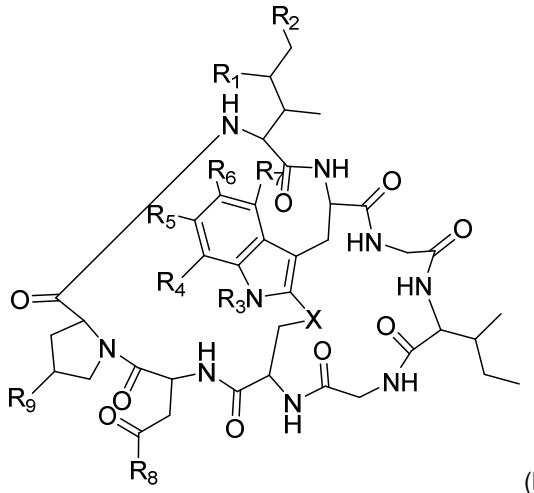
CLAIMS

1. Use of an effective amount of a drug-antibody conjugate comprising an anti-CD45 antibody and an amatoxin in the manufacture of a medicament for depleting a population of CD45+ cells in a human patient in need of a hematopoietic stem cell (HSC) transplant,

wherein the anti-CD45 antibody is an antibody or antigen-binding fragment thereof that specifically binds to human CD45, wherein the anti-CD45 antibody comprises an Fc domain and is internalized by a CD45+ cell, wherein the amatoxin is conjugated to the anti-CD45 antibody via a linker by way of a cysteine residue in a constant region of the antibody, and wherein the 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, when present, together with the oxygen atoms to which they are bound, combine to form a 5-membered heterocycloalkyl group;

R_3 is H, R_C, or R_D;

R_4 is H, OH, OR_C, or OR_D;

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

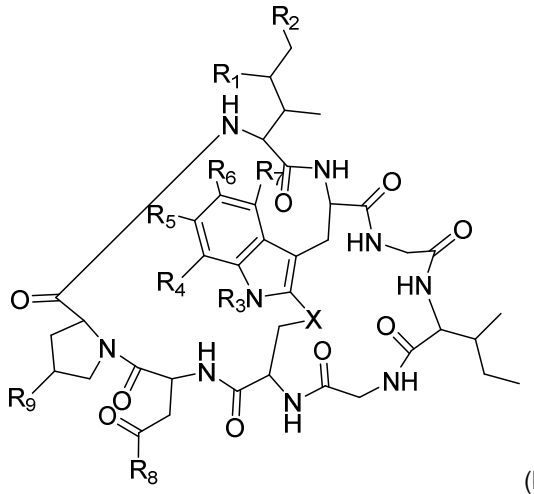
L is a linker, which is C_1-C_6 alkylene, C_1-C_6 heteroalkylene, C_2-C_6 alkenylene, C_2-C_6 heteroalkenylene, C_2-C_6 alkynylene, C_2-C_6 heteroalkynylene, or comprises a peptide; and

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

wherein the amatoxin comprises exactly one R_C substituent.

2. Use of an effective amount of a drug-antibody conjugate comprising an anti-CD45 antibody and an amatoxin in the manufacture of a medicament for conditioning a human patient for receiving a hematopoietic stem cell (HSC) transplant,

wherein the anti-CD45 antibody is an antibody or antigen-binding fragment thereof that specifically binds to human CD45, wherein the anti-CD45 antibody comprises an Fc domain and is internalized by a CD45+ cell, wherein the amatoxin is conjugated to the anti-CD45 antibody via a linker by way of a cysteine residue in a constant region of the antibody, and wherein the amatoxin is 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, when present, together with the oxygen atoms to which they are bound, combine to form a 5-membered heterocycloalkyl group;

R_3 is H, R_C, or R_D;

R_4 is H, OH, OR_C, or OR_D;

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

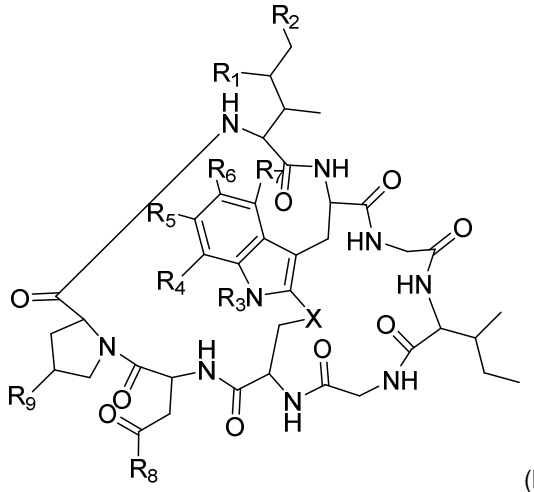
L is a linker, which is C_1-C_6 alkylene, C_1-C_6 heteroalkylene, C_2-C_6 alkenylene, C_2-C_6 heteroalkenylene, C_2-C_6 alkynylene, C_2-C_6 heteroalkynylene, or comprises a peptide; and

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

wherein the amatoxin comprises exactly one R_C substituent.

3. Use of an effective amount of a drug-antibody conjugate comprising an anti-CD45 antibody and an amatoxin in the manufacture of a medicament for use in a method of promoting engraftment of a hematopoietic stem cell (HSC) transplant in a human patient,

wherein the anti-CD45 antibody is an antibody or antigen-binding fragment thereof that specifically binds to human CD45, wherein the anti-CD45 antibody comprises an Fc domain and is internalized by a CD45+ cell, wherein the amatoxin is conjugated to the anti-CD45 antibody via a linker by way of a cysteine residue in a constant region of the antibody, and wherein the amatoxin is 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, when present, together with the oxygen atoms to which they are bound, combine to form a 5-membered heterocycloalkyl group;

R_3 is H, R_C, or R_D;

R_4 is H, OH, OR_C, or OR_D;

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

L a linker, which is C_1-C_6 alkylene, C_1-C_6 heteroalkylene, C_2-C_6 alkenylene, C_2-C_6 heteroalkenylene, C_2-C_6 alkynylene, C_2-C_6 heteroalkynylene, or comprises a peptide; and

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

wherein the amatoxin comprises exactly one R_C substituent.

4. The use of any one of claims 1-3, wherein the HSC transplant comprises allogeneic cells.

5. The use of any one of claims 1-4, wherein the anti-CD45 antibody is capable of specifically binding to CD45RO, and wherein the antibody is internalized by a CD45RO+ cell.

6. The use of any one of claims 1-5, wherein the anti-CD45 antibody is a human antibody or a humanized antibody.

7. The use of any one of claims 1-6, wherein the antibody has an IgG1 isotype.

8. The use of any one of claims 1-7, wherein the medicament is for use in conjunction with a transplant comprising hematopoietic stem cells.

9. The use of claim 8, 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.

10. The use of claim 8, 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.

11. The use of claim 9 or claim 10, 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.

12. The use of any one of claims 1-11, wherein the human patient has a stem cell disorder.

13. The use of claim 12, wherein the stem cell disorder is a hematological cancer or an autoimmune disease.

14. The use of any one of claims 1-11, wherein the human patient has a hematological cancer.

15. The use of claim 14, wherein the hematological cancer is leukemia or lymphoma.

16. The use of claim 15, wherein the hematological cancer is acute myeloid leukemia, acute lymphoid leukemia, chronic myeloid leukemia, diffuse large B-cell lymphoma, or non-Hodgkin’s lymphoma.

17. The use of any one of claims 1-11, wherein the human patient has an autoimmune disorder.

18. The use of claim 17, wherein the autoimmune disorder is scleroderma.

19. The use of claim 17, wherein the autoimmune disorder is multiple sclerosis.

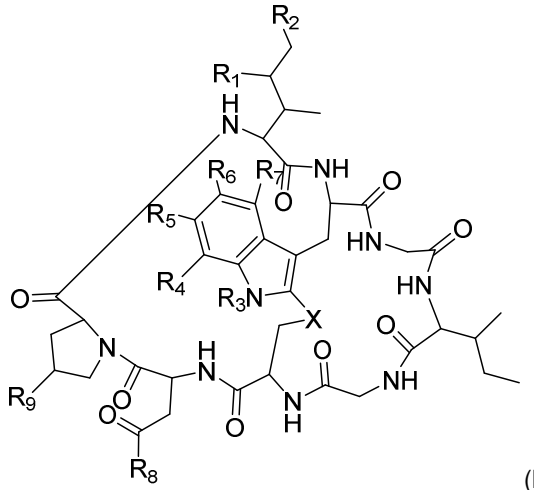
20. The use of claim 17, wherein the autoimmune disorder is ulcerative colitis.

21. The use of claim 17, wherein the autoimmune disorder is Crohn's disease.

22. The use of claim 17, wherein the autoimmune disorder is Type 1 diabetes.

23. Use of an effective amount of a drug-antibody conjugate comprising an anti-CD45 antibody and an amatoxin in the manufacture of a medicament for conditioning a human patient for receiving a hematopoietic stem cell (HSC) transplant, wherein the human patient has a stem cell disorder,

wherein the anti-CD45 antibody is an antibody or antigen-binding fragment thereof that specifically binds to human CD45, wherein the anti-CD45 antibody comprises an Fc domain and is internalized by a CD45+ cell, wherein the amatoxin is conjugated to the anti-CD45 antibody via a linker by way of a cysteine residue in a constant region of the antibody, and wherein the 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, when present, together with the oxygen atoms to which they are bound, combine to form a 5-membered heterocycloalkyl group;

R_3 is H, R_C, or R_D;

R_4 is H, OH, OR_C, or OR_D;

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

L is a linker, which is C_1-C_6 alkylene, C_1-C_6 heteroalkylene, C_2-C_6 alkenylene, C_2-C_6 heteroalkenylene, C_2-C_6 alkynylene, C_2-C_6 heteroalkynylene, or comprises a peptide; and

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

wherein the amatoxin comprises exactly one R_C substituent.

24. The use of claim 23, wherein the antibody is capable of specifically binding to CD45RO, and wherein the antibody is internalized by a CD45RO+ cell.

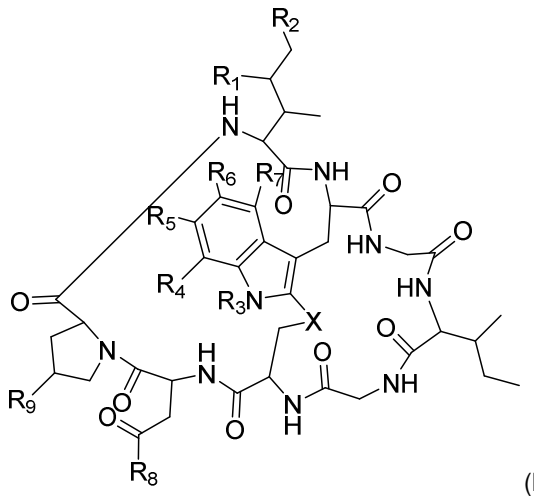
25. The use of claim 23 or claim 24, wherein the medicament is for use in conjunction with a transplant comprising hematopoietic stem cells, wherein the transplant comprising hematopoietic cells is to be administered to the human patient once the drug-antibody conjugate has substantially cleared from the blood of the human patient.

26. The use of any one of claims 23-25, wherein the stem cell disorder is a hematological cancer or an autoimmune disease.

27. The use of claim 26, wherein the hematological cancer is lymphoma or leukemia.

28. Use of an effective amount of a drug-antibody conjugate comprising an anti-CD45 antibody and an amatoxin in the manufacture of a medicament for promoting engraftment of a hematopoietic stem cell transplant in a human patient having a hematological cancer,

wherein the anti-CD45 antibody is an antibody or antigen-binding fragment thereof that specifically binds to human CD45, wherein the anti-CD45 antibody comprises an Fc domain and is internalized by a CD45+ cell, wherein the amatoxin is conjugated to the anti-CD45 antibody via a linker by way of a cysteine residue in a constant region of the antibody, and wherein the amatoxin is 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, when present, together with the oxygen atoms to which they are bound, combine to form a 5-membered heterocycloalkyl group;

R_3 is H, R_C, or R_D;

R_4 is H, OH, OR_C, or OR_D;

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

L a linker, which is C_1-C_6 alkylene, C_1-C_6 heteroalkylene, C_2-C_6 alkenylene, C_2-C_6 heteroalkenylene, C_2-C_6 alkynylene, C_2-C_6 heteroalkynylene, or comprises a peptide; and

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

wherein the amatoxin comprises exactly one R_C substituent.

29. The use of claim 28, wherein the antibody is capable of specifically binding to CD45RO, and wherein the antibody is internalized by a CD45RO+ cell.

30. The use of claim 28 or claim 29, wherein the medicament is for use in conjunction with a transplant comprising hematopoietic stem cells, wherein the transplant comprising hematopoietic cells is to be administered to the human patient once the drug-antibody conjugate has substantially cleared from the blood of the human patient.

31. The use of any one of claims 1-30, wherein

R_1 is OH;

R_2 is OH;

R_3 is H;

R_4 is H;

R_5 is H, OH, OR_C, or R_C;

$R_{6,}$is H;

R_7 is H;

R_8 is OH, NH_2, OR_C, or NHR_C;

R_9 is OH;

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

R_C is -L-Z;

L is a linker, which is C_1-C_6 alkylene, C_1-C_6 heteroalkylene, C_2-C_6 alkenylene, C_2-C_6 heteroalkenylene, C_2-C_6 alkynylene, C_2-C_6 heteroalkynylene, or comprises a peptide; 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 the amatoxin comprises exactly one R_C substituent.

32. The use of any one of claims 1-31, wherein R_5 is OR_C.

33. The use of any one of claims 1-31, wherein R_8 is NHR_C.

34. The use of any one of claims 1-33, wherein L is a linker which is C_1-C_6 alkylene, C_1-C_6 heteroalkylene, C_2-C_6 alkenylene, C_2-C_6 heteroalkenylene, C_2-C_6 alkynylene, or C_2-C_6 heteroalkynylene.

35. The use of any one of claims 1-33, wherein L is a linker which comprises a peptide.

36. The use of any one of claims 1-35, wherein the cysteine residue is selected from the group consisting of Cys118, Cys239, and Cys265, wherein the numbering of residues is based on the Kabat numbering system.

37. The use of any one of claims 1-35, wherein the cysteine residue is selected from the group consisting of Cys261, Cys321, Cys367, and Cys425, wherein the numbering of residues is based on the Kabat numbering system.