[0008a] According to an aspect, there is provided an antibody conjugate comprising an antibody that specifically binds to CD74 linked site-specifically to at least one payload moiety, and wherein the payload is conjugated to a non-natural amino acid at a site selected from the group consisting of HC-F404, HC-K121, HC-Y180, HC-F241, HC-221, LC-T22, LC-S7, LC-N152, LC-K42, LC-E161, LC-D170, HC-S136, HC-S25, HC-A40, HC-S119, HC-S190, HC-K222, HC-R19, HC-Y52, or HC-S70, according to the Kabat, Chothia, or EU numbering scheme, either directly or indirectly, and wherein the antibody further comprises:

a. three heavy chain CDRs and three light chain CDRs of the V_H region SEQ ID NO: 236, and the V_L region SEQ ID NO: 256.

[0008b] According to another aspect there is provided a kit comprising an antibody conjugate described herein, and instructions for use of the antibody conjugate.

[0008c] According to another aspect there is provided a pharmaceutical composition comprising the antibody conjugate described herein and a pharmaceutically acceptable carrier.

[0008d] According to another aspect there is provided an antibody conjugate described herein, or a pharmaceutical composition described herein for use in treating or preventing a disease or condition in a subject

[0008e] According to another aspect there is provided an antibody conjugate described herein, or a pharmaceutical composition described herein for use in diagnosing a disease or condition in a subject.

WHAT IS CLAIMED IS:

1. An antibody conjugate comprising an antibody that specifically binds to CD74 linked site-specifically to at least one payload moiety, and wherein the payload is conjugated to a non-natural amino acid at a site selected from the group consisting of HC-F404, HC-K121, HC-Y180, HC-F241, HC-221, LC-T22, LC-S7, LC-N152, LC-K42, LC-E161, LC-D170, HC-S136, HC-S25, HC-A40, HC-S119, HC-S190, HC-K222, HC-R19, HC-Y52, or HC-S70, according to the Kabat, Chothia, or EU numbering scheme, either directly or indirectly, and wherein the antibody further comprises:

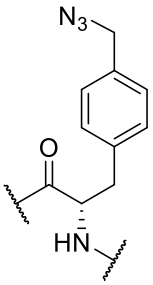
   a. three heavy chain CDRs and three light chain CDRs of the V_H region SEQ ID NO: 236, and the V_L region SEQ ID NO: 256.

2. The antibody conjugate of claim 1, wherein the non-natural amino acid is selected from the group consisting of p-acetyl-L-phenylalanine, O-methyl-L-tyrosine, an -3-(2-naphthyl)alanine, 3-methyl-phenylalanine, O-4-allyl-L-tyrosine, 4-propyl-L-tyrosine, a tri-O-acetyl-GlcNAcβ-serine, L-Dopa, fluorinated phenylalanine, isopropyl-L-phenylalanine, p-azido-L-phenylalanine, p-azidomethyl-L-phenylalanine, compound 56, p-acyl-L-phenylalanine, p-benzoyl-L-phenylalanine, L-phosphoserine, phosphonoserine, phosphonotyrosine, p-iodo-phenylalanine, p-bromophenylalanine, p-amino-L-phenylalanine, isopropyl-L-phenylalanine, and p-propargyloxy-phenylalanine.

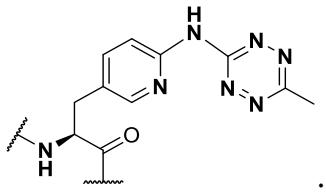
3. The antibody conjugate of claim 2, wherein the antibody is linked to the payload moiety via a linker that is hydrolytically stable.

4. The antibody conjugate of claim 2, wherein the antibody is linked to the payload moiety via a linker that is cleavable.

5. The antibody conjugate of any one of claims 2 to 4 wherein the non-natural amino acid residue is according to formula 30:

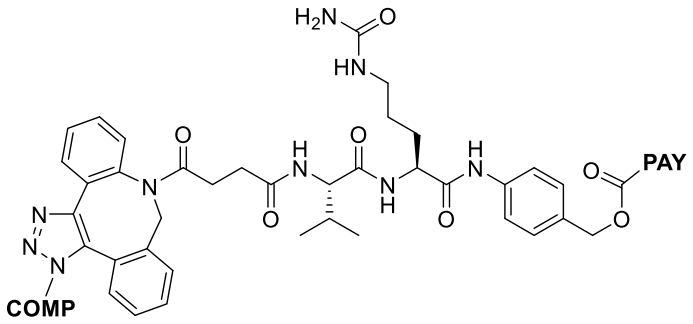


or formula 56:

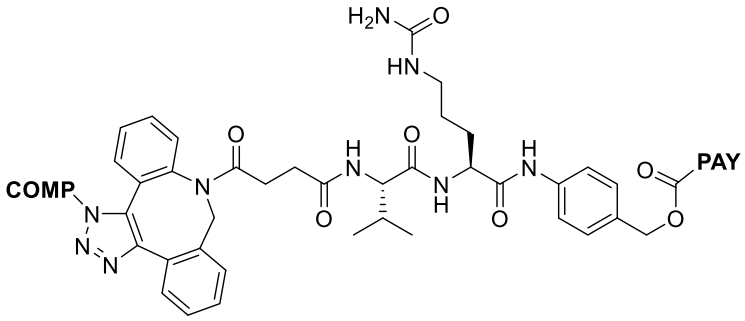


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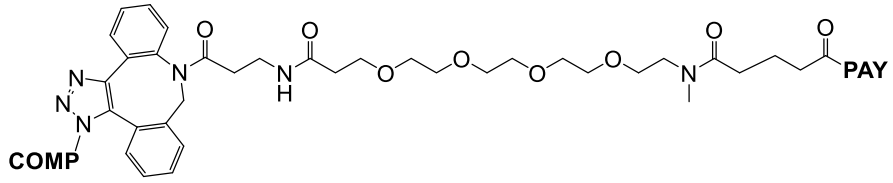
6. The antibody conjugate of any of the preceding claims according to any of formulas 101a-104b:



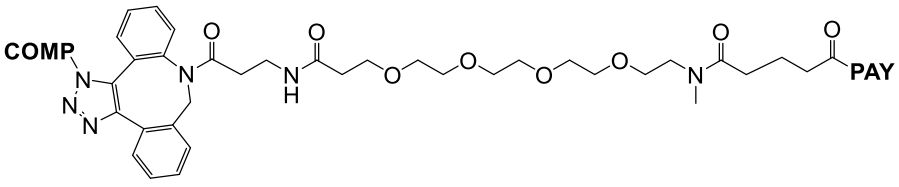
(101a)



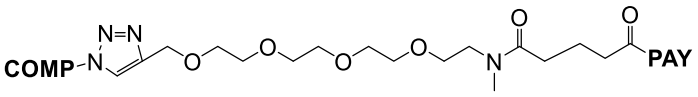
(101b)



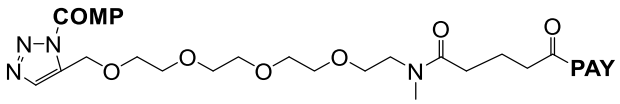
(102a)



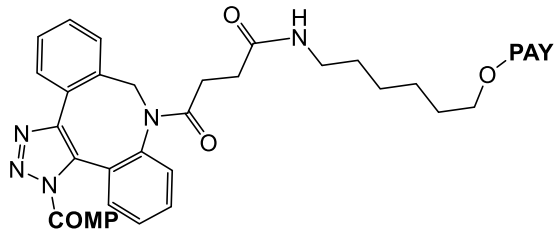
(102b)



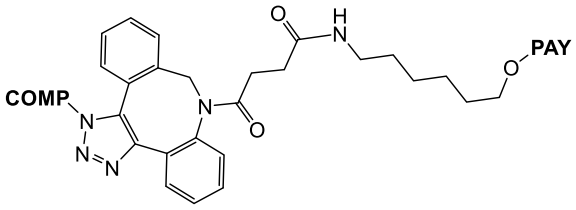
(103a)



(103b)



(104a)



(104b)

wherein **COMP** is an amino acid residue of the antibody bearing the indicated bond and **PAY** is a payload moiety.

7. The antibody conjugate of any of the preceding claims wherein the payload moiety is selected from the group consisting of maytansines, hemiasterlins, amanitins, and auristatins.

8. The antibody conjugate of any of the preceding claims wherein the payload moiety is selected from the group consisting of DM1, hemiasterlin, amanitin, MMAF, and MMAE.

9. The antibody conjugate of any of the preceding claims, wherein the antibody comprises:

a. a V_L comprising: a CDR-L1 comprising SEQ ID NO: 161; a CDR-L2 comprising SEQ ID NO: 181; and a CDR-L3 comprising SEQ ID NO: 201.

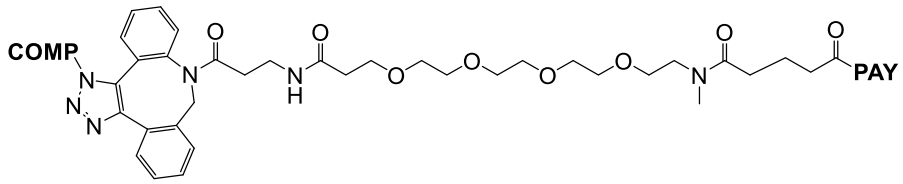
10. The antibody conjugate of any of the preceding claims, wherein the antibody comprises:

a. the V_H region is SEQ ID NO: 236, or the conservative modified variants, glycosylation variants, and the V_L region is SEQ ID NO: 256, or the conservative modified variants, glycosylation variants.

11. The antibody conjugate of claim 10, wherein the antibody comprises a non-natural amino acid at site HC-F404 according to the EU numbering scheme of Kabat.

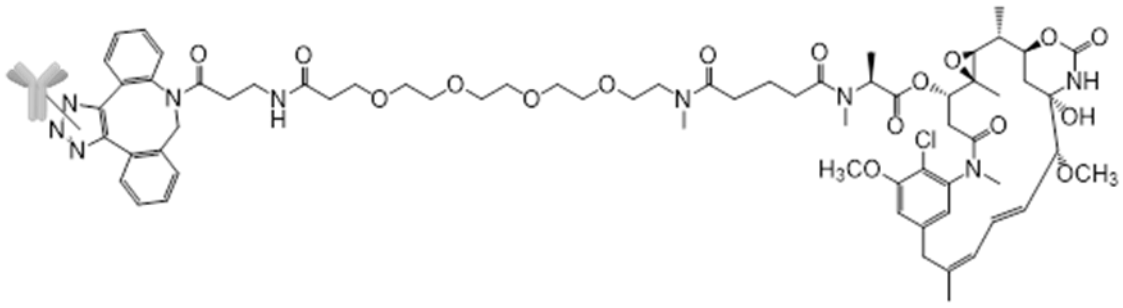
12. The antibody conjugate of claim 9, wherein the non-natural amino acid is para-azidomethylphenylalanine or p-azidomethyl-L-phenylalanine.

13. The antibody conjugate of claim 8, wherein the antibody conjugate has the formula of (102b):



wherein **COMP** is the non-natural amino acid residue of the antibody bearing the indicated bond and **PAY** is DM1.

14. The antibody conjugate of claim 13, wherein the antibody conjugate has the structure of **Conjugate A**:



and the antibody comprises a V_H region comprising SEQ ID NO: 236 and a V_L region comprising SEQ ID NO: 256.

15. The antibody conjugate of any of the preceding claims, further comprising at least one constant region domain.

16. The antibody conjugate of claim 15, wherein the constant region comprises a sequence selected from SEQ ID NOs: 304-305.

17. The antibody conjugate of any of the preceding claims, wherein the antibody is a monoclonal antibody.

18. The antibody conjugate of any of the preceding claims, wherein the antibody is an IgA, an IgD, an IgE, an IgG, or an IgM.

19. The antibody conjugate of any of the preceding claims, wherein the antibody is humanized or human.

20. The antibody conjugate of any of the preceding claims, wherein the antibody is aglycosylated.

21. The antibody conjugate of any of the preceding claims, wherein the antibody is an antibody fragment.

22. The antibody conjugate of claim 21, wherein the antibody fragment is selected from an Fv fragment, a Fab fragment, a $F(ab')_2$ fragment, a Fab′ fragment, an scFv (sFv) fragment, and an scFv-Fc fragment.

23. The antibody conjugate of claim 22, wherein the antibody is an scFv fragment.

24. The antibody conjugate of claim 23, wherein the scFv fragment comprises a sequence selected from SEQ ID NOs: 221-228.

25. The antibody conjugate of claim 22, wherein the antibody is an scFv-Fc fragment.

26. The antibody conjugate of claim 25, wherein the scFv-Fc fragment comprises SEQ ID NO: 229.

27. The antibody conjugate of any of the preceding claims, wherein the antibody has a k_a of at least 10^5 $M^{-1}\times sec^{-1}$ at a temperature of 25°C.

28. The antibody conjugate of any of the preceding claims, wherein the antibody has a k_d of 10^{-3} sec^{-1} or less at a temperature of 25°C.

29. The antibody conjugate of any of the preceding claims, wherein the antibody has a K_D of 10^{-9} M or less at a temperature of 25°C.

30. The antibody conjugate of any of the preceding claims, wherein the antibody is internalized after binding to CD74 on the surface of a cell.

31. The antibody conjugate of any of the preceding claims, wherein the Tm2 of the antibody is at least 75°C, 75.5°C, 76°C, 76.5°C, 77°C, 77.5°C, 78°C, 78.5°C, or 79°C.

32. The antibody conjugate of any of the preceding claims, wherein the Tm1 of the antibody is less than 61°C or less than 60°C.

33. A kit comprising an antibody conjugate of any of the preceding claims, and instructions for use of the antibody conjugate.

34. The kit of claim 33, wherein the antibody conjugate is lyophilized.

35. The kit of claim 34, further comprising a fluid for reconstitution of the lyophilized antibody conjugate.

36. A pharmaceutical composition comprising the antibody conjugate of any of claims 1 to 32 and a pharmaceutically acceptable carrier.

37. An antibody conjugate of any one of claims 1 to 32, or a pharmaceutical composition of claim 36 for use in treating or preventing a disease or condition in a subject.

38. An antibody conjugate of any one of claims 1 to 32, or a pharmaceutical composition of claim 36 for use in diagnosing a disease or condition in a subject.

39. The antibody conjugate or pharmaceutical composition of any of claims 37 or 38, wherein the disease or condition involves an upregulation of CD74 in a cancer, an autoimmune disease, an inflammatory disease, or an infection.

40. The antibody conjugate or pharmaceutical composition of claim 39, wherein the cancer is selected from multiple myeloma or pancreatic cancer.

41. The antibody conjugate or pharmaceutical composition of claim 39, wherein the disease or condition is B-cell lymphoma.

42. The antibody conjugate or pharmaceutical composition of claim 39, wherein the disease or condition is non-Hodgkin’s lymphoma.

43. The antibody conjugate or pharmaceutical composition of claim 39, wherein the disease or condition is leukemia.

44. The antibody conjugate of any of the preceding claims, wherein the antibody comprises:

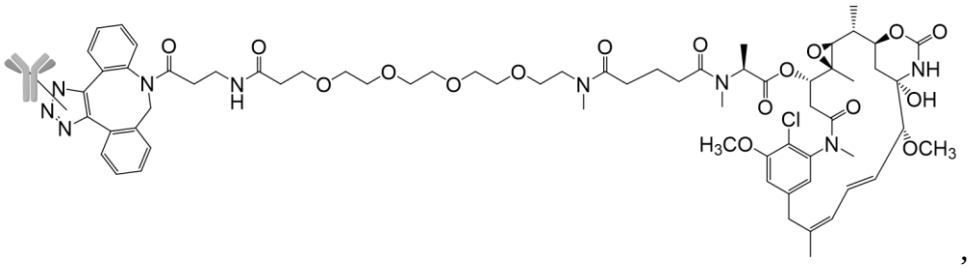
a. a VH comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 1 and 33; a CDR-H2 comprising at least one of SEQ ID NOs: 65 and 97; and a CDR-H3 comprising SEQ ID NO: 129.

45. The antibody conjugate of claim 1, wherein the antibody comprises:

a. a VH comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 1 and 33; a CDR-H2 comprising at least one of SEQ ID NOs: 65 and 97; and a CDR-H3 comprising SEQ ID NO: 129; and a VL comprising: a CDR-L1 comprising SEQ ID NO: 161; a CDR-L2 comprising SEQ ID NO: 181; and a CDR-L3 comprising SEQ ID NO: 201.

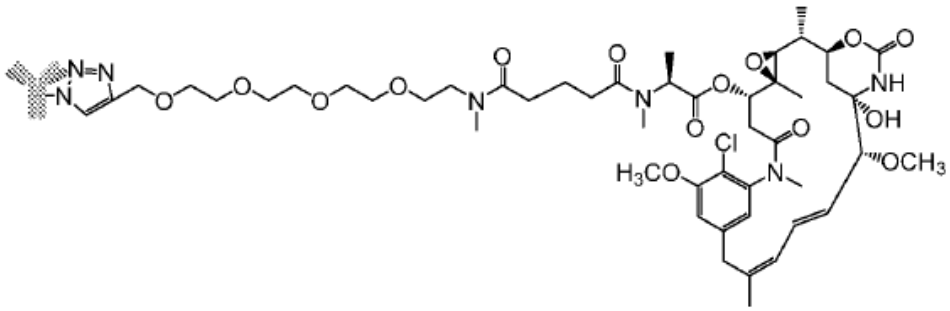
46. The antibody conjugate of claim 2, wherein the antibody conjugate has the structure of:

Conjugate A:



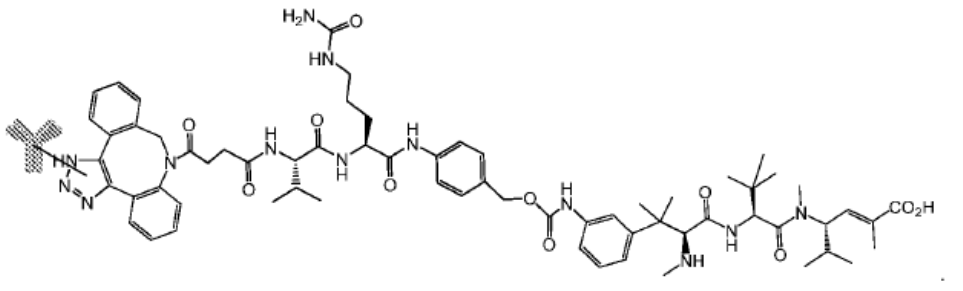
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Conjuage B:



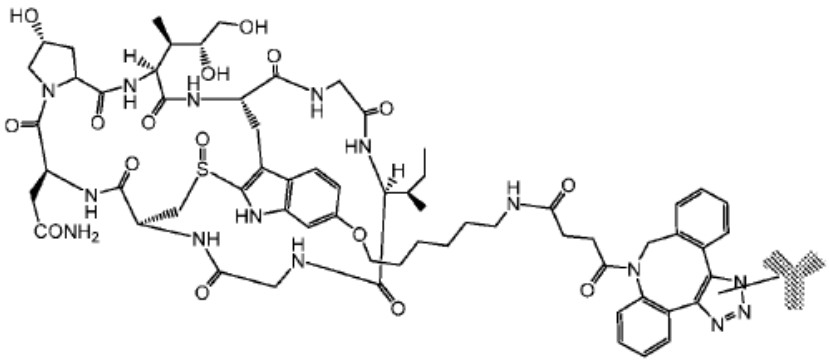
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Conjugate C:



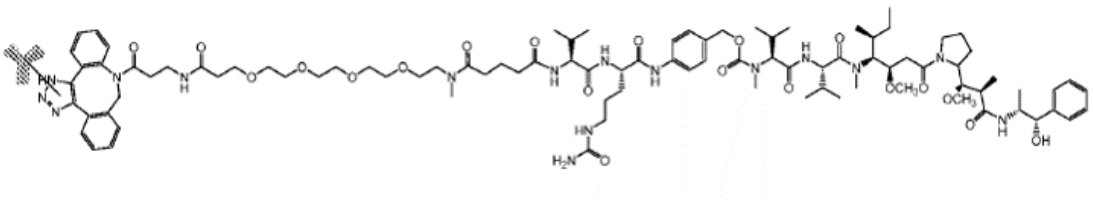
,

Conjugate D



, or

Conjugate F:



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