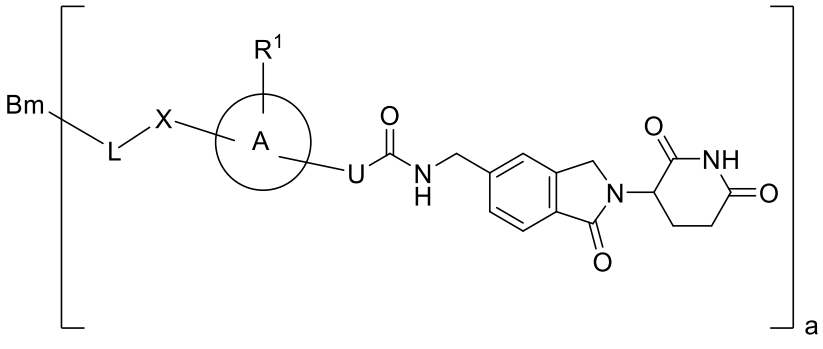
CLAIMS

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; wherein the constant region comprises at least one amino acid different from gemtuzumab.

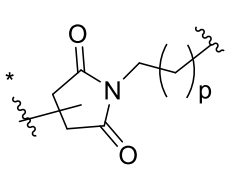
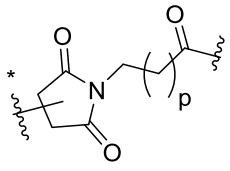
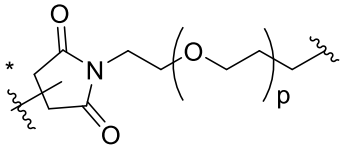
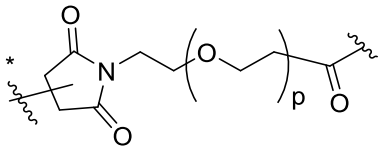
2. The conjugate of claim 1, wherein the anti-CD33 antibody or antigen-binding portion thereof comprises a VH comprising the amino acid sequence set forth in SEQ ID NO: 4 and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 8.

3. The conjugate of claim 1, wherein the anti-CD33 antibody comprises a heavy chain as set forth in SEQ ID NO: 9 and a light chain as set forth in SEQ ID NO: 10.

4. The conjugate of any one of claims 1 to 3, wherein a is an integer from 2 to 8.

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

6. The conjugate of claim 5, wherein the non-cleavable linkers is selected from the group consisting of

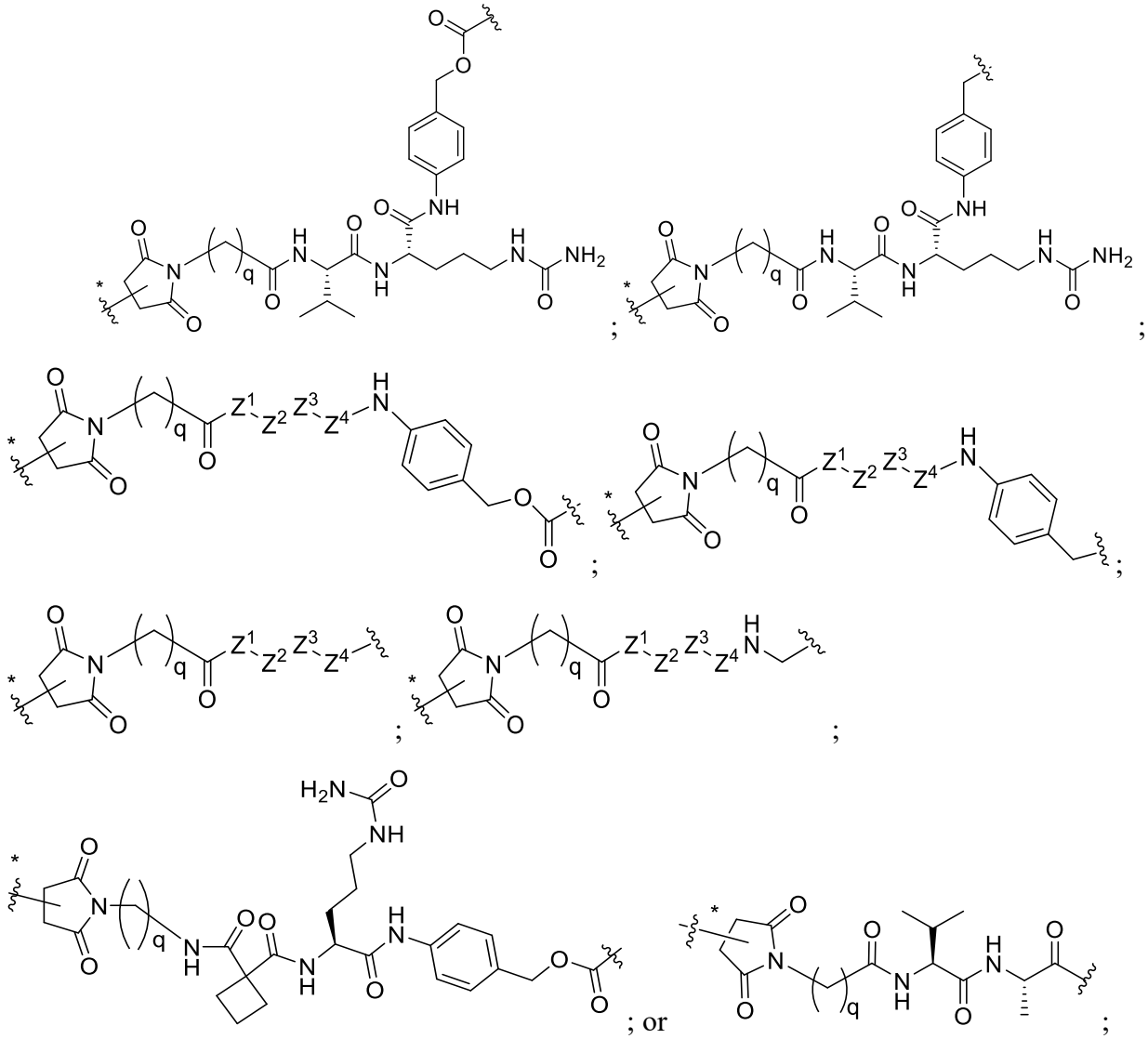

, 
, 
, and 
;

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.

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

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

9. The conjugate of claim 8, wherein the linker cleavable by a protease is



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.

10. The conjugate of claim 7, wherein the cleavable linker is:

(a) a bioreducible linker;

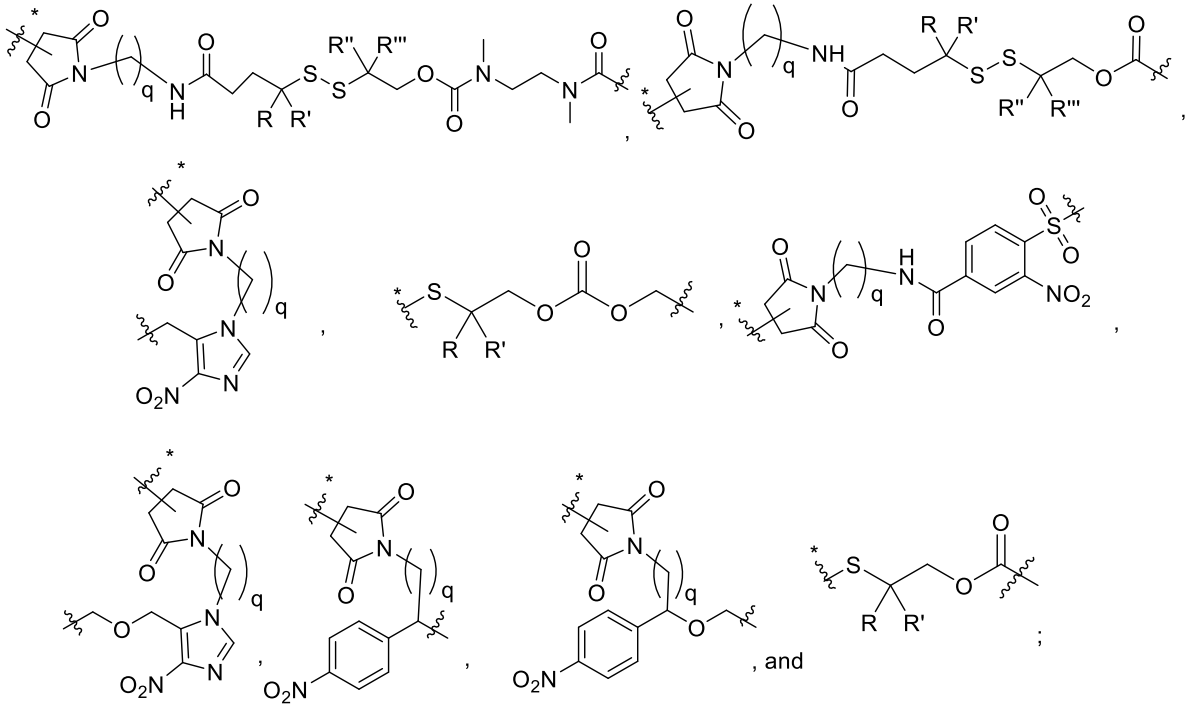
(b) an acid cleavable linker;

(c) a click-to-release linker; or

(d) a pyrophosphatase cleavable linker.

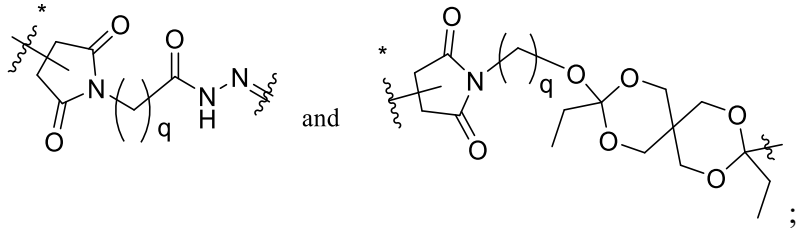
11. The conjugate of claim 10, wherein

(a) the bioreducible linker is selected from the group consisting of:



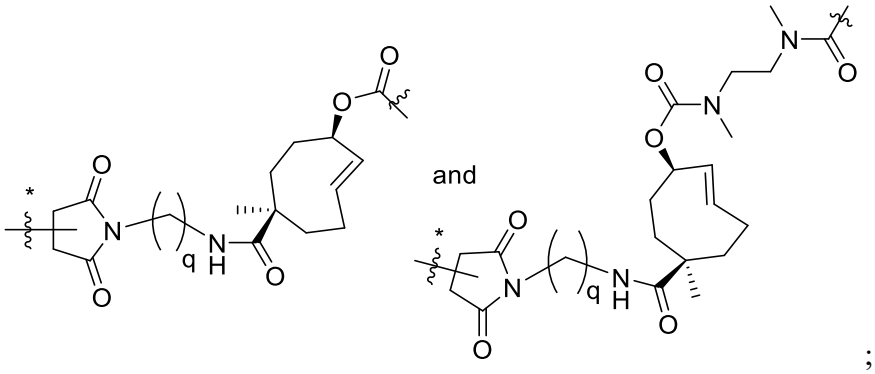
wherein q is an integer from 2 to 10; R, R', R'', and R''' are each independently selected from hydrogen, C_1-C_6alkoxyC_1-C_6alkyl, $(C_1$-$C_6)_2$NC_1-C_6alkyl, and C_1-C_6alkyl, or, two geminal R groups, together with the carbon atom to which they are attached, can form a cyclobutyl or cyclopropyl ring; is the point of attachment to X; and is the point of attachment to the anti-CD33 antibody or antigen-binding portion thereof.

(b) the acid cleavable linker 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;

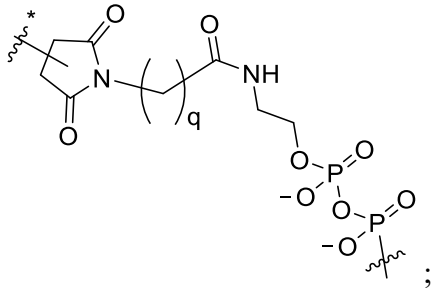
(c) the click-to-release linker is:



;

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.

(d) the pyrophosphatase cleavable linker is

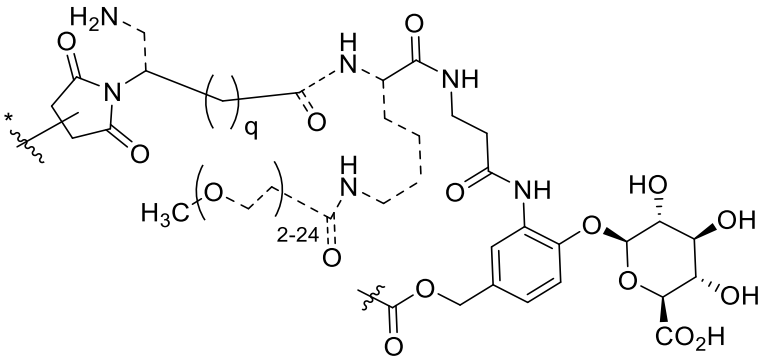


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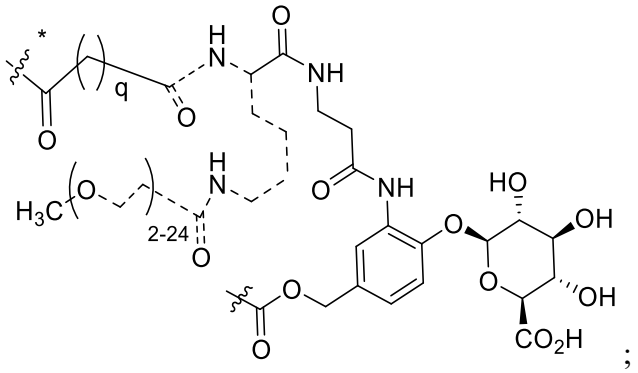
wherein q is an integer from 2 to 10; ~ is the point of attachment to X; and ~* is the point of attachment to the anti-CD33 antibody or antigen-binding portion thereof.

12. The conjugate of any one of claims 1 to 4, wherein the cleavable linker is a beta-glucuronidase cleavable linker.

13. The conjugate of claim 12, wherein the beta-glucuronidase cleavable linker is



or



;

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.

14. The conjugate of any one of claims 1 to 13, 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;

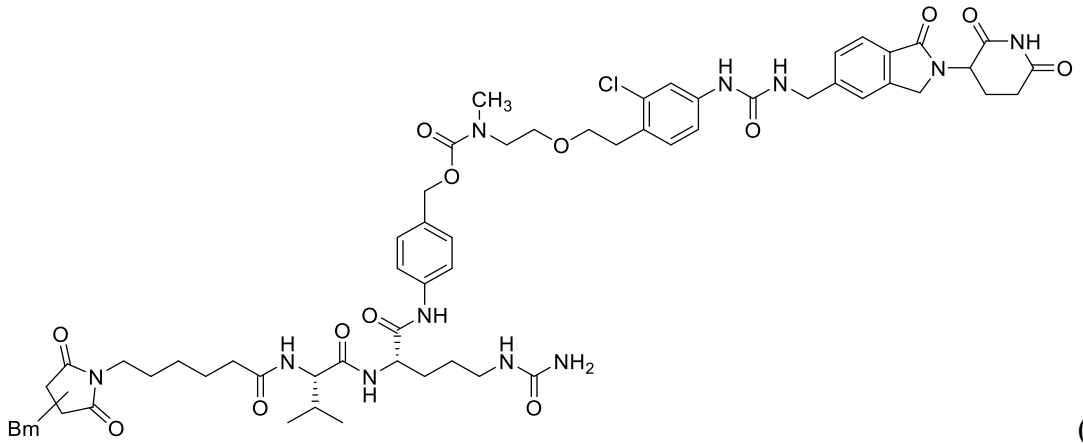
(g) A is phenyl; U is NH; R^1 is hydrogen; and X is $–C(CH_3)=$;

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

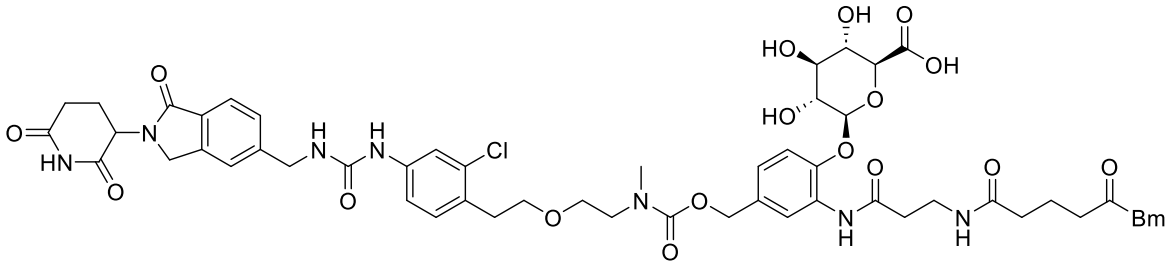
(i) A is a C_4-C_{10}cycloalkyl ring; U is NH; R^1 is hydrogen; and X is $-N(R^2)(CH_2)_mO(CH_2)_n-$; wherein: n is 1; m is 2; and R^2 is methyl.

15. A conjugate, wherein the conjugate is selected from the group consisting of a conjugate of formula (V), a pharmaceutically acceptable salt of a conjugate of Formula (V), a conjugate of formula (VI), a pharmaceutically acceptable salt of a conjugate of Formula (VI), a

conjugate of formula (VII), or a pharmaceutically acceptable salt of a conjugate of (VII):

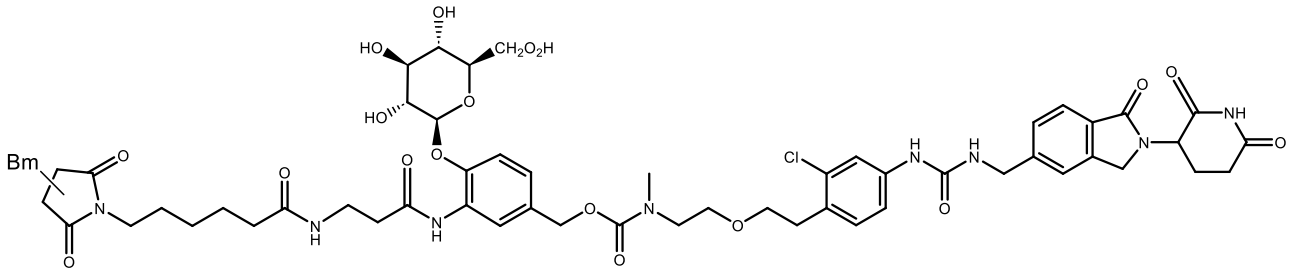


(V);



(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; wherein the constant region comprises at least one amino acid different from gemtuzumab.

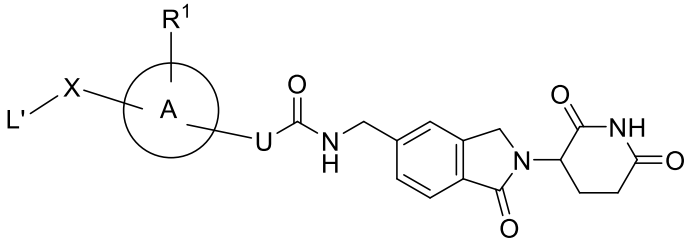
16. The conjugate of claim 15, wherein the anti-CD33 antibody or antigen-binding porition thereof comprises (i) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 4 and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 8 or (ii) a heavy chain comprising the amino acid 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.

17. A pharmaceutical composition comprising the conjugate of any one of claims 1 to 16, and one or more pharmaceutically acceptable carriers.

18. A conjugate of any one of claims 1 to 16 for use in treating cancer or myelodysplastic syndrome.

19. The conjugate for use of claim 18, wherein the cancer is a multiple myeloma, leukemia, malignant lymphoma, Hodgkin's disease, or chronic myeloproliferative disease.

20. A process of preparing the conjugate of any one of claims 1 to 14, 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; wherein the constant region comprises at least one amino acid different from gemtuzumab.

21. The process of claim 20, wherein the anti-CD33 antibody or antigen-binding portion thereof comprises a heavy chain as set forth in SEQ ID NO: 9 and a light chain as set forth in SEQ ID NO: 10.