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(54) Title: COMPOSITIONS AND METHODS FOR THE DEPLETION OF CD5+ CELLS

(57) Abstract: The invention provides anti-CD5 antibodies, antigen-binding fragments thereof, and antibody drug conjugates thereof, for use in treating, for example, a stem cell disorder, cancer, or autoimmune disease, among other hematological and proliferative diseases. Compositions and methods for depleting populations of CD5+ cells, such as CD5+ cancer cells and CD5+ immune cells are described, and can be used to treat cancers and autoimmune diseases directly as stand-alone therapies by eradicating cancerous cells and autoreactive immune cells that express CD5 and/or to prepare a patient for hematopoietic stem cell transplantation, for instance, by depleting populations of CD5+ immune cells that cross-react with, and mount an immune response against, non-self hematopoietic stem cells.



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AMENDED CLAIMS
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CLAIMS

1. A method of depleting a population of CD5+ cells in a human patient, the method comprising administering to the patient an effective amount of an anti-CD5 antibody or antigen-binding fragment thereof, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

2. A method of depleting a population of CD5+ 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 anti-CD5 antibody, or antigen-binding fragment thereof, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

3. A method of preventing rejection of a hematopoietic stem cell graft in a human patient in need of a hematopoietic stem cell transplant, the method comprising administering to the patient an effective amount of an anti-CD5 antibody, or antigen-binding fragment thereof, prior to the human patient receiving a transplant comprising hematopoietic stem cells, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

4. A method of depleting a population of CD5+ 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 anti-CD5 antibody, or antigen-binding fragment thereof, prior to the patient receiving a transplant comprising hematopoietic stem cells, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

5. A method comprising administering to a human patient a transplant comprising hematopoietic stem cells, wherein the patient has been previously administered an anti-CD5 antibody or antigen-binding fragment thereof, in an amount sufficient to deplete a population of CD5+ cells in the patient, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

6. A method comprising:
- a. administering to a human patient an anti-CD5 antibody or antigen-binding fragment thereof, that binds to CD5, in an amount sufficient to deplete a population of CD5+ cells in the patient, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin; and
 - b. subsequently administering to the patient a transplant comprising hematopoietic stem cells.

7. A method of treating a stem cell disorder in a human patient, the method comprising administering to the patient a therapeutically effective amount of an anti-CD5 antibody or antigen-binding fragment thereof, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

8. A method of treating a hemoglobinopathy disorder in a human patient, the method comprising administering to the patient a therapeutically effective amount of an anti-CD5 antibody or antigen-binding fragment thereof, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

9. A method of treating a myelodysplastic disorder in a human patient, the method comprising administering to the patient a therapeutically effective amount of an antibody or antigen-binding fragment thereof capable of binding CD5, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

10. A method of treating an immunodeficiency disorder in a human patient, the method comprising administering to the patient a therapeutically effective amount of an antibody or antigen-binding fragment thereof capable of binding CD5, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

11. A method of treating a metabolic disorder in a human patient, the method comprising administering to the patient a therapeutically effective amount of an antibody or antigen-binding fragment thereof capable of binding CD5, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

12. A method of treating cancer in a human patient, the method comprising administering to the patient a therapeutically effective amount of an antibody or antigen-binding fragment thereof capable of binding CD5, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

13. A method of treating 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 in a human patient, the method comprising administering to the patient a therapeutically effective amount of an

anti-CD5 antibody or antigen-binding fragment thereof, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

14. A method of treating an autoimmune disorder in a human patient, the method comprising administering to the patient a therapeutically effective amount of an anti-CD5 antibody or antigen-binding fragment thereof, wherein the antibody, or antigen-binding fragment thereof, is conjugated to a cytotoxin.

15. The method of any one of claims 1-14, wherein the antibody or antigen-binding fragment thereof is produced by the hybridoma cell line ATCC CRL 8000.

16. The method of any one of claims 1-14, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region CDR set (CDR1, CDR2, and CDR3) and a light chain variable region CDR set (CDR1, CDR2, and CDR3) of antibody OKT1 produced by the hybridoma cell line having ATCC accession number CRL 8000.

17. The method of any one of claims 1-14, wherein said antibody or antigen-binding fragment thereof comprises the following variable domains:

- a. a V_L having the amino acid sequence
DIQMTQSPSSMSASLGDRVTITCRASQDINSYLSWFQQKPGKSPKTLIYRAN
RL
VDGVPSRFSGSGSGTDYTLTISSLQYEDFGIYYCQQYDESPWTFGGGKLE
IK (SEQ ID NO: 1); and
- b. a V_H having the amino acid sequence
QIQLVQSGPGLKKPGGSGVRISCAASGYTFTNYGMNWVKQAPGKGLRWMG
WI
NHTHGEPTYADDFKGRFTFSLDTSKSTAYLQINSLRAEDTATYFCTRRGYD
WY FDVWGQGTTVTVSS (SEQ ID NO: 2); or
- a. V_L having the amino acid sequence
NIVMTQSPSSLSASVGDRVTITCQASQDVGTAVAWYQQKPDQSPKLLIYWT
STRHTGVPDRFTGSGSGTDFTLTISLQPEDATYFCHQYNSYNTFGSGTKL
EIK (SEQ ID NO: 258); and
- b. V_H having the amino acid sequence
QVTLKESGPVLVKPTETLTCTFSGFSLSTSGMGVGVIRQAPGKGLEWVA
HIWWDDDDVYNNPSLKSRLTITKDASKDQVSLKLSSVTAADTAVYYCVRRRA
TGTGFDYWGGGTLTVTVSS (SEQ ID NO: 257).

18. The method of any one of claims 1-14, wherein said antibody or antigen-binding fragment thereof comprises the following complementarity determining regions (CDRs):

- a. a CDR-H1 having the amino acid sequence GYTFTNY (SEQ ID NO: 3);
- b. a CDR-H2 having the amino acid sequence NTHTGE (SEQ ID NO: 4);
- c. a CDR-H3 having the amino acid sequence RGYDWYFDV (SEQ ID NO: 5);
- d. a CDR-L1 having the amino acid sequence RASQDINSYLS (SEQ ID NO: 6);
- e. a CDR-L2 having the amino acid sequence RANRLVD (SEQ ID NO: 7); and
- f. a CDR-L3 having the amino acid sequence QQYDESPWT (SEQ ID NO: 8);

or

- a. a CDR-H1 having the amino acid sequence FSLSTSGMG (SEQ ID NO: 29);
- b. a CDR-H2 having the amino acid sequence WWDDD (SEQ ID NO: 30);
- c. a CDR-H3 having the amino acid sequence RRATGTGFDY (SEQ ID NO: 31);
- d. a CDR-L1 having the amino acid sequence QDVGTA (SEQ ID NO: 32);
- e. a CDR-L2 having the amino acid sequence WTSTRHT (SEQ ID NO: 33);
- f. a CDR-L3 having the amino acid sequence YNSYNT (SEQ ID NO: 34).

19. The method of any one of claims 1-14, wherein said antibody or antigen-binding fragment thereof comprises the following variable domains:

- a. a V_L having the amino acid sequence
DIQMTQSPSSLSASVGDRVTITCRASQDINSYLSWFQQKPGKAPKTLIYRAN
RL ESGVPSRFSGSGSGTDYTLTIS
SLQYEDFGIYYCQQYDESPWTFGGGTKLEIK (SEQ ID NO: 9); and
- b. a V_H having the amino acid sequence
EIQLVQSGGGLVKPGGSVRISCAASGYTFTNYGMNWRQAPGKGLEWMG
WI
NTHYGEPTYADSFKGTRTFSLDDSKNTAYLQINSLRAEDTAVYFCTRRGYD
W YFDVWGQGGTTVTVSS (SEQ ID NO: 10).

20. The method of any one of claims 1-14, wherein said antibody or antigen-binding fragment thereof comprises the following CDRs:

- a. a CDR-H1 having the amino acid sequence GYTFTNY (SEQ ID NO: 11);
- b. a CDR-H2 having the amino acid sequence NTHYGE (SEQ ID NO: 12);
- c. a CDR-H3 having the amino acid sequence RRGYDWYFDV (SEQ ID NO: 13);

- d. a CDR-L1 having the amino acid sequence RASQDINSYLS (SEQ ID NO: 14);
- e. a CDR-L2 having the amino acid sequence RANRLES (SEQ ID NO: 15); and
- f. a CDR-L3 having the amino acid sequence QQYDESPWT (SEQ ID NO: 16).

21. The method of any one of claims 1-20, 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, an intact antibody, 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.

22. The method of claim 21, wherein the antibody or antigen-binding fragment thereof is a humanized antibody, or an antigen-binding fragment thereof.

23. The method of any one of claims 1-22, wherein the antibody has an isotype selected from the group consisting of IgG, IgA, IgM, IgD, and IgE.

24. The method of claim 23, wherein the IgG isotype is an IgG1 or an IgG4.

25. The method of any one of claims 1-24, wherein the cytotoxin is selected from the group consisting of pseudomonas exotoxin A, deBouganin, diphtheria toxin, an amatoxin, 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.

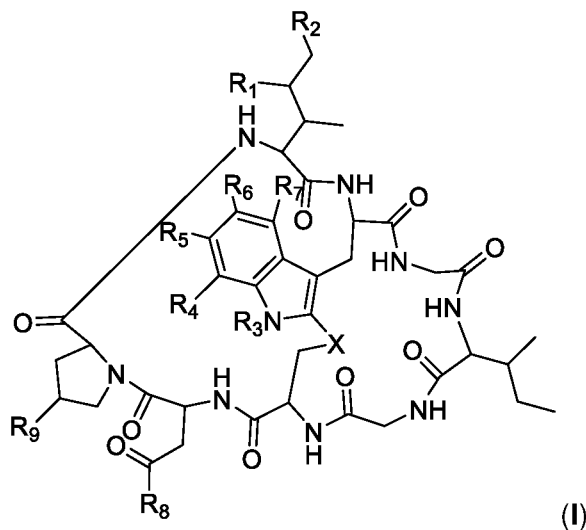
26. The method of claim 25, wherein the cytotoxin is an RNA polymerase inhibitor.

27. The method of claim 26, wherein the RNA polymerase inhibitor is an RNA polymerase II inhibitor.

28. The method of claim 27, wherein the RNA polymerase II inhibitor is amatoxin.

29. The method of any one of claims 1-24, wherein the antibody or antigen-binding fragment thereof conjugated to a cytotoxin is represented by the formula Ab-Z-L-Am,

wherein Ab is the antibody or antigen-binding fragment thereof, L is a linker, Z is a chemical moiety, and Am an amatoxin represented by formula (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 , when present, 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 $NR_C R_D$;

R_9 is H, OH, OR_C , or OR_D ;

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

R_C is $-L-Z$;

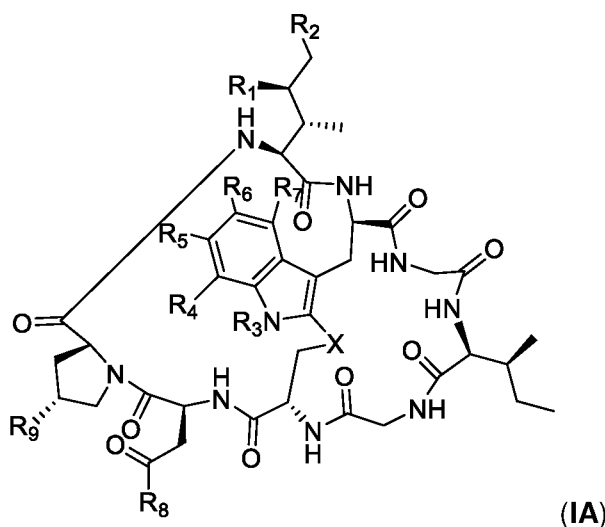
R_D is optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted C_2 - C_6 alkynyl, optionally substituted C_2 - C_6 heteroalkynyl, optionally substituted cycloalkyl, 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, optionally substituted heteroarylene; a dipeptide, $-C(=O)-$, a peptide, or a combination thereof; 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.

30. The method of claim 29, wherein Am-L-Z is represented by formula (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 , when present, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocycloalkyl 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 $NR_C R_D$;

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;

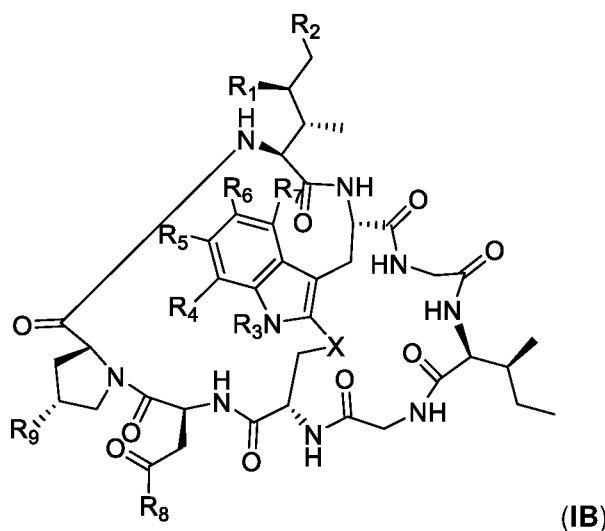
L is optionally substituted C_1 - C_6 alkylene, optionally substituted C_1 - C_6 heteroalkylene, optionally substituted C_2 - C_6 alkenylene, optionally substituted C_2 - C_6 heteroalkenylene, optionally substituted C_2 - C_6 alkynylene, optionally substituted C_2 - C_6 heteroalkynylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene, optionally substituted arylene, optionally substituted heteroarylene, a dipeptide, $-C(=O)-$, a peptide, or a combination thereof;

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; and

wherein Am comprises exactly one R_C substituent.

31. The method of claim 29, wherein Am-L-Z is represented by formula (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 , when present, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocycloalkyl 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 $-L-Z$;

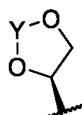
R_D is optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 heteroalkyl, optionally substituted C_2 - C_6 alkenyl, optionally substituted C_2 - C_6 heteroalkenyl, optionally substituted C_2 - C_6 alkynyl, optionally substituted C_2 - C_6 heteroalkynyl, optionally substituted cycloalkyl, 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, optionally substituted heteroarylene, a dipeptide, $-C(=O)-$, a peptide, or a combination thereof; 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.

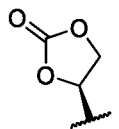
32. The method of claim 30 or 31, wherein R_A and R_B , together with the oxygen atoms to which they are bound, combine to form a 5 membered heterocycloalkyl group of formula:



wherein Y is $-C(=O)-$, $-C(=S)-$, $-C(=NR_E)-$, or $-C(R_E R_{E'})-$; 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 .

33. The method of claim 32, wherein R_A and R_B , together with the oxygen atoms to which they are bound, combine to form:

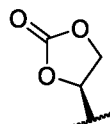


34. The method of claim 30 or 31, wherein:

(a) 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;

(b) 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;

(c) 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;

or

(d) R_1 and R_2 are each independently H or OH;

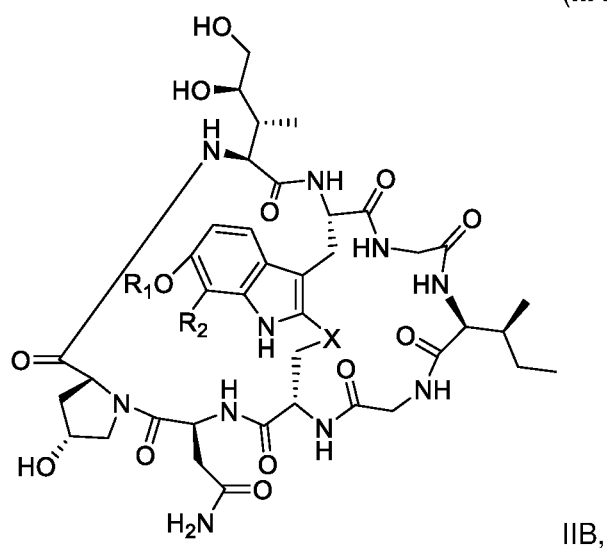
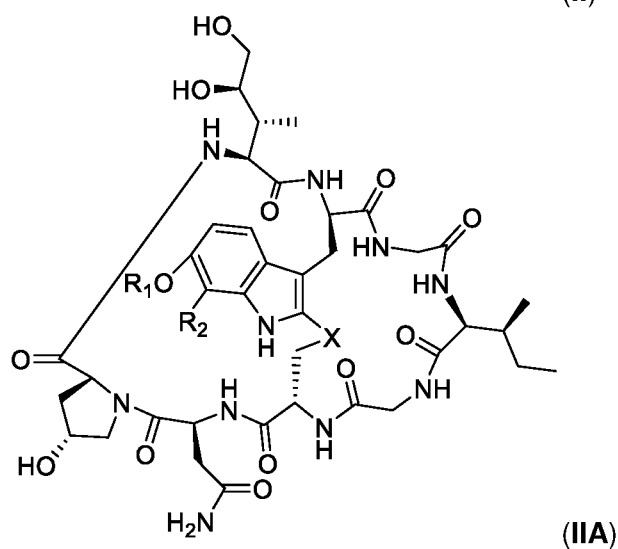
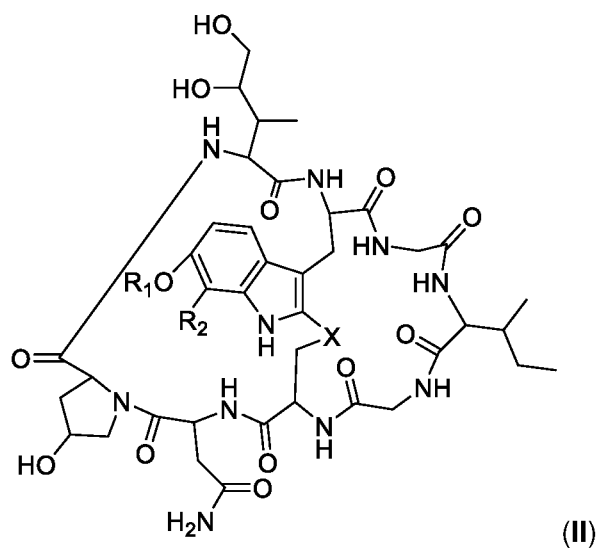
R_3 , R_6 , and R_7 are each H;

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.

35. The method of any one of claims 1-24, wherein the antibody or antigen-binding fragment thereof conjugated to a cytotoxin is represented by the formula Ab-L-Z-Am, wherein Ab is the antibody or antigen-binding fragment thereof, Z is a chemical moiety, L is a linker, and Am is an amatoxin, and the amatoxin-linker conjugate Am-L-Z is represented by formula (II), formula (IIA), or formula (IIB)



wherein X is S, SO, or SO₂;

R₁ is H or a linker covalently bound to the antibody or antigen-binding fragment thereof through a chemical moiety Z, formed from a coupling reaction between a reactive

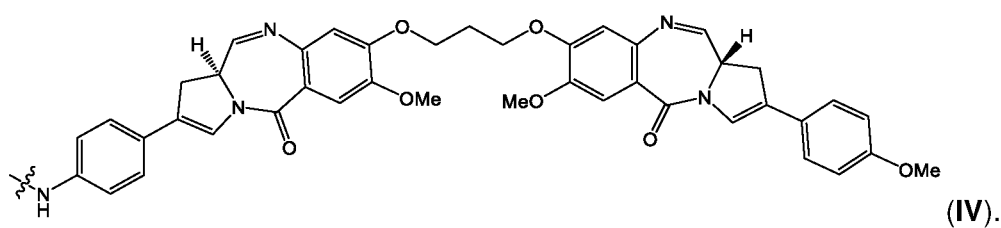
substituent present on the linker and a reactive substituent present within an antibody, or antigen-binding fragment thereof; and

R_2 is H or a linker covalently bound to the antibody or antigen-binding fragment thereof through a chemical moiety Z, formed from a coupling reaction between a reactive substituent present on the linker and a reactive substituent present within an 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.

36. The method of any one of claims 1-24, wherein the cytotoxin is:

- (a) a maytansinoid selected from the group consisting of DM1 and DM4;
- (b) an auristatin;
- (c) an anthracycline selected from the group consisting of daunorubicin, doxorubicin, epirubicin, and idarubicin; or
- (d) a pyrrolobenzodiazepine dimer derivative represented by formula (IV)



37. The method of claim 36, wherein the auristatin is selected from the group consisting of monomethyl auristatin E and monomethyl auristatin F.

38. The method of any one of claims 1-6 and 15-37, wherein the antibody, or antigen-binding fragment thereof, conjugated to the cytotoxin is internalized by an immune cell following administration to the patient.

39. The method of any one of claims 1-6 and 15-38, wherein the antibody, or antigen-binding fragment thereof, conjugated to the cytotoxin is capable of promoting necrosis of an immune cell.

40. The method of any one of claims 1-6 and 15-37, wherein the antibody, or antigen-binding fragment thereof, conjugated to the cytotoxin is capable of recruiting one or more complement proteins to an immune cell upon administration to the patient.

41. The method of any one of claims 38-40, wherein the immune cell is selected from the group consisting of a T cell, B cell, and NK cell.

42. The method of any one of claims 3-6 and 15-41, wherein the transplant comprising hematopoietic stem cells is administered to the patient after the concentration of the antibody, or antigen-binding fragment thereof, conjugated to the cytotoxin has substantially cleared from the blood of the patient.

43. The method of claim 42, wherein:

(a) the transplant comprising hematopoietic stem cells is administered to the patient between 1 hour and 7 days after the concentration of the antibody, or antigen-binding fragment thereof, conjugated to the cytotoxin has substantially cleared from the blood of the patient;

(b) the transplant comprising hematopoietic stem cells is administered to the patient between 6 hours and 3 days after the concentration of the antibody, or antigen-binding fragment thereof, conjugated to the cytotoxin has substantially cleared from the blood of the patient;

(c) the transplant comprising hematopoietic stem cells is administered to the patient between 12 hours and 36 hours after the concentration of the antibody, or antigen-binding fragment thereof, conjugated to the cytotoxin has substantially cleared from the blood of the patient; or

(d) the transplant comprising hematopoietic stem cells is administered to the patient 24 hours after the concentration of the antibody, or antigen-binding fragment thereof, conjugated to the cytotoxin has substantially cleared from the blood of the patient.

44. The method of any one of claims 3-6 and 15-1, 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.

45. The method of any one of claims 3-6 and 15-44, wherein the hematopoietic stem cells are autologous with respect to the patient.

46. The method of any one of claims 3-6 and 15-44, wherein the hematopoietic stem cells are allogeneic with respect to the patient.

47. The method of claim 46, wherein the hematopoietic stem cells are HLA-matched with respect to the patient or the hematopoietic stem cells are HLA-mismatched with respect to the patient.

48. The method of any one of claims 1, 2, 4-6, and 15-47, wherein the population of CD5+ cells comprises CD34+ cells.

49. The method of any one of claims 1, 2, 4-6, and 15-48, wherein the population of CD5+ cells comprises T cells.

50. The method of any one of claims 3-6 and 15-49, 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.

51. The method of any one of claims 3-6 and 15-50, 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, myeloblasts, basophils, neutrophils, eosinophils, microglia, granulocytes, monocytes, osteoclasts, antigen-presenting cells, macrophages, dendritic cells, natural killer cells, T lymphocytes, and B lymphocytes.

52. The method of any one of claims 1-6 and 15-51, wherein the patient is suffering from a stem cell disorder, a hemoglobinopathy disorder, a myelodysplastic disorder, an immunodeficiency disorder, a metabolic disorder, a cancer, or an autoimmune disorder.

53. The method of claim 8 or 52, wherein the hemoglobinopathy disorder is selected from the group consisting of sickle cell anemia, thalassemia, Fanconi anemia, aplastic anemia, and Wiskott-Aldrich syndrome.

54. The method of claim 10 or 52, wherein the immunodeficiency disorder is a congenital immunodeficiency or an acquired immunodeficiency.

55. The method of claim 54, wherein the acquired immunodeficiency is human immunodeficiency virus or acquired immune deficiency syndrome.

56. The method of claim 11 or 52, wherein the metabolic disorder is selected from the group consisting of glycogen storage diseases, mucopolysaccharidoses, Gaucher's Disease, Hurlers Disease, sphingolipidoses, and metachromatic leukodystrophy.

57. The method of claim 12 or 52, wherein the cancer is selected from the group consisting of leukemia, lymphoma, multiple myeloma, and neuroblastoma.

58. The method of claim 12 or 52, wherein the cancer is a hematological cancer.

59. The method of claim 12 or 52, wherein the cancer is acute myeloid leukemia, acute lymphoid leukemia, chronic myeloid leukemia, or chronic lymphoid leukemia.

60. The method of claim 12 or 52, wherein the cancer is multiple myeloma.

61. The method of claim 12 or 52, wherein the cancer is diffuse large B-cell lymphoma or non-Hodgkin's lymphoma.

62. The method of any one of claims 1-6 and 15-61, 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.

63. The method of claim 14 or 52, 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 spondylitis, 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, cicatricial 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.

64. The method of claim 14 or 52, wherein the autoimmune disorder is scleroderma, multiple sclerosis, ulcerative colitis, Crohn's disease, or Type 1 diabetes.

65. The method of any one of claims 52-64, wherein the method treats the disorder or cancer.

66. A conjugate represented by the formula Ab-Cy, wherein Ab is an antibody or antigen-binding fragment thereof that binds CD5 and Cy is a cytotoxin, wherein the cytotoxin is selected from the group consisting of pseudomonas exotoxin A, deBouganin, diphtheria toxin, an amatoxin, 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.

67. The conjugate of claim 66, wherein the antibody or antigen-binding fragment thereof is produced by the hybridoma cell line ATCC HB 8000.

68. The conjugate of claim 66, wherein the antibody or antigen-binding fragment thereof comprises the following complementarity determining regions (CDRs):

- a. a CDR-H1 having the amino acid sequence GYTFTNY (SEQ ID NO: 3);
- b. a CDR-H2 having the amino acid sequence NTHTGE (SEQ ID NO: 4);
- c. a CDR-H3 having the amino acid sequence RGYDWYFDV (SEQ ID NO: 5);
- d. a CDR-L1 having the amino acid sequence RASQDINSYLS (SEQ ID NO: 6);
- e. a CDR-L2 having the amino acid sequence RANRLVD (SEQ ID NO: 7); and

- f. a CDR-L3 having the amino acid sequence QQYDESPWT (SEQ ID NO: 8);
or
- a. a CDR-H1 having the amino acid sequence FSLSTSGMG (SEQ ID NO: 29);
- b. a CDR-H2 having the amino acid sequence WWDDD (SEQ ID NO: 30);
- c. a CDR-H3 having the amino acid sequence RRATGTGFDY (SEQ ID NO: 31);
- d. a CDR-L1 having the amino acid sequence QDVGTA (SEQ ID NO: 32);
- e. a CDR-L2 having the amino acid sequence WTSTRHT (SEQ ID NO: 33);
- f. a CDR-L3 having the amino acid sequence YNSYNT (SEQ ID NO: 34).

69. The conjugate of claim 66, wherein the antibody or antigen-binding fragment thereof comprises the following CDRs:

- a. a CDR-H1 having the amino acid sequence GYTFTNY (SEQ ID NO: 11);
- b. a CDR-H2 having the amino acid sequence NTHYGE (SEQ ID NO: 12);
- c. a CDR-H3 having the amino acid sequence RRGYDWYFDV (SEQ ID NO: 13);
- d. a CDR-L1 having the amino acid sequence RASQDINSYLS (SEQ ID NO: 14);
- e. a CDR-L2 having the amino acid sequence RANRLES (SEQ ID NO: 15); and
- f. a CDR-L3 having the amino acid sequence QQYDESPWT (SEQ ID NO: 16).

70. The conjugate of any one of claims 66-69 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.

71. The conjugate of claim 70, wherein the antibody or antigen-binding fragment thereof is a humanized antibody or antigen-binding fragment thereof.

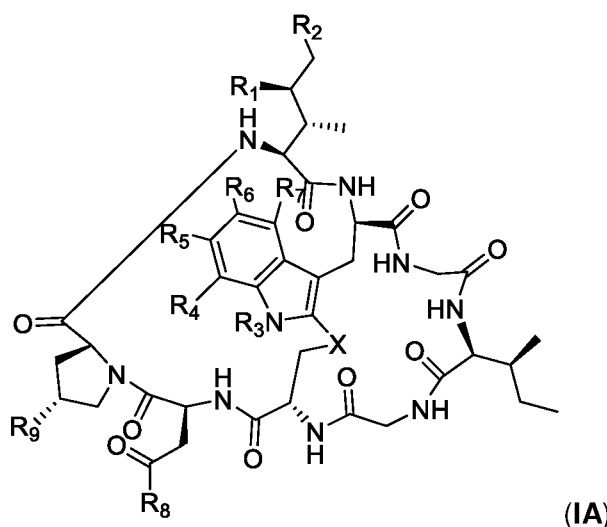
72. The conjugate of any one of claims 66-71, wherein the antibody has an isotype selected from the group consisting of IgG, IgA, IgM, IgD, and IgE.

73. The conjugate of claim 72, wherein the IgG is IgG1 or IgG4.

74. The conjugate of any one of claims 66-72, wherein Cy is an amatoxin (Am) represented by formula (I)

wherein Am comprises exactly one R_C substituent.

75. The conjugate of claim 74, wherein Am is an amatoxin represented by formula (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 , when present, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocycloalkyl 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 -SO₂-;

R_C is -L-Z;

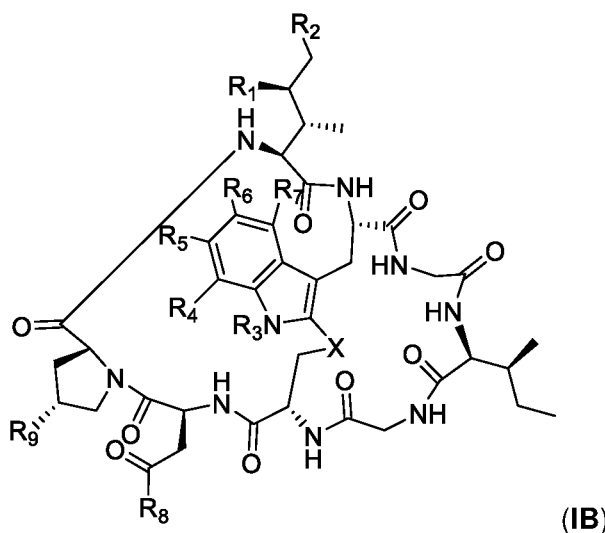
R_D is optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ heteroalkyl, optionally substituted C₂-C₆ alkenyl, optionally substituted C₂-C₆ heteroalkenyl, optionally substituted C₂-C₆ alkynyl, optionally substituted C₂-C₆ heteroalkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

L is optionally substituted C₁-C₆ alkylene, optionally substituted C₁-C₆ heteroalkylene, optionally substituted C₂-C₆ alkenylene, optionally substituted C₂-C₆ heteroalkenylene, optionally substituted C₂-C₆ alkynylene, optionally substituted C₂-C₆ heteroalkynylene, optionally substituted cycloalkylene, optionally substituted heterocycloalkylene, optionally substituted arylene, optionally substituted heteroarylene, a dipeptide, -C(=O)-, a peptide, or a combination thereof;

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; and

wherein Am comprises exactly one R_C substituent.

76. The conjugate of claim 74, wherein Am is an amatoxin represented by formula (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 , when present, together with the oxygen atoms to which they are bound, combine to form an optionally substituted 5-membered heterocycloalkyl 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;

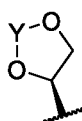
L is optionally substituted C_1 - C_6 alkylene, optionally substituted C_1 - C_6 heteroalkylene, optionally substituted C_2 - C_6 alkenylene, optionally substituted C_2 - C_6 heteroalkenylene, optionally substituted C_2 - C_6 alkynylene, optionally substituted C_2 - C_6 heteroalkynylene, optionally substituted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

heterocycloalkylene, optionally substituted arylene, optionally substituted heteroarylene, a dipeptide, $-C(=O)-$, a peptide, or a combination thereof; 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.

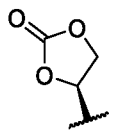
77. The conjugate of claim 71 or 72, wherein R_A and R_B , together with the oxygen atoms to which they are bound, combine to form a 5 membered heterocycloalkyl group of formula:



wherein Y is $-C(=O)-$, $-C(=S)-$, $-C(=NR_E)-$, or $-C(R_E R_{E'})-$; 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 .

78. The conjugate of claim 77, wherein R_A and R_B , together with the oxygen atoms to which they are bound, combine to form:

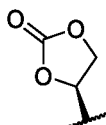


79. The conjugate of claim 75 or 76, wherein:

(a) 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 ;

R₈ is OH or NH₂; and

R₉ is H or OH;

(b) R₁ and R₂ are each independently H or OH;

R₃ is R_C;

R₄, R₆, and R₇ are each H;

R₅ is H, OH, or OC₁-C₆ alkyl;

R₈ is OH or NH₂; and

R₉ is H or OH;

(c) R₁ and R₂ are each independently H or OH;

R₃, R₆, and R₇ are each H;

R₄ and R₅ are each independently H, OH, OR_C, or R_C;

R₈ is OH or NH₂; and

R₉ is H or OH;

or

(c) R₁ and R₂ are each independently H or OH;

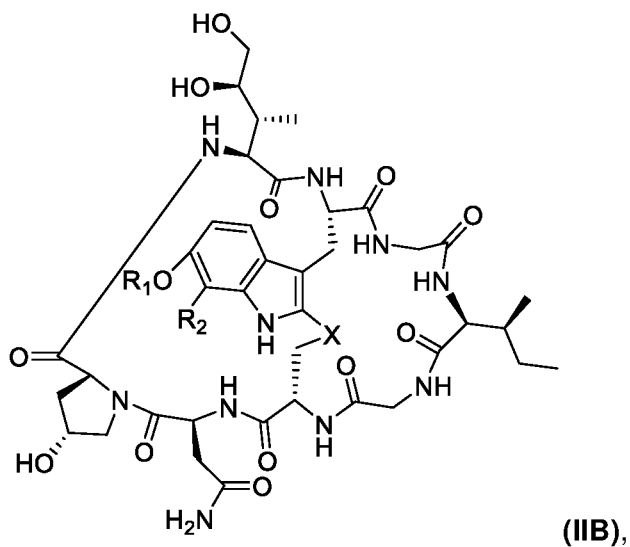
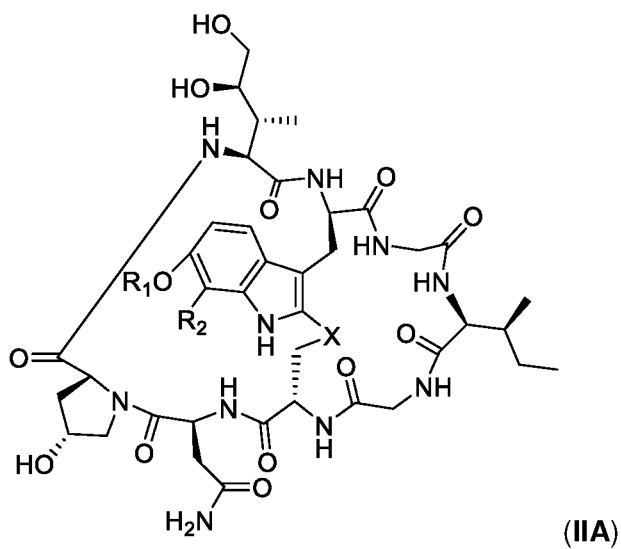
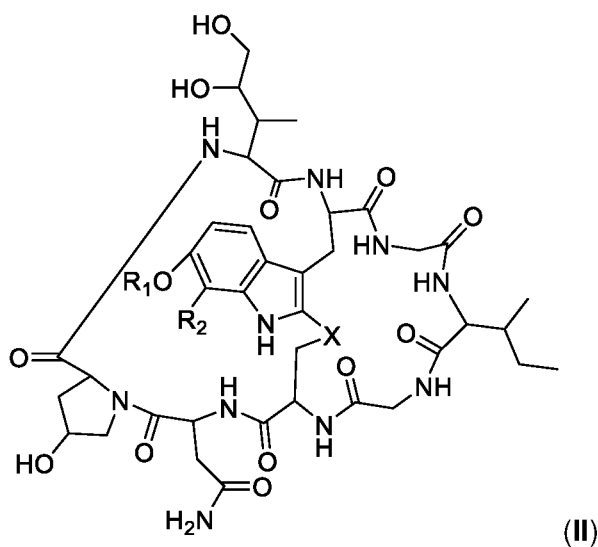
R₃, R₆, and R₇ are each H;

R₄ and R₅ are each independently H or OH;

R₈ is OR_C or NHR_C; and

R₉ is H or OH.

80. The conjugate of any one of claims 66-72, wherein Cy is an amatoxin (Am) represented by formula (II), formula (IIA), or formula (IIB)



wherein X is S, SO, or SO₂;

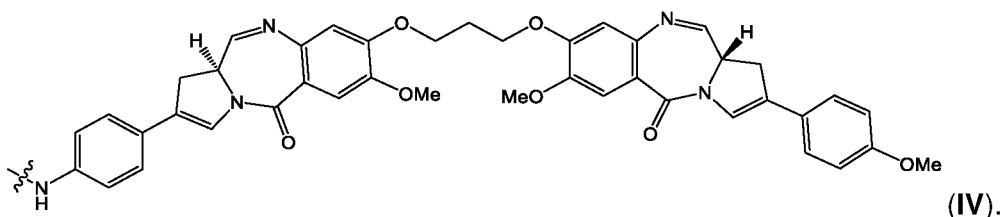
R_1 is H or a linker covalently bound to the antibody or antigen-binding fragment thereof through a chemical moiety Z, formed from a coupling reaction between a reactive substituent present on the linker and a reactive substituent present within an antibody, or antigen-binding fragment thereof; and

R_2 is H or a linker covalently bound to the antibody or antigen-binding fragment thereof through a chemical moiety Z, formed from a coupling reaction between a reactive substituent present on the linker and a reactive substituent present within an 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.

81. The conjugate of any one of claims 66-72, wherein:

- (a) Cy is a maytansinoid selected from the group consisting of DM1 and DM4;
- (b) Cy is an auristatin selected from the group consisting of monomethyl auristatin E and monomethyl auristatin F;
- (c) Cy is an anthracycline selected from the group consisting of daunorubicin, doxorubicin, epirubicin, and idarubicin; or
- (d) Cy is a pyrrolobenzodiazepine dimer derivative represented by formula (IV)



82. A pharmaceutical composition comprising the conjugate of any one of claims 66-80 and a pharmaceutically acceptable excipient.

83. The pharmaceutical composition of claim 82, wherein the pharmaceutical composition is formulated for transdermal, subcutaneous, intravenous, intramuscular, intraocular, intratumoral, parenteral, intrathecal or intracerebroventricular administration to a human patient.

84. The pharmaceutical composition of claim 83, wherein the pharmaceutical composition is formulated for intravenous administration to a human patient.

85. A method of depleting a population of CD5+ cells in a human patient, the method comprising administering to the patient an effective amount of an anti-CD5 antibody or antigen-binding fragment thereof.

86. A method of depleting a population of CD5+ 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 anti-CD5 antibody, or antigen-binding fragment thereof.

87. A method of preventing rejection of a hematopoietic stem cell graft in a human patient in need of a hematopoietic stem cell transplant, the method comprising administering to the patient an effective amount of an anti-CD5 antibody, or antigen-binding fragment thereof, prior to the human patient receiving a transplant comprising hematopoietic stem cells.

88. A method of depleting a population of CD5+ 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 anti-CD5 antibody, or antigen-binding fragment thereof, prior to the patient receiving a transplant comprising hematopoietic stem cells.

89. A method comprising administering to a human patient a transplant comprising hematopoietic stem cells, wherein the patient has been previously administered an anti-CD5 antibody or antigen-binding fragment thereof, in an amount sufficient to deplete a population of CD5+ cells in the patient.

90. A method comprising:

- a. administering to a human patient an anti-CD5 antibody or antigen-binding fragment thereof in an amount sufficient to deplete a population of CD5+ cells in the patient; and
- b. subsequently administering to the patient a transplant comprising hematopoietic stem cells.

91. The method of any one of claims 85-90, wherein the antibody or antigen-binding fragment thereof is produced by the hybridoma cell line ATCC CRL 8000.

92. The method of any one of claims 85-90, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region CDR set (CDR1, CDR2, and

CDR3) and a light chain variable region CDR set (CDR1, CDR2, and CDR3) of antibody OKT1 produced by the hybridoma cell line having ATCC accession number CRL 8000.

93. The method of any one of claims 85-90, wherein said antibody or antigen-binding fragment thereof comprises the following variable domains:

- a. a V_L having the amino acid sequence
DIQMTQSPSSMSASLGDRVTITCRASQDINSYLSWFQQKPGKSPKTLIY
RANRL
VDGVPSRFSGSGSGTDYTLTISSLQYEDFGIYYCQQYDESPWTFGGGT
KLEIK (SEQ ID NO: 1); and
- b. a V_H having the amino acid sequence
QIQLVQSGPGLKPKGGSVRISCAASGYTFTNYGMNWVKQAPGKGLRW
MGWI
NTHTGEPTYADDFKGRFTFSLDTSKSTAYLQINSLRAEDTATYFCTRRG
YDWY FDVWGQGTTVTVSS (SEQ ID NO: 2); or
- c. V_L having the amino acid sequence
NIVMTQSPSSLSASVGDRVTITCQASQDVGTAVAWYQQKPDQSPKLLIY
WTSTRHTGVPDRFTGSGSGTDFTLTISLQPEDATYFCHQYNSYNTFG
SGTKLEIK (SEQ ID NO: 258); and
- d. V_H having the amino acid sequence
QVTLKESGPVLVKPTETLTCTFSGFSLSTSGMGVGWIRQAPGKGLE
WVAHIWWDDDVYYNP SLKSRLTITKDASKDQVSLKLSSVTAADTAVYYC
VRRRATGTGFDYWGGTTLTVSS (SEQ ID NO: 257).

94. The method of any one of claims 85-90, wherein said antibody or antigen-binding fragment thereof comprises the following complementarity determining regions (CDRs):

- a. a CDR-H1 having the amino acid sequence GYTFTNY (SEQ ID NO: 3);
- b. a CDR-H2 having the amino acid sequence NTHTGE (SEQ ID NO: 4);
- c. a CDR-H3 having the amino acid sequence RGYDWYFDV (SEQ ID NO: 5);
- d. a CDR-L1 having the amino acid sequence RASQDINSYLS (SEQ ID NO: 6);
- e. a CDR-L2 having the amino acid sequence RANRLVD (SEQ ID NO: 7);
and
- f. a CDR-L3 having the amino acid sequence QQYDESPWT (SEQ ID NO: 8); or

- g. a CDR-H1 having the amino acid sequence FSLSTSGMG (SEQ ID NO: 29);
- h. a CDR-H2 having the amino acid sequence WWDDD (SEQ ID NO: 30);
- i. a CDR-H3 having the amino acid sequence RRATGTGFDY (SEQ ID NO: 31);
- j. a CDR-L1 having the amino acid sequence QDVGTA (SEQ ID NO: 32);
- k. a CDR-L2 having the amino acid sequence WTSTRHT (SEQ ID NO: 33);
- l. a CDR-L3 having the amino acid sequence YNSYNT (SEQ ID NO: 34).

95. The method of any one of claims 85-90, wherein said antibody or antigen-binding fragment thereof comprises the following variable domains:

- a. a V_L having the amino acid sequence
DIQMTQSPSSLSASVGDRVTITCRASQDINSYLSWFQQKPGKAPKTLIYR
ANRL ESGVPSRFSGSGSGTDYTLTIS
SLQYEDFGIYYCQQYDESPWTFGGGTKLEIK (SEQ ID NO: 9); and
- b. a V_H having the amino acid sequence
EIQLVQSGGGLVKPGGSVRISCAASGYTFTNYGMNWVRQAPGKGLEW
MGWI
NTHYGEPTYADSFKGTRTFSLDDSKNTAYLQINSLRAEDTAVYFCTRRG
YDW YFDVWGQGGTTVTVSS (SEQ ID NO: 10).

96. The method of any one of claims 85-90, wherein said antibody or antigen-binding fragment thereof comprises the following CDRs:

- a. a CDR-H1 having the amino acid sequence GYTFTNY (SEQ ID NO: 11);
- b. a CDR-H2 having the amino acid sequence NTHYGE (SEQ ID NO: 12);
- c. a CDR-H3 having the amino acid sequence RRGYDWYFDV (SEQ ID NO: 13);
- d. a CDR-L1 having the amino acid sequence RASQDINSYLS (SEQ ID NO: 14);
- e. a CDR-L2 having the amino acid sequence RANRLES (SEQ ID NO: 15);
and
- f. a CDR-L3 having the amino acid sequence QQYDESPWT (SEQ ID NO: 16).

97. The method of any one of claims 85-96, wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of a monoclonal antibody, a polyclonal antibody, a humanized antibody, a bispecific antibody, a dual-variable

immunoglobulin domain, an intact antibody, 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.

98. The method of claim 97, wherein the antibody or antigen-binding fragment thereof is a humanized antibody, or an antigen-binding fragment thereof.

99. The method of any one of claims 85-98, wherein the antibody has an isotype selected from the group consisting of IgG, IgA, IgM, IgD, and IgE.

100. The method of claim 99, wherein the IgG is IgG1 or IgG4.

101. The method of any one of claims 85-100, wherein the antibody or antigen-binding fragment thereof is internalized by an immune cell following administration to the patient.

102. The method of any one of claims 85-101, wherein the antibody or antigen-binding fragment thereof is capable of promoting necrosis of an immune cell.

103. The method of any one of claims 85-100, wherein the antibody or antigen-binding fragment thereof is capable of recruiting one or more complement proteins to an immune cell upon administration to the patient.

104. The method of any one of claims 101-103, wherein the immune cell is selected from the group consisting of a T cell, B cell, and NK cell.

105. The method of any one of claims 87-104, wherein the transplant comprising hematopoietic stem cells is administered to the patient after the concentration of the antibody or antigen-binding fragment thereof has substantially cleared from the blood of the patient.

106. The method of claim 105, wherein:

(a) the transplant comprising hematopoietic stem cells is administered to the patient between 1 hour and 7 days after the concentration of the antibody or antigen-binding fragment thereof has substantially cleared from the blood of the patient;

(b) the transplant comprising hematopoietic stem cells is administered to the patient between 6 hours and 3 days after the concentration of the antibody or antigen-binding fragment thereof has substantially cleared from the blood of the patient;

(c) the transplant comprising hematopoietic stem cells is administered to the patient between 12 hours and 36 hours after the concentration of the antibody or antigen-binding fragment thereof has substantially cleared from the blood of the patient; or

(d) the transplant comprising hematopoietic stem cells is administered to the patient 24 hours after the concentration of the antibody or antigen-binding fragment thereof has substantially cleared from the blood of the patient.

107. The method of any one of claims 87-106, 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.

108. The method of any one of claims 87-107, wherein the hematopoietic stem cells are autologous with respect to the patient or the hematopoietic stem cells are allogeneic with respect to the patient.

109. The method of claim 108, wherein the hematopoietic stem cells are HLA-matched with respect to the patient or the hematopoietic stem cells are HLA-mismatched with respect to the patient.

110. The method of any one of claims 87-109, wherein the population of CD5+ cells comprises CD34+ cells.

111. The method of any one of claims 85, 86, and 88-110, wherein the population of CD5+ cells comprises T cells.

112. The method of any one of claims 87-111, 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.

113. The method of any one of claims 87-112, 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, myeloblasts, basophils, neutrophils, eosinophils, microglia, granulocytes,

monocytes, osteoclasts, antigen-presenting cells, macrophages, dendritic cells, natural killer cells, T lymphocytes, and B lymphocytes.

114. The method of any one of claims 85-113, wherein the patient is suffering from a stem cell disorder, a hemoglobinopathy disorder, a myelodysplastic disorder, an immunodeficiency disorder, a metabolic disorder, a cancer, and/or an autoimmune disorder.

115. The method of claim 114, wherein the hemoglobinopathy disorder is selected from the group consisting of sickle cell anemia, thalassemia, Fanconi anemia, aplastic anemia, and Wiskott-Aldrich syndrome.

116. The method of claim 114, wherein the immunodeficiency disorder is a congenital immunodeficiency or an acquired immunodeficiency.

117. The method of claim 116, wherein the acquired immunodeficiency is human immunodeficiency virus or acquired immune deficiency syndrome.

118. The method of claim 114, wherein the metabolic disorder is selected from the group consisting of glycogen storage diseases, mucopolysaccharidoses, Gaucher's Disease, Hurlers Disease, sphingolipidoses, and metachromatic leukodystrophy.

119. The method of claim 114, wherein the cancer is selected from the group consisting of leukemia, lymphoma, multiple myeloma, and neuroblastoma.

120. The method of claim 114, wherein the cancer is a hematological cancer.

121. The method of claim 114, wherein the cancer is acute myeloid leukemia, acute lymphoid leukemia, chronic myeloid leukemia, or chronic lymphoid leukemia.

122. The method of claim 114, wherein the cancer is multiple myeloma.

123. The method of claim 114, wherein the cancer is diffuse large B-cell lymphoma or non-Hodgkin's lymphoma.

124. The method of any one of claims 85-123, 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.

125. The method of claim 114, 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 spondylitis, 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.

126. The method of claim 114, wherein the autoimmune disorder is scleroderma, multiple sclerosis, ulcerative colitis, Crohn's disease, or Type 1 diabetes.

127. The method of any one of claims 114-126, wherein the method treats the disorder or cancer.