CLAIMS

What is claimed is:

1. A method of depleting a population of CD45RO+ cells in a human patient, the method comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof capable of binding CD45RO.

2. A method of depleting a population of CD45RO+ cells in a human patient in need of a hematopoietic stem cell transplant, the method comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof capable of binding CD45RO prior to the patient receiving a transplant comprising hematopoietic stem cells.

3. A method comprising administering to a human patient a transplant comprising hematopoietic stem cells, wherein the patient has been previously administered an antibody or antigen-binding fragment thereof capable of binding CD45RO in an amount sufficient to deplete a population of CD45RO+ cells in the patient.

4. A method comprising:
   a. administering to a human patient an antibody or antigen-binding fragment thereof capable of binding CD45RO in an amount sufficient to deplete a population of CD45RO+ cells in the patient; and
   b. subsequently administering to the patient a transplant comprising hematopoietic stem cells.

5. The method of any one of claims 1-4, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

6. A method of depleting a population of CD135+ cells in a human patient, the method comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof capable of binding CD135, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

7. A method of depleting a population of CD135+ cells in a human patient in need of a hematopoietic stem cell transplant, the method comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof capable of binding CD135 prior to the patient receiving a transplant comprising hematopoietic stem cells, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

8. A method comprising administering to a human patient a transplant comprising hematopoietic stem cells, wherein the patient has been previously administered an antibody or antigen-binding fragment thereof capable of binding CD135 in an amount sufficient to deplete a population of CD135+ cells in the patient, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

9. A method comprising:
   a. administering to a human patient an antibody or antigen-binding fragment thereof capable of binding CD135 in an amount sufficient to deplete a population of CD135+ cells in the patient; and
   b. subsequently administering to the patient a transplant comprising hematopoietic stem cells,

wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

10. The method of any one of claims 6-9, wherein the antibody or antigen-binding fragment thereof comprises the following complementarity determining regions (CDRs):
   a. a CDR-H1 having the amino acid sequence SYYMH (SEQ ID NO: 1);
   b. a CDR-H2 having the amino acid sequence IINPSGGSTSYAQKFQG (SEQ ID NO: 2);
   c. a CDR-H3 having the amino acid sequence GVGAHDAFDI (SEQ ID NO: 3) or VVAAAVADY (SEQ ID NO: 4);
   d. a CDR-L1 having the amino acid sequence RSSQSLLHSNGNNYLD (SEQ ID NO: 5) or RSSQSLLHSNGYNYLD (SEQ ID NO: 6);
   e. a CDR-L2 having the amino acid sequence LGSNRAS (SEQ ID NO: 7); and
   f. a CDR-L3 having the amino acid sequence MQGTHPAIS (SEQ ID NO: 8) or MQSLQTPFT (SEQ ID NO: 9).

11. The method of any one of claims 6-9, wherein the antibody or antigen-binding fragment thereof comprises the following CDRs:
   a. a CDR-H1 having the amino acid sequence SYAIS (SEQ ID NO: 10);
   b. a CDR-H2 having the amino acid sequence GIIPIFGTANYAQKFQG (SEQ ID NO: 11);
   c. a CDR-H3 having the amino acid sequence FALFGFREQAFDI (SEQ ID NO: 12);
   d. a CDR-L1 having the amino acid sequence RASQSISSYLN (SEQ ID NO: 13);
   e. a CDR-L2 having the amino acid sequence AASSLQS (SEQ ID NO: 14); and
   f. a CDR-L3 having the amino acid sequence QQSYSTPFT (SEQ ID NO: 15).

12. A method of depleting a population of CD135+ cells in a human patient, the method comprising administering to the patient an effective amount of human Flt3 ligand, or a fragment thereof capable of binding CD135.

13. A method of depleting a population of CD135+ cells in a human patient in need of a hematopoietic stem cell transplant, the method comprising administering to the patient an effective amount of human Flt3 ligand, or a fragment thereof capable of binding CD135, prior to the patient receiving a transplant comprising hematopoietic stem cells.

14. A method comprising administering to a human patient a transplant comprising hematopoietic stem cells, wherein the patient has been previously administered human Flt3 ligand, or a fragment thereof capable of binding CD135, in an amount sufficient to deplete a population of CD135+ cells in the patient.

15. A method comprising:
    a. administering to a human patient human Flt3 ligand, or a fragment thereof capable of binding CD135, in an amount sufficient to deplete a population of CD135+ cells in the patient; and
    b. subsequently administering to the patient a transplant comprising hematopoietic stem cells.

16. The method of any one of claims 12-15, wherein the human Flt3 ligand or fragment thereof is covalently bound to an Fc domain.

17. The method of claim 16, wherein the N-terminus of the human Flt3 ligand or fragment thereof is covalently bound to the Fc domain.

18. The method of claim 16, wherein the C-terminus of the human Flt3 ligand or fragment thereof is covalently bound to the Fc domain.

19. The method of any one of claims 16-18, wherein the Fc domain is covalently bound to a cytotoxin.

20. The method of any one of claims 12-15, wherein the human Flt3 ligand or fragment thereof is covalently bound to a cytotoxin.

21. The method of claim 20, wherein the N-terminus of the human Flt3 ligand or fragment thereof is covalently bound to the cytotoxin.

22. The method of claim 20, wherein the C-terminus of the human Flt3 ligand or fragment thereof is covalently bound to the cytotoxin.

23. The method of any one of claims 20-22, wherein the cytotoxin is covalently bound to an Fc domain.

24. The method of any claim 20, wherein the human Flt3 ligand or fragment thereof is covalently bound to the cytotoxin at one site and is covalently bound to an Fc domain at a different site.

25. The method of any one of claims 16-19, 23, and 24, wherein the Fc domain is a human IgG1, IgG2, IgG3, or IgG4 isotype Fc domain.

26. A method of depleting a population of CD34+ cells in a human patient, the method comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof capable of binding CD34, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

27. A method of depleting a population of CD34+ cells in a human patient in need of a hematopoietic stem cell transplant, the method comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof capable of binding CD34 prior to the patient receiving a transplant comprising hematopoietic stem cells, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

28. A method comprising administering to a human patient a transplant comprising hematopoietic stem cells, wherein the patient has been previously administered an antibody or antigen-binding fragment thereof capable of binding CD34 in an amount sufficient to deplete a population of CD34+ cells in the patient, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

29. A method comprising:

a. administering to a human patient an antibody or antigen-binding fragment thereof capable of binding CD34 in an amount sufficient to deplete a population of CD34+ cells in the patient; and
b. subsequently administering to the patient a transplant comprising hematopoietic stem cells,

wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

30. A method of depleting a population of CD90+ cells in a human patient, the method comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof capable of binding CD90, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

31. A method of depleting a population of CD90+ cells in a human patient in need of a hematopoietic stem cell transplant, the method comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof capable of binding CD90 prior to the patient

receiving a transplant comprising hematopoietic stem cells, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

32. A method comprising administering to a human patient a transplant comprising hematopoietic stem cells, wherein the patient has been previously administered an antibody or antigen-binding fragment thereof capable of binding CD90 in an amount sufficient to deplete a population of CD90+ cells in the patient, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

33. A method comprising:

a. administering to a human patient an antibody or antigen-binding fragment thereof capable of binding CD90 in an amount sufficient to deplete a population of CD90+ cells in the patient; and
b. subsequently administering to the patient a transplant comprising hematopoietic stem cells,

wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

34. A method of depleting a population of CD110+ cells in a human patient, the method comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof capable of binding CD110, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

35. A method of depleting a population of CD110+ cells in a human patient in need of a hematopoietic stem cell transplant, the method comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof capable of binding CD110 prior to the patient receiving a transplant comprising hematopoietic stem cells, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

36. A method comprising administering to a human patient a transplant comprising hematopoietic stem cells, wherein the patient has been previously administered an antibody or antigen-binding fragment thereof capable of binding CD110 in an amount sufficient to deplete a population of CD110+ cells in the patient, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

37. A method comprising:

a. administering to a human patient an antibody or antigen-binding fragment thereof capable of binding CD110 in an amount sufficient to deplete a population of CD110+ cells in the patient; and
b. subsequently administering to the patient a transplant comprising hematopoietic stem cells,

wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin.

38. The method of any one of claims 5-11 and 19-37, wherein the cytotoxin is selected from the group consisting of an amatoxin, pseudomonas exotoxin A, deBouganin, diphtheria toxin, saporin, maytansine, a maytansinoid, an auristatin, an anthracycline, a calicheamicin, irinotecan, SN-38, a duocarmycin, a pyrrolobenzodiazepine, a pyrrolobenzodiazepine dimer, an indolinobenzodiazepine, and an indolinobenzodiazepine dimer, or a variant thereof.

39. A method of depleting a population of CD45+ cells in a human patient, the method comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof capable of binding CD45, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin selected from the group consisting of an amatoxin, pseudomonas exotoxin A, deBouganin, diphtheria toxin, saporin, maytansine, a maytansinoid, an auristatin, an anthracycline, a calicheamicin, irinotecan, SN-38, a duocarmycin, a pyrrolobenzodiazepine, a pyrrolobenzodiazepine dimer, an indolinobenzodiazepine, and an indolinobenzodiazepine dimer, or a variant thereof.

40. A method of depleting a population of CD45+ cells in a human patient in need of a hematopoietic stem cell transplant, the method comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof capable of binding CD45 prior to the patient receiving a transplant comprising hematopoietic stem cells, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin selected from the group consisting of an amatoxin, pseudomonas exotoxin A, deBouganin, diphtheria toxin, saporin, maytansine, a maytansinoid, an auristatin, an anthracycline, a calicheamicin, irinotecan, SN-38, a duocarmycin, a pyrrolobenzodiazepine, a pyrrolobenzodiazepine dimer, an indolinobenzodiazepine, and an indolinobenzodiazepine dimer, or a variant thereof.

41. A method of comprising administering to a human patient a transplant comprising hematopoietic stem cells, wherein the patient has been previously administered an antibody or antigen-binding fragment thereof capable of binding CD45 in an amount sufficient to deplete a population of CD45+ cells in the patient, wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin selected from the group consisting of an amatoxin, pseudomonas exotoxin A, deBouganin, diphtheria toxin, saporin, maytansine, a maytansinoid, an auristatin, an anthracycline, a calicheamicin, irinotecan, SN-38, a duocarmycin, a pyrrolobenzodiazepine, a pyrrolobenzodiazepine dimer, an indolinobenzodiazepine, and an indolinobenzodiazepine dimer, or a variant thereof.

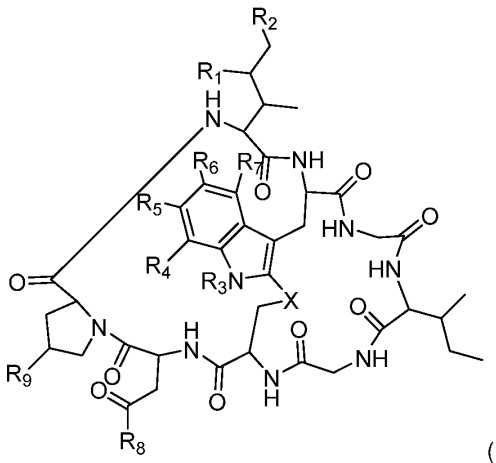
42. A method comprising:

a. administering to a human patient an antibody or antigen-binding fragment thereof capable of binding CD45 in an amount sufficient to deplete a population of CD45+ cells in the patient; and

b. subsequently administering to the patient a transplant comprising hematopoietic stem cells,

wherein the antibody or antigen-binding fragment thereof is conjugated to a cytotoxin selected from the group consisting of an amatoxin, pseudomonas exotoxin A, deBouganin, diphtheria toxin, saporin, maytansine, a maytansinoid, an auristatin, an anthracycline, a calicheamicin, irinotecan, SN-38, a duocarmycin, a pyrrolobenzodiazepine, a pyrrolobenzodiazepine dimer, an indolinobenzodiazepine, and an indolinobenzodiazepine dimer, or a variant thereof.

43. The method of any one of claims 5-11 and 19-42, wherein the antibody, antigen-binding fragment thereof, or ligand conjugated to a cytotoxin is represented by the formula Ab-Am, wherein Ab is the antibody, antigen-binding fragment thereof, or ligand and Am is an amatoxin represented by formula (I)



(I)

wherein R_1 is H, OH, OR_A, or OR_C;

R_2 is H, OH, OR_B, or OR_C;

R_A and R_B, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocyclolalkyl group;

R_3 is H, R_C, or R_D;

R_4, R_5, R_6, and R_7 are each independently H, OH, OR_C, OR_D, R_C, or R_D;

R_8 is OH, NH_2, OR_C, OR_D, NHR_C, or NR_CR_D;

R_9 is H, OH, OR_C, or OR_D;

X is -S-, -S(O)-, or $-SO_2-$;

R_C is -L-Z;

R_D is optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 heteroalkenyl, optionally substituted C_2-C_6 alkynyl, optionally substituted C_2-C_6 heteroalkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

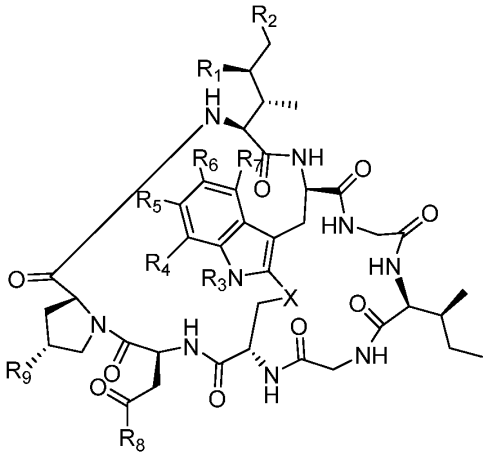
L is optionally substituted C_1-C_6 alkylene, optionally substituted C_1-C_6 heteroalkylene, optionally

substituted C_2-C_6 alkenylene, optionally substituted C_2-C_6 heteroalkenylene, optionally substituted C_2-C_6 alkynylene, optionally substituted C_2-C_6 heteroalkynylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene, optionally substituted arylene, or optionally substituted heteroarylene; and

Z is a chemical moiety formed from a coupling reaction between a reactive substituent present on L and a reactive substituent present within the antibody or antigen-binding fragment thereof,

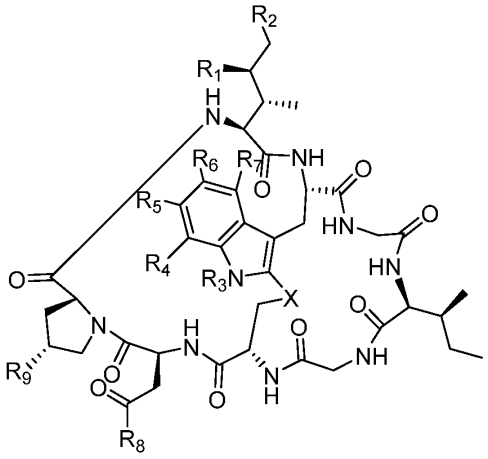
wherein Am comprises exactly one R_C substituent.

44. The method of claim 43, wherein Am is an amatoxin represented by formula (**IA**).



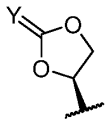
(**IA**)

45. The method of claim 43, wherein Am is an amatoxin represented by formula (**IB**).



(**IB**)

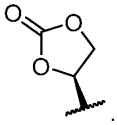
46. The method of claim 44 or 45, wherein R_A and R_B, together with the oxygen atoms to which they are bound, combine to form:



wherein Y is selected from O, S, NR_E, and $CR_ER_{E'}$, and

R_E and $R_{E'}$ are each independently optionally substituted C_1-C_6 alkylene-R_C, optionally substituted C_1-C_6 heteroalkylene-R_C, optionally substituted C_2-C_6 alkenylene-R_C, optionally substituted C_2-C_6 heteroalkenylene-R_C, optionally substituted C_2-C_6 alkynylene-R_C, optionally substituted C_2-C_6 heteroalkynylene-R_C, optionally substituted cycloalkylene-R_C, optionally substituted heterocycloalkylene-R_C, optionally substituted arylene-R_C, or optionally substituted heteroarylene-R_C.

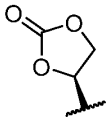
47. The method of claim 46, wherein R_A and R_B, together with the oxygen atoms to which they are bound, combine to form:



48. The method of claim 44 or 45, wherein R_1 is H, OH, or OR_A;

R_2 is H, OH, or OR_B;

R_A and R_B, together with the oxygen atoms to which they are bound, combine to form:



R_3, R_4, R_6, and R_7 are each H;

R_5 is OR_C;

R_8 is OH or NH_2; and

R_9 is H or OH.

49. The method of claim 44 or 45, wherein R_1 and R_2 are each independently H or OH;

R_3 is R_C;

R_4, R_6, and R_7 are each H;

R_5 is H, OH, or OC_1-C_6 alkyl;

R_8 is OH or NH_2; and

R_9 is H or OH.

50. The method of claim 44 or 45, wherein R_1 and R_2 are each independently H or OH;

R_3, R_6, and R_7 are each H;

R_4 and R_5 are each independently H, OH, OR_C, or R_C;

R_8 is OH or NH_2; and

R_9 is H or OH.

51. The method of claim 44 or 45, wherein R_1 and R_2 are each independently H or OH;

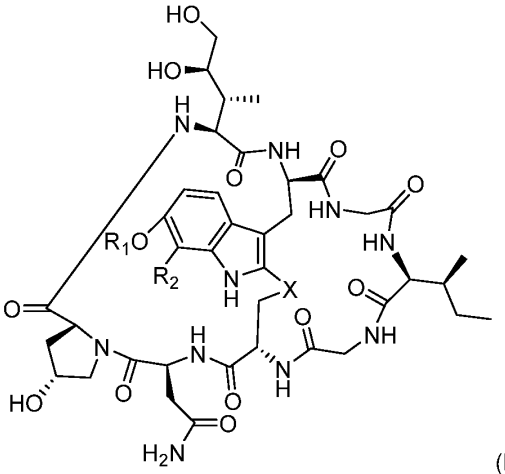
R_3, R_6, and R_7 are each H;

R_4 and R_5 are each independently H or OH;

R_8 is OR_C or NHR_C; and

R_9 is H or OH.

52. The method of any one of claims 5-11 and 19-42, wherein the antibody, antigen-binding fragment thereof, or ligand conjugated to a cytotoxin is represented by the formula Ab-Am, wherein Ab is the antibody, antigen-binding fragment thereof, or ligand and Am is an amatoxin represented by formula (**II**)



(**II**)

wherein X is S, SO, or SO_2;

R_1 is H or a linker covalently bound to the antibody or antigen-binding fragment thereof; and

R_2 is H or a linker covalently bound to the antibody or antigen-binding fragment thereof;

wherein when R_1 is H, R_2 is the linker, and when R_2 is H, R_1 is the linker.

53. The method of any one of claims 5-11 and 19-42, wherein the cytotoxin is a maytansinoid selected from the group consisting of DM1 and DM4.

54. The method of any one of claims 5-11 and 19-42, wherein the cytotoxin is an auristatin selected from the group consisting of monomethyl auristatin E and monomethyl auristatin F.

55. The method of any one of claims 5-11 and 19-42, wherein the cytotoxin is an anthracycline selected from the group consisting of daunorubicin, doxorubicin, epirubicin, and idarubicin.

56. The method of any one of claims 1-11 and 26-55, wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of a monoclonal antibody or antigen-binding fragment thereof, a polyclonal antibody or antigen-binding fragment thereof, a humanized antibody or antigen-binding fragment thereof, a bispecific antibody or antigen-binding fragment thereof, a dual-variable immunoglobulin domain, a single-chain Fv molecule (scFv), a diabody, a triabody, a nanobody, an antibody-like protein scaffold, a Fv fragment, a Fab fragment, a $F(ab')_2$ molecule, and a tandem di-scFv.

57. The method of any one of claims 1-11 and 26-56, wherein the antibody has an isotype selected from the group consisting of IgG, IgA, IgM, IgD, and IgE.

58. The method of any one of claims 1-57, wherein the antibody, antigen-binding fragment thereof, or ligand is internalized by a cancer cell, autoimmune cell, or hematopoietic stem cell following administration to the patient.

59. The method of any one of claims 1-58, wherein the antibody, antigen-binding fragment thereof, or ligand is capable of promoting necrosis of a cancer cell, autoimmune cell, or hematopoietic stem cell.

60. The method of any one of claims 2-5, 7-11, 13-25, 27-29, 31-33, 35-38, and 40-59, wherein the antibody, antigen-binding fragment thereof, or ligand is capable of recruiting one or more complement proteins to the hematopoietic stem cell upon administration to the patient.

61. The method of any one of claims 2-5, 7-11, 13-25, 27-29, 31-33, 35-38, and 40-60, wherein the transplant comprising hematopoietic stem cells is administered to the patient after the concentration of the antibody, antigen-binding fragment thereof, or ligand has substantially cleared from the blood of the patient.

62. The method of any one of claims 2-5, 7-11, 13-25, 27-29, 31-33, 35-38, and 40-61, wherein the hematopoietic stem cells or progeny thereof maintain hematopoietic stem cell functional potential after two or more days following transplantation of the hematopoietic stem cells into the patient.

63. The method of any one of claims 2-5, 7-11, 13-25, 27-29, 31-33, 35-38, and 40-62, wherein the hematopoietic stem cells or progeny thereof are capable of localizing to hematopoietic tissue and/or reestablishing hematopoiesis following transplantation of the hematopoietic stem cells into the patient.

64. The method of any one of claims 2-5, 7-11, 13-25, 27-29, 31-33, 35-38, and 40-63, wherein upon transplantation into the patient, the hematopoietic stem cells give rise to recovery of a population of cells selected from the group consisting of megakaryocytes, thrombocytes, platelets, erythrocytes, mast

cells, myeoblasts, basophils, neutrophils, eosinophils, microglia, granulocytes, monocytes, osteoclasts, antigen-presenting cells, macrophages, dendritic cells, natural killer cells, T-lymphocytes, and B-lymphocytes.

65. The method of any one of claims 1-64, wherein the patient is suffering from a stem cell disorder.

66. The method of any one of claims 1-65, wherein the patient is suffering from a hemoglobinopathy disorder.

67. The method of claim 66, wherein the hemoglobinopathy disorder is selected from the group consisting of sickle cell anemia, thalassemia, Fanconi anemia, aplastic anemia, and Wiskott-Aldrich syndrome.

68. The mehod of claim 66, wherein the hemoglobinopathy disorder is Fanconi anemia.

69. The mehod of claim 66, wherein the hemoglobinopathy disorder is aplastic anemia.

70. The mehod of claim 66, wherein the hemoglobinopathy disorder is sickle cell anemia.

71. The mehod of claim 66, wherein the hemoglobinopathy disorder is thalassemia.

72. The method of any one of claims 1-71, wherein the patient is suffering from a myelodysplastic disorder.

73. The method of any one of claims 1-72, wherein the patient is suffering from an immunodeficiency disorder.

74. The method of claim 73, wherein the immunodeficiency disorder is a congenital immunodeficiency.

75. The method of claim 73, wherein the immunodeficiency disorder is an acquired immunodeficiency.

76. The method of claim 75, wherein the acquired immunodeficiency is human immunodeficiency virus or acquired immune deficiency syndrome.

77. The method of any one of claims 1-76, wherein the patient is suffering from a metabolic disorder.

78. The method of claim 77, wherein the metabolic disorder is selected from the group consisting of glycogen storage diseases, mucopolysaccharidoses, Gaucher's Disease, Hurlers Disease, sphingolipidoses, and metachromatic leukodystrophy.

79. The method of any one of claims 1-78, wherein the patient is suffering from cancer.

80. The method of claim 79, wherein the cancer is selected from the group consisting of leukemia, lymphoma, multiple myeloma, and neuroblastoma.

81. The method of claim 79, wherein the cancer is a hematological cancer.

82. The method of claim 79, wherein the cancer is acute myeloid leukemia.

83. The method of claim 79, wherein the cancer is acute lymphoid leukemia.

84. The method of claim 79, wherein the cancer is chronic myeloid leukemia.

85. The method of claim 79, wherein the cancer is chronic lymphoid leukemia.

86. The method of claim 79, wherein the cancer is diffuse large B-cell lymphoma.

87. The method of claim 79, wherein the cancer is non-Hodgkin's lymphoma.

88. The method of any one of claims 1-87, wherein the patient is suffering from a disorder selected from the group consisting of adenosine deaminase deficiency and severe combined immunodeficiency, hyper immunoglobulin M syndrome, Chediak-Higashi disease, hereditary lymphohistiocytosis, osteopetrosis, osteogenesis imperfecta, storage diseases, thalassemia major, systemic sclerosis, systemic lupus erythematosus, multiple sclerosis, and juvenile rheumatoid arthritis.

89. The method of any one of claims 1-88, wherein the patient is suffering from an autoimmune disorder.

90. The method of claim 89, wherein the autoimmune disorder is selected from the group consisting of multiple sclerosis, human systemic lupus, rheumatoid arthritis, inflammatory bowel disease, treating psoriasis, Type 1 diabetes mellitus, acute disseminated encephalomyelitis, Addison's disease, alopecia universalis, ankylosing spondylitisis, antiphospholipid antibody syndrome, aplastic anemia, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune inner ear disease, autoimmune lymphoproliferative syndrome, autoimmune oophoritis, Balo disease, Behcet's disease, bullous

pemphigoid, cardiomyopathy, Chagas' disease, chronic fatigue immune dysfunction syndrome, chronic inflammatory demyelinating polyneuropathy, Crohn's disease, cicatrical pemphigoid, coeliac sprue-dermatitis herpetiformis, cold agglutinin disease, CREST syndrome, Degos disease, discoid lupus, dysautonomia, endometriosis, essential mixed cryoglobulinemia, fibromyalgia-fibromyositis, Goodpasture' s syndrome, Grave's disease, Guillain-Barre syndrome, Hashimoto' s thyroiditis, Hidradenitis suppurativa, idiopathic and/or acute thrombocytopenic purpura, idiopathic pulmonary fibrosis, IgA neuropathy, interstitial cystitis, juvenile arthritis, Kawasaki's disease, lichen planus, Lyme disease, Meniere disease, mixed connective tissue disease, myasthenia gravis, neuromyotonia, opsoclonus myoclonus syndrome, optic neuritis, Ord's thyroiditis, pemphigus vulgaris, pernicious anemia, polychondritis, polymyositis and dermatomyositis, primary biliary cirrhosis, polyarteritis nodosa, polyglandular syndromes, polymyalgia rheumatica, primary agammaglobulinemia, Raynaud phenomenon, Reiter' s syndrome, rheumatic fever, sarcoidosis, scleroderma, Sjögren's syndrome, stiff person syndrome, Takayasu's arteritis, temporal arteritis, ulcerative colitis, uveitis, vasculitis, vitiligo, vulvodynia, and Wegener's granulomatosis.

91. The method of claim 89, wherein the autoimmune disorder is scleroderma.

92. The method of claim 89, wherein the autoimmune disorder is multiple sclerosis.

93. The method of claim 89, wherein the autoimmune disorder is ulcerative colitis.

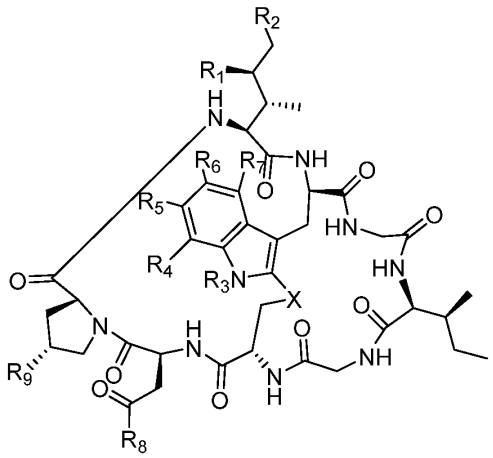
94. The method of claim 89, wherein the autoimmune disorder is Chrohn's disease.

95. The method of claim 89, wherein the autoimmune disorder is Type 1 diabetes.

96. The method of any one of claims 65-95, wherein the methods treats the disorder or cancer.

97. A method of depleting a population of CD45+ cells, the method comprising contacting the population with an effective amount of a conjugate represented by the formula Ab-Am, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD45 and Am is an amatoxin.

98. The method of claim 97, wherein Am is represented by formula (**IA**)



(**IA**)

wherein R_1 is H, OH, OR_A, or OR_C;

R_2 is H, OH, OR_B, or OR_C;

R_A and R_B, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocyclolalkyl group;

R_3 is H, R_C, or R_D;

R_4, R_5, R_6, and R_7 are each independently H, OH, OR_C, OR_D, R_C, or R_D;

R_8 is OH, NH_2, OR_C, OR_D, NHR_C, or NR_CR_D;

R_9 is H, OH, OR_C, or OR_D;

X is -S-, -S(O)-, or $-SO_2-$;

R_C is -L-Z;

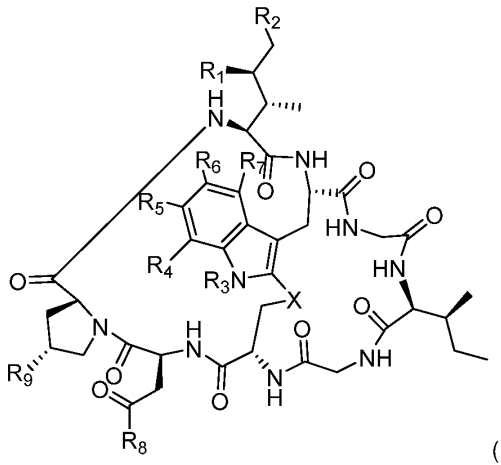
R_D is optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 heteroalkenyl, optionally substituted C_2-C_6 alkynyl, optionally substituted C_2-C_6 heteroalkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

L is optionally substituted C_1-C_6 alkylene, optionally substituted C_1-C_6 heteroalkylene, optionally substituted C_2-C_6 alkenylene, optionally substituted C_2-C_6 heteroalkenylene, optionally substituted C_2-C_6 alkynylene, optionally substituted C_2-C_6 heteroalkynylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene, optionally substituted arylene, or optionally substituted heteroarylene; and

Z is a chemical moiety formed from a coupling reaction between a reactive substituent present on L and a reactive substituent present within the antibody or antigen-binding fragment thereof,

wherein Am comprises exactly one R_C substituent.

99. The method of claim 97, wherein Am is represented by formula (**IB**)



(**IB**)

wherein R_1 is H, OH, OR_A, or OR_C;

R_2 is H, OH, OR_B, or OR_C;

R_A and R_B, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocyclolalkyl group;

R_3 is H, R_C, or R_D;

R_4, R_5, R_6, and R_7 are each independently H, OH, OR_C, OR_D, R_C, or R_D;

R_8 is OH, NH_2, OR_C, OR_D, NHR_C, or NR_CR_D;

R_9 is H, OH, OR_C, or OR_D;

X is -S-, -S(O)-, or $-SO_2-$;

R_C is -L-Z;

R_D is optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 heteroalkenyl, optionally substituted C_2-C_6 alkynyl, optionally substituted C_2-C_6 heteroalkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

L is optionally substituted C_1-C_6 alkylene, optionally substituted C_1-C_6 heteroalkylene, optionally substituted C_2-C_6 alkenylene, optionally substituted C_2-C_6 heteroalkenylene, optionally substituted C_2-C_6 alkynylene, optionally substituted C_2-C_6 heteroalkynylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene, optionally substituted arylene, or optionally substituted heteroarylene; and

Z is a chemical moiety formed from a coupling reaction between a reactive substituent present on L and a reactive substituent present within the antibody or antigen-binding fragment thereof,

wherein Am comprises exactly one R_C substituent

100. The method of claim 97, wherein the wherein the antibody or antigen-binding fragment thereof is conjugated to the amatoxin by way of a cysteine residue in the Fc domain of the antibody or antigen-binding fragment thereof.

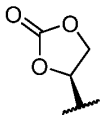
101. The method of claim 100, wherein the cysteine residue is introduced by way of a mutation in the Fc domain of the antibody or antigen-binding fragment thereof.

102. The method of claim 101, wherein the cysteine residue is selected from the group consisting of Cys118, Cys239, and Cys265.

103. The method of claim 100, wherein the cysteine residue is naturally occurring in the Fc domain of the antibody or antigen-binding fragment thereof.

104. The method of claim 103, wherein the Fc domain is an IgG Fc domain and the cysteine residue is selected from the group consisting of Cys261, Csy321, Cys367, and Cys425.

105. The method of claim 98 or 99, wherein R_1 is H, OH, or OR_A;
R_2 is H, OH, or OR_B;
R_A and R_B, together with the oxygen atoms to which they are bound, combine to form:



R_3, R_4, R_6, and R_7 are each H;
R_5 is OR_C;
R_8 is OH or NH_2; and
R_9 is H or OH.

106. The method of claim 98 or 99, wherein R_1 and R_2 are each independently H or OH;
R_3 is R_C;
R_4, R_6, and R_7 are each H;
R_5 is H, OH, or OC_1-C_6 alkyl;
R_8 is OH or NH_2; and
R_9 is H or OH.

107. The method of claim 98 or 99, wherein R_1 and R_2 are each independently H or OH;
R_3, R_6, and R_7 are each H;
R_4 is OR_C, or R_C;
R_5 is H, OH, or OC_1-C_6 alkyl;
R_8 is OH or NH_2; and
R_9 is H or OH.

108. The method of claim 98 or 99, wherein R_1 and R_2 are each independently H or OH;

R_3, R_6, and R_7 are each H;

R_4 and R_5 are each independently H or OH;

R_8 is OR_C or NHR_C; and

R_9 is H or OH.

109. The method of claim 97, wherein the antibody or antigen-binding fragment thereof is internalized by a CD45+ cell.

110. The method of claim 97, wherein the antibody or antigen-binding fragment thereof binds CD45 with a K_d of from about 0.1 pM to about 1 μM.

111. The method of claim 97, wherein the antibody or antigen-binding fragment thereof binds CD45 with a k_{on} of from about 9 x 10^{-2} M^{-1} s^{-1} to about 1 x 10^2 M^{-1} s^{-1}.

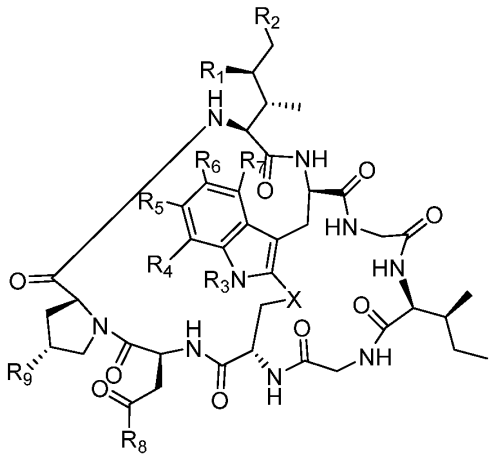
112. The method of claim 97, wherein the antibody or antigen-binding fragment thereof competitively inhibits the binding of CD45 to a second antibody or antigen binding fragment thereof, wherein the second antibody or antigen-binding fragment thereof comprises the following complementarity determining regions (CDRs):

a. a CDR-H1 having the amino acid sequence SYAMS (SEQ ID NO: 16);
b. a CDR-H2 having the amino acid sequence AISGSGGSTFYADSVRG (SEQ ID NO: 17);
c. a CDR-H3 having the amino acid sequence EVMGPIFFDY (SEQ ID NO: 18);
d. a CDR-L1 having the amino acid sequence RASQSIISSALA (SEQ ID NO: 19);
e. a CDR-L2 having the amino acid sequence GASSRAT (SEQ ID NO: 20); and
f. a CDR-L3 having the amino acid sequence QQYGSTPLT (SEQ ID NO: 21).

113. The method of claim 97, wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of a monoclonal antibody or antigen-binding fragment thereof, a polyclonal antibody or antigen-binding fragment thereof, a humanized antibody or antigen-binding fragment thereof, a bispecific antibody or antigen-binding fragment thereof, a dual-variable immunoglobulin domain, a single-chain Fv molecule (scFv), a diabody, a triabody, a nanobody, an antibody-like protein scaffold, a Fv fragment, a Fab fragment, a $F(ab')_2$ molecule, and a tandem di-scFV.

114. A conjugate represented by the formula Ab-Am, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD45 and Am is an amatoxin.

115. The conjugate of claim 114, wherein Am is represented by formula (**IA**)



(**IA**)

wherein R_1 is H, OH, OR_A, or OR_C;

R_2 is H, OH, OR_B, or OR_C;

R_A and R_B, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocyclolalkyl group;

R_3 is H, R_C, or R_D;

R_4, R_5, R_6, and R_7 are each independently H, OH, OR_C, OR_D, R_C, or R_D;

R_8 is OH, NH_2, OR_C, OR_D, NHR_C, or NR_CR_D;

R_9 is H, OH, OR_C, or OR_D;

X is -S-, -S(O)-, or $-SO_2-$;

R_C is -L-Z;

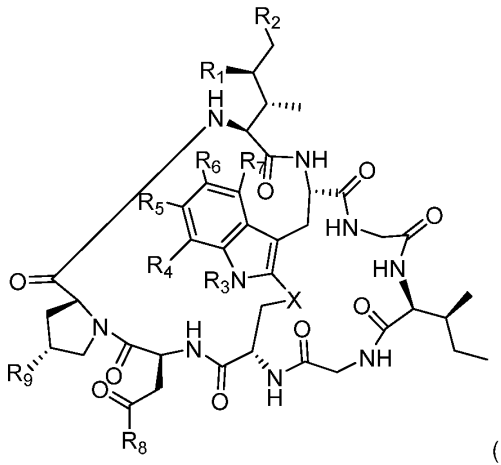
R_D is optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 heteroalkenyl, optionally substituted C_2-C_6 alkynyl, optionally substituted C_2-C_6 heteroalkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

L is optionally substituted C_1-C_6 alkylene, optionally substituted C_1-C_6 heteroalkylene, optionally substituted C_2-C_6 alkenylene, optionally substituted C_2-C_6 heteroalkenylene, optionally substituted C_2-C_6 alkynylene, optionally substituted C_2-C_6 heteroalkynylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene, optionally substituted arylene, or optionally substituted heteroarylene; and

Z is a chemical moiety formed from a coupling reaction between a reactive substituent present on L and a reactive substituent present within the antibody or antigen-binding fragment thereof,

wherein Am comprises exactly one R_C substituent.

116. The conjugate of claim 114, wherein Am is represented by formula (**IB**)



(**IB**)

wherein R_1 is H, OH, OR_A, or OR_C;

R_2 is H, OH, OR_B, or OR_C;

R_A and R_B, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocyclolalkyl group;

R_3 is H, R_C, or R_D;

R_4, R_5, R_6, and R_7 are each independently H, OH, OR_C, OR_D, R_C, or R_D;

R_8 is OH, NH_2, OR_C, OR_D, NHR_C, or NR_CR_D;

R_9 is H, OH, OR_C, or OR_D;

X is -S-, -S(O)-, or $-SO_2-$;

R_C is -L-Z;

R_D is optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 heteroalkenyl, optionally substituted C_2-C_6 alkynyl, optionally substituted C_2-C_6 heteroalkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

L is optionally substituted C_1-C_6 alkylene, optionally substituted C_1-C_6 heteroalkylene, optionally substituted C_2-C_6 alkenylene, optionally substituted C_2-C_6 heteroalkenylene, optionally substituted C_2-C_6 alkynylene, optionally substituted C_2-C_6 heteroalkynylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene, optionally substituted arylene, or optionally substituted heteroarylene; and

Z is a chemical moiety formed from a coupling reaction between a reactive substituent present on L and a reactive substituent present within the antibody or antigen-binding fragment thereof,

wherein Am comprises exactly one R_C substituent

117. The conjugate of claim 114, wherein the antibody or antigen-binding fragment thereof is conjugated to the amatoxin by way of a cysteine residue in the Fc domain of the antibody or antigen-binding fragment thereof.

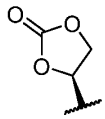
118. The conjugate of claim 117, wherein the cysteine residue is introduced by way of a mutation in the Fc domain of the antibody or antigen-binding fragment thereof.

119. The conjugate of claim 118, wherein the cysteine residue is selected from the group consisting of Cys118, Cys239, and Cys265.

120. The conjugate of claim 117, wherein the cysteine residue is naturally occurring in the Fc domain of the antibody or antigen-binding fragment thereof.

121. The conjugate of claim 120, wherein the Fc domain is an IgG Fc domain and the cysteine residue is selected from the group consisting of Cys261, Csy321, Cys367, and Cys425.

122. The conjugate of claim 115 or 116, wherein R_1 is H, OH, or OR_A;
R_2 is H, OH, or OR_B;
R_A and R_B, together with the oxygen atoms to which they are bound, combine to form:



R_3, R_4, R_6, and R_7 are each H;
R_5 is OR_C;
R_8 is OH or NH_2; and
R_9 is H or OH.

123. The conjugate of claim 115 or 116, wherein R_1 and R_2 are each independently H or OH;
R_3 is R_C;
R_4, R_6, and R_7 are each H;
R_5 is H, OH, or OC_1-C_6 alkyl;
R_8 is OH or NH_2; and
R_9 is H or OH.

124. The conjugate of claim 115 or 116, wherein R_1 and R_2 are each independently H or OH;
R_3, R_6, and R_7 are each H;
R_4 is OR_C, or R_C;
R_5 is H, OH, or OC_1-C_6 alkyl;
R_8 is OH or NH_2; and
R_9 is H or OH.

125. The conjugate of claim 115 or 116, wherein R_1 and R_2 are each independently H or OH;

R_3, R_6, and R_7 are each H;

R_4 and R_5 are each independently H or OH;

R_8 is OR_C or NHR_C; and

R_9 is H or OH.

126. The conjugate of claim 114, wherein the antibody or antigen-binding fragment thereof is internalized by a CD45+ cell.

127. The conjugate of claim 114, wherein the antibody or antigen-binding fragment thereof binds CD45 with a K_d of from about 0.1 pM to about 1 μM.

128. The conjugate of claim 114, wherein the antibody or antigen-binding fragment thereof binds CD45 with a k_{on} of from about 9 x 10^{-2} M^{-1} s^{-1} to about 1 x 10^2 M^{-1} s^{-1}.

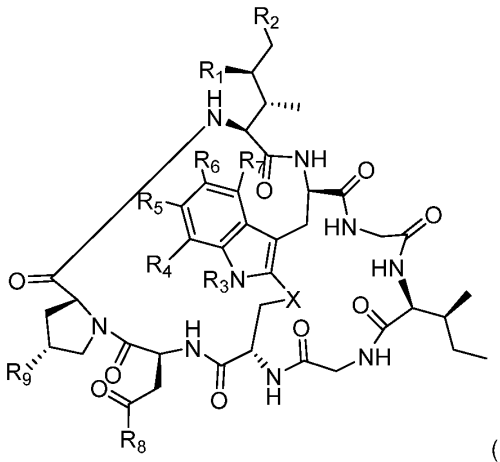
129. The conjugate of claim 114, wherein the antibody or antigen-binding fragment thereof competitively inhibits the binding of CD45 to a second antibody or antigen binding fragment thereof, wherein the second antibody or antigen-binding fragment thereof comprises the following complementarity determining regions (CDRs):

a. a CDR-H1 having the amino acid sequence SYAMS (SEQ ID NO: 16);
b. a CDR-H2 having the amino acid sequence AISGSGGSTFYADSVRG (SEQ ID NO: 17);
c. a CDR-H3 having the amino acid sequence EVMGPIFFDY (SEQ ID NO: 18);
d. a CDR-L1 having the amino acid sequence RASQSIISSALA (SEQ ID NO: 19);
e. a CDR-L2 having the amino acid sequence GASSRAT (SEQ ID NO: 20); and
f. a CDR-L3 having the amino acid sequence QQYGSTPLT (SEQ ID NO: 21).

130. The conjugate of claim 114, wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of a monoclonal antibody or antigen-binding fragment thereof, a polyclonal antibody or antigen-binding fragment thereof, a humanized antibody or antigen-binding fragment thereof, a bispecific antibody or antigen-binding fragment thereof, a dual-variable immunoglobulin domain, a single-chain Fv molecule (scFv), a diabody, a triabody, a nanobody, an antibody-like protein scaffold, a Fv fragment, a Fab fragment, a $F(ab')_2$ molecule, and a tandem di-scFV.

131. A method of depleting a population of CD135+ cells, the method comprising contacting the population with an effective amount of a conjugate represented by the formula Ab-Am, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD135 and Am is an amatoxin.

132. The method of claim 131, wherein Am is represented by formula (**IA**)



(**IA**)

wherein R_1 is H, OH, OR_A, or OR_C;

R_2 is H, OH, OR_B, or OR_C;

R_A and R_B, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocyclolalkyl group;

R_3 is H, R_C, or R_D;

R_4, R_5, R_6, and R_7 are each independently H, OH, OR_C, OR_D, R_C, or R_D;

R_8 is OH, NH_2, OR_C, OR_D, NHR_C, or NR_CR_D;

R_9 is H, OH, OR_C, or OR_D;

X is -S-, -S(O)-, or $-SO_2-$;

R_C is -L-Z;

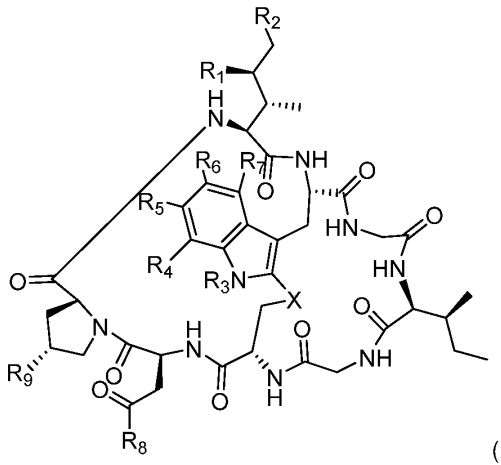
R_D is optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 heteroalkenyl, optionally substituted C_2-C_6 alkynyl, optionally substituted C_2-C_6 heteroalkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

L is optionally substituted C_1-C_6 alkylene, optionally substituted C_1-C_6 heteroalkylene, optionally substituted C_2-C_6 alkenylene, optionally substituted C_2-C_6 heteroalkenylene, optionally substituted C_2-C_6 alkynylene, optionally substituted C_2-C_6 heteroalkynylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene, optionally substituted arylene, or optionally substituted heteroarylene; and

Z is a chemical moiety formed from a coupling reaction between a reactive substituent present on L and a reactive substituent present within the antibody or antigen-binding fragment thereof,

wherein Am comprises exactly one R_C substituent.

133. The method of claim 131, wherein Am is represented by formula (**IB**)



(**IB**)

wherein R_1 is H, OH, OR_A, or OR_C;

R_2 is H, OH, OR_B, or OR_C;

R_A and R_B, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocyclolalkyl group;

R_3 is H, R_C, or R_D;

R_4, R_5, R_6, and R_7 are each independently H, OH, OR_C, OR_D, R_C, or R_D;

R_8 is OH, NH_2, OR_C, OR_D, NHR_C, or NR_CR_D;

R_9 is H, OH, OR_C, or OR_D;

X is -S-, -S(O)-, or $-SO_2-$;

R_C is -L-Z;

R_D is optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 heteroalkenyl, optionally substituted C_2-C_6 alkynyl, optionally substituted C_2-C_6 heteroalkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

L is optionally substituted C_1-C_6 alkylene, optionally substituted C_1-C_6 heteroalkylene, optionally substituted C_2-C_6 alkenylene, optionally substituted C_2-C_6 heteroalkenylene, optionally substituted C_2-C_6 alkynylene, optionally substituted C_2-C_6 heteroalkynylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene, optionally substituted arylene, or optionally substituted heteroarylene; and

Z is a chemical moiety formed from a coupling reaction between a reactive substituent present on L and a reactive substituent present within the antibody or antigen-binding fragment thereof,

wherein Am comprises exactly one R_C substituent

134. The method of claim 131, wherein the wherein the antibody or antigen-binding fragment thereof is conjugated to the amatoxin by way of a cysteine residue in the Fc domain of the antibody or antigen-binding fragment thereof.

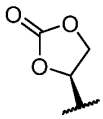
135. The method of claim 134, wherein the cysteine residue is introduced by way of a mutation in the Fc domain of the antibody or antigen-binding fragment thereof.

136. The method of claim 135, wherein the cysteine residue is selected from the group consisting of Cys118, Cys239, and Cys265.

137. The method of claim 134, wherein the cysteine residue is naturally occurring in the Fc domain of the antibody or antigen-binding fragment thereof.

138. The method of claim 137, wherein the Fc domain is an IgG Fc domain and the cysteine residue is selected from the group consisting of Cys261, Csy321, Cys367, and Cys425.

139. The method of claim 132 or 133, wherein R_1 is H, OH, or OR_A;
R_2 is H, OH, or OR_B;
R_A and R_B, together with the oxygen atoms to which they are bound, combine to form:



R_3, R_4, R_6, and R_7 are each H;
R_5 is OR_C;
R_8 is OH or NH_2; and
R_9 is H or OH.

140. The method of claim 132 or 133, wherein R_1 and R_2 are each independently H or OH;
R_3 is R_C;
R_4, R_6, and R_7 are each H;
R_5 is H, OH, or OC_1-C_6 alkyl;
R_8 is OH or NH_2; and
R_9 is H or OH.

141. The method of claim 132 or 133, wherein R_1 and R_2 are each independently H or OH;
R_3, R_6, and R_7 are each H;
R_4 is OR_C, or R_C;
R_5 is H, OH, or OC_1-C_6 alkyl;
R_8 is OH or NH_2; and
R_9 is H or OH.

142. The method of claim 132 or 133, wherein R_1 and R_2 are each independently H or OH;

R_3, R_6, and R_7 are each H;

R_4 and R_5 are each independently H or OH;

R_8 is OR_C or NHR_C; and

R_9 is H or OH.

143. The method of claim 131, wherein the antibody or antigen-binding fragment thereof is internalized by a CD135+ cell.

144. The method of claim 131, wherein the antibody or antigen-binding fragment thereof binds CD135 with a K_d of from about 0.1 pM to about 1 μM.

145. The method of claim 131, wherein the antibody or antigen-binding fragment thereof binds CD135 with a k_{on} of from about 9 x 10^{-2} M^{-1} s^{-1} to about 1 x 10^2 M^{-1} s^{-1}.

146. The method of claim 131, wherein the antibody or antigen-binding fragment thereof competitively inhibits the binding of CD135 to a second antibody or antigen binding fragment thereof, wherein the second antibody or antigen-binding fragment thereof comprises the following complementarity determining regions (CDRs):

a. a CDR-H1 having the amino acid sequence SYYMH (SEQ ID NO: 1);
b. a CDR-H2 having the amino acid sequence IINPSGGSTSYAQKFQG (SEQ ID NO: 2);
c. a CDR-H3 having the amino acid sequence GVGAHDAFDI (SEQ ID NO: 3) or VVAAAVADY (SEQ ID NO: 4);
d. a CDR-L1 having the amino acid sequence RSSQSLLHSNGNNYLD (SEQ ID NO: 5) or RSSQSLLHSNGYNYLD (SEQ ID NO: 6);
e. a CDR-L2 having the amino acid sequence LGSNRAS (SEQ ID NO: 7); and
f. a CDR-L3 having the amino acid sequence MQGTHPAIS (SEQ ID NO: 8) or MQSLQTPFT (SEQ ID NO: 9).

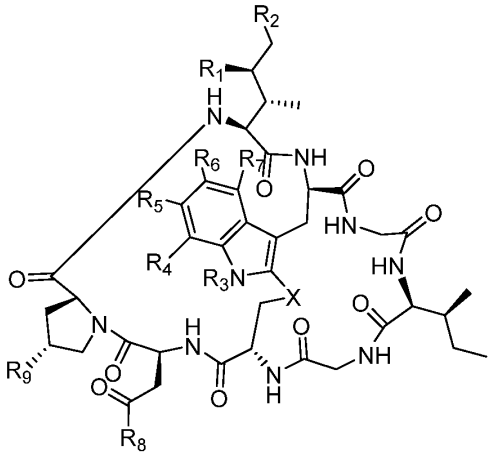
147. The method of claim 131, wherein the antibody or antigen-binding fragment thereof competitively inhibits the binding of CD135 to a second antibody or antigen binding fragment thereof, wherein the second antibody or antigen-binding fragment thereof comprises the following complementarity determining regions (CDRs):

a. a CDR-H1 having the amino acid sequence SYAIS (SEQ ID NO: 10);
b. a CDR-H2 having the amino acid sequence GIIPIFGTANYAQKFQG (SEQ ID NO: 11);
c. a CDR-H3 having the amino acid sequence FALFGFREQAFDI (SEQ ID NO: 12);
d. a CDR-L1 having the amino acid sequence RASQSISSYLN (SEQ ID NO: 13);
e. a CDR-L2 having the amino acid sequence AASSLQS (SEQ ID NO: 14); and
f. a CDR-L3 having the amino acid sequence QQSYSTPFT (SEQ ID NO: 15).

148. The method of claim 131, wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of a monoclonal antibody or antigen-binding fragment thereof, a polyclonal antibody or antigen-binding fragment thereof, a humanized antibody or antigen-binding fragment thereof, a bispecific antibody or antigen-binding fragment thereof, a dual-variable immunoglobulin domain, a single-chain Fv molecule (scFv), a diabody, a triabody, a nanobody, an antibody-like protein scaffold, a Fv fragment, a Fab fragment, a $F(ab')_2$ molecule, and a tandem di-scFV.

149. A conjugate represented by the formula Ab-Am, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD135 and Am is an amatoxin.

150. The conjugate of claim 149, wherein Am is represented by formula (**IA**)



(**IA**)

wherein R_1 is H, OH, OR_A, or OR_C;

R_2 is H, OH, OR_B, or OR_C;

R_A and R_B, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocyclolalkyl group;

R_3 is H, R_C, or R_D;

R_4, R_5, R_6, and R_7 are each independently H, OH, OR_C, OR_D, R_C, or R_D;

R_8 is OH, NH_2, OR_C, OR_D, NHR_C, or NR_CR_D;

R_9 is H, OH, OR_C, or OR_D;

X is -S-, -S(O)-, or $-SO_2-$;

R_C is -L-Z;

R_D is optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 heteroalkenyl, optionally substituted C_2-C_6 alkynyl, optionally substituted C_2-C_6 heteroalkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

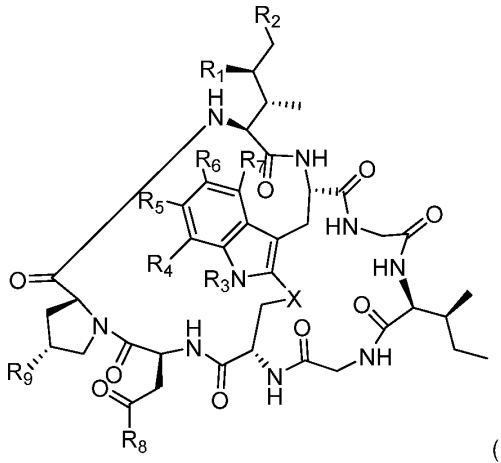
L is optionally substituted C_1-C_6 alkylene, optionally substituted C_1-C_6 heteroalkylene, optionally substituted C_2-C_6 alkenylene, optionally substituted C_2-C_6 heteroalkenylene, optionally

substituted C_2-C_6 alkynylene, optionally substituted C_2-C_6 heteroalkynylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene, optionally substituted arylene, or optionally substituted heteroarylene; and

Z is a chemical moiety formed from a coupling reaction between a reactive substituent present on L and a reactive substituent present within the antibody or antigen-binding fragment thereof,

wherein Am comprises exactly one R_C substituent.

151. The conjugate of claim 149, wherein Am is represented by formula (**IB**)



(**IB**)

wherein R_1 is H, OH, OR_A, or OR_C;

R_2 is H, OH, OR_B, or OR_C;

R_A and R_B, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocyclolalkyl group;

R_3 is H, R_C, or R_D;

R_4, R_5, R_6, and R_7 are each independently H, OH, OR_C, OR_D, R_C, or R_D;

R_8 is OH, NH_2, OR_C, OR_D, NHR_C, or NR_CR_D;

R_9 is H, OH, OR_C, or OR_D;

X is -S-, -S(O)-, or -SO_2-;

R_C is -L-Z;

R_D is optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted C_2-C_6 alkenyl, optionally substituted C_2-C_6 heteroalkenyl, optionally substituted C_2-C_6 alkynyl, optionally substituted C_2-C_6 heteroalkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

L is optionally substituted C_1-C_6 alkylene, optionally substituted C_1-C_6 heteroalkylene, optionally substituted C_2-C_6 alkenylene, optionally substituted C_2-C_6 heteroalkenylene, optionally substituted C_2-C_6 alkynylene, optionally substituted C_2-C_6 heteroalkynylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene, optionally substituted arylene, or optionally substituted heteroarylene; and

Z is a chemical moiety formed from a coupling reaction between a reactive substituent present on L and a reactive substituent present within the antibody or antigen-binding fragment thereof,

wherein Am comprises exactly one R_C substituent

152. The conjugate of claim 149, wherein the wherein the antibody or antigen-binding fragment thereof is conjugated to the amatoxin by way of a cysteine residue in the Fc domain of the antibody or antigen-binding fragment thereof.

153. The conjugate of claim 152, wherein the cysteine residue is introduced by way of a mutation in the Fc domain of the antibody or antigen-binding fragment thereof.

154. The conjugate of claim 153, wherein the cysteine residue is selected from the group consisting of Cys118, Cys239, and Cys265.

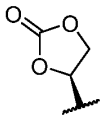
155. The conjugate of claim 152, wherein the cysteine residue is naturally occurring in the Fc domain of the antibody or antigen-binding fragment thereof.

156. The conjugate of claim 155, wherein the Fc domain is an IgG Fc domain and the cysteine residue is selected from the group consisting of Cys261, Csy321, Cys367, and Cys425.

157. The conjugate of claim 150 or 151, wherein R_1 is H, OH, or OR_A;

R_2 is H, OH, or OR_B;

R_A and R_B, together with the oxygen atoms to which they are bound, combine to form:



R_3, R_4, R_6, and R_7 are each H;

R_5 is OR_C;

R_8 is OH or NH_2; and

R_9 is H or OH.

158. The conjugate of claim 150 or 151, wherein R_1 and R_2 are each independently H or OH;

R_3 is R_C;

R_4, R_6, and R_7 are each H;

R_5 is H, OH, or OC_1-C_6 alkyl;

R_8 is OH or NH_2; and

R_9 is H or OH.

159. The conjugate of claim 150 or 151, wherein R_1 and R_2 are each independently H or OH;
R_3, R_6, and R_7 are each H;
R_4 is OR_C, or R_C;
R_5 is H, OH, or OC_1-C_6 alkyl;
R_8 is OH or NH_2; and
R_9 is H or OH.

160. The conjugate of claim 150 or 151, wherein R_1 and R_2 are each independently H or OH;
R_3, R_6, and R_7 are each H;
R_4 and R_5 are each independently H or OH;
R_8 is OR_C or NHR_C; and
R_9 is H or OH.

161. The conjugate of claim 149, wherein the antibody or antigen-binding fragment thereof is internalized by a CD135+ cell.

162. The conjugate of claim 149, wherein the antibody or antigen-binding fragment thereof binds CD135 with a K_d of from about 0.1 pM to about 1 μM.

163. The conjugate of claim 149, wherein the antibody or antigen-binding fragment thereof binds CD135 with a k_{on} of from about 9×10^{-2} M^{-1} s^{-1} to about 1×10^{2} M^{-1} s^{-1}.

164. The conjugate of claim 149, wherein the antibody or antigen-binding fragment thereof competitively inhibits the binding of CD135 to a second antibody or antigen binding fragment thereof, wherein the second antibody or antigen-binding fragment thereof comprises the following complementarity determining regions (CDRs):

a. a CDR-H1 having the amino acid sequence SYYMH (SEQ ID NO: 1);
b. a CDR-H2 having the amino acid sequence IINPSGGSTSYAQKFQG (SEQ ID NO: 2);
c. a CDR-H3 having the amino acid sequence GVGAHDAFDI (SEQ ID NO: 3) or VVAAAVADY (SEQ ID NO: 4);
d. a CDR-L1 having the amino acid sequence RSSQSLLHSNGNNYLD (SEQ ID NO: 5) or RSSQSLLHSNGYNYLD (SEQ ID NO: 6);
e. a CDR-L2 having the amino acid sequence LGSNRAS (SEQ ID NO: 7); and
f. a CDR-L3 having the amino acid sequence MQGTHPAIS (SEQ ID NO: 8) or MQSLQTPFT (SEQ ID NO: 9).

165. The conjugate of claim 149, wherein the antibody or antigen-binding fragment thereof competitively inhibits the binding of CD135 to a second antibody or antigen binding fragment thereof,

wherein the second antibody or antigen-binding fragment thereof comprises the following complementarity determining regions (CDRs):

a. a CDR-H1 having the amino acid sequence SYAIS (SEQ ID NO: 10);
b. a CDR-H2 having the amino acid sequence GIIPIFGTANYAQKFQG (SEQ ID NO: 11);
c. a CDR-H3 having the amino acid sequence FALFGFREQAFDI (SEQ ID NO: 12);
d. a CDR-L1 having the amino acid sequence RASQSISSYLN (SEQ ID NO: 13);
e. a CDR-L2 having the amino acid sequence AASSLQS (SEQ ID NO: 14); and
f. a CDR-L3 having the amino acid sequence QQSYSTPFT (SEQ ID NO: 15).

166. The conjugate of claim 149, wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of a monoclonal antibody or antigen-binding fragment thereof, a polyclonal antibody or antigen-binding fragment thereof, a humanized antibody or antigen-binding fragment thereof, a bispecific antibody or antigen-binding fragment thereof, a dual-variable immunoglobulin domain, a single-chain Fv molecule (scFv), a diabody, a triabody, a nanobody, an antibody-like protein scaffold, a Fv fragment, a Fab fragment, a $F(ab')_2$ molecule, and a tandem di-scFV.

167. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD45 and Cy is pseudomonas exotoxin A.

168. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD45 and Cy is deBouganin.

169. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD45 and Cy is diphtheria toxin.

170. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD45 and Cy is saporin.

171. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD45 and Cy is maytansine or a maytansinoid.

172. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD45 and Cy is an auristatin.

173. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD45 and Cy is an anthracycline.

174. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD45 and Cy is a calicheamicin.

175. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD45 and Cy is irinotecan.

176. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD45 and Cy is SN-38.

177. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD45 and Cy is a duocarmycin.

178. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD45 and Cy is a pyrrolobenzodiazepine or a pyrrolobenzodiazepine dimer.

179. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD45 and Cy is an indolinobenzodiazepine or an indolinobenzodiazepine dimer.

180. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD135 and Cy is pseudomonas exotoxin A.

181. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD135 and Cy is deBouganin.

182. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD135 and Cy is diphtheria toxin.

183. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD135 and Cy is saporin.

184. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD135 and Cy is maytansine or a maytansinoid.

185. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD135 and Cy is an auristatin.

186. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD135 and Cy is an anthracycline.

187. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD135 and Cy is a calicheamicin.

188. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD135 and Cy is irinotecan.

189. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD135 and Cy is SN-38.

190. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD135 and Cy is a duocarmycin.

191. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD135 and Cy is a pyrrolobenzodiazepine or a pyrrolobenzodiazepine dimer.

192. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD135 and Cy is an indolinobenzodiazepine or an indolinobenzodiazepine dimer.

193. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD34 and Cy is pseudomonas exotoxin A.

194. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD34 and Cy is deBouganin.

195. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD34 and Cy is diphtheria toxin.

196. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD34 and Cy is saporin.

197. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD34 and Cy is maytansine or a maytansinoid.

198. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD34 and Cy is an auristatin.

199. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD34 and Cy is an anthracycline.

200. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD34 and Cy is a calicheamicin.

201. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD34 and Cy is irinotecan.

202. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD34 and Cy is SN-38.

203. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD34 and Cy is a duocarmycin.

204. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD34 and Cy is a pyrrolobenzodiazepine or a pyrrolobenzodiazepine dimer.

205. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD34 and Cy is an indolinobenzodiazepine or an indolinobenzodiazepine dimer.

206. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD90 and Cy is pseudomonas exotoxin A.

207. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD90 and Cy is deBouganin.

208. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD90 and Cy is diphtheria toxin.

209. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD90 and Cy is saporin.

210. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD90 and Cy is maytansine or a maytansinoid.

211. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD90 and Cy is an auristatin.

212. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD90 and Cy is an anthracycline.

213. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD90 and Cy is a calicheamicin.

214. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD90 and Cy is irinotecan.

215. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD90 and Cy is SN-38.

216. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD90 and Cy is a duocarmycin.

217. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD90 and Cy is a pyrrolobenzodiazepine or a pyrrolobenzodiazepine dimer.

218. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD90 and Cy is an indolinobenzodiazepine or an indolinobenzodiazepine dimer.

219. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD110 and Cy is pseudomonas exotoxin A.

220. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD110 and Cy is deBouganin.

221. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD110 and Cy is diphtheria toxin.

222. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD110 and Cy is saporin.

223. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD110 and Cy is maytansine or a maytansinoid.

224. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD110 and Cy is an auristatin.

225. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD110 and Cy is an anthracycline.

226. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD110 and Cy is a calicheamicin.

227. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD110 and Cy is irinotecan.

228. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD110 and Cy is SN-38.

229. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD110 and Cy is a duocarmycin.

230. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD110 and Cy is a pyrrolobenzodiazepine or a pyrrolobenzodiazepine dimer.

231. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or an antigen-binding fragment thereof that binds CD110 and Cy is an indolinobenzodiazepine or an indolinobenzodiazepine dimer.