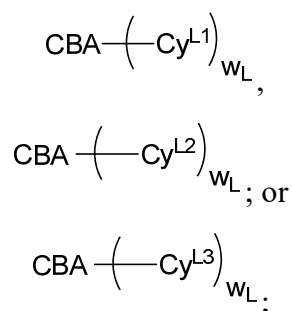


CLAIMS:

1. An antibody or antigen-binding fragment thereof that:
 - (a) binds an epitope within amino acids 101 to 346 of human CD123 / IL3-R α antigen, and
 - (b) inhibits IL3-dependent proliferation in antigen-positive TF-1 cells.
2. An antibody or antigen-binding fragment thereof that:
 - (a) binds an epitope within amino acids 1 to 100 of human CD123 antigen, and
 - (b) inhibits IL3-dependent proliferation in antigen-positive TF-1 cells, with an IC₅₀ value of 0.1 nM or less (*e.g.*, 0.08 nM, 0.05 nM, 0.03 nM).
3. The antibody or antigen-binding fragment thereof of any of claims 1 and 2, comprising:
 - a) at least one heavy chain variable region or fragment thereof comprising three sequential complementarity-determining regions (CDR) CDR1, CDR2, and CDR3, respectively, wherein, with the exception of 1, 2, or 3 conservative amino acid substitutions, CDR1 is selected from the group consisting of: SEQ ID NOs: 1, 5, and 12, CDR2 is selected from the group consisting of: SEQ ID NOs: 2, 3, 6-10, 13, and 14, and, optionally, CDR3 is selected from the group consisting of: SEQ ID NOs: 4, 11, and 15; and
 - b) at least one light chain variable region or fragment thereof comprising three sequential complementarity-determining regions (CDR) CDR1, CDR2, and CDR3, respectively, wherein, with the exception of 1, 2, or 3 conservative amino acid substitutions, CDR1 is selected from the group consisting of: SEQ ID NOs: 16, 19, 20, and 23, CDR2 is selected from the group consisting of: SEQ ID NOs: 17, 21, and 24, and, optionally, CDR3 is selected from the group consisting of: SEQ ID NOs: 18, 22, and 25.
4. The antibody or antigen-binding fragment thereof of any of claims 1-3, comprising:
 - a) an immunoglobulin heavy chain variable region having the amino acid sequence set forth in SEQ ID NO: 34; and
 - b) an immunoglobulin light chain variable region having the amino acid sequence set forth in SEQ ID NO: 35.

5. The antibody or antigen-binding fragment thereof of claim 4, wherein Xaa, the second residue from the N-terminus of SEQ ID NO: 34, is Phe.
6. The antibody or antigen-binding fragment thereof of claim 4, wherein Xaa, the second residue from the N-terminus of SEQ ID NO: 34, is Val.
7. The antibody or antigen-binding fragment thereof of any of claims 1-6, comprising:
 - a) an immunoglobulin heavy chain variable region having the amino acid sequence set forth in SEQ ID NO: 34; and
 - b) an immunoglobulin light chain variable region having the amino acid sequence set forth in SEQ ID NO: 37.
8. The antibody or antigen-binding fragment thereof of any of claims 1-3, comprising:
 - a) an immunoglobulin heavy chain region having the amino acid sequence set forth in SEQ ID NO: 54; and
 - b) an immunoglobulin light chain variable region having the amino acid sequence set forth in SEQ ID NO: 35.
9. The antibody or antigen-binding fragment thereof of claim 8, wherein Xaa, the second residue from the N-terminus of SEQ ID NO: 54 or 56, is Phe.
10. The antibody or antigen-binding fragment thereof of claim 8, wherein Xaa, the second residue from the N-terminus of SEQ ID NO: 54 or 56, is Val.
11. The antibody or antigen-binding fragment thereof of any one of claims 1-3, comprising:
 - a) an immunoglobulin heavy chain variable region comprising a CDR1 having an amino acid sequence set forth in SEQ ID NO: 5, a CDR2 having an amino acid sequence set forth in SEQ ID NO: 6, 7, 8, 9, or 10, and a CDR3 having an amino acid sequence set forth in SEQ ID NO: 11; and
 - b) an immunoglobulin light chain variable region comprising a CDR1 having an amino acid sequence set forth in SEQ ID NO: 19 or 20, a CDR2 having an amino acid sequence set forth in SEQ ID NO: 21, and a CDR3 having an amino acid sequence set forth in SEQ ID NO: 22.
12. The antibody or antigen-binding fragment thereof of any one of claims 1-11, comprising a V_H sequence of SEQ ID NO: 34 and a V_L sequence of SEQ ID NO: 35.

13. A polypeptide comprising the V_H and V_L sequences of any of claims 1-12.
14. A cell producing the antibody or antigen-binding fragment thereof of any one of claims 1-12, or the polypeptide of claim 13.
15. A method of producing the antibody or antigen-binding fragment thereof of any one of claims 1-12, or the polypeptide of claim 13, comprising:
 - (a) culturing a cell producing said antibody or antigen-binding fragment thereof; and
 - (b) isolating said antibody, antigen-binding fragment thereof, or polypeptide from said cultured cell.
16. An immunoconjugate having the following formula:

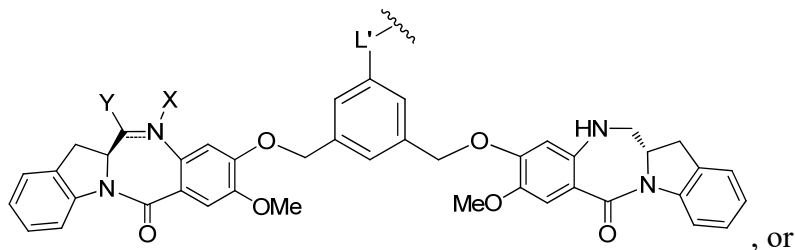


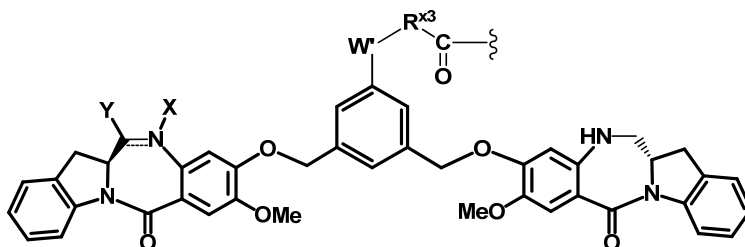
wherein:

CBA is an antibody or antigen-binding fragment thereof of any one of claims 3-6, or the polypeptide thereof of claim 13, that is covalently linked through a lysine residue to Cy^{L1}, Cy^{L2} or Cy^{L3};

w_L is an integer from 1 to 20;

Cy^{L1} is represented by the following formula:





or a pharmaceutically acceptable salt thereof, wherein:

the double line $\equiv$ between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H or a (C₁-C₄)alkyl; and when it is a single bond, X is -H or an amine protecting moiety, and Y is -OH or -SO₃M;

W' is -NR^{e'},

R^{e'} is -(CH₂-CH₂-O)_n-R^k;

n is an integer from 2 to 6;

R^k is -H or -Me;

R^{x3} is a (C₁-C₆)alkyl;

L' is represented by the following formula:

-NR₅-P-C(=O)-(CR_aR_b)_m-C(=O)- (B1'); or

-NR₅-P-C(=O)-(CR_aR_b)_m-S-Z^{s1}- (B3');

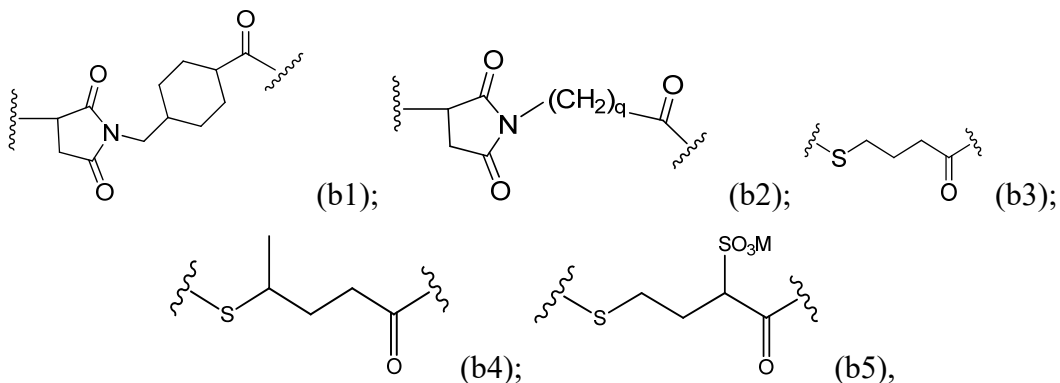
R₅ is -H or a (C₁-C₃)alkyl;

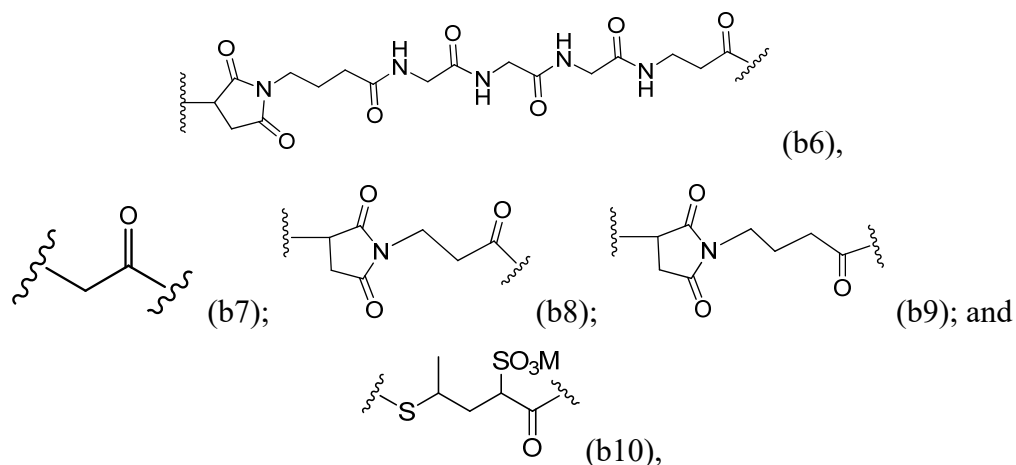
P is an amino acid residue or a peptide containing between 2 to 20 amino acid residues;

R_a and R_b, for each occurrence, are each independently -H, (C₁-C₃)alkyl, or a charged substituent or an ionizable group Q;

m is an integer from 1 to 6; and

Z^{s1} is selected from any one of the following formulas:



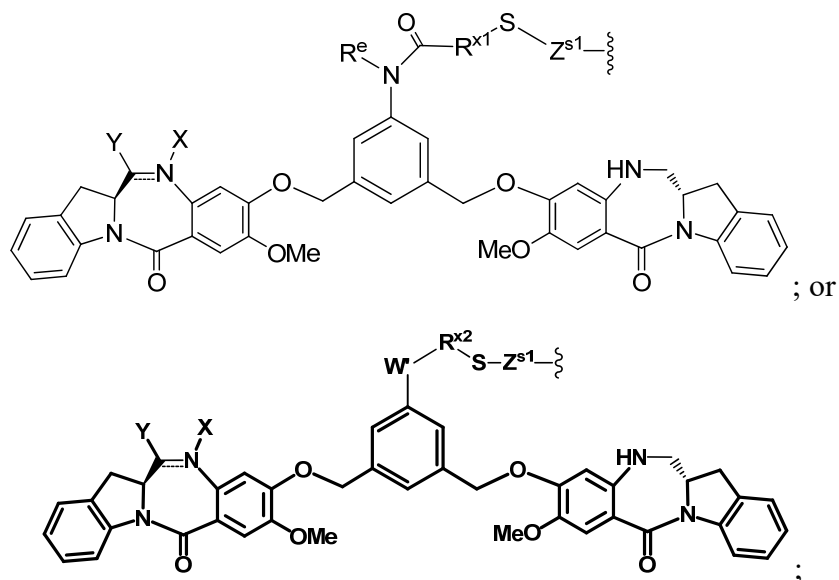


wherein:

q is an integer from 1 to 5; and

M is H^+ or a cation;

Cy^{L2} is represented by the following formula:



or a pharmaceutically acceptable salt thereof, wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H or a (C₁-C₄)alkyl; and when it is a single bond, X is -H or an amine protecting moiety, and Y is -OH or -SO₃M;

R^{x1} and R^{x2} are independently (C₁-C₆)alkyl;

R^e is -H or a (C₁-C₆)alkyl;

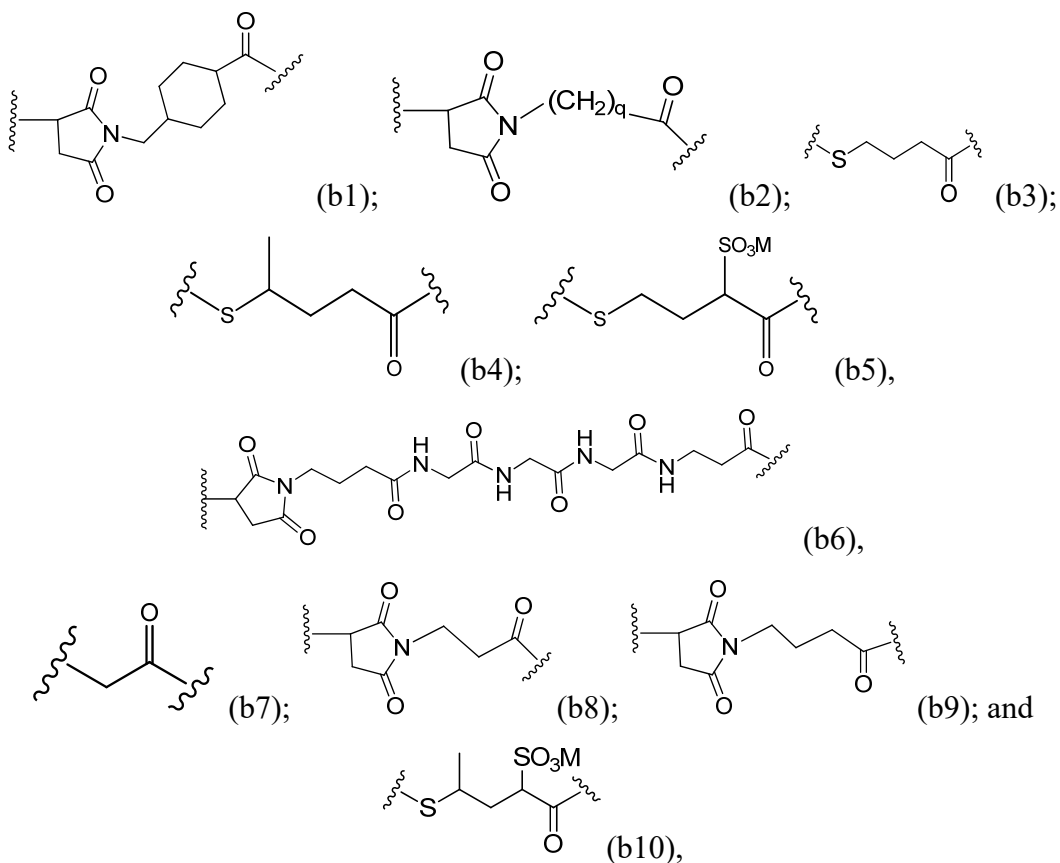
W' is -NR^{e'},

R^{e'} is -(CH₂-CH₂-O)_n-R^k;

n is an integer from 2 to 6;

R^k is -H or -Me;

Z^{s1} is selected from any one of the following formulas:

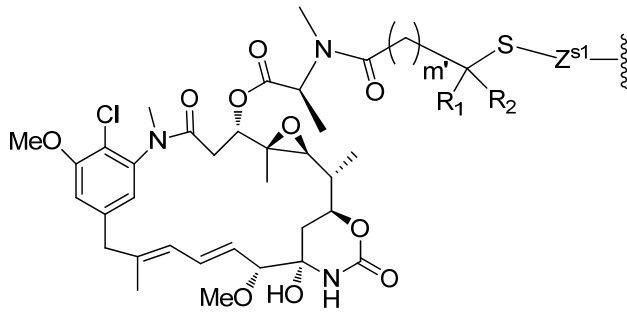


wherein:

q is an integer from 1 to 5; and

M is -H⁺ or a cation; and

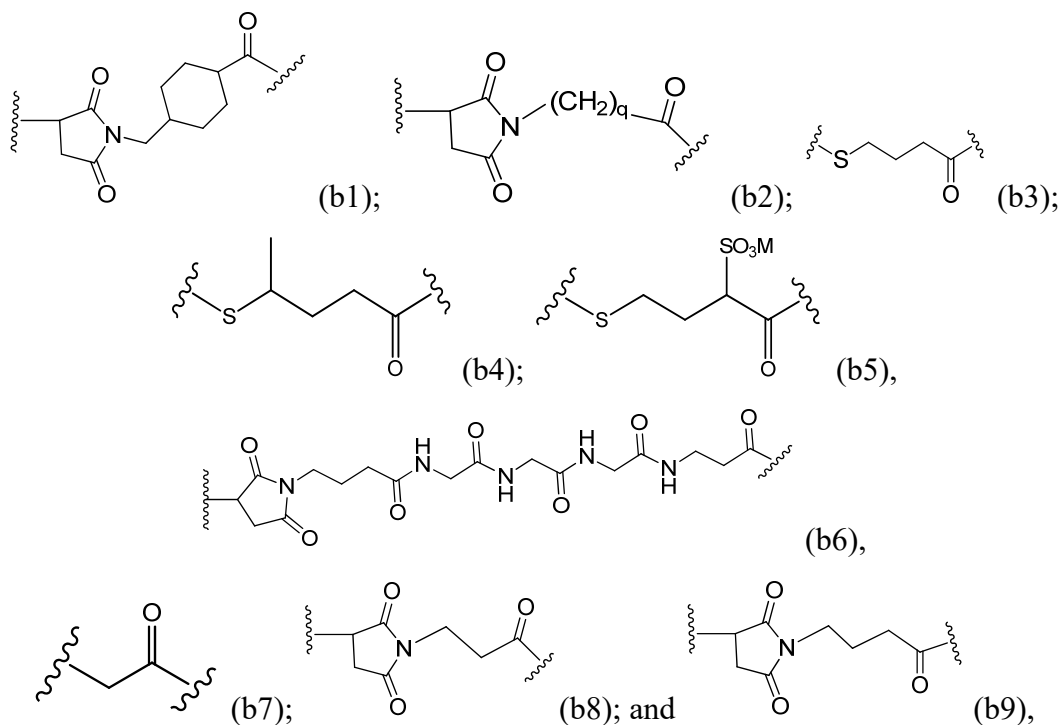
Cy^{L3} is represented by the following formula:



m' is 1 or 2;

R₁ and R₂, are each independently H or a (C₁-C₃)alkyl; and

Z^{s1} is selected from any one of the following formulas:

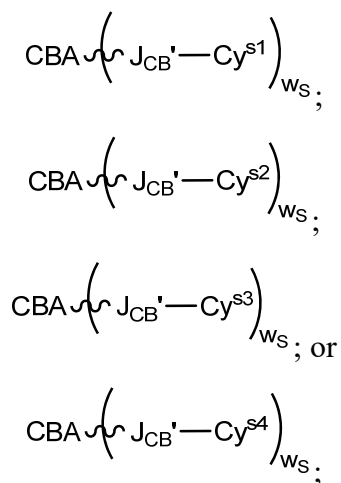


wherein:

q is an integer from 1 to 5; and

M is H^+ or a cation.

17. An immunoconjugate having the following formula:

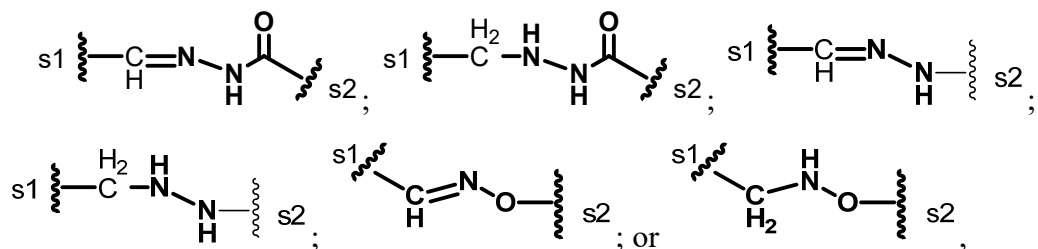


wherein:

CBA is the antibody or antigen-binding fragment thereof of claim 7, or the polypeptide of claim 13, covalently linked to the $J_{CB'}$ group;

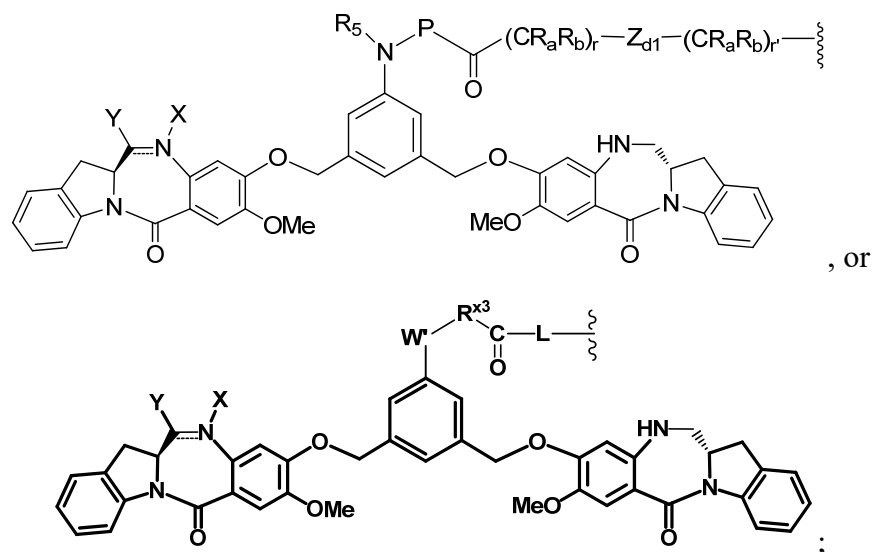
W_s is 1, 2, 3, or 4;

JCB' is a moiety formed by reacting an aldehyde group derived from oxidation of a 2-hydroxyethylamine moiety on an N-terminal of said antibody or antigen-binding fragment thereof, or said polypeptide thereof, and an aldehyde reactive group on Cy^{s1} , Cy^{s2} , Cy^{s3} , or Cy^{s4} and is represented by the following formula:



wherein $s1$ is the site covalently linked to the CBA; and $s2$ is the site covalently linked to Cy^{s1} ;

Cy^{s1} is represented by the following formula:



or a pharmaceutically acceptable salt thereof, wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H or a (C₁-C₄)alkyl; and when it is a single bond, X is -H or an amine protecting moiety, Y is -OH or -SO₃M, and M is H⁺ or a cation;

R₅ is -H or a (C₁-C₃)alkyl;

P is an amino acid residue or a peptide containing 2 to 20 amino acid residues;

Z_{d1} is absent, -C(=O)-NR₉-, or -NR₉-C(=O)-;

R₉ is -H or a (C₁-C₃)alkyl;

R_a and R_b, for each occurrence, are independently -H, (C₁-C₃)alkyl, or a charged substituent or an ionizable group Q;

r and r' are independently an integer from 1 to 6;

W' is -NR^{e'},

R^{e'} is -(CH₂-CH₂-O)_n-R^k;

n is an integer from 2 to 6;

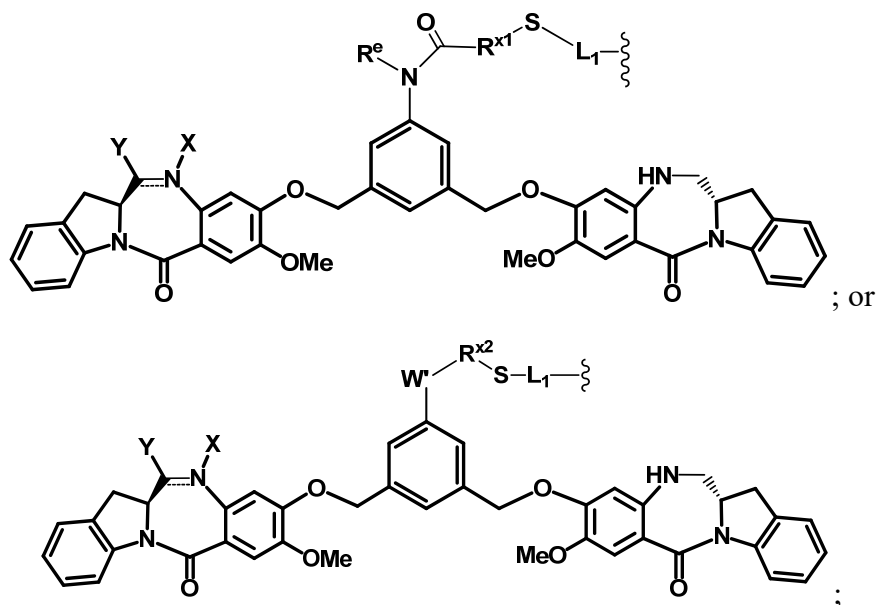
R^k is -H or -Me;

R^{x3} is a (C₁-C₆)alkyl;

L is -NR₉-(CR_aR_b)_{r''} or absent; and

r'' is an integer from 0 to 6;

Cy^{s2} is represented by the following formula:



or a pharmaceutically acceptable salt thereof, wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H or a (C₁-C₄)alkyl; and when it is a single bond, X is -H or an amine protecting moiety, and Y is -OH or -SO₃M;

M is H⁺ or a cation;

R^{x1} is a (C₁-C₆)alkyl;

R^e is -H or a (C₁-C₆)alkyl;

W' is -NR^{e'},

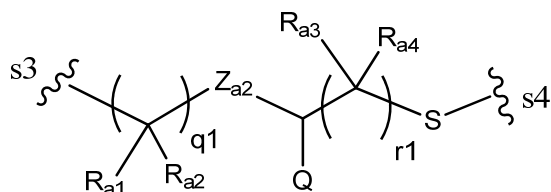
R^{e'} is -(CH₂-CH₂-O)_n-R^k;

n is an integer from 2 to 6;

R^k is -H or -Me;

R^{x2} is a (C₁-C₆)alkyl;

L₁ is represented by the following formula:



wherein:

s₃ is the site covalently linked to the group J_{CB}';

s₄ is the site covalently linked to the -S- group on Cy^{s2};

Z_{a2} is absent, -C(=O)-NR₉-, or -NR₉-C(=O)-;

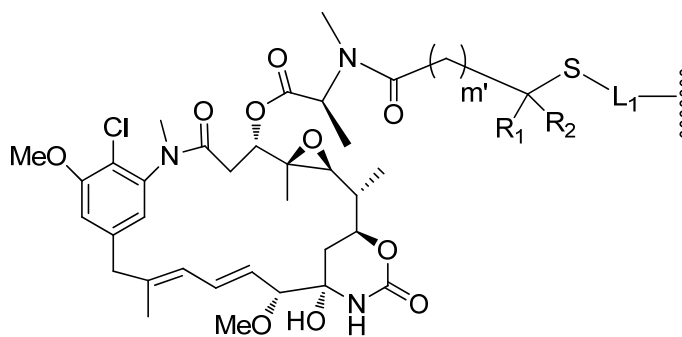
R₉ is -H or a (C₁-C₃)alkyl;

Q is H, a charged substituent or an ionizable group;

R_{a1}, R_{a2}, R_{a3}, R_{a4}, for each occurrence, are independently H or (C₁-C₃)alkyl; and

q₁ and r₁ are each independently an integer from 0 to 10, provided that q₁ and r₁ are not both 0;

Cy^{s3} is represented by the following formula:

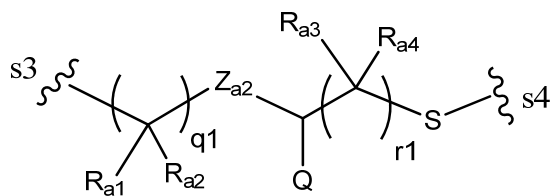


wherein:

m' is 1 or 2;

R₁ and R₂, are each independently H or a (C₁-C₃)alkyl;

L₁ is represented by the following formula:



wherein:

s3 is the site covalently linked to the group J_{CB'};

s4 is the site covalently linked to the -S- group on Cy^{s3};

Z_{a2} is absent, -C(=O)-NR₉-, or -NR₉-C(=O)-;

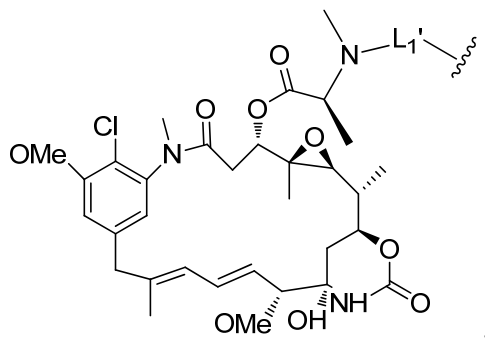
R₉ is -H or a (C₁-C₃)alkyl;

Q is H, a charged substituent or an ionizable group;

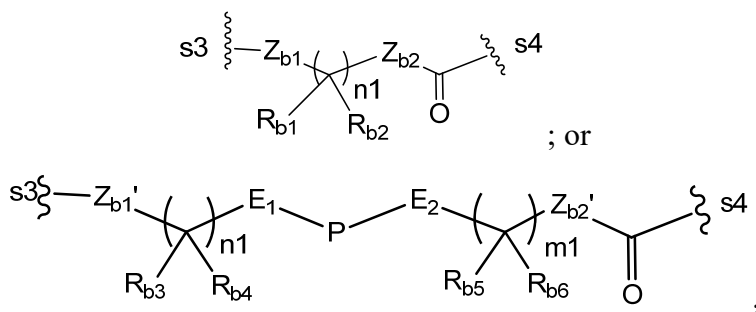
R_{a1}, R_{a2}, R_{a3}, R_{a4}, for each occurrence, are independently H or a (C₁-C₃)alkyl; and

q1 and r1 are each independently an integer from 0 to 10, provided that q1 and r1 are not both 0;

Cy^{s4} is represented by the following formula:



L_{1'} is represented by the following formula:



wherein:

s3 is the site covalently linked to the group J_{CB'} group;

s4 is the site covalently linked to -NMe- group on Cy^{s4};

Z_{b1} and Z_{b2} are both absent, or one of Z_{b1} and Z_{b2} is absent and the other is -CH₂-

O- or -O-CH₂-;

Z_{b1}' and Z_{b2}' are each independently absent, -CH₂-O-, -O-CH₂-, -NR₉-C(=O)-CH₂-, or -CH₂-C(=O)-NR₉-;

R₉ is H or (C₁-C₃)alkyl;

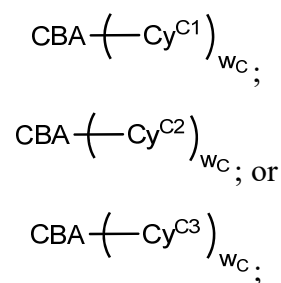
n₁ and m₁ are each independently an integer from 1 to 6;

one of E₁ and E₂ is -C(=O)-, and the other is -NR₉-; or one of E₁ and E₂ is -C(=O)- or -NR₉-, and the other is absent;

P is an amino acid residue or a peptide containing between 2 to 20 amino acid residues; and

R_{b1}, R_{b2}, R_{b3}, R_{b4}, R_{b5} and R_{b6}, for each occurrence, are each independently H or a (C₁-C₃)alkyl.

18. An immunoconjugate represented by the following formula:

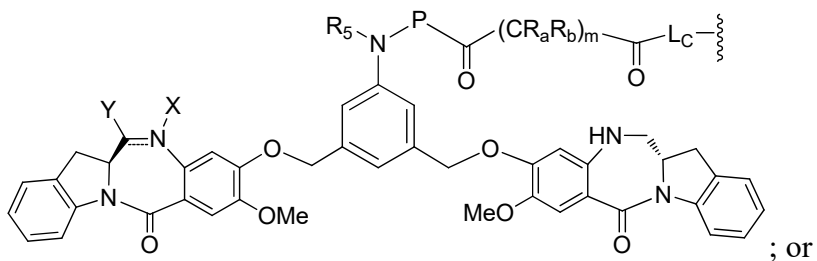


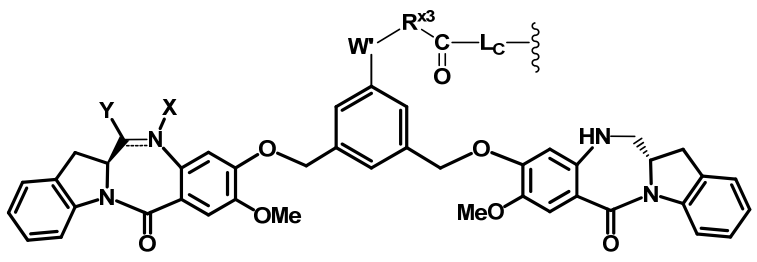
wherein:

CBA is an antibody or antigen-binding fragment thereof of claim 8, or the polypeptide of claim 13, covalently linked to Cy^{C1}, Cy^{C2} or Cy^{C3} through a cysteine residue;

W_C is 1 or 2;

Cy^{C1} is represented by the following formula:





or a pharmaceutically acceptable salt thereof, wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H or a (C₁-C₄)alkyl; and when it is a single bond, X is -H or an amine protecting moiety, Y is -OH or -SO₃M, and M is H⁺ or a cation;

R₅ is -H or a (C₁-C₃)alkyl;

P is an amino acid residue or a peptide containing 2 to 20 amino acid residues;

R_a and R_b, for each occurrence, are independently -H, (C₁-C₃)alkyl, or a charged substituent or an ionizable group Q;

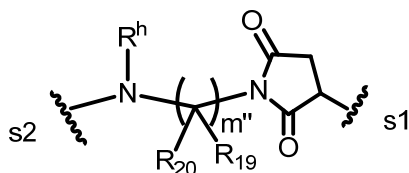
W' is -NR^{e'},

R^{e'} is -(CH₂-CH₂-O)_n-R^k;

n is an integer from 2 to 6;

R^k is -H or -Me;

R^{x3} is a (C₁-C₆)alkyl; and,



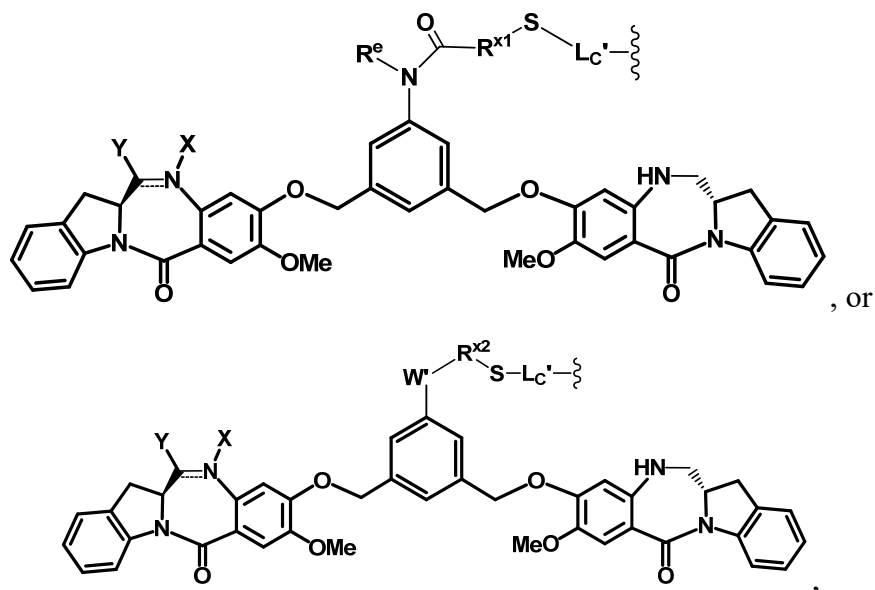
Lc is represented by , s1 is the site covalently linked to CBA, and s2 is the site covalently linked to the -C(=O)- group on Cy^{C1};
wherein:

R₁₉ and R₂₀, for each occurrence, are independently -H or a (C₁-C₃)alkyl;

m'' is an integer between 1 and 10; and

R^h is -H or a (C₁-C₃)alkyl;

Cy^{C2} is represented by the following formula:



or a pharmaceutically acceptable salt thereof, wherein:

the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H or a (C₁-C₄)alkyl; and when it is a single bond, X is -H or an amine protecting moiety, Y is -OH or -SO₃M, and M is H⁺ or a cation;

R^{x1} is a (C₁-C₆)alkyl;

R^e is -H or a (C₁-C₆)alkyl;

W' is -NR^{e'};

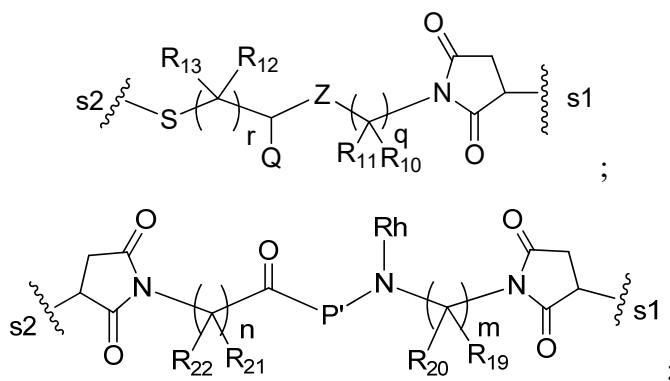
R^{e'} is -(CH₂-CH₂-O)_n-R^k;

n is an integer from 2 to 6;

R^k is -H or -Me;

R^{x2} is a (C₁-C₆)alkyl;

L_C' is represented by the following formula:



wherein:

s1 is the site covalently linked to the CBA and s2 is the site covalently linked to -S- group on Cy^{C2};

Z is -C(=O)-NR₉-, or -NR₉-C(=O)-;

Q is -H, a charged substituent, or an ionizable group;

R₉, R₁₀, R₁₁, R₁₂, R₁₃, R₁₉, R₂₀, R₂₁ and R₂₂, for each occurrence, are independently -H or a (C₁-C₃)alkyl;

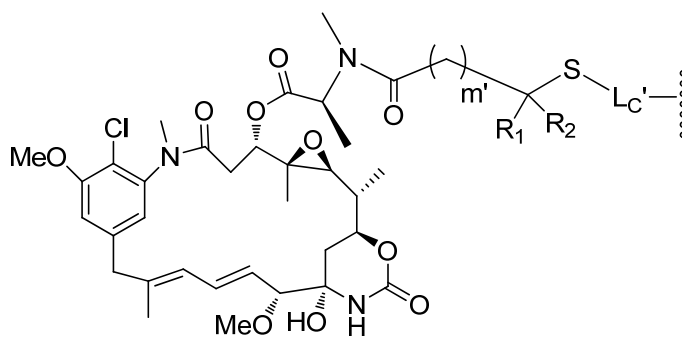
q and r, for each occurrence, are independently an integer between 0 and 10;

m and n are each independently an integer between 0 and 10;

R^h is -H or a (C₁-C₃)alkyl; and

P' is an amino acid residue or a peptide containing 2 to 20 amino acid residues;

Cy^{C3} is represented by the following formula:

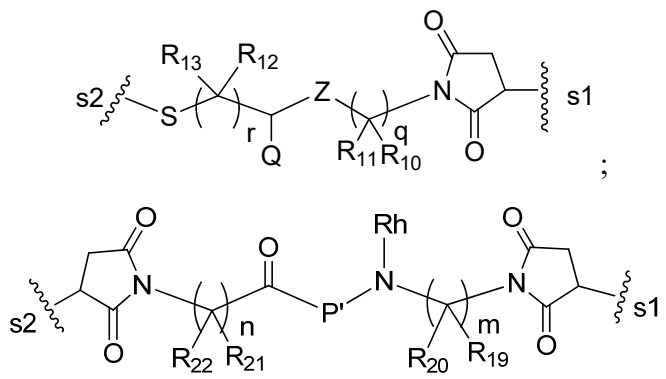


wherein:

m' is 1 or 2;

R₁ and R₂, are each independently -H or a (C₁-C₃)alkyl;

Lc' is represented by the following formula:



wherein:

s1 is the site covalently linked to the CBA and s2 is the site covalently linked

to -S- group on Cy^{C3};

Z is -C(=O)-NR₉-, or -NR₉-C(=O)-;

Q is H, a charged substituent, or an ionizable group;

R₉, R₁₀, R₁₁, R₁₂, R₁₃, R₁₉, R₂₀, R₂₁ and R₂₂, for each occurrence, are independently -H or a (C₁-C₃)alkyl;

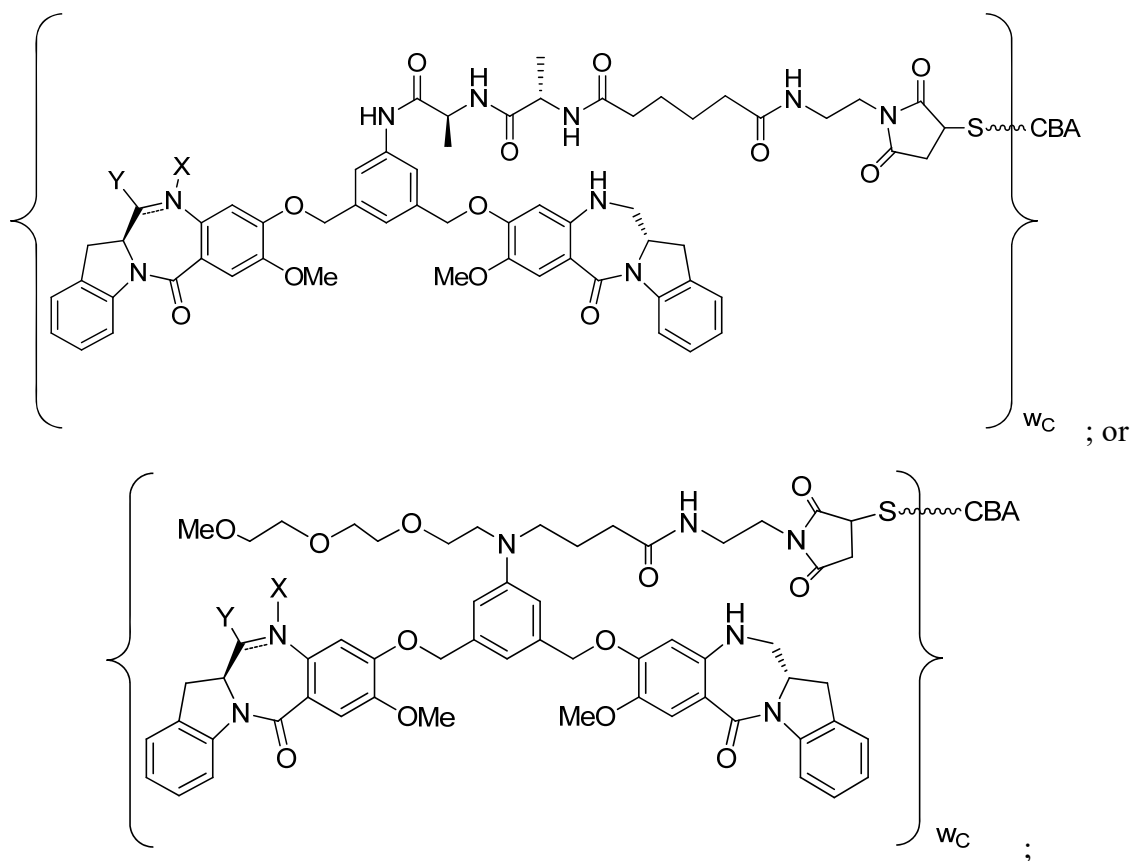
q and r, for each occurrence, are independently an integer between 0 and 10;

m and n are each independently an integer between 0 and 10;

R^h is -H or a (C₁-C₃)alkyl; and

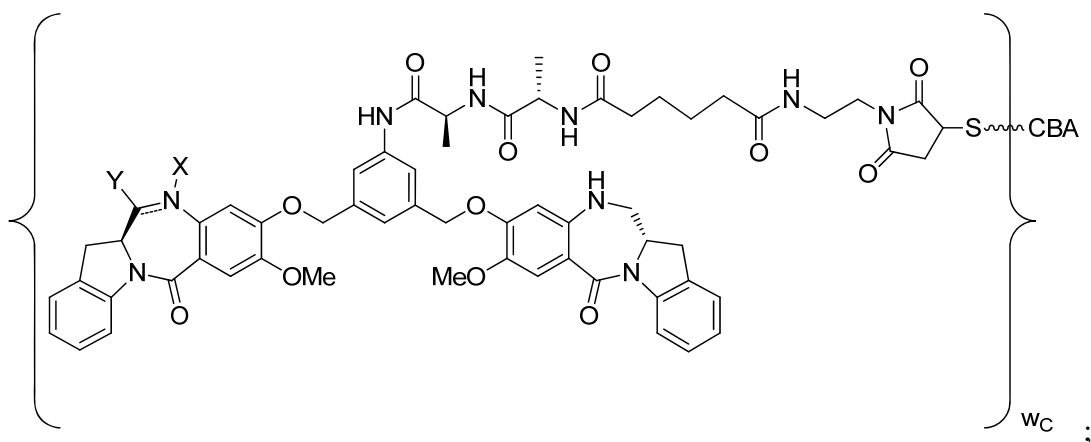
P' is an amino acid residue or a peptide containing 2 to 20 amino acid residues.

19. The immunoconjugate of claim 18, which is represented by the following formula:



or a pharmaceutically acceptable salt thereof, wherein the double line == between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H, and when it is a single bond, X is -H, and Y is -OH or -SO₃M.

20. The immunoconjugate of claim 19, which is represented by the following formula:



or a pharmaceutically acceptable salt thereof, wherein:

CBA is an antibody comprising an immunoglobulin heavy chain region having the amino acid sequence set forth in SEQ ID NO: 54; and an immunoglobulin light chain region having the amino acid sequence set forth in SEQ ID NO: 51; and

the double line $\equiv$ between N and C represents a single bond or a double bond, provided that when it is a double bond, X is absent and Y is -H, and when it is a single bond, X is -H, and Y is -OH or -SO₃M.

21. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-12, or the polypeptide of claim 13, or the immunoconjugate of any one of claims 14-20, and a pharmaceutically acceptable carrier.
22. A method for inhibiting the growth of a cell expressing CD123, comprising contacting the cell with the antibody or antigen-binding fragment thereof of any one of claims 1-12, or the polypeptide of claim 13, or the immunoconjugate of any one of claims 14-20, or the pharmaceutical composition of claim 21.
23. Use of the antibody or antigen-binding fragment thereof any one of claims 1-12, or the polypeptide of claim 13, or the immunoconjugate of any one of claims 14-20 in the manufacture of a medicament for treating a subject having cancer, wherein cells of the cancer expresses CD123.
24. The use of claim 23, wherein said cancer is leukemia or lymphoma.
25. The use of claim 23, wherein said cancer is selected from the group consisting of: acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), and Chronic

lymphocytic leukemia (CLL).

26. The use of claim 25, wherein said cancer is acute myeloid leukemia (AML).
27. The use of claim 25, wherein said cancer is B-cell acute lymphoblastic leukemia (B-ALL).
28. Use of the antibody or antigen-binding fragment thereof any one of claims 1-12, or the polypeptide of claim 13, or the immunoconjugate of any one of claims 14-20 in the manufacture of a medicament for treating a cell-proliferative disorder in a subject, wherein cells of the cell-proliferative disorder expresses CD123.
29. The use of claim 28, wherein said cell-proliferative disorder is selected from the group consisting of: acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL), B-cell lineage acute lymphoblastic leukemia (B-ALL), chronic lymphocytic leukemia (CLL), hairy cell leukemia (HCL), myelodysplastic syndrome, basic plasmacytoid DC neoplasm (BPDCN) leukemia, non-Hodgkin lymphomas (NHL), mantle cell lymphoma, and Hodgkin's leukemia (HL).