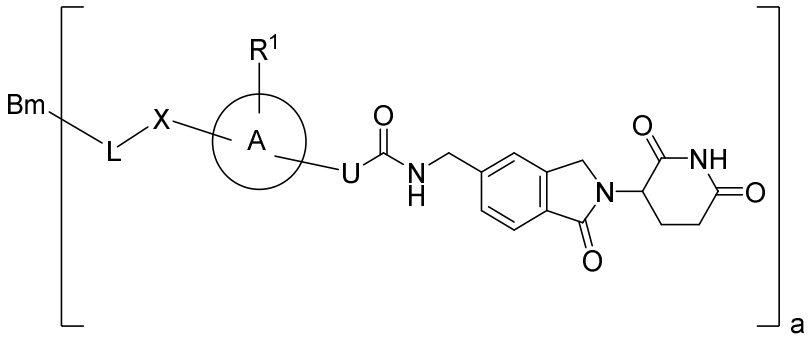
WHAT IS CLAIMED IS:

1. A conjugate of formula (I):



(I),

or a pharmaceutically acceptable salt thereof, wherein:

a is an integer from 1 to 10;

A is phenyl or a C_4-C_{10}cycloalkyl ring;

U is selected from NH and CF_2;

R^1 is independently selected from hydrogen and halo;

X is selected from $–NR^2$-, $=C(CH_3)$-, $-Q-(CH_2)_n$-, and $–Q(CH_2)_mQ'(CH_2)_n$-; wherein

Q and Q' are each independently O, S, or $N(R^2)_v$;

v is 1 or 2;

each R^2 is independently hydrogen or C_1-C_6alkyl;

n is an integer from 1 to 6; and

m is an integer from 2 to 6;

wherein the left side of each group is attached to L and the right side is attached to A;

provided that when X is NH or $-Q-(CH_2)_n$-, R^1 is halo;

L is a cleavable linker or non-cleavable linker; and

Bm is an anti-CD33 antibody or antigen-binding portion thereof comprising a heavy chain variable region (VH) complementarity determining region (CDR) 1 (VH-CDR1) compising the amino acid sequence as set forth in SEQ ID NO: 1, a VH-CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 2, a VH-CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 3, a light chain variable region (VL) CDR1 (VL-CDR1) comprising the amino acid sequence as set forth in SEQ ID NO: 5, a VL-CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 6, and a VL-CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 7.

2. The conjugate of claim 1, wherein the anti-CD33 antibody or antigen-binding portion thereof is an IgG1 antibody or antigen-binding portion thereof and/or wherein the anti-CD33 antibody or antigen-binding portion thereof comprises:

(i) a VH comprising the amino acid sequence set forth in SEQ ID NO: 4 and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 8;

(ii) a constant region, wherein the constant region comprises at least one amino acid different from gemtuzumab;

(iii) alanine at amino acid 297 corresponding to the constant region;

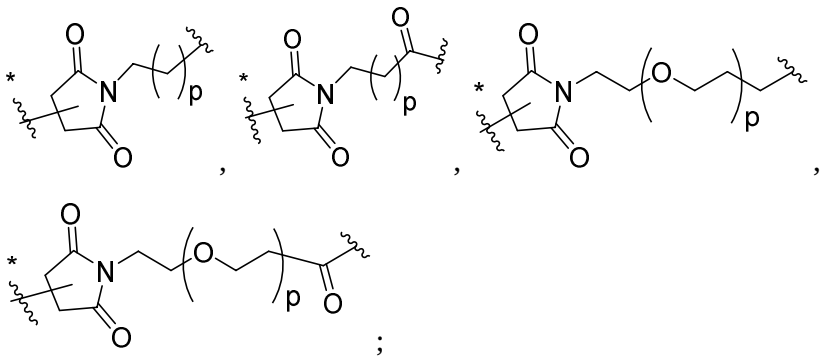
(iv) a heavy chain as set forth in SEQ ID NO: 9 and a light chain as set forth in SEQ ID NO: 10; or

(v) two or more of (i)-(v).

3. The conjugate of claim 1 or 2, wherein a is an integer from 2 to 8.

4. The conjugate of any one of claims 1 to 3, wherein L is a non-cleavable linker.

5. The conjugate of claim 4, wherein L is selected from the group consisting of


, and

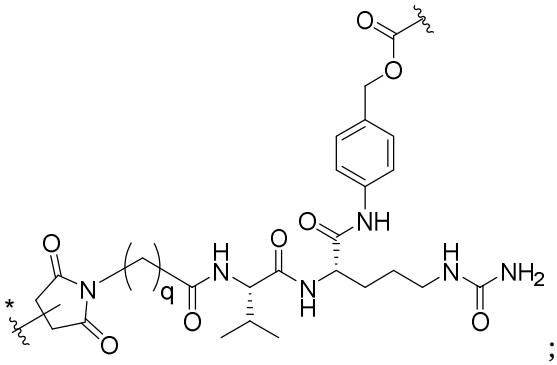
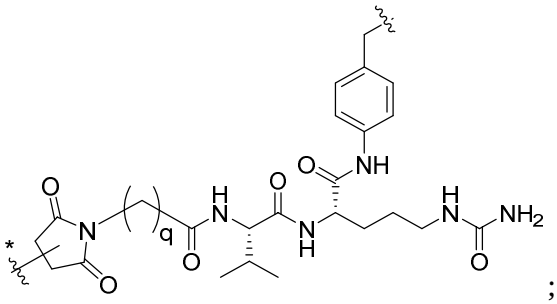
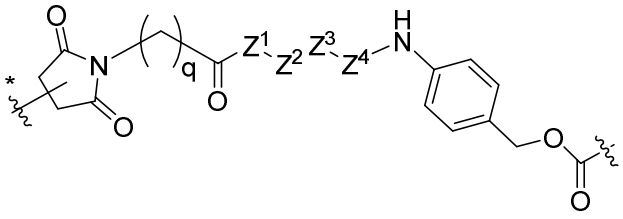
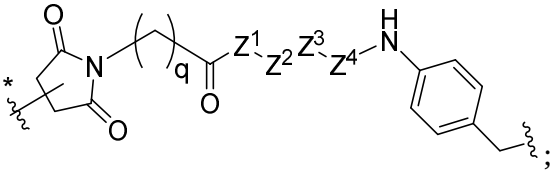
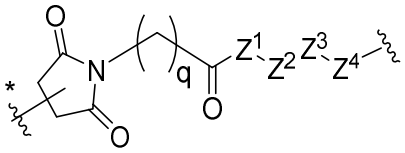
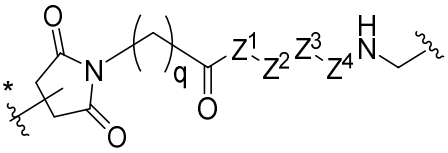
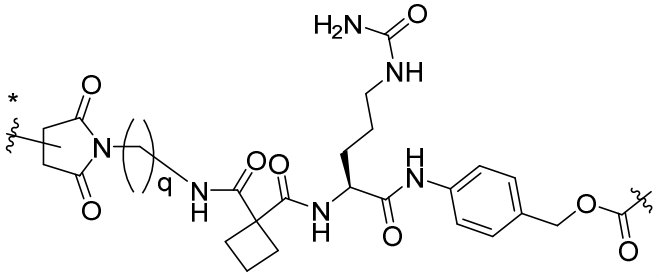
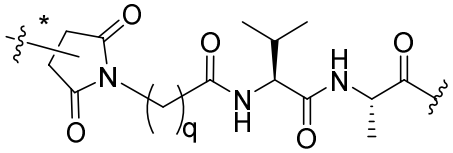
;

wherein: p is an integer from 1 to 10; ~ is the point of attachment to X; and ~* is the point of attachment to the anti-CD33 antibody or antigen-binding portion thereof.

6. The conjugate of any one of claims 1 to 3, wherein L is a cleavable linker.

7. The conjugate of claim 6, wherein the cleavable linker is cleavable by a protease.

8. The conjugate of claim 6 or 7, wherein L is selected from the group consisting of


;

;

;

;

;

;

; and

;

wherein:

q is an integer from 2 to 10;

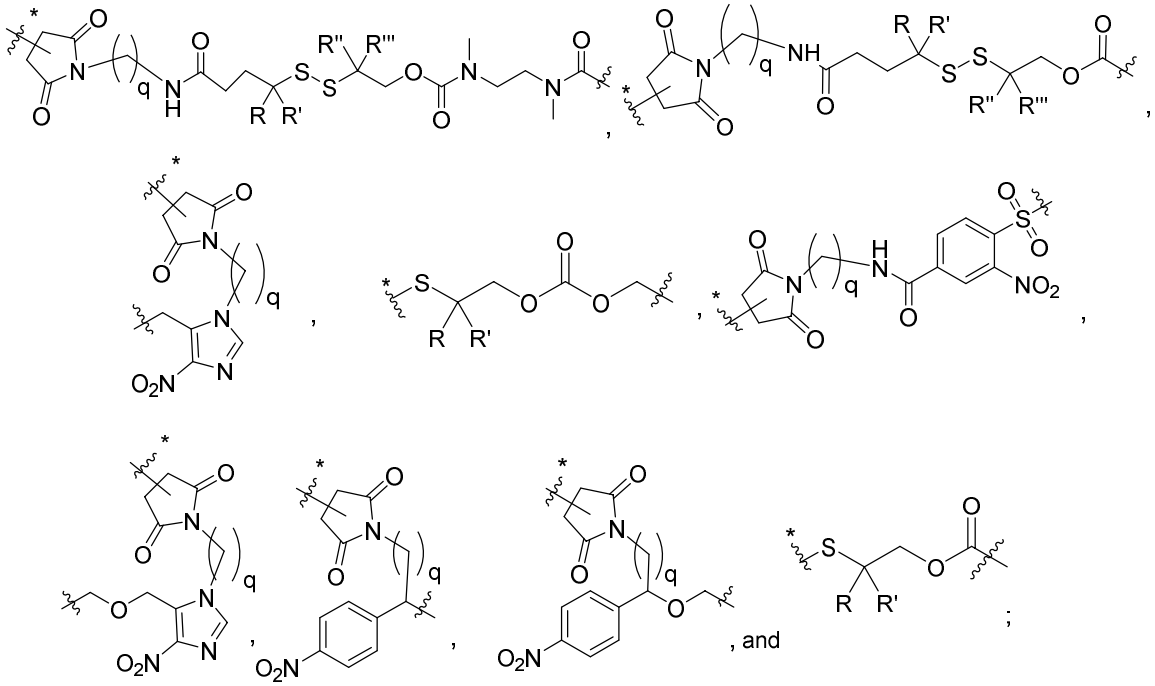
Z^1, Z^2, Z^3, and Z^4 are each independently absent or a naturally-occurring amino acid residue in the L- or D-configuration, provided that at least two of Z^1, Z^2, Z^3, and Z^4 are amino acid residues;

~ is the point of attachment to X; and

~* is the point of attachment to the anti-CD33 antibody or antigen-binding portion thereof.

9. The conjugate of claim 6, wherein L is a bioreducible linker.

10. The conjugate of claim 6 or 9, wherein L is selected from the group consisting of



wherein:

q is an integer from 2 to 10;

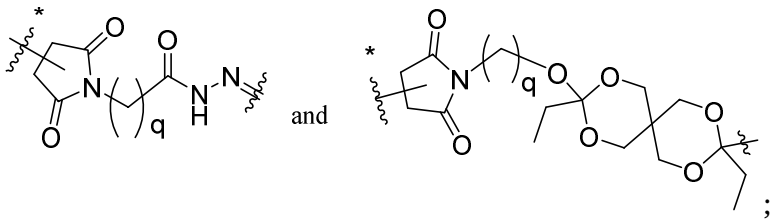
R, R', R'', and R''' are each independently selected from hydrogen, C_1-C_6alkoxyC_1-C_6alkyl, $(C_1$-$C_6)_2$NC_1-C_6alkyl, and C_1-C_6alkyl, or, two geminal R groups, together with the carbon atom to which they are attached, can form a cyclobutyl or cyclopropyl ring;

~ is the point of attachment to X; and

~* is the point of attachment to the anti-CD33 antibody or antigen-binding portion thereof.

11. The conjugate of claim 6, wherein L is an acid cleavable linker.

12. The conjugate of claim 6 or 11, wherein L is selected from the group consisting of



wherein:

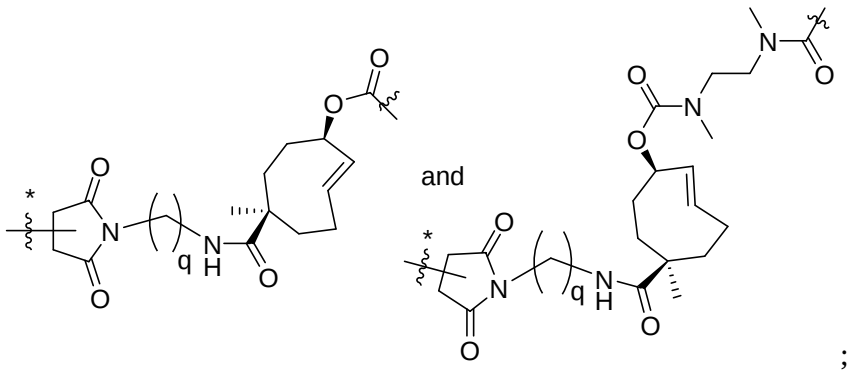
q is an integer from 2 to 10;

~ is the point of attachment to X; and

~* is the point of attachment to the anti-CD33 antibody or antigen-binding portion thereof.

13. The conjugate of claim 6, wherein L is a click-to-release linker.

14. The conjugate of claim 6 or 13, wherein L is selected from



;

wherein:

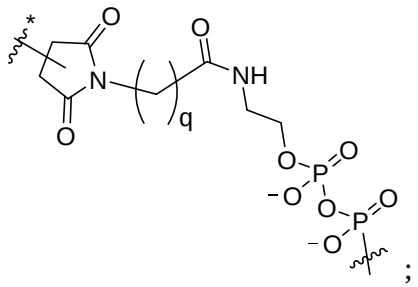
q is an integer from 2 to 10;

~ is the point of attachment to X; and

~* is the point of attachment to the anti-CD33 antibody or antigen-binding portion thereof.

15. The conjugate of claim 6, wherein L is a pyrophosphatase cleavable linker.

16. The conjugate of claim 15, wherein L is



;

wherein:

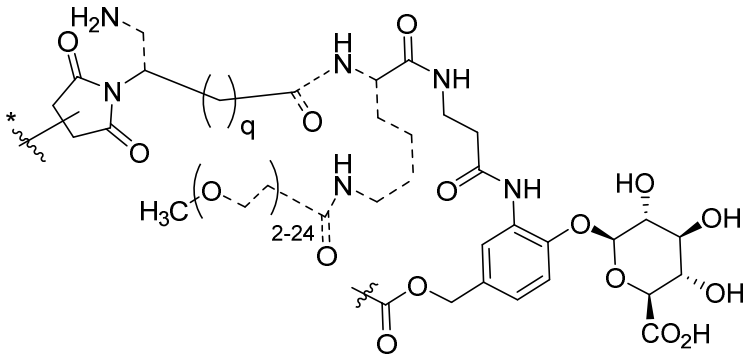
q is an integer from 2 to 10;

~ is the point of attachment to X; and

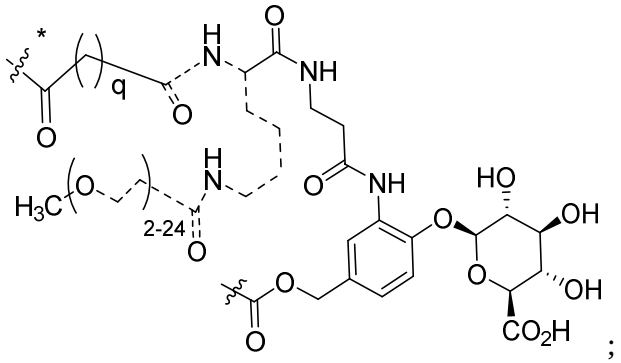
~* is the point of attachment to the anti-CD33 antibody or antigen-binding portion thereof.

17. The conjugate of claim 6, wherein L is a beta-glucuronidase cleavable linker.

18. The conjugate of claim 6 or 17, wherein L is selected from



and



;

wherein:

q is an integer from 2 to 10;

---- is absent or a bond;

 is the point of attachment to X; and

 is the point of attachment to the anti-CD33 antibody or antigen-binding portion thereof.

19. The conjugate of any one of claims 1 to 18, wherein:

(a) A is phenyl; U is NH; R^1 is halo; and X is $-N(R^2)_v(CH_2)_mO(CH_2)_n-$; wherein: v is 1; m and n are 2; and R^2 is methyl;

(b) A is phenyl; U is NH; R^1 is halo; and X is $-N(R^2)_v(CH_2)_mO(CH_2)_n-$; wherein: v is 2; m and n are 2; and each R^2 is methyl;

(c) A is phenyl; U is NH; R^1 is halo; and X is $-O(CH_2)_n-$; wherein: n is 2;

(d) A is phenyl; U is NH; R^1 is halo; and X is $-S(CH_2)_n-$; wherein: n is 2;

(e) A is phenyl; U is NH; R^1 is hydrogen; and X is –NR^2-; wherein: R^2 is

methyl;

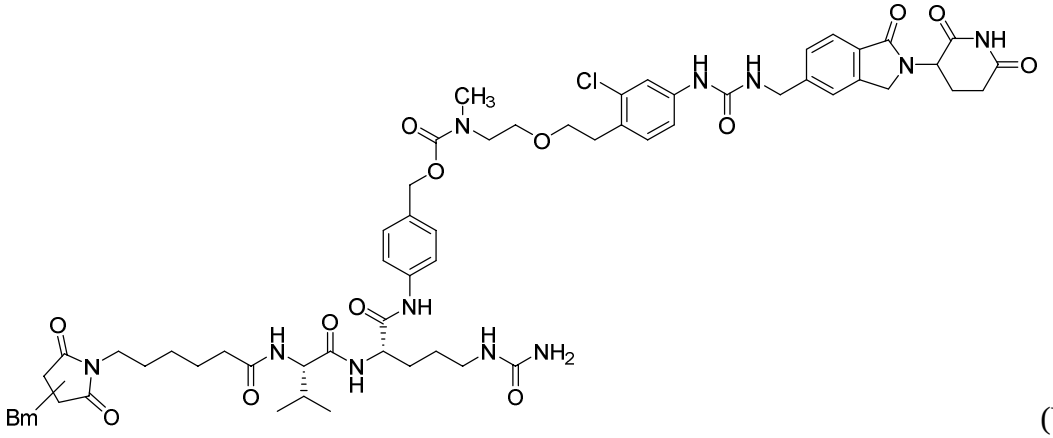
(f) A is phenyl; U is NH; R^1 is halo; and X is -–NR^2-; wherein: R^2 is hydrogen;

(g) A is phenyl; U is NH; R^1 is hydrogen; and X is –$C(CH_3)$=;

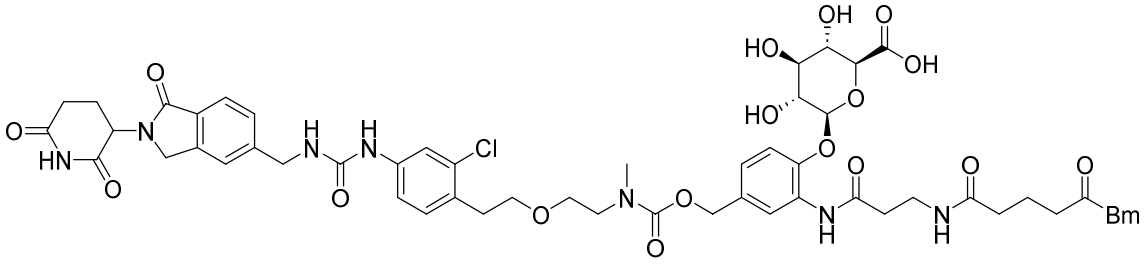
(h) A is phenyl; U is NH; R^1 is hydrogen; and X is –$C(CH_3)$=; or

(i) A is a C_4-C_{10}cycloalkyl ring; U is NH; R^1 is hydrogen; and X is -$N(R^2)(CH_2)_mO(CH_2)_n$-; wherein: n is 1; m is 2; and R^2 is methyl.

20. A conjugate of formula (V) formula (VI), or formula (VII):

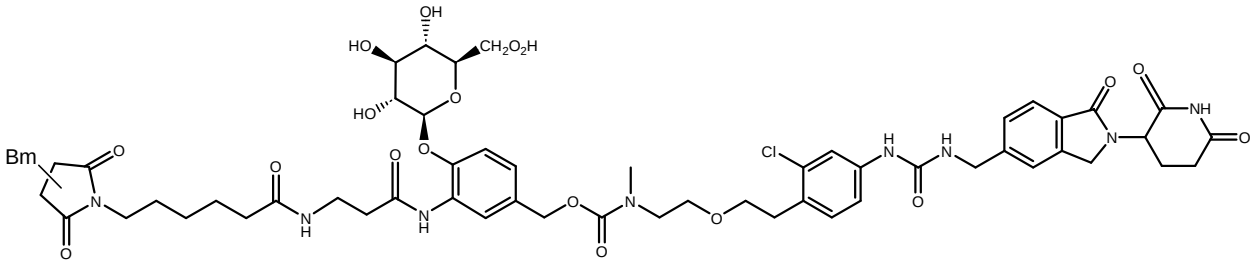


(V);



(VI);

or



(VII);

or a pharmaceutically acceptable salt of one of the foregoing, wherein Bm is an anti-CD33 antibody or antigen-binding portion thereof comprising a VH-CDR1 compising the amino acid

sequence as set forth in SEQ ID NO: 1, a VH-CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 2, a VH-CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 3, a VL-CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 5, a VL-CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 6, and a VL-CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 7.

21. The conjugate of claim 20, wherein the anti-CD33 antibody or antigen-binding porition thereof comprises (i) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 4 and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 8 or (ii) a heavy chain comprising the amino acid sequence as set forth in SEQ ID NO: 9 and a light chain comprising the amino acid sequence as set forth in SEQ ID NO: 10.

22. A pharmaceutical composition comprising the conjugate of any one of claims 1 to 21, and one or more pharmaceutically acceptable carriers.

23. A conjugate of any one of claims 1 to 21 for use in the treatment of cancer or myelodysplastic syndrome.

24. The conjugate for use of claim 23, wherein the cancer is a hematological/blood cancer.

25. The conjugate for use of claim 23, wherein the cancer is a multiple myeloma, leukemia, lymphoma, Hodgkin’s disease, or chronic myeloproliferative disease.

26. The conjugate for use of claim 23, wherein the cancer is acute myeloid leukemia.

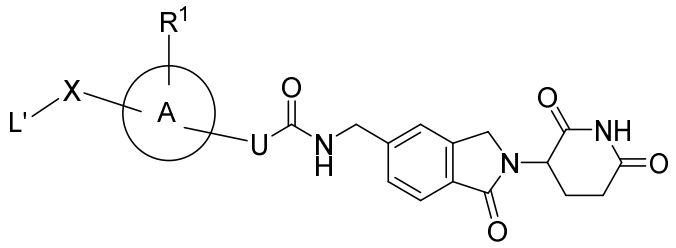
27. The conjugate for use of any one of claims 23 to 26, wherein a pharmaceutically acceptable amount of an additional agent is to be administered to the subject, wherein the additional agent is selected from the group consisting of:

(i) a cytotoxic agent or an immune response modifier;

(ii) a checkpoint inhibitor; and

(iii) a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a TIM3 inhibitor, and/or a LAG-3 inhibitor.

28. A method of preparing the conjugate of any one of claims 1 to 21, the process comprising reacting an anti-CD33 antibody or antigen-binding portion thereof with a compound of formula (I-1):



(I-1),

or a pharmaceutically acceptable salt thereof, wherein:

a is an integer from 1 to 10;

A is phenyl or a C_4-C_{10}cycloalkyl ring;

R^1 is independently selected from hydrogen and halo;

U is selected from NH and CF_2;

X is selected from $–N(R^2)_v$-, $=C(CH_3)$-, -Q-$(CH_2)_n$-, and $–Q(CH_2)_mQ'(CH_2)_n$-; wherein

v is 1 or 2;

Q and Q' are each independently O, S, or NR^2;

each R^2 is independently hydrogen or C_1-C_6alkyl;

n is an integer from 1 to 6; and

m is an integer from 2 to 6;

wherein the left side of each group is attached to L' and the right side is attached to A;

provided that when X is NH or -Q-$(CH_2)_n$-, R^1 is halo;

L' is a cleavable or non-cleavable linker precursor that conjugates to the anti-CD33 antibody or antigen-binding portion thereof, wherein the anti-CD33 antibody or antigen-binding portion thereof comprises a VH-CDR1 compising the amino acid sequence as set forth in SEQ ID NO: 1, a VH-CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 2, a VH-CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 3, a light chain variable region (VL) CDR1 comprising the amino acid sequence as set forth in SEQ ID NO: 5, a VL-CDR2 comprising the amino acid sequence as set forth in SEQ ID NO: 6, and a VL-CDR3 comprising the amino acid sequence as set forth in SEQ ID NO: 7.

29. An antibody comprising a heavy chain as set forth in SEQ ID NO: 9 and a light chain as set forth in SEQ ID NO: 10.

30. A pharmaceutical composition comprising the antibody of claim 29 and a pharmaceutically acceptable carrier.