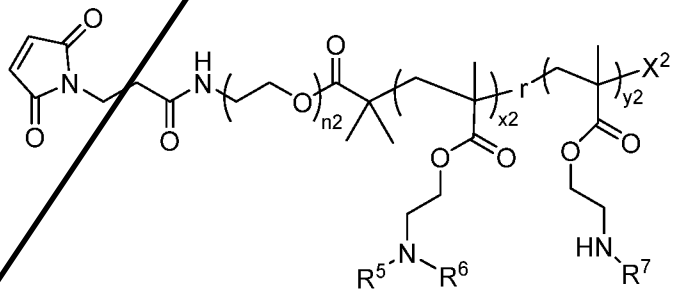
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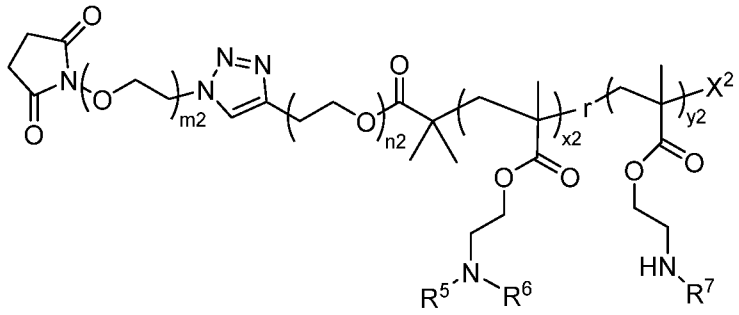
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, or



, wherein m_2 is 2-200; or a pharmaceutically acceptable salt, solvate, or hydrate thereof.