CLAIMS

What is claimed is:

1. Use of a menin-MLL inhibitor or a pharmaceutical composition comprising a menin-MLL inhibitor in the manufacture of a medicament for treating, preventing, or reducing the severity of a colorectal cancer in a subject in need thereof, wherein the menin-MLL inhibitor or the pharmaceutical composition comprising a menin-MLL inhibitor is to be administered to the subject.

2. Use of a pharmaceutical composition consisting essentially of a menin-MLL inhibitor in the manufacture of a medicament for treating, preventing, or reducing the severity of a colorectal cancer in a subject in need thereof, wherein the pharmaceutical composition consisting essentially of a menin-MLL inhibitor is to be administered to the subject.

3. Use of a pharmaceutical composition comprising a menin-MLL inhibitor in the manufacture of a medicament for treating, preventing, or reducing the severity of a colorectal cancer in a subject in need thereof, wherein the use is consisting essentially of administration of the pharmaceutical composition comprising a menin-MLL inhibitor to the subject.

4. Use of a single anti-cancer agent in the manufacture of a medicament for treating, preventing, or reducing the severity of colorectal cancer in a subject in need thereof, wherein the single anti-cancer agent is to be administered to the subject and the single anti-cancer agent is a menin-MLL inhibitor.

5. The use of any one of the preceding claims, wherein the menin-MLL inhibitor is Compound A, Compound B, DSP-5336, DS-1594, KO-539, MI-503, MI-3454, MI-463, M-808, MI-136, JNJ-75276617, MI-227, BMF-219, the antibody A300-105A, MI-0202, MI-503, MI-463, MI-136, ML-227, MI-2-2, or ISC-30.

6. The use of any one of the preceding claims, wherein the menin-MLL inhibitor is Compound A or Compound B.

7. The use of any one of the preceding claims, wherein the menin-MLL inhibitor is Compound A.

8. The use of any one of the preceding claims, wherein the menin-MLL inhibitor is to be administered at least once daily.

9. The use of any one of the preceding claims, wherein the menin-MLL inhibitor is to be administered twice daily.

10. The use of any one of the preceding claims, wherein the menin-MLL inhibitor is to be administered three times daily.

11. The use of any one of the preceding claims, wherein the menin-MLL inhibitor is to be administered in combination with a CYP3A inhibitor.

12. The use of any one of the preceding claims, wherein the menin-MLL inhibitor is to be administered in combination with a CYP3A4 inhibitor.

13. The use of claim 12, wherein the CYP3A4 inhibitor is a strong CYP3A4 inhibitor.

14. The use of claim 13, wherein the strong CYP3A4 inhibitor is boceprevir, cobicistat, clarithromycin, conivaptan, grapefruit juice, indinavir, itraconazole, ketoconazole, lopinavir, mibefradil, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, or voriconazole.

15. The use of any one of claims 1-10, wherein the menin-MLL inhibitor is to be further administered with cobicistat.

16. The use of any one of claims 1-10, wherein the menin-MLL inhibitor is to be further administered with cobicistat at least once daily.

17. The use of any one of claims 1-10, wherein the menin-MLL inhibitor is to be further administered with cobicistat once daily.

18. The use of claim 12, wherein the CYP3A4 inhibitor is a moderate CYP3A4 inhibitor.

19. The use of claim 18, wherein the moderate CYP3A4 inhibitor is amprenavir, aprepitant, atazanavir, ciprofloxacin, darunavir, diltiazem, erythromycin, fluconazole, fosamprenavir, imatinib, or verapamil.

20. The use of any one of the preceding claims, wherein the menin-MLL inhibitor is to be administered at a dosage of between 25 mg and 276 mg every 12 hours.

21. The use of any one of the preceding claims, wherein the menin-MLL inhibitor is to be administered at a dosage of about 163 mg every 12 hours.

22. The use of any one of claims 1-10, wherein the subject does not receive a CYP3A inhibitor.

23. The use of any one of claims 1-10, wherein the pharmaceutical composition does not comprise a CYP3A inhibitor.

24. The use of either claim 22 or 23, wherein the menin-MLL inhibitor is to be administered at a dosage of between 25 mg and 276 mg.

25. The use of either claim 22 or 23, wherein the menin-MLL inhibitor is to be administered at a dosage of between 25 mg and 276 mg, and wherein the menin-MLL inhibitor is to be administered three times per day.

26. The use of either claim 22 or 23, wherein the menin-MLL inhibitor is to be administered at a dosage of about 276 mg.

27. The use of either claim 22 or 23, wherein the menin-MLL inhibitor is to be administered at a dosage of about 276 mg, and wherein the menin-MLL inhibitor is to be administered three times per day.

28. The use of any one of claims 1-19, 22-25, and 27, wherein the menin-MLL inhibitor is to be administered at a dosage of up to 828 mg per day.

29. The use of any one of the preceding claims, wherein the menin-inhibitor is contained within a capsule or oral solution.

30. The use of any one of the preceding claims, wherein the subject previously received at least one prior line of therapy for colorectal cancer.

31. The use of any one of the preceding claims, wherein the subject previously received at least one prior line of therapy for colorectal cancer, and wherein the subject did not respond to previous therapy.

32. The use of either claim 30 or 31, wherein the at least one prior line of therapy was a chemotherapy, radiation therapy, immunotherapy, targeted small molecule therapy or biologic therapy (e.g., monoclonal antibody therapy).

33. The use of any one of the preceding claims, wherein the subject has previously received a treatment for colorectal cancer selected from trifluridine, tipiracil and or regorafenib.

34. The use of any one of the preceding claims, wherein the subject has previously received trifluridine, tipiracil, or a combination thereof.

35. The use of any one of the preceding claims, wherein the subject has previously received regorafenib.

36. The use of any one of the preceding claims, wherein the subject progressed on at least one prior line of therapy for colorectal cancer.

37. The use of any one of the preceding claims, wherein the subject is being treated for microsatellite stable/proficient mismatch repair (MSS/pMMR) mCRC.

38. The use of any one of the preceding claims, wherein subject is not receiving an EGFR inhibitor.

39. Use of a first pharmaceutical composition and a second pharmaceutical composition in the manufacture of a medicament for treating, preventing, or reducing the severity of a colorectal cancer in a subject in need thereof, wherein:

the first pharmaceutical composition comprising Compound A, and the first pharmaceutical composition is to be administered at least once daily,

the second pharmaceutical composition comprising cobicistat, and the second pharmaceutical composition is to be administered at least once daily, and

wherein the subject is not receiving an EGFR inhibitor.

40. Use of a Compound A in the manufacture of a medicament for treating, preventing, or reducing the severity of a colorectal cancer in a subject in need thereof, wherein the Compound A is to be administered at a dose between 150 mg and 200 mg dose three times daily, and wherein the subject does not receive a CYP3A inhibitor and an EGFR inhibitor.

41. Use of any one of the preceding claims, wherein the colorectal cancer is characterized by dysregulation of the WNT/β-catenin signaling pathway.

42. Use of any one of the preceding claims, wherein the subject has progressed on a prior colorectal cancer therapy due to developing resistance to the prior colorectal cancer therapy.

43. Use of a pharmaceutical composition comprising Compound A in the manufacture of a medicament for treating, preventing, or reducing the severity of a cancer in a subject, wherein 220 to 280 mg of Compound A is to be administered to the subject three times per day, wherein the subject does not receive a CYP3A inhibitor.

44. The use of claim 43, wherein the cancer is a leukemia.

45. The use of claim 44, wherein the cancer is an AML leukemia.

46. The use of claim 44, wherein the cancer is an acute lymphoblastic leukemia.

47. The use of claim 44, wherein the cancer is an NMP1-mutated leukemia.

48. The use of claim 44, wherein the cancer is a colorectal cancer.

49. The use of claim 43, wherein the cancer is a microsatellite stable/proficient mismatch repair (MSS/pMMR) mCRC.

50. The use of any one of claims 43-49, wherein the menin-MLL inhibitor is to be administered at a dosage of 270 mg to 280 mg.

51. The use of any one of claims 43-50, wherein the menin-MLL inhibitor is to be administered three times per day.

52. The use of any one of the preceding claims, wherein the menin-MLL inhibitor is to be administered with food.

53. Use of a menin-MLL inhibitor in the preparation of a medicament for the treatment of colorectal cancer, wherein the medicament and/or treatment does not involve the use of an EGFR inhibitor.

54. Use of a menin-MLL inhibitor in the preparation of a medicament for the treatment of colorectal cancer, wherein the medicament does not comprise an EGFR inhibitor.

55. A kit comprising a menin-MLL inhibitor, and printed instructions for using the menin-MLL inhibitor in a subject for the treatment for colorectal cancer.

56. Use of a Compound A or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising Compound A in the manufacture of a medicament for treating, preventing, or reducing the severity of a cancer in a subject in need thereof, wherein the Compound A is to be administered at a dosage of between 163 mg and 276 mg every 8 hours, wherein upon administration, the area under plasma concentration versus time curve from time 0 to 24 hours ($AUC_{(0-24)}$) of Compound A is from 1,000 ng*h/mL to 100,000 ng*h/mL.

57. The use of claim 56, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 163 mg every 8 hours, wherein upon administration the

area under plasma concentration versus time curve from time 0 to 24 hours ($AUC_{(0-24)}$) of Compound A is from 10,000 ng*h/mL to 60,000 ng*h/mL.

58. The use of claim 56, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 226 mg every 8 hours, wherein upon administration the area under plasma concentration versus time curve from time 0 to 24 hours ($AUC_{(0-24)}$) of the Compound A is from 14,000 ng*h/mL to 65,000 ng*h/mL.

59. The use of claim 56, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 276 mg every 8 hours, wherein upon administration the area under plasma concentration versus time curve from time 0 to 24 hours ($AUC_{(0-24)}$) of the Compound A is from 17,000 ng*h/mL to 90,000 ng*h/mL.

60. The use of claim 56, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 163 mg every 8 hours, wherein upon administration the area under plasma concentration versus time curve from time 0 to 24 hours ($AUC_{(0-24)}$) of the Compound A is about 22,000 ng*h/mL.

61. The use of claim 56, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 226 mg every 8 hours, wherein upon administration the area under plasma concentration versus time curve from time 0 to 24 hours ($AUC_{(0-24)}$) of the Compound A is about 30,500 ng*h/mL.

62. The use of claim 56, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 276 mg every 8 hours, wherein upon administration the area under plasma concentration versus time curve from time 0 to 24 hours ($AUC_{(0-24)}$) of the Compound A is about 41,000 ng*h/mL.

63. Use of Compound A, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising Compound A in the manufacture of a medicament for treating, preventing, or reducing the severity of a cancer in a subject in need thereof, wherein the Compound A is to be administered at a dosage from 163 mg to 276 mg every 8 hours, and wherein upon administration the minimum observed concentration (C_{min}) of Compound A is from 100 ng/mL to 2,400 ng/mL.

64. The use of claim 63, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 163 mg every 8 hours, wherein upon administration the minimum observed concentration (C_{min}) of the Compound A is from 100 ng/mL to 1,400 ng/mL.

65. The use of claim 63, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 226 mg every 8 hours, wherein upon administration the minimum observed concentration (C_{min}) of the Compound A is from 100 ng/mL to 1,600 ng/mL.

66. The use of claim 63, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 276 mg every 8 hours, wherein upon administration the minimum observed concentration (C_{min}) of the Compound A is from 100 ng/mL to 2,400 ng/mL.

67. The use of claim 63, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 163 mg every 8 hours, wherein upon administration the minimum observed concentration (C_{min}) of the Compound A is about 400 ng/mL.

68. The use of claim 63, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 226 mg every 8 hours, wherein upon administration the minimum observed concentration (C_{min}) of the Compound A is about 500 ng/mL.

69. The use of claim 63, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 276 mg every 8 hours, wherein upon administration the minimum observed concentration (C_{min}) of the Compound A is about 800 ng/mL.

70. Use of Compound A, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising Compound A in the manufacture of a medicament for treating, preventing, or reducing the severity of a cancer in a subject in need thereof, wherein the Compound A is to be administered at a dosage from 163 mg to 276 mg every 8 hours, and wherein upon administration the maximum observed concentration (C_{max}) of Compound A is from 1,000 ng/mL to 6,000 ng/mL.

71. The use of claim 70, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 163 mg every 8 hours, wherein upon administration the maximum observed concentration (C_{max}) of the Compound A is from 1,000 ng/mL to 3,400 ng/mL.

72. The method of claim 70, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is administered at a dosage of about 226 mg every 8 hours, wherein upon administration the maximum observed concentration (C_{max}) of the Compound A is from 1,300 ng/mL to 4,400 ng/mL.

73. The use of claim 70, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 276 mg every 8 hours, wherein upon administration the maximum observed concentration (C_{max}) of the Compound A is from 1,700 ng/mL to 5,400 ng/mL.

74. The use of claim 70, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 163 mg every 8 hours, wherein upon administration maximum observed concentration (C_{max}) of the Compound A is about 1700 ng/mL.

75. The use of claim 70, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 226 mg every 8 hours, wherein upon administration the maximum observed concentration (C_{max}) of the Compound A is about 2400 ng/mL.

76. The use of claim 70, wherein the Compound A, or the pharmaceutically acceptable salt thereof, or the pharmaceutical composition comprising Compound A is to be administered at a dosage of about 276 mg every 8 hours, wherein upon administration the maximum observed concentration (C_{max}) of the Compound A is about 3,100 ng/mL.

77. Use of Compound A, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising Compound A and a CYP3A4 inhibitor in the manufacture of a medicament for treating, preventing, or reducing the severity of a cancer in a subject in need thereof, , wherein the Compound A is to be administered at a dosage of about 163 mg every 12 hours, and wherein upon administration the area under plasma concentration versus time curve from time 0 to 24 hours ($AUC_{(0-24)}$) of the Compound A is from 19,000 ng*h /mL to 110,000 ng*h/mL.

78. The use of claim 77, wherein the Compound A is to be administered at a dosage of about 163 mg every 12 hours, and wherein upon administration the area under plasma concentration versus time curve from time 0 to 24 hours ($AUC_{(0-24)}$) of the Compound A is about 43,000 ng*h /mL.

79. Use of Compound A, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising Compound A and a CYP3A4 inhibitor in the manufacture of a medicament for treating, preventing, or reducing the severity of a cancer in a subject in need thereof, wherein the Compound A is to be administered at a dosage of about 163 mg every 12 hours, and wherein upon administration the minimum observed concentration (C_{min}) of the Compound A is from 200 ng/mL to 2,800 ng/mL.

80. The use of claim 79, wherein the Compound A is to be administered at a dosage of about 163 mg every 12 hours, and wherein upon administration the minimum observed concentration (C_{min}) of the Compound A is about 900 ng/mL.

81. Use of Compound A, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising Compound A and a CYP3A4 inhibitor in the manufacture of a medicament for treating, preventing, or reducing the severity of a cancer in a subject in need thereof, wherein the Compound A is to be administered at a dosage of about 163 mg every 12 hours, and wherein upon administration the maximum observed concentration (C_{max}) of the Compound A is from 1,700 ng/mL to 6,200 ng/mL.

82. The use of claim 81, wherein the Compound A is to be administered at a dosage of about 163 mg every 12 hours, and wherein upon administration the maximum observed concentration (C_{max}) of the Compound A is about 3,200 ng/mL.