[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, ~~according to the Kabat, Chothia, or EU numbering scheme,~~ and wherein the payload is conjugated to ~~the~~ 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~~, according to the Kabat, Chothia, or EU numbering scheme~~, and wherein the payload is conjugated to ~~the~~ 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.

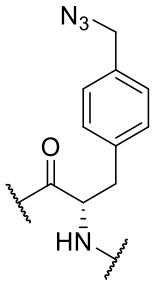
~~2. The antibody of claim 1, wherein the antibody further comprises a non-natural amino acid at a site selected from the group consisting of HC-F404, HC-K121, HC-Y180, HC-F241, HC-221, LC-T22, LC-S7, LC-N152, LC-K42, LC-E161, LC-D170, HC-S136, HC-S25, HC-A40, HC-S119, HC-S190, HC-K222, HC-R19, HC-Y52, or HC-S70.~~

~~3.~~2. The antibody conjugate of claim 1 ~~or 2~~, 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.

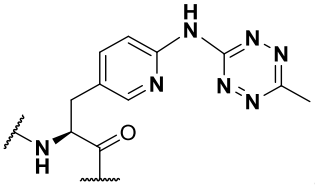
~~4.~~3. The antibody conjugate of claim ~~3~~2, wherein the antibody is linked to the payload moiety via a linker that is hydrolytically stable.

~~5.~~4. The antibody conjugate of claim ~~3~~2, wherein the antibody is linked to the payload moiety via a linker that is cleavable.

~~6.~~5. The antibody conjugate of any one of claims ~~3~~ 2 to ~~5~~ 4 wherein the non-natural amino acid residue is according to formula 30:

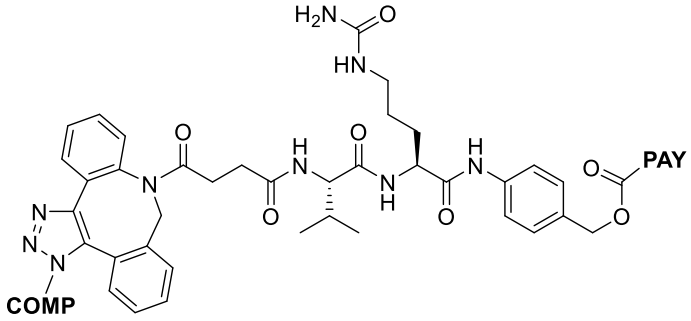


or formula 56:

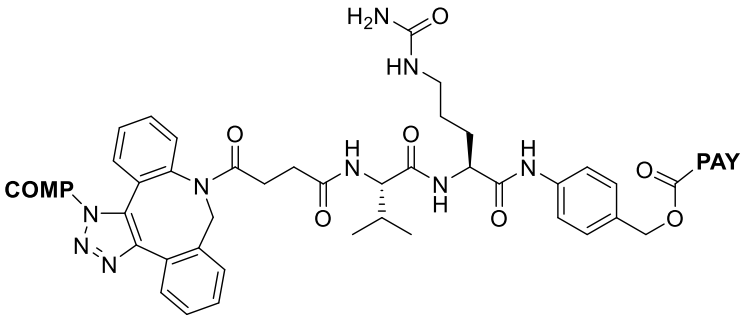


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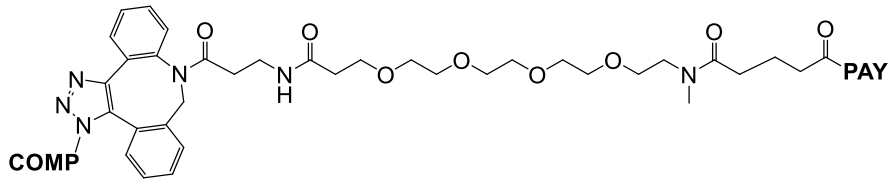
~~7.~~6. The antibody conjugate of any of the preceding claims according to any of formulas 101a-104b:



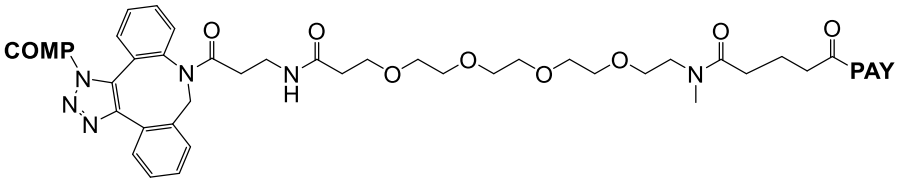
(101a)



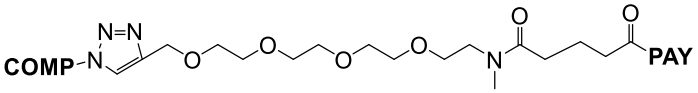
(101b)



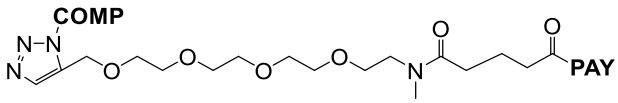
(102a)



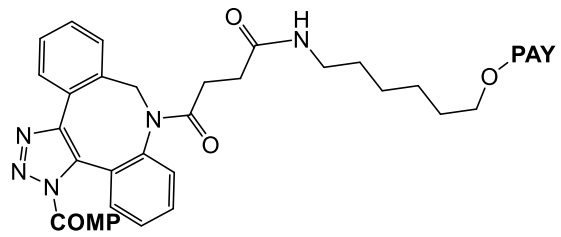
(102b)



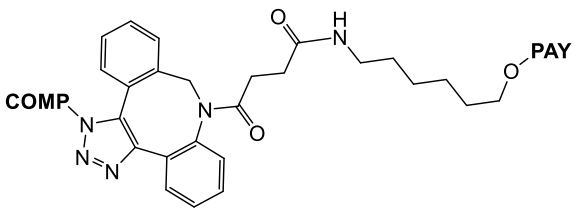
(103a)



(103b)



(104a)



(104b)

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

~~8.~~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.

~~9.~~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.

~~10.~~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.

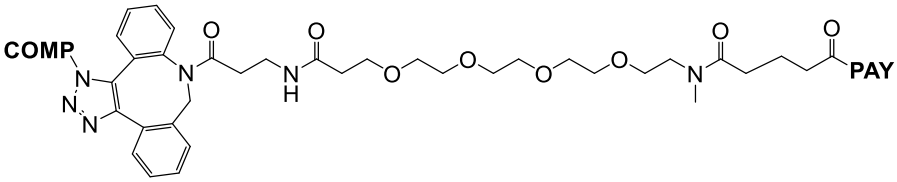
~~11.~~10. The antibody conjugate of any of the preceding claims, wherein the antibody comprises:

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

~~12.~~11. The antibody conjugate of claim ~~11~~10, wherein the antibody comprises a non-natural amino acid at site HC-F404 according to the EU numbering scheme of Kabat.

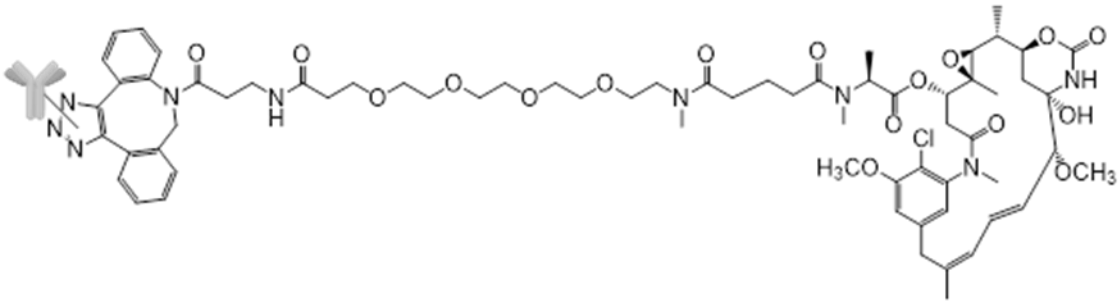
~~13.~~12. The antibody conjugate of claim ~~12~~9, wherein the non-natural amino acid is para-azidomethylphenylalanine or p-azidomethyl-L-phenylalanine.

~~14.~~13. The antibody conjugate of claim ~~13~~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.

~~15.~~14. The antibody conjugate of claim ~~14~~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.

~~16.~~15. The antibody conjugate of any of the preceding claims, further comprising at least one constant region domain.

~~17.~~16. The antibody conjugate of claim ~~16~~15, wherein the constant region comprises a sequence selected from SEQ ID NOs: 304-305.

~~18.~~17. The antibody conjugate of any of the preceding claims, wherein the antibody is a monoclonal antibody.

~~19.~~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.

~~20.~~19. The antibody conjugate of any of the preceding claims, wherein the antibody is humanized or human.

~~21.~~20. The antibody conjugate of any of the preceding claims, wherein the antibody is aglycosylated.

~~22.~~21. The antibody conjugate of any of the preceding claims, wherein the antibody is an antibody fragment.

~~23.~~22. The antibody conjugate of claim ~~22~~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.

~~24.~~23. The antibody conjugate of claim ~~23~~22, wherein the antibody is an scFv fragment.

~~25.~~24. The antibody conjugate of claim ~~24~~23, wherein the scFv fragment comprises a sequence selected from SEQ ID NOs: 221-228.

~~26.~~25. The antibody conjugate of claim ~~23~~22, wherein the antibody is an scFv-Fc fragment.

~~27.~~26. The antibody conjugate of claim ~~26~~25, wherein the scFv-Fc fragment comprises SEQ ID NO: 229.

~~28.~~27. The antibody conjugate of any of the preceding claims, wherein the antibody has a k_a of at least ~~about~~ 10^5 $M^{-1}\times sec^{-1}$ at a temperature of 25°C.

~~29.~~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.

~~30.~~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.

~~31.~~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.

~~32.~~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.

~~33.~~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.

~~34.~~33. A kit comprising an antibody conjugate of any of the preceding claims, and instructions for use of the antibody conjugate.

~~35.~~34. The kit of claim ~~34~~33, wherein the antibody conjugate is lyophilized.

~~36.~~35. The kit of claim ~~35~~34, further comprising a fluid for reconstitution of the lyophilized antibody conjugate.

~~37.~~36. A pharmaceutical composition comprising the antibody conjugate of any of claims 1 to ~~33~~ 32 and a pharmaceutically acceptable carrier.

~~38.~~37. An antibody conjugate of any one of claims 1 to ~~33~~32, or a pharmaceutical composition of claim ~~37~~ 36 for use in treating or preventing a disease or condition in a subject.

~~39.~~38. An antibody conjugate of any one of claims 1 to ~~33~~32, or a pharmaceutical composition of claim ~~37~~ 36 for use in diagnosing a disease or condition in a subject.

~~40.~~39. The antibody conjugate or pharmaceutical composition of any of claims ~~38~~ 37 or ~~39~~38, wherein the disease or condition involves an upregulation of CD74 in a cancer, an autoimmune disease, an inflammatory disease, or an infection.

~~41.~~40. The antibody conjugate or pharmaceutical composition of claim ~~40~~39, wherein the cancer is selected from multiple myeloma or pancreatic cancer.

~~42.~~41. The antibody conjugate or pharmaceutical composition of claim ~~40~~39, wherein the disease or condition is B-cell lymphoma.

~~43.~~42. The antibody conjugate or pharmaceutical composition of claim 39~~40~~, wherein the disease or condition is non-Hodgkin's lymphoma.

~~44.~~43. The antibody conjugate or pharmaceutical composition of claim 39~~40~~, wherein the disease or condition is leukemia.

~~45~~44. The antibody conjugate of any of the preceding claims, wherein the antibody comprises:

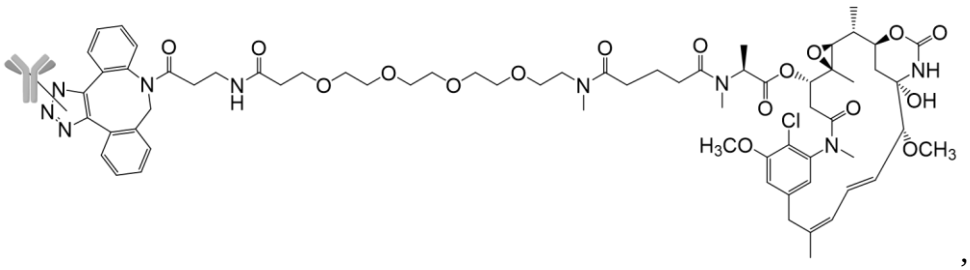
a. a VH comprising: a CDR-H1 comprising at least one of SEQ ID NOs: 1 and 33; a CDR-H2 comprising at least one of SEQ ID NOs: 65 and 97; and a CDR-H3 comprising SEQ ID NO: 129.

~~46~~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.

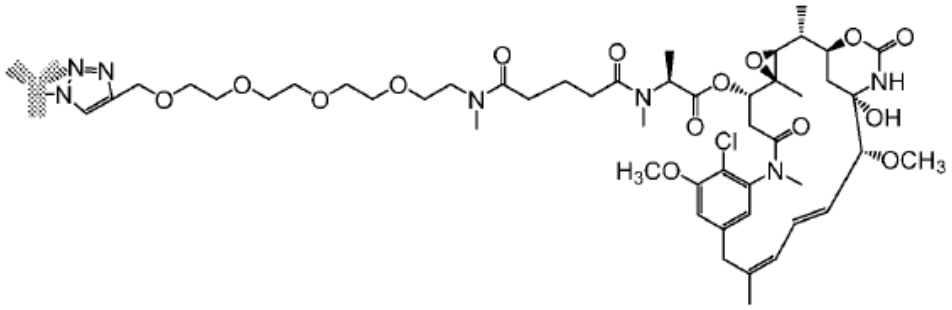
~~47~~46. The antibody conjugate of claim ~~3~~2, wherein the antibody conjugate has the structure of:

Conjugate A:



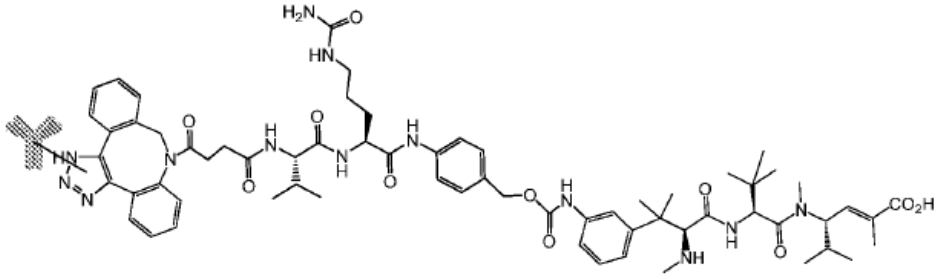
,

Conjuage B:



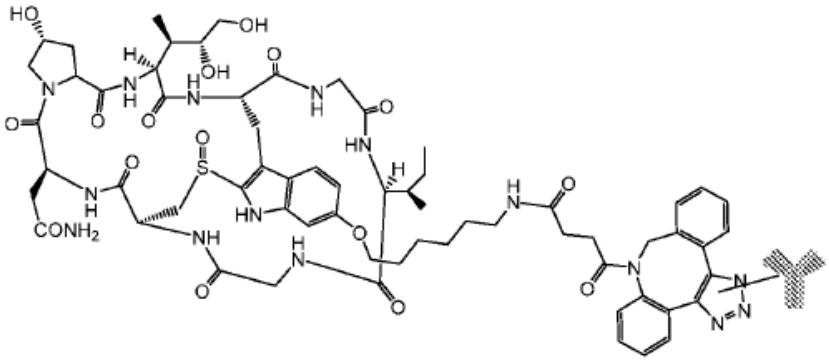
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Conjugate C:



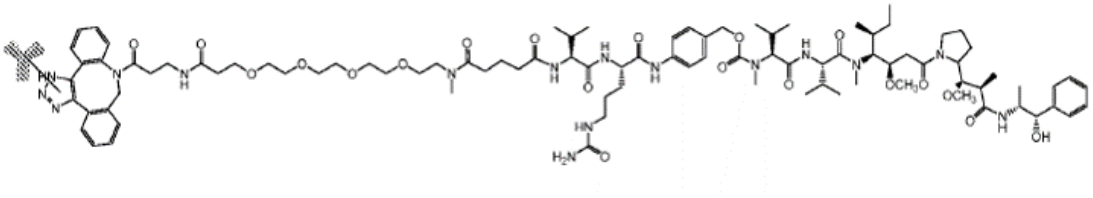
,

Conjugate D



, or

Conjugate F:



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