CLAIMS:

1. Use of an immunoconjugate that binds to CD123 in the manufacture of a medicament for the treatment of a hematologic malignancy in a subject, wherein said immunoconjugate (i) comprises a cytotoxin, wherein the cytotoxin is a DNA-alkylating agent and (ii) comprises an antibody or antigen-binding fragment thereof comprising a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO: 5; a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO: 6; and a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO: 7; and a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO: 8; a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO: 9; and a light chain variable region CDR3 comprising the amino acid sequence of: SEQ ID NO: 10, wherein the medicament is to be administered in combination with venetoclax and azacitidine.

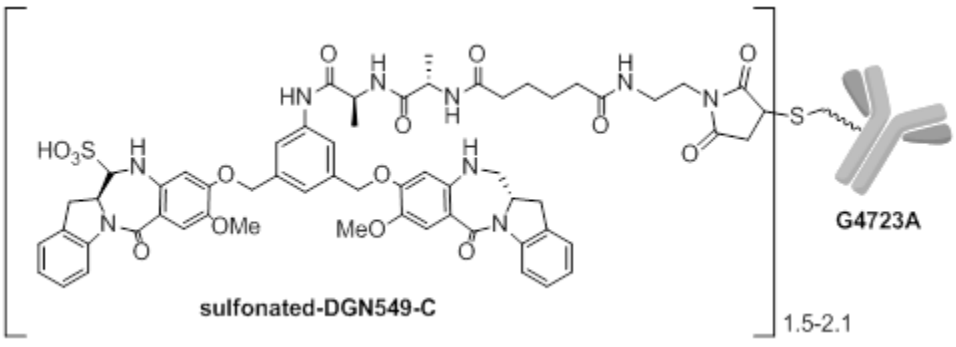
2. The use of claim 1, wherein the antibody or antigen-binding fragment thereof comprises a VH comprising the amino acid sequence set forth in SEQ ID NO:1 and a VL comprising the amino acid sequence set forth in SEQ ID NO: 2.

3. The use of claim 1 or 2, wherein the antibody comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:3 and a light chain comprising the amino acid sequence set forth in SEQ ID NO:4.

4. The use of any one of claims 1-3, wherein the DNA-alkylating agent is an indolino-benzodiazepine (IGN) DNA-alkylator.

5. The use of claim 4, wherein the indolino-benzodiazepine (IGN) DNA-alkylator is DGN549-C.

6. The use of any one of claims 1-5, wherein the medicament comprises immunoconjugates with the following structure:




,wherein G4723A is an antibody comprising a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:3 and a light chain comprising the amino acid sequence set forth in SEQ ID NO:4.

7. The use of any one of claims 1-6, wherein the administration is a front-line therapy.

8. The use of any one of claims 1-7, wherein the medicament is to be administered intravenously.

9. The use of any one of claims 1-8, wherein the administration of the immunoconjugate with the venetoclax, and the azacitidine produces a synergistic effect.

10. The use of any one of claims 1-9, wherein administration of the immunoconjugate, the venetoclax, and the azacitidine does not produce more toxicity than the administration of the immunoconjugate and the venetoclaxor the immunoconjugate and the azacitidine.

11. The use of any one of claims 1-10, wherein the medicament is to be administered once in a 21-day cycle.

12. The use of claim 11, wherein the medicament is to be administered at a dose of about 0.015 mg/kg to about 0.09 mg/kg once in the 21-day cycle, optionally wherein the dose is about 0.015 mg/kg, about 0.045 mg/kg, or about 0.09 mg/kg.

13. The use of claim 12, wherein the medicament is to be administered at a dose of about 0.045 mg/kg once in the 21-day cycle.

14. The use of claim 12, wherein the medicament is to be administered at a dose of about 0.03 mg/kg once in the 21-day cycle.

15. The use of claim 12, wherein the medicament is to be administered at a dose of about 0.015 mg/kg once in the 21-day cycle.

16. The use of any one of claims 1-12, wherein the venetoclax is to be administered daily in a 21-day cycle.

17. The use of any one of claims 1-12, wherein the venetoclax is to be administered at a dose of 100 mg on day 1 of a 21-day cycle, at a dose of 200 mg on day 2 of the 21-day cycle, and at a dose of 400 mg on days 3-21 of the 21-day cycle.

18. The use of any one of claims 1-12, wherein the venetoclax is to be administered at a dose of 100 mg on day 1 of a 21-day cycle, at a dose of 200 mg on day 2 of the 21-day cycle, and a dose of 400 mg on days 3-7 or days 3-14 of the 21-day cycle.

19. The use of any one of claims 1-10, wherein the medicament is to be administered once in a 28-day cycle.

20. The use of claim 19, wherein the medicament is to be administered at a dose of about 0.015 mg/kg to about 0.09 mg/kg once in the 28-day cycle, optionally wherein the dose is about 0.015 mg/kg, about 0.045 mg/kg, or about 0.09 mg/kg.

21. The use of claim 19, wherein the medicament is to be administered at a dose of about 0.03 mg/kg once in the 28-day cycle.

22. The use of claim 19, wherein the medicament is to be administered at a dose of about 0.045 mg/kg once in the 28-day cycle.

23. The use of any one of claims 1-16 and 18-22, wherein the venetoclax is to be administered at a dose of 400 mg.

24. The use of any one of claims 1-16 and 18-22, wherein the venetoclax is to be administered at dose of 200 mg.

25. The use of any one of claims 18-24, wherein the venetoclax is to be administered daily in a 28-day cycle.

26. The use of any one of claims 16 and 23-25, wherein the venetoclax is to be administered daily on days 1-7 of the cycle.

27. The use of any one of claims 16 and 23-25, wherein the venetoclax is to be administered daily on days 1-8 of the cycle.

28. The use of any one of claims 16 and 23-25, wherein the venetoclax is to be administered daily on days 1-14 of the cycle.

29. The use of any one of claims 16 and 23-25, wherein the venetoclax is to be administered daily on days 1-18 of the cycle.

30. The use of any one of claims 16 and 23-25, wherein the venetoclax is to be administered daily on days 1-21 of the cycle.

31. The use of claim 25, wherein the venetoclax is to be administered daily on days 1-28 of the cycle.

32. The use of any one of claims 19-22, wherein the venetoclax is to be administered at a dose of 100 mg on day 1 of a 28-day cycle, at a dose of 200 mg on day 2 of the 28-day cycle, and at a dose of 400 mg on days 3-28 of the 28-day cycle.

33. The use of any one of claims 19-22, wherein the venetoclax is to be administered at a dose of 100 mg on day 1 of a 28-day cycle, at a dose of 200 mg on day 2 of the 28-day cycle, and a dose of 400 mg on days 3-7 or days 3-14 of the 28-day cycle.

34. The use of any one of claims 19-22, wherein the venetoclax is to be administered at a dose of 100 mg on day 1 of the 28-day cycle, and at a dose of 200 mg on days 2-28, 2-14, or 2-7 of the 28-day cycle.

35. The use of any one of claims 1-34, wherein the venetoclax is to be administered orally.

36. The use of any one of claims 1-35, wherein administration of the medicament is initiated six days after initiation of the administration of the venetoclax.

37. The use of any one of claims 1-36, wherein the azacitidine is to be administered in a 28-day cycle.

38. The use of claim 37, wherein the azacitidine is to be administered once daily on days 1-7 of a 28-day cycle.

39. The use of claim 37, wherein the azacitidine is to be administered once daily on days 1-5 of a 28-day cycle.

40. The use of claim 37, wherein the azacitidine is to be administered once daily on days 3-7 of a 28-day cycle.

41. The use of any one of claims 37-40, wherein the azacitidine is to be administered at a dose of about 75 $mg/m^2$.

42. The use of any one of claims 37-41, wherein the azacitidine is to be administered subcutaneously or intravenously.

43. The use of any one of claims 1-42, wherein the hematological malignancy is present in the subject as minimal residual disease (MRD).

44. The use of any one of claims 11-43, wherein the administration is for one cycle.

45. The use of any one of claims 11-43, wherein the administration is for more than one cycle, optionally wherein the administration is for at least 2 cycles, at least 3 cycles, at least 4 cycles, at least 5 cycles, at least 6 cycles, at least 7 cycles, at least 8 cycles, at least 9 cycles, or at least 10 cycles or wherein the administration is for about 2-4 cycles, about 2-6 cycles, about 2-8 cycles, about 2-10 cycles, or about 2-12 cycles.

46. The use of any one of claims 1-45, wherein a reduced dose of the medicament is to be administered after a dose-limiting toxicity has occurred in the subject and has been reduced to baseline or $\leq$ Grade 2.

47. The use of any one of claims 1-46, wherein the medicament is to be further administered as a maintenance therapy.

48. The use of claim 47, wherein the maintenance therapy is to be administered once in a 21-day cycle.

49. The use of claim 48, wherein the maintenance therapy is to be administered at a dose of about 0.015 mg/kg to about 0.09 mg/kg once in the 21-day cycle, optionally wherein the dose is about 0.015 mg/kg, about 0.045 mg/kg, or about 0.09 mg/kg.

50. The use of claim 48, wherein the medicament of the maintenance therapy is to be administered at a dose of about 0.045 mg/kg once in the 21-day cycle.

51. The use of any one of claims 1-6, 8-42, and 44-50, wherein the hematological malignancy is a relapsed hematological malignancy.

52. The use of any one of claims 1-6, 8-42, and 44-51, wherein the hematological malignancy is a refractory hematological malignancy.

53. The use of any one of claims 1-52, wherein the hematological malignancy is acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), B-cell acute lymphoblastic leukemia (B-ALL), chronic myeloid leukemia in blast crisis/phase (BP-CML), and blastic plasmacytoid dendritic cell neoplasm (BPDCN).

54. The use of any one of claims 1-52, wherein the hematological malignancy is AML.

55. The use of claim 54, wherein the AML is unfit AML.

56. The use of claim 54 or 55, wherein the AML is relapsed and/or refractory AML.

57. The use of any one of claims 1-52, wherein the hematological malignancy is BPDCN.

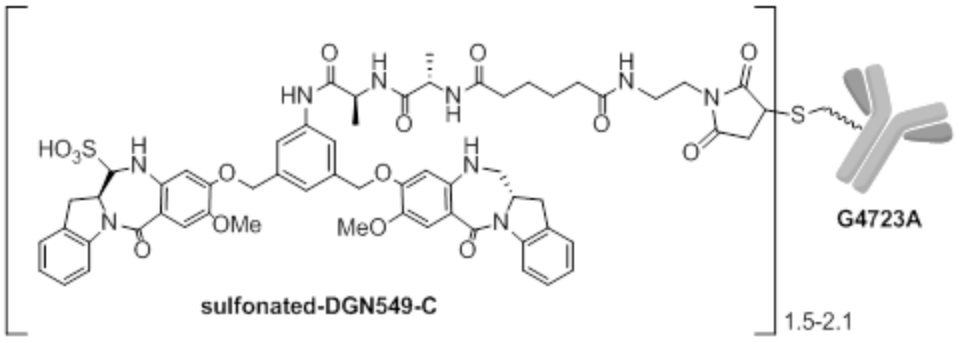
58. The use of any one of claims 1-52, wherein the hematological malignancy is ALL.

59. The use of any one of claims 1-58, wherein the hematological malignancy is a CD123-expressing hematological malignancy.

60. The use of any one of claims 1-59, wherein CD123 has been detected in a sample obtained from the hematological malignancy prior to the administration

61. The use of claim 60, wherein the CD123 was detected using flow cytometry.

62. The use of any one of claims 1-61, wherein the hematological malignancy is resistant to an immunoconjugate with the following structure:




, wherein G4723A is an antibody comprising a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:3 and a light chain comprising the amino acid sequence set forth in SEQ ID NO:4.

63. The use of any one of claims 1-62, wherein the hematological malignancy expresses multidrug resistance 1 (MDR1).

64. The use of any one of claims 1-63, wherein the hematological malignancy expresses P-glycoprotein (P-gp).

65. The use of any one of claims 1-64, wherein the subject has an absolute neutrophil count of greater than 500 neutrophils/μL.

66. The use of any one of claims 1-6 and 8-65, wherein the subject received at least one prior line of therapy.

67. The use of any one of claims 1-6 and 8-65, wherein the subject received at least two prior lines of therapy or at least three prior lines of therapy.

68. The use of any one of claims 1-6 and 8-67, wherein the cancer has previously been treated with venetoclax.

69. The use of any one of claims 1-67, wherein the cancer has not previously been treated with venetoclax.

70. The use of any one of claims 1-6 and 8-69, wherein the cancer has previously been treated with a hyomethylating agent.

71. The use of any one of claims 1-69, wherein the cancer has not previously been treated with a hypomethylating agent.

72. The use of any one of claims 1-71, wherein the subject has been pretreated with a corticosteroid prior to administration of the medicament, optionally wherein the corticosteroid is prednisone, prednisolone, methylprednisolone, beclamethasone, betamethasone, fludrocortisone, hydrocortisone, triamcinolone, dexamethasone, or a combination thereof.

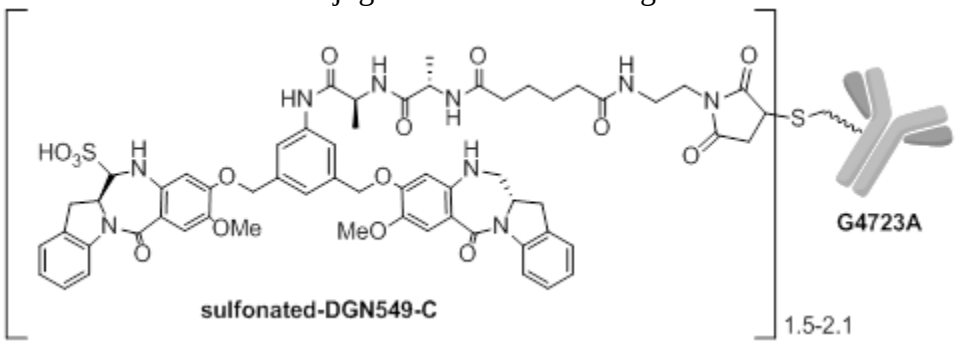
73. The use of any one of claims 1-71, wherein the subject is to be pre-treated with a corticosteroid prior to administration of the immunoconjugate, optionally wherein the corticosteroid is

prednisone, prednisolone, methylprednisolone, beclamethasone, betamethasone, fludrocortisone, hydrocortisone, triamcinolone,-dexamethasone, or a combination thereof.

74. The use of any one of claims 1-73, wherein the immunoconjugate and the venetoclax, the azacitidine are to be administered in separate pharmaceutical compositions.

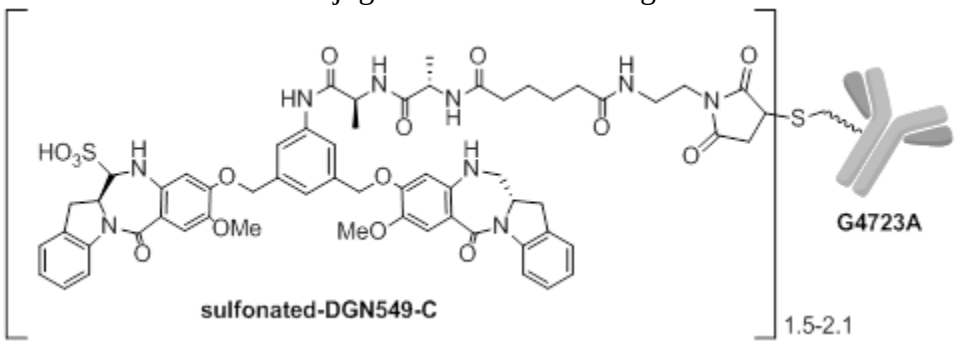
75. The use of any one of claims 1-74, wherein the subject is human.

76. Use of an immunoconjugate with the following structure:




, wherein G4723A is an antibody comprising a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:3 and a light chain comprising the amino acid sequence set forth in SEQ ID NO:4 in the manufacture of a medicament for the treatment of a hematologic malignancy in a human subject, wherein the medicament is to be administered in combination with venetoclax and azacytidine, wherein the medicament, the venetoclax, and the azacytidine are to be administered in a 28-day cycle, wherein the immunoconjugate in the medicament is to be administered intravenously on day 7 of the cycle at a dose of about 0.045 mg/kg, wherein the venetoclax is to be administered orally on days 1-14 of the cycle, and wherein the azacytidine is to be administered subcutaneously or intravenously on days 1-7 of the cycle.

77. Use of an immunoconjugate with the following structure:




, wherein G4723A is an antibody comprising a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:3 and a light chain comprising the amino acid sequence set forth in SEQ ID NO:4 in the manufacture of a medicament for the treatment of a hematologic malignancy in a human subject, wherein the medicament is to be administered in combination with venetoclax and azacytidine, wherein the medicament, the venetoclax, and the azacytidine are to be administered

in a 28-day cycle, wherein the immunoconjugate in the medicament is to be administered intravenously on day 7 of the cycle at a dose of about 0.045 mg/kg, wherein the venetoclax is to be administered orally on days 1-14 of the cycle, and wherein the azacytidine is to be administered subcutaneously or intravenously at a dose of 75 $mg/m^2$ on days 1-7 of the cycle.

78. The use of claim 76 or 77, wherein the venetoclax is to be administered at a dose of 100 mgon days 1-14 of the cycle.

79. The use of claim 76 or 77, wherein the venetoclax is to be administered at a dose of 200 mg on days 1-14 of the cycle.

80. The use of claim 76 or 77, wherein the venetoclax is to be administered at a dose of 400 mg on days 1-14 of the cycle.

81. The use of any one of claims 76-80, wherein the hematologic malignancy is AML.

82. The use of any one of claims 76-81, wherein the hematologic malignancy is unfit AML.

83. The use of any one of claims 76-82, wherein the hematologic malignancy is relapsed and/or refractory AML.

84. The use of any one of claims 76-82, wherein the administration is a front-line therapy.

85. The use of any one of claims 1-75, wherein at least 80% of cells in the hematological malignancy express CD123.

86. The use of any one of claims 1-75 and 85, wherein CD123 has been detected in at least 80% of cells in a sample obtained from the hematological malignancy prior to the administration.