WHAT IS CLAIMED IS:

1. A method of treating cancer in a subject who previously received treatment with a first poly ADP-ribose polymerase (PARP) inhibitor, the method comprising administering to the subject a ubiquitin-specific-processing protease (USP1) inhibitor and a second PARP inhibitor, wherein the first and the second PARP inhibitors are the same or different PARP inhibitors.

2. The method of claim 1, wherein the subject did not previously receive treatment with a USP1 inhibitor.

3. The method of claim 1 or 2, wherein the treatment with the first PARP inhibitor was interrupted or discontinued.

4. The method of claim 3, wherein the interruption is for at least one week, at least two weeks, at least three weeks, or at least four weeks.

5. The method of any one of claims 1-4, wherein the subject experienced unacceptable toxicity and/or unacceptable adverse reactions during treatment with the first PARP inhibitor.

6. The method of claim 1, wherein the unacceptable toxicity or adverse reaction was a hematological toxicity such as thrombocytopenia, anemia, or neutropenia, pneumonitis, dyspnea, fever, cough, wheezing, a radiological abnormality, hypertension, myelodysplastic syndrome/acute myeloid leukemia (MDS/AML), nausea, and/or fatigue.

7. The method of any one of claims 1-6, wherein during treatment with the first PARP inhibitor, the dose of the first PARP inhibitor was reduced.

8. The method of claim 7, wherein the dose of the first PARP inhibitor was reduced to one quarter, one third, one half, two thirds, or three quarters of the dose prior to the reduction.

9. The method of claim 7, wherein the first PARP inhibitor was olaparib and the dose prior to the reduction was 400 mg taken twice daily.

10. The method of claim 7 or 9, wherein the first PARP inhibitor was olaparib and the dose after the reduction was 200 mg taken twice daily or 100 mg taken twice daily.

11. The method of claim 7, wherein the first PARP inhibitor was niraparib and the dose prior to reduction was 300 mg taken once daily.

12. The method of claim 7 or 11, wherein the first PARP inhibitor was niraparib and the dose after the reduction was 200 mg taken once daily or 100 mg taken once daily.

13. The method of claim 7, wherein the first PARP inhibitor was talazoparib and the dose prior to reduction was 1 mg taken once daily.

14. The method of claim 7 or 13, wherein the first PARP inhibitor was talazoparib and the dose after the reduction was 0.75 mg taken once daily, 0.5 mg taken once daily, or 0.25 mg taken once daily.

15. The method of claim 7, wherein the first PARP inhibitor was rucaparib and the dose prior to reduction was 600 mg taken twice daily.

16. The method of claim 7 or 15, wherein the first PARP inhibitor was rucaparib and the dose after the reduction was 500 mg taken twice daily, 400 mg taken twice daily, or 300 mg taken twice daily.

17. The method of any one of claims 1-8, wherein the first PARP inhibitor was olaparib, niraparib, talazoparib, or rucaparib.

18. The method of any one of claims 1-17, wherein the second PARP inhibitor is olaparib, niraparib, talazoparib, or rucaparib.

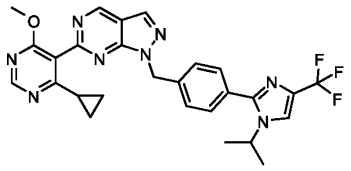
19. The method of any one of claims 1-18, wherein the first PARP inhibitor and the second PARP inhibitor are the same PARP inhibitor.

20. The method of any one of claims 1-19, wherein the first PARP inhibitor and the second PARP inhibitor are different PARP inhibitors.

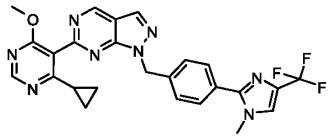
21. The method of any one of claims 1-20, wherein the dose of the second PARP inhibitor is reduced compared to the dose of first PARP inhibitor.

22. The method of any one of claims 1-21, wherein the USP1 inhibitor is a compound selected from the group consisting of

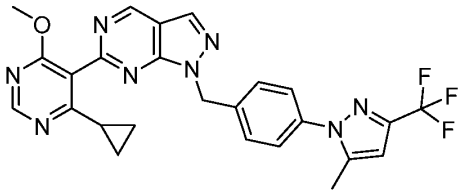
(a) Formula I:



(b) Formula II:



(c) Formula III:



and pharmaceutically acceptable salts, hydrates, solvates, amorphous solids, or polymorphs thereof.

23. The method of any one of claims 1-22, wherein the USP1 inhibitor and the second PARP inhibitor are well tolerated.

24. The method of any one of claims 1-23, wherein the USP1 inhibitor decreases the exposure of the subject to the second PARP inhibitor.

25. The method of any one of claims 1-24, wherein the USP1 inhibitor and the second PARP inhibitor inhibit rebounding and/or regrowth of the cancer.

26. The method of any one of claims 1-25, wherein the USP1 inhibitor and the second PARP inhibitor are administered sequentially.

27. The method of any one of claims 1-26, wherein the USP1 inhibitor and the second PARP inhibitor are administered simultaneously.

28. The method of any one of claims 1-27, wherein the subject is human.

29. The method of any one of claims 1-28, wherein the cancer is selected from the group consisting of brain cancer, lung cancer, non-small cell lung cancer (NSCLC), colon cancer, bladder cancer, osteosarcoma, ovarian cancer, skin cancer, uterine cancer, peritoneal cancer, and endometrial cancer, and breast cancer.

30. The method of claim 29, wherein the cancer is breast cancer.

31. The method of claim 30, wherein the breast cancer is triple negative breast cancer (TNBC).

32. The method of any one of claims 1-31, wherein the cancer is a BRCA1 mutant cancer, a BRCA2 mutant cancer, or a BRCA1 mutant and BRCA2 mutant cancer.

33. The method of claim 29, wherein the cancer is ovarian cancer.

34. The method of claim 33, wherein the ovarian cancer is a BRCA1 mutant cancer, a BRCA2 mutant cancer, or a p53 mutant cancer.

35. The method of claim 33 or 34, wherein the ovarian cancer is a BRCA1 mutant cancer and a p53 mutant cancer.

36. The method of claim 33 or 34, wherein the ovarian cancer is a BRCA1 and BRCA2 mutant cancer.

37. The method of claim 33 or 34, wherein the ovarian cancer is a BRCA2 mutant cancer.

38. The method of any one of claims 1-28, wherein the cancer is selected from the group consisting of a hematological cancer and a lymphatic cancer.

39. The method of any one of claims 1-38, wherein the cancer comprises cells with elevated levels of RAD51.

40. The method of claim 39, wherein the elevated levels of RAD51 are elevated RAD51 protein levels.

41. The method of claim 39, wherein the elevated levels of RAD51 are elevated RAD51 protein foci levels.

42. The method of claim 39, wherein at least 10% of cells that are in the S/G2 phase of the cell cycle in a sample obtained from the cancer are RAD51-positive.

43. The method of claim 39, wherein the elevated levels of RAD51 are elevated RAD51 mRNA levels.

44. The method of any one of claims 39-43, wherein the elevated levels of RAD51 have been detected prior to the administration.

45. The method of claim 44, further comprising detecting RAD51 levels in a cancer sample obtained from the subject prior to the administration.

46. The method of any one of claims 1-45, wherein the cancer is selected from the group consisting of a DNA damage repair pathway deficient cancer, a homologous-recombination deficient cancer, a cancer comprising cancer cells with a mutation in a gene encoding p53, a cancer comprising cancer cells with a loss of function mutation in a gene encoding p53, and a cancer comprising cells with a mutation in the gene encoding ATM.

47. The method of any one of claims 1-46, wherein the cancer is a PARP inhibitor resistant or refractory cancer.

48. A method of treating cancer in a subject comprising administering to the subject a USP1 inhibitor, wherein the cancer comprises cancer cells with elevated levels of RAD51.

49. The method of claim 48, wherein the elevated levels of RAD51 have been detected prior to the administration.

50. The method of claim 49, further comprising detecting RAD51 levels in a cancer sample obtained from the subject.

51. The method of any one of claims 48-50, wherein the method further comprises administering to the subject a PARP inhibitor in combination with the USP1 inhibitor.

52. The method of claim 51, wherein the PARP inhibitor is olaparib, niraparib, talazoparib, or rucaparib.

53. A method of selecting a subject with cancer for treatment with a USP1 inhibitor, comprising detecting whether the cancer comprises cells with elevated levels of RAD51, wherein if the cancer comprises cells with elevated levels of RAD51, the subject is selected for treatment with a USP1 inhibitor.

54. An *in vitro* method for identifying a subject with cancer to be responsive to the treatment with a USP1 inhibitor, comprising detecting RAD51 levels in a cancer sample obtained from the subject, wherein elevated levels of RAD51 in the cancer sample are indicative for the patient to be responsive to the treatment with a USP1 inhibitor.

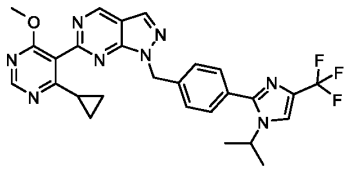
55. An *in vitro* use of at least one agent capable of specifically detecting RAD51, for identifying a subject with cancer to be responsive to the treatment with a USP1 inhibitor.

56. The method or use of any one of claims 53-55, wherein the treatment with a USP1 inhibitor further comprises treatment with a PARP inhibitor in combination with the USP1 inhibitor.

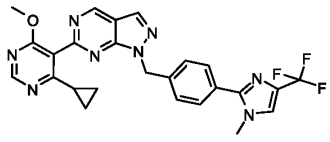
57. The method or use of claim 56, wherein the PARP inhibitor is olaparib, niraparib, talazoparib, or rucaparib.

58. The method or use of any one of claims 53-57, wherein the USP1 inhibitor is a compound selected from the group consisting of

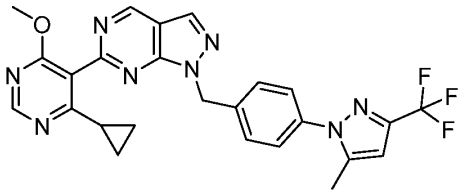
(a) Formula I:



(b) Formula II:



(c) Formula III:



and pharmaceutically acceptable salts, hydrates, solvates, amorphous solids, or polymorphs thereof.

59. The method or use of any one of claims 48-58, wherein the subject is human.

60. The method or use of any one of claims 48-59, wherein the cancer is selected from the group consisting of brain cancer, lung cancer, non-small cell lung cancer (NSCLC), colon cancer, bladder cancer, osteosarcoma, ovarian cancer, skin cancer, uterine cancer, peritoneal cancer, and endometrial cancer, and breast cancer.

61. The method of claim 60, wherein the cancer is breast cancer.

62. The method of claim 61, wherein the breast cancer is triple negative breast cancer (TNBC).

63. The method of any one of claims 48-62, wherein the cancer is a BRCA1 mutant cancer, a BRCA2 mutant cancer, or a BRCA1 mutant and BRCA2 mutant cancer.

64. The method of claim 60, wherein the cancer is ovarian cancer.

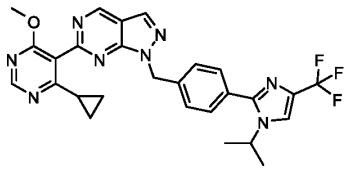
65. The method of claim 64, wherein the ovarian cancer is a BRCA1 mutant cancer, a BRCA2 mutant cancer, or a p53 mutant cancer.

66. The method of claim 64 or 65, wherein the ovarian cancer is a BRCA1 mutant cancer and a p53 mutant cancer.

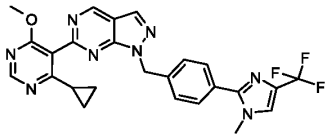
67. The method of claim 64 or 65, wherein the ovarian cancer is a BRCA1 and BRCA2 mutant cancer.

68. The method of claim 64 or 65, wherein the ovarian cancer is a BRCA2 mutant cancer.

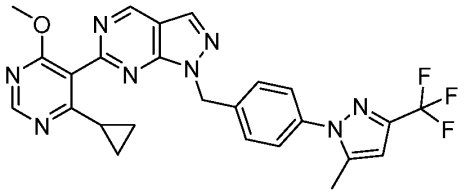
69. A method of delaying, reducing, or preventing rebounding of a tumor in a subject comprising administering to the subject (i) a ubiquitin-specific-processing protease 1 (USP1) inhibitor and (ii) a poly ADP-ribose polymerase (PARP) inhibitor, or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof,
wherein the USP1 inhibitor is a compound selected from the group consisting of
(a) Formula I:



(b) Formula II:

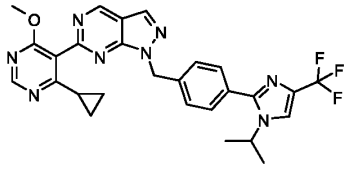


(c) Formula III:

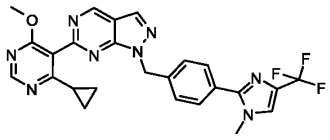


and pharmaceutically acceptable salts, hydrates, solvates, amorphous solids, or polymorphs thereof.

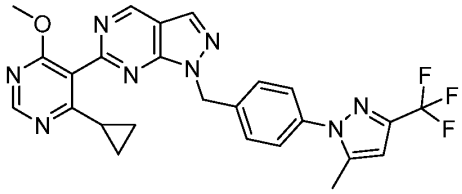
70. A method of treating cancer in a subject comprising administering to the subject (i) a ubiquitin-specific-processing protease 1 (USP1) inhibitor and (ii) a poly ADP-ribose polymerase (PARP) inhibitor, or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof,
wherein the USP1 inhibitor is a compound selected from the group consisting of
(a) Formula I:



(b) Formula II:



(c) Formula III:



and pharmaceutically acceptable salts, hydrates, solvates, amorphous solids, or polymorphs thereof.

71. The method of claim 69 or 70, wherein said PARP inhibitor is selected from the group consisting of niraparib, olaparib and pharmaceutically acceptable salts, hydrates, solvates, amorphous solids, or polymorphs thereof.

72. The method of claim 71, wherein said PARP inhibitor is niraparib or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof.

73. The method of claim 71, wherein said PARP inhibitor is olaparib or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof.

74. The method of any one of claims 69 to 73, wherein the USP1 inhibitor is the compound of Formula I, or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof.

75. The method of any one of claims 69 to 73, wherein the USP1 inhibitor is the compound of Formula II, or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof.

76. The method of any one of claims 69 to 73, wherein the USP1 inhibitor is the compound of Formula III, or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof.

77. The method of any one of claims 69 to 76, wherein the administration of the USP1 inhibitor, or said pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, and said PARP inhibitor, or said pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, provides a synergistic effect.

78. The method of any one of claims 70 to 77, wherein said USP1 inhibitor, or said pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, and said PARP inhibitor, or said pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, are administered in a therapeutically effective amount sufficient to produce one or more therapeutic effects selected from the group consisting of (i) reduction in tumor size, (ii) increase in tumor regression rate, and (iii) reduction or inhibition of tumor growth.

79. The method of any one of claims 69 to 78, wherein said USP1 inhibitor, or said pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, and said PARP inhibitor, or said pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, are administered in an amount effective to reduce the toxicity effects of a PARP inhibitor administered as a monotherapy.

80. The method of any one of claims 70 to 79, wherein said USP1 inhibitor, or said pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, and said PARP inhibitor, or said pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, delay, reduce, or prevent rebounding of a tumor.

81. The method of any one of claims 69 to 80, wherein the USP1 inhibitor, or said pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, and said PARP inhibitor, or said pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, are administered sequentially.

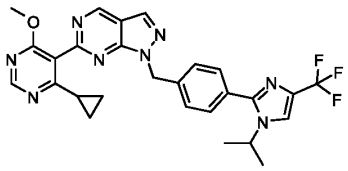
82. The method of any one of claims 69 to 80, wherein the USP1 inhibitor, or said pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, and said PARP inhibitor, or said pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, are administered simultaneously.

83. The method of any one of claims 69 to 82, wherein the USP1 inhibitor and/or the PARP inhibitor is administered at a dose that is not effective as a single agent.

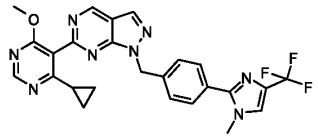
84. The method of any one of claims 69 to 83, wherein the subject is a mammal, optionally, wherein the mammal is a human.

85. A combination composition comprising (i) a ubiquitin-specific-processing protease 1 (USP1) inhibitor and (ii) a poly ADP-ribose polymerase (PARP) inhibitor, or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof, wherein the USP1 inhibitor is a compound selected from the group consisting of

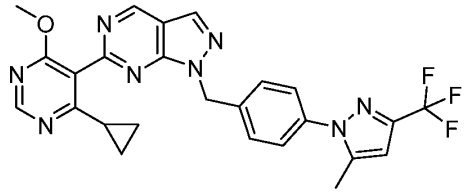
(a) Formula I:



(b) Formula II:



(c) Formula III:



and pharmaceutically acceptable salts, hydrates, solvates, amorphous solids, or polymorphs thereof.

86. The composition of claim 85, wherein said PARP inhibitor is selected from the group consisting of niraparib, olaparib and pharmaceutically acceptable salts, hydrates, solvates, amorphous solids, or polymorphs thereof.

87. The composition of claim 86, wherein said PARP inhibitor is niraparib or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof.

88. The composition of claim 86, wherein said PARP inhibitor is olaparib or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof.

89. The composition of any one of claims 85 to 88, wherein the USP1 inhibitor is the compound of Formula I, or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof.

90. The composition of any one of claims 85 to 88, wherein the USP1 inhibitor is the compound of Formula II, or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof.

91. The composition of any one of claims 85 to 88, wherein the USP1 inhibitor is the compound of Formula III, or a pharmaceutically acceptable salt, hydrate, solvate, amorphous solid, or polymorph thereof.

92. Use of the composition of any one of claims 85 to 91 for the manufacture of a medicament for treatment of cancer.

93. A pharmaceutical composition comprising the composition of any one of claims 85 to 91 and a pharmaceutically acceptable carrier.

94. The pharmaceutical composition of claim 93 for use in the treatment of cancer.

95. A kit comprising the composition of any one of claims 85 to 91, or the pharmaceutical composition of claim 93 or 94, and instructions for administering the combination to a subject having cancer.

96. The method of any one of claims 69 to 84, the use of claim 92, the pharmaceutical composition of claim 94, or the kit of claim 95, wherein the cancer is selected from the group consisting of a hematological cancer, a lymphatic cancer, a DNA damage repair pathway deficient cancer, a homologous-recombination deficient cancer, a cancer comprising cancer cells with a mutation in a gene encoding p53, and a cancer comprising cancer cells with a loss of function mutation in a gene encoding p53.

97. The method, use, pharmaceutical composition, or kit of any one of claims 69 to 84, 92, 94, 95, or 96, wherein the cancer is selected from the group consisting of brain cancer, lung cancer, non-small cell lung cancer (NSCLC), colon cancer, bladder cancer, osteosarcoma, ovarian cancer, skin cancer, uterine cancer, peritoneal cancer, and endometrial cancer, and breast cancer.

98. The method, use, pharmaceutical composition, or kit of any one of claims 69 to 84, 92, 94, 95, or 96, wherein the cancer is ovarian cancer or breast cancer.

99. The method, use, pharmaceutical composition, or kit of any one of claims 69 to 84, 92, 94, 95, or 96, wherein the cancer is ovarian cancer.

100. The method, use, pharmaceutical composition, or kit of any one of claims 69 to 84, 92, 94, 95, or 96, wherein the cancer is a breast cancer.

101. The method, use, pharmaceutical composition, or kit of any one of claims 69 to 84, 92, 94, 95, or 96, wherein the cancer is a triple negative breast cancer.

102. The method, use, pharmaceutical composition, or kit of any one of claims 69 to 84, 92, 94 to 101, wherein the cancer is a DNA damage repair pathway deficient cancer.

103. The method, use, pharmaceutical composition, or kit of claim 102, wherein the cancer is a homologous-recombination deficient cancer.

104. The method, use, pharmaceutical composition, or kit of any one of claims 69 to 84, 92, 94 to 103, wherein the cancer is a BRCA1 mutant cancer.

105. The method, use, pharmaceutical composition, or kit of any one of claims 69 to 84, 92, 94 to 103, wherein the cancer is a BRCA2 mutant cancer.

106. The method, use, pharmaceutical composition, or kit of any one of claims 69 to 84, 92, 94 to 103, wherein the cancer is a BRCA1 mutant cancer and a BRCA2 mutant cancer.

107. The method, use, pharmaceutical composition, or kit of any one of claims 69 to 84, 92, 94 to 106, wherein the cancer is a PARP inhibitor resistant or refractory cancer.

108. The method, use, pharmaceutical composition, or kit of any one of claims 69 to 84, 92, 94 to 107, wherein the cancer comprises cancer cells with a mutation in a gene encoding ATM.

109. The method, use, pharmaceutical composition, or kit of any one of claims 69 to 84, 92, 94 to 108, wherein the cancer comprises cells with elevated levels of RAD51.

110. The method, use, pharmaceutical composition, or kit of claim 109, wherein the elevated levels of RAD51 are elevated RAD51 protein levels.

111. The method, use, pharmaceutical composition, or kit of claim 109, wherein the elevated levels of RAD51 are elevated RAD51 protein foci levels.

112. The method, use, pharmaceutical composition, or kit of claim 109, wherein at least 10% of cells that are in the S/G2 phase of the cell cycle in a sample obtained from the cancer are RAD51-positive.

113. The method, use, pharmaceutical composition, or kit of claim 109, wherein the elevated levels of RAD51 are elevated RAD51 mRNA levels.

114. The method, use, pharmaceutical composition, or kit of any one of claims 109-113, wherein the elevated levels of RAD51 have been detected prior to the administration or the treatment.

115. The method or use of claim 114, further comprising detecting RAD51 levels in a cancer sample obtained from the subject prior to the administration or the treatment.

116. A method of treating a USP1 protein mediated disorder and/or a PARP protein mediated disorder comprising administering to a subject in need thereof a composition of any one of claims 85 to 91, or the pharmaceutical composition of claim 93 in an effective amount to treat the USP1 protein mediated disorder and/or the PARP protein mediated disorder.

117. A method of inhibiting a USP1 protein and/or a PARP protein comprising contacting a USP1 protein and/or a PARP protein with the composition of any one of claims 85 to 91, or the pharmaceutical composition of claim 93.

118. The method of claim 117, wherein the contacting occurs *in vitro*.

119. The method of claim 117, wherein the contacting occurs *in vivo*.