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 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 a BCL-2 inhibitor, a hypomethylating agent, or a combination thereof.

2. The use of claim 1, wherein the medicament is to be administered in combination with the BCL-2 inhibitor.

3. The use of claim 1, wherein the medicament is to be administered in combination with the hypomethylating agent.

4. The use of claim 1, wherein the medicament is to be administered in combination with the BCL-2 inhibitor and the hypomethylating agent.

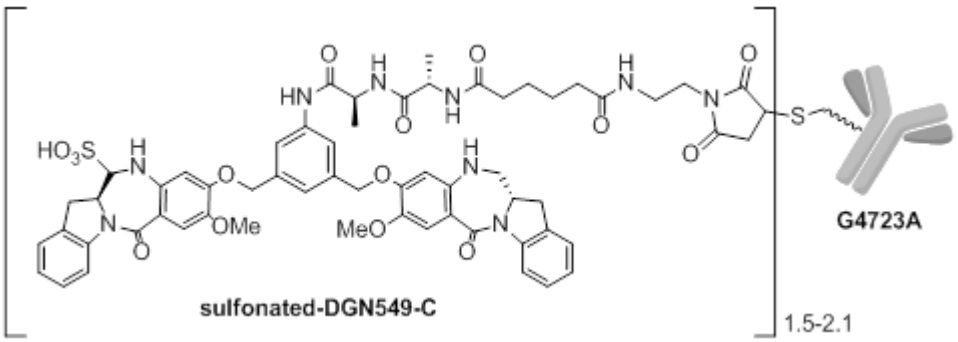
5. The use of any one of claims 1-4, wherein the antibody or antigen-binding fragment thereof comprises a VH comprising the amino acid sequence set forth in SEQ ID NO:1 and/or a VL comprising the amino acid sequence set forth in SEQ ID NO: 2.

6. The use of any one of claims 1-4, wherein the antibody or antigen-binding fragment comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:3 and/or 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 immunoconjugate comprises a cytotoxin, optionally wherein the cytotoxin is a DNA-alkylating agent, optionally wherein the DNA-alkylating agent is indolino-benzodiazepine (IGN) DNA-alkylator.

8. The method use of any one of claims 1-7, wherein the immunoconjugate is IMGN632.

9. The use of any one of claims 1-7, wherein the medicament comprises immunoconjugates with the following structure:




,wherein G4723A 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.

10. The use of any one of claims 1-9, wherein the administration is a front-line therapy.

11. The use of any one of claims 1-10, wherein the medicament is to be administered intravenously.

12. The use of any one of claims 1-11, wherein the administration of the immunoconjugate with the BCL-2 inhibitor, the hypomethylating agent, or a combination thereof produces a synergistic effect.

13. The use of any one of claims 1, 2, and 4-12, wherein upon administration of the immunoconjugate and the BCL-2 inhibitor does not produce more toxicity than administration of the immunoconjugate alone or the BCL-2 inhibitor alone.

14. The use of any one of claims 1 and 3-12, wherein upon administration of the immunoconjugate and the hypomethylating agent does not produce more toxicity than administration of the immunoconjugate alone or the hypomethylating agent alone.

15. The use of any one of claims 1 and 4-12, wherein upon administration of the immunoconjugate, the BCL-2 inhibitor, and the hypomethylating agent does not produce more toxicity than the administration of the immunoconjugate, the BCL-2 inhibitor, and/or the hypomethylating agent.

16. The use of any one of claims 1, 2, and 5-15, wherein the medicament is to be administered once in a 21-day cycle.

17. The use of claim 16, wherein the immunoconjugate in 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.

18. The use of claim 17, wherein the immunoconjugate in the medicament is to be administered at a dose of about 0.045 mg/kg once in the 21-day cycle.

19. The use of claim 17, wherein the immunoconjugate in the medicament is to be administered at a dose of about 0.03 mg/kg once in the 21-day cycle.

20. The use of claim 17, wherein the immunoconjugate in the medicament is to be administered at a dose of about 0.015 mg/kg once in the 21-day cycle.

21. The use of any one of claims 1, 2, and 4-20, wherein the BCL-2 inhibitor is to be administered daily in a 21-day cycle.

22. The use of any one of claims 1, 2, and 4-20, wherein the BCL-2 inhibitor 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.

23. The use of any one of claims 1, 2, and 4-20, wherein the BCL-2 inhibitor 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.

24. The use of any one of claims 1 and 3-15, wherein the medicament is to be administered once in a 28-day cycle.

25. The use of claim 24, wherein the immunoconjugate in 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.

26. The use of claim 24, wherein the immunoconjugate in the medicament is to be administered at a dose of about 0.03 mg/kg once in the 28-day cycle.

27. The use of claim 24, wherein the immunoconjugate in the medicament is to be administered at a dose of about 0.045 mg/kg once in the 28-day cycle.

28. The use of any one of claims 1, 2, and 4-27, wherein the BCL-2 inhibitor is venetoclax.

29. The use of any one of claims 1, 2, 4-21, and 23-28, wherein the BCL-2 inhibitor is to be administered at a dose of 400 mg.

30. The use of any one of claims 1, 2, 4-21, and 23-28, wherein the BCL-2 inhibitor is to be administered at dose of 200 mg.

31. The use of any one of claims 23-30, wherein the BCL-2 inhibitor is to be administered daily in a 28-day cycle.

32. The use of any one of claims 21 and 28-31, wherein the BCL-2 inhibitor is to be administered daily on days 1-7 of the cycle.

33. The use of any one of claims 21 and 28-31, wherein the BCL-2 inhibitor is to be administered daily on days 1-8 of the cycle.

34. The use of any one of claims 21 and 28-31, wherein the BCL-2 inhibitor is to be administered daily on days 1-14 of the cycle.

35. The use of any one of claims 21 and 28-31, wherein the BCL-2 inhibitor is to be administered daily on days 1-18 of the cycle.

36. The use of any one of claims 21 and 28-31, wherein the BCL-2 inhibitor is to be administered daily on days 1-21 of the cycle.

37. The use of claim 31, wherein the BCL-2 inhibitor is to be administered daily on days 1-28 of the cycle.

38. The use of any one of claims 24-28, wherein the BCL-2 inhibitor 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.

39. The use of any one of claims 24-28, wherein the BCL-2 inhibitor 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.

40. The use of any one of claims 24-28, wherein the BCL-2 inhibitor 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.

41. The use of any one of claims 1, 2, and 4-40, wherein the BCL-2 inhibitior is to be administered orally.

42. The use of any one of claims 1, 2, and 4-41, wherein administration of the medicament is initiated six days after initation of the administration of the BCL-2 inhibitor.

43. The use of any one of claims 1, 3-15, and 23-42, wherein the hypomethylating agent is azacitidine.

44. The use of claim 43, wherein the azacitidine is to be administered in a 28-day cycle.

45. The use of claim 43 or claim 44, wherein the azacitidine is to be administered once daily on days 1-7 of a 28-day cycle.

46. The use of claim 43 or claim 44, wherein the azacitidine is to be administered once daily on days 1-5 of a 28-day cycle.

47. The use of claim 43 or claim 44, wherein the azacitidine is to be administered once daily on days 3-7 of a 28-day cycle.

48. The use of any one of claims 43-47, wherein the azacitidine is to be administered at a dose of about 75 $mg/m^2$.

49. The use of any one of claims 43-48, wherein the azacitidine is to be administered subcutaneously or intravenously.

50. The use of any one of claims 1 and 3-42, wherein the hypomethylating agent is decitabine.

51. The use of claim 50, wherein the decitabine is to be administered intravenously.

52. The use of any one of claims 1-51, wherein the hematological malignancy is present in the subject as minimal residual disease (MRD).

53. Use of an anti-CD123 immunoconjugate comprising an anti-CD123 antibody or antigen-binding fragment thereof linked to a cytotoxic agent in the manufacture of a medicament for the treatment of a hematologic malignancy present as a minimal residual disease in a human subject.

54. The use of any one of claims 16-52, wherein the administration is for one cycle.

55. The use of any one of claims 16-52, 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.

56. The use of any one of claims 1-55, wherein a reduced dose of the medicament after a dose-limiting toxicity has occurred in the subject and has been reduced to baseline or ≤ Grade 2 is to be administered.

57. The use of any one of claims 1-56, wherein the medicament is to be further administered as a maintenance therapy.

58. The use of claim 57, wherein the medicament in the maintenance therapy is to be administered once in a 21-day cycle.

59. The use of claim 58, wherein the immunoconjugate in the medicament of 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.

60. The use of claim 58, wherein the immunoconjugate in 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.

61. The use of any one of claims 1-9, 11-50, and 54-60, wherein the hematological malignancy is a relapsed hematological malignancy.

62. The use of any one of claims 1-9, 11-50, and 54-61, wherein the hematological malignancy is a refractory hematological malignancy.

63. The use of any one of claims 1-62, 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).

64. The use of claim 1-62, wherein the hematological malignancy is AML.

65. The use of any one of claims 1-62, wherein the hematological malignancy is BPDCN.

66. The use of any one of claims 1-62, wherein the hematological malignancy is ALL.

67. The use of any one of claims 1-66, wherein the hematological malignancy is a CD123-expressing hematological malignancy.

68. The use of any one of claims 1-67, wherein CD123 has been detected in a sample obtained from the hematological malignancy prior to the administration, optionally wherein the CD123 was detected using flow cytometry.

69. The use of any one of claims 1-68, further comprising detecting CD123 in a sample obtained from the hematological malignancy prior to the administration.

70. The use of any one of claims 1-69, wherein at least 80% of cells in the hematological malignancy express CD123.

71. The use of any one of claims 1-70, wherein CD123 has been detected in at least 80% of cells in a sample obtained from the hematological malignancy prior to the administration.

72. The use of any one of claims 1-71, further comprising detecting CD123 in at least 80% of cells in a sample obtained from the hematological malignancy prior to the administration.

73. The use of any one of claims 1-52 and 54-72, wherein the hematological malignancy is resistant to IMGN632.

74. The use of any one of claims 1-73, wherein the hematological malignancy expresses multidrug resistance 1 (MDR1).

75. The use of any one of claims 1-74, wherein the hematological malignancy expresses P-glycoprotein (P-gp).

76. The use of any one of claims 1-75, wherein the subject has an absolute neutrophil count of greater than 500/μL.

77. The use of any one of claims 1-9 and 11-76, wherein the subject received at least one prior line of therapy, at least two prior lines of therapy, or at least three prior lines of therapy.

78. The use of any one of claims 1-9 and 11-77, wherein the cancer has previously been treated with venetoclax.

79. The use of any one of claims 1-77, wherein the cancer has not previously been treated with venetoclax.

80. The use of any one of claims 1-9 and 11-79, wherein the cancer has previously been treated with a hyomethylating agent.

81. The use of any one of claims 1-79, wherein the cancer has not previously been treated with a hypomethylating agent.

82. The use of any one of claims 1-81, wherein the subject has been pretreated with a corticosteroid prior to administration of the medicament, optionally wherein the corticosteroid is diphenhydramine, acetaminophen, paracetamol, dexamethasone, or a combination thereof.

83. The use of any one of claims 1-81, wherein the subject is to be pre-treated with a corticosteroid prior to administration of the immunoconjugate, optionally wherein the corticosteroid is diphenhydramine, acetaminophen, paracetamol, dexamethasone, or a combination thereof.

84. The use of any one of claims 1-52 and 54-83, wherein the immunoconjugate and the BCL-2 inhibitor, the hypomethylating agent, or combination thereof are to be administered in separate pharmaceutical compositions.

85. The use of any one of claims 1-84, wherein the subject is human.

86. Use of venetoclax in the manufacture of a medicament for the treatment of a hematologic malignancy in a human subject, wherein the medicament is to be administerd in combination with IMGN632 wherein the medicament and the IMGN632 are to be administered in a 21-day cycle, wherein the IMGN632 is to be administered intravenously on day 7 of the cycle at a dose of about 0.015 mg/kg to about 0.09 mg/kg, and wherein the venetoclax in the medicament is to be administered at an oral daily dose of 400 mg.

87. Use of IMGN632 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, wherein the medicament and the venetoclax are to be administered in a 21-day cycle, wherein the IMGN632 in the medicament is to be administered intravenously on day 7 of the cycle at a dose of about 0.015 mg/kg to about 0.09 mg/kg, and wherein the venetoclax is to be administered at an oral daily dose of 400 mg.

88. The method of claim 92 or claim 93, wherein IMGN632 is to be administered at a dose of about 0.045 mg/kg.

89. The method of claim 92 or claim 93, wherein IMGN632 is to be administered at a dose of about 0.03 mg/kg.

90. Use of IMGN632 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 azacitidine wherein the medicament and the azacitidine are to be administered in a 28-day cycle wherein the IMGN632 in the medicament is to be administered intravenously on day 7 of the cycle at a dose of about 0.015 mg/kg to about 0.09 mg/kg, and wherein the azacitdine is to be administered subcutaneously or intravenously at a dose of 75 $mg/m^2$.

91. Use of azacytidine in the manufacture of a medicmament for the treatment of a hematologic malignancy in a human subject, wherein the medicament is to be administered in combination with IMGN632 wherein the medicament and the IMGN632 are to be administered in a 28-day cycle wherein the IMGN632 is to be administered intravenously on day 7 of the cycle at a dose of about 0.015 mg/kg to about 0.09 mg/kg, and wherein the azacitidinein in the medicament is to be administered subcutaneously or intravenously at a dose of 75 $mg/m^2$.

92. The use of claim 96 or claim 97, wherein the azacitdine is to be administered on days 1-7 of the cycle.

93. The use of claim 96 or claim 97, wherein the azacitdine is to be administered on days 1-5 of the cycle

94. The use of any one of claims 96-99, wherein IMGN632 is to be administered at a dose of about 0.045 mg/kg.

95. The use of any one of claims 96-99, wherein IMGN632 is to be administered at a dose of about 0.03 mg/kg.

96. The use of any one of claims 96-99, wherein IMGN632 is to be administered at a dose of about 0.015 mg/kg.

97. The use of any one of claims 96-102, wherein venetoclax is to be administered at an oral daily dose of 400 mg.

98. The use of any one of claims 92-95 and 103, wherein venetoclax is to be administered on days 1-7 of the cycle.

99. The use of any one of claims 92-95 and 103, wherein venetoclax is to be administered on days 1-8 of the cycle.

100. The use of any one of claims 92-95 and 103, wherein venetoclax is to be administered on days 1-14 of the cycle.

101. The use of any one of claims 92-95 and 103, wherein venetoclax is to be administered on days 1-18 of the cycle.

102. The use of any one of claims 92-95 and 103, wherein venetoclax is to be administered on days 1-21 of the cycle.

103. The use of claim 103, wherein venetoclax is to be administered on days 1-28 of the cycle.

104. The use of any one of claims 92-109, wherein the hematologic malignancy is AML, BPDCN, or ALL.

105. Use of IMGN632 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 IMGN632 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 dasy 1-14 of the cycle, and wherein the azacytidine is to be administered subcutaneously or intravenously on days 1-7 of the cycle.

106. Use of IMGN632 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 IMGN632 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 dasy 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.

107. The use of claim 105 or 106, wherein the venetoclax is to be administered at a dose of 100 mg, 200 mg, or 400 mg on days 1-14 of the cycle.

108. An immunoconjugate that binds to CD123 for use in treating a hematologic malignancy in a subject, wherein said immunoconjugate 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 immunoconjugate is for use in combination with a BCL-2 inhibitor, a hypomethylating agent, or a combination thereof.