

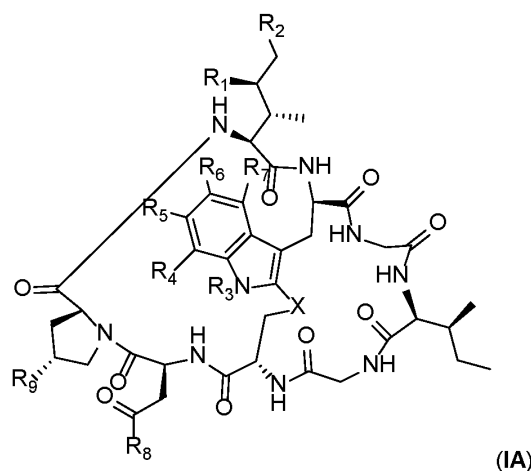
CLAIMS

1. A method of depleting a population of CD45+ cells in a human patient having an autoimmune disease, the method comprising administering to the patient having the autoimmune disease an effective amount of an antibody-drug conjugate (ADC) comprising an anti-CD45 antibody, or antigen binding portion thereof, conjugated to a cytotoxin via a linker.
2. A method of conditioning a human patient having an autoimmune disease for receiving a hematopoietic stem cell (HSC) transplant, the method comprising administering to the human patient having the autoimmune disease an antibody-drug conjugate (ADC) comprising an anti-CD45 antibody, or antigen binding portion thereof, conjugated to a cytotoxin via a linker.
3. The method of claim 1 or 2, wherein the autoimmune disease is an inflammatory arthritis (for example, rheumatoid arthritis), autoimmune encephalitis, scleroderma, multiple sclerosis, type 1 diabetes, or systemic sclerosis.
4. The method of any one of claims 1-3, further comprising administering a transplant comprising hematopoietic stem cells (HSCs) to the patient.
5. The method of claim 4, wherein the HSC transplant is an autologous HSC transplant (autoH SCT).
6. The method of claim 4 or 5, wherein the anti-CD45 ADC is administered to the patient about three days prior to the patient receiving the transplant comprising HSCs
7. The method of any one of claim 4-6, wherein the HSC transplant is administered to the patient after the anti-CD45 ADC has substantially cleared from the blood of the human patient.
8. A method of treating a patient having scleroderma or multiple sclerosis, said method comprising administering an anti-CD45 antibody drug conjugate (ADC) to the patient having scGVHD, such that the scGVHD is treated, wherein the anti-CD45 ADC comprises an anti-CD45 antibody, or fragment thereof, conjugated to a cytotoxin via a linker.
9. The method of any one of the preceding claims, wherein the anti-CD45 ADC is administered to the patient as a single dose or as a fractionated dose.
10. The method of any one of the preceding claims, wherein the patient does not require treatment for the autoimmune disease following transplantation.

11. The method of any one of claim 1-10, wherein the patient has multiple sclerosis, and wherein the patient does not require treatment with natalizumab, dimethyl fumarate, or monomethyl fumarate following transplantation.
12. The method of any one of claim 1-10, wherein the patient has arthritis, and wherein the patient does not require treatment with a TNF inhibitor following transplantation.
13. The method of claim 12, wherein the TNF inhibitor is an anti-TNF α antibody.
14. The method of any one of claims 1-13, wherein the patient enters remission for at least 1 year following transplantation.
15. The method of any one of claims 1-13, wherein the patient enters remission for at least 2 years following transplantation.
16. The method of any one of claims 1-13, wherein the patient enters remission for at least 5 years following transplantation.
17. The method of any one of claims 14-16, wherein the remission is clinical remission.
18. The method of any one of claims 14-16, wherein the remission is biochemical remission.
19. The method of any one of claims 14-16, wherein the remission is histologic remission.
20. The method of any one of the preceding claims, wherein the anti-CD45 antibody is a chimeric antibody or a humanized antibody.
21. The method of any one of the preceding claims, wherein the anti-CD45 antibody is a human antibody.
22. The method of any one of the preceding claims, wherein the anti-CD45 antibody is intact.
23. The method of any one of the preceding claims, wherein the anti-CD45 antibody or antigen-binding portion thereof is selected from the group consisting of a monoclonal antibody or antigen-binding portion thereof, a polyclonal antibody or antigen-binding portion thereof, a bispecific antibody or antigen-binding portion 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.

24. The method of any one of the preceding claims, wherein the anti-CD45 antibody has an isotype selected from the group consisting of IgG, IgA, IgM, IgD, and IgE.
25. The method of claim 24, wherein the anti-CD45 antibody contains a human IgG1, IgG2, IgG3, or IgG4 isotype Fc domain.
26. The method of any one of the preceding claims, wherein the anti-CD45 antibody, or antigen binding portion thereof, comprises an Fc domain, and wherein the anti-CD45 antibody, or antigen binding portion thereof, is conjugated to the cytotoxin by way of a cysteine residue in the Fc domain.
27. The method of claim 26, wherein the cysteine residue is introduced by way of an amino acid substitution in the Fc domain.
28. The method of claim 27, wherein the amino acid substitution is D265C (EU numbering).
29. The method of any one of the preceding claims, wherein the cytotoxin is selected from the group consisting of an 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.
30. The method of any one of claims 1-28, wherein the cytotoxin is an auristatin.
31. The method of claim 30, wherein the auristatin is MMAE or MMAF.
32. The method of any one of claim 1-28, wherein the cytotoxin is a pyrrolobenzodiazepine, a pyrrolobenzodiazepine dimer, an indolinobenzodiazepine, an indolinobenzodiazepine dimer, or an indolinobenzodiazepine pseudodimer.
33. The method of any one of claim 1-28, wherein the cytotoxin is an RNA polymerase inhibitor.
34. The method of claim 33, wherein the RNA polymerase inhibitor is an amatotoxin.

35. The method of claim 34, wherein the amatoxin is represented by formula (IA)



wherein R₁ is H, OH, OR_A, or OR_C;

R₂ 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 heterocycloalkyl group;

R₃ is H, R_C, or R_D;

R₄, R₅, R₆, and R₇ are each independently H, OH, OR_C, OR_D, R_C, or R_D;

R₈ is OH, NH₂, OR_C, OR_D, NHR_C, or NR_CR_D;

R₉ is H, OH, OR_C, or OR_D;

X is -S-, -S(O)-, or -SO₂-;

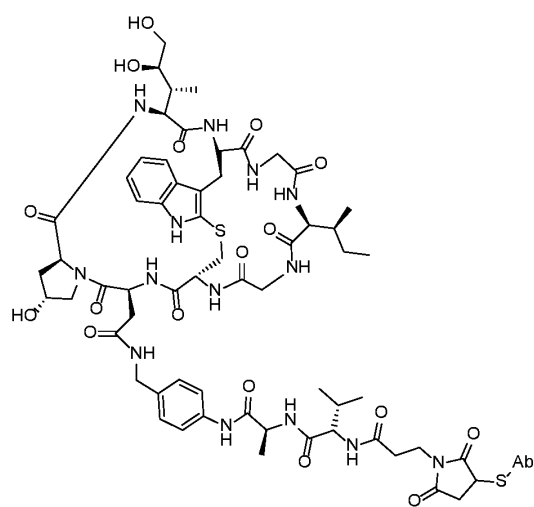
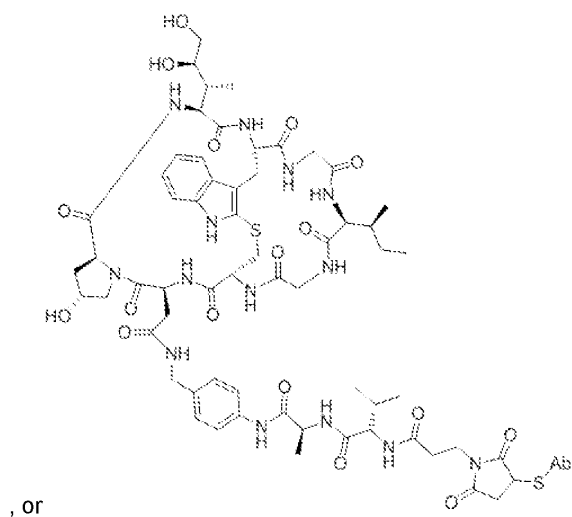
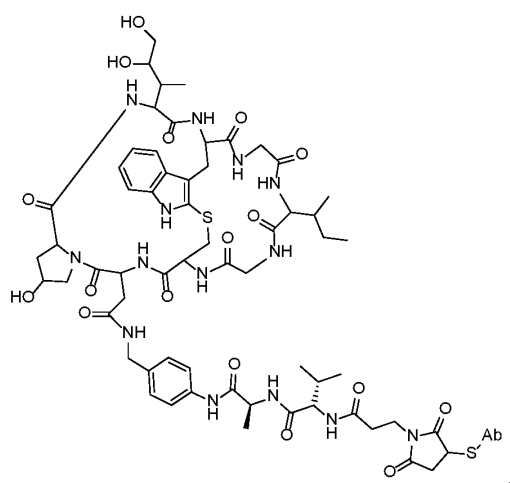
R_C is -L-Z;

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, or a combination thereof; and

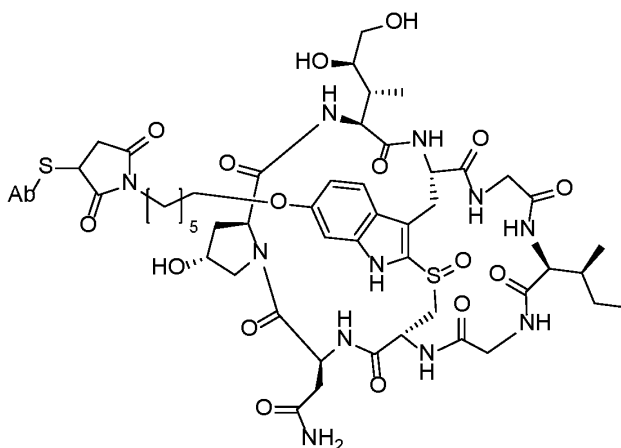
Z is a chemical moiety formed from a coupling reaction between a reactive substituent present on L and a reactive substituent present within the antibody or antigen-binding fragment thereof, wherein Am comprises exactly one R_C substituent.

36. The method of any one of the preceding claims, wherein the anti-CD45 ADC has a formula of

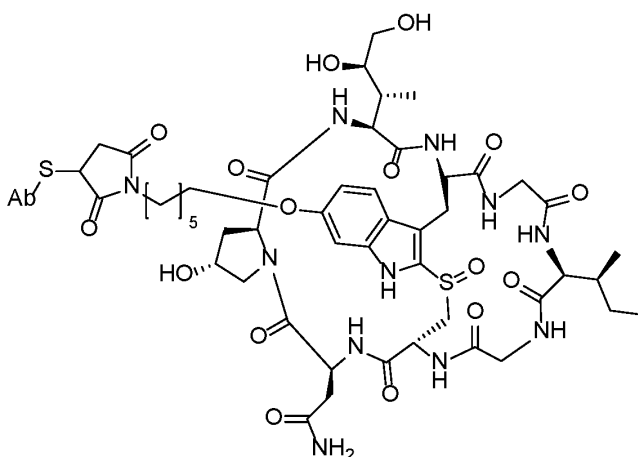


, wherein Ab represents the anti-CD45 antibody.

37. The method of any one of the preceding claims, wherein the anti-CD45 ADC has a formula of



or



, wherein Ab represents the anti-CD45 antibody.

38. The method of claim 33, wherein the RNA polymerase inhibitor is an amanitin.

39. A method of depleting a population of CD45+ cells in a human patient having an autoimmune disease, the method comprising administering to the patient having the autoimmune disease an effective amount of an engineered toxin body targeting CD45.

40. The method of claim 39, wherein the engineered toxin body comprises an antibody, or antigen binding fragment thereof, that specifically binds to CD45.

41. The method of claim 39, wherein the engineered toxin body comprises an scFv that specifically binds to CD45.
42. The method of any one of claims 39-41, wherein the engineered toxin body comprises a protein-based toxin.
43. The method of claim 42, wherein the protein-based toxin is a protein synthesis inhibitor, e.g., a ribosome inactivating protein.
44. The method of claim 42 or 43, wherein the protein-based toxin is selected from the group consisting of Shiga toxin, Shiga-like toxin A subunit, saporin, ricin, and mutants, fragments, and derivatives thereof.