WHAT IS CLAIMED IS:

1. An immunoconjugate comprising an antibody that binds CD22 covalently attached to a cytotoxic agent, wherein the antibody binds an epitope within amino acids 20 to 240 of SEQ ID NO: 28, and wherein the cytotoxic agent is a pyrrolobenzodiazepine.

2. The immunoconjugate of claim 1, wherein the antibody comprises (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10.

3. The immunoconjugate of claim 1 or claim 2, wherein the antibody comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11.

4. The immunoconjugate of claim 1, wherein the antibody comprises:

a) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (iv) HVR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 12 and 15 to 22, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14; or

b) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 15, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14.

5. The immunoconjugate of any one of claims 1 to 3, wherein the antibody comprises:

a) (i) HVR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 12 and 15 to 22, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14; or

b) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 15, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14.

6. The immunoconjugate of any one of claims 1 to 5, wherein the antibody comprises:

a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 7; or

b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 8; or

c) a VH sequence as in (a) and a VL sequence as in (b).

7. The immunoconjugate of claim 6, comprising a VH sequence having the amino acid sequence of SEQ ID NO: 7.

8. The immunoconjugate of claim 6, comprising a VL sequence having the amino acid sequence of SEQ ID NO: 6 or a VL sequence having the amino acid sequence of SEQ ID NO:8.

9. An immunoconjugate comprising an antibody that binds CD22 covalently attached to a cytotoxic agent, wherein the antibody comprises (a) a VH sequence having the amino acid sequence of SEQ ID NO: 7 and a VL sequence having the amino acid sequence of SEQ ID NO: 8, and wherein the cytotoxic agent is a pyrrolobenzodiazepine.

10. The immunoconjugate of any one of claims 1 to 9, wherein the antibody is an IgG1, IgG2a or IgG2b antibody.

11. An immunoconjugate of any one of claims 1 to 10, wherein the immunoconjugate has the formula Ab-(L-D)p, wherein:

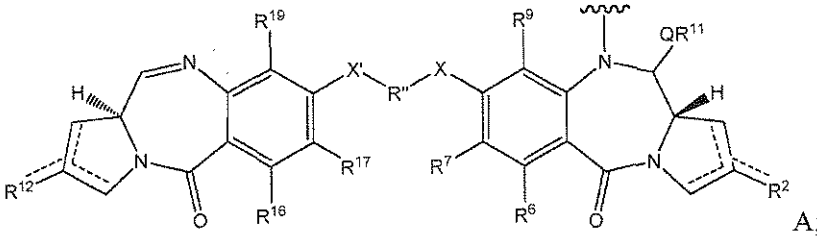
(a) Ab is the antibody;

(b) L is a linker;

(c) D is the cytotoxic agent; and

(d) p ranges from 1-8.

12. The immunoconjugate of claim 11, wherein D is a pyrrolobenzodiazepine of Formula A:



A;

wherein the wavy line indicates the covalent attachement site to the linker;

the dotted lines indicate the optional presence of a double bond between C1 and C2 or C2 and C3;

R^2 is independently selected from H, OH, =O, $=CH_2$, CN, R, OR, $=CH\text{-}R^D$, $=C(R^D)_2$, $O\text{-}SO_2\text{-}R$, CO_2R and COR, and optionally further selected from halo or dihalo, wherein R^D is independently selected from R, CO_2R, COR, CHO, CO_2H, and halo;

R^6 and R^9 are independently selected from H, R, OH, OR, SH, SR, NH_2, NHR, NRR', NO_2, Me_3Sn and halo;

R^7 is independently selected from H, R, OH, OR, SH, SR, NH_2, NHR, NRR', NO_2, Me_3Sn and halo;

Q is independently selected from O, S and NH;

R^{11} is either H, or R or, where Q is O, SO_3M, where M is a metal cation;

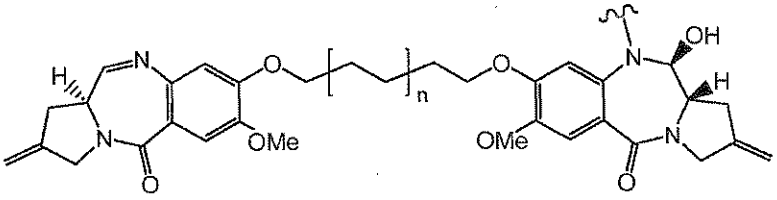
R and R' are each independently selected from optionally substituted C_{1-12} alkyl, C_{3-20} heterocyclyl and C_{5-20} aryl groups, and optionally in relation to the group NRR', R and R' together with the nitrogen atom to which they are attached form an optionally substituted 4-, 5-, 6- or 7-membered heterocyclic ring;

R^{12}, R^{16}, R^{19} and R^{17} are as defined for R^2, R^6, R^9 and R^7 respectively;

R″ is a C_{3-12} alkylene group, which chain may be interrupted by one or more heteroatoms and/or aromatic rings that are optionally substituted; and

X and X' are independently selected from O, S and N(H).

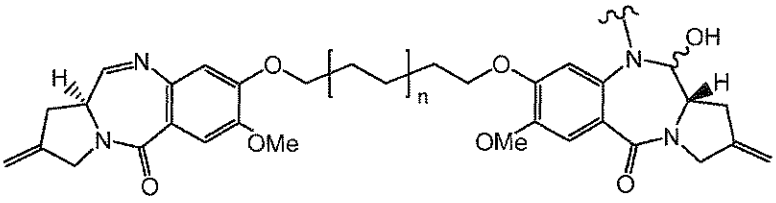
13. The immunoconjugate of claim 12, wherein D has the structure:



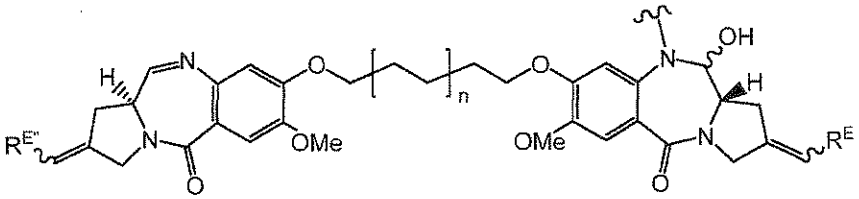
A(II);

wherein n is 0 or 1.

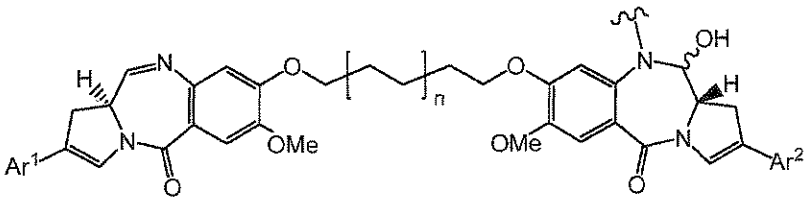
14. The immunoconjugate of claim 12, wherein D has a structure selected from:



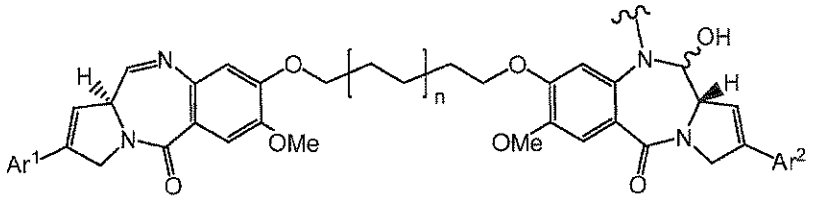
A(I);



A(III);



A(IV); and



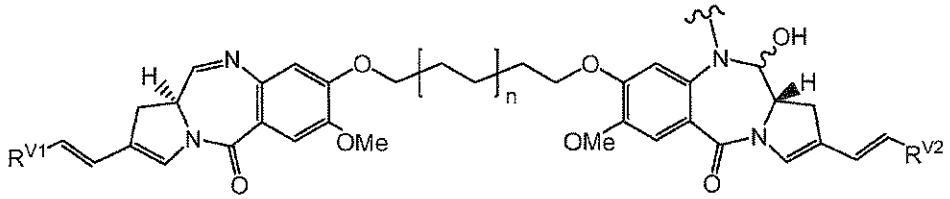
A(V);

wherein R^E and $R^{E''}$ are each independently selected from H or R^D, wherein R^D is independently selected from R, CO_2R, COR, CHO, CO_2H, and halo;

wherein Ar^1 and Ar^2 are each independently optionally substituted C_{5-20} aryl; and

wherein n is 0 or 1.

15. The immunoconjugate of claim 11, wherein D is a pyrrolobenzodiazepine of Formula B:



wherein the horizontal wavy line indicates the covalent attachement site to the linker;

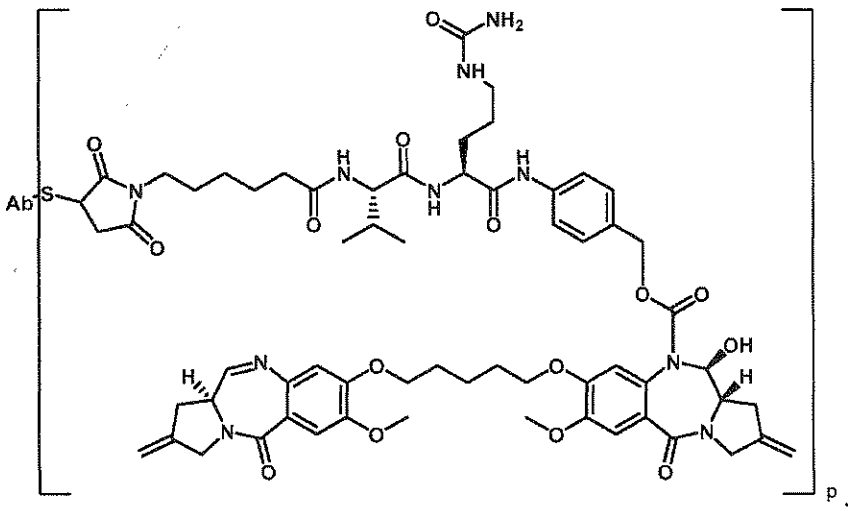
R^{V1} and R^{V2} are independently selected from H, methyl, ethyl, phenyl, fluoro-substituted phenyl, and C_{5-6} heterocyclyl; and

n is 0 or 1.

16. The immunoconjugate of any one of claims 11 to 15, wherein the linker is cleavable by a protease.

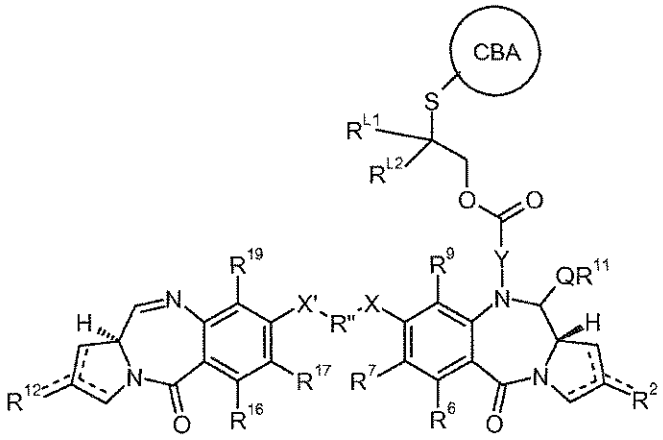
17. The immunoconjugate of claim 16, wherein the linker comprises a val-cit dipeptide or a Phe-Lys dipeptide.

18. The immunoconjugate of claim 11 having the formula



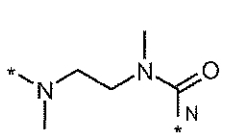
19. The immunoconjugate of any one of claims 11 to 18, wherein p ranges from 1-3.

20. The immunoconjugate of claim 12, comprising the structure:

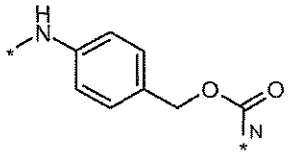


D ;

wherein CBA represents the antibody (Ab); R^{L1} and R^{L2} are each independently selected from H and methyl, or together with the carbon atom to which they are bound form a cyclopropylene group; and Y is selected from a single bond, (a1), and (a2):



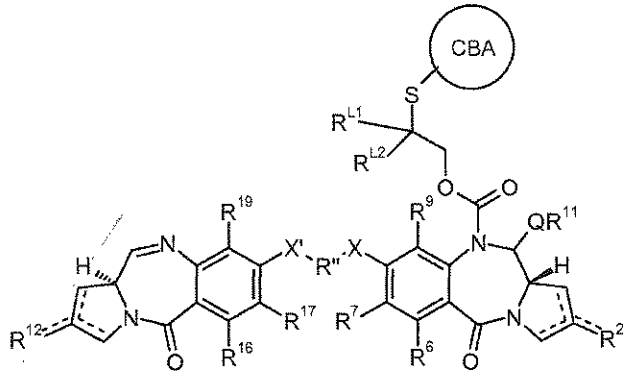
(a1)



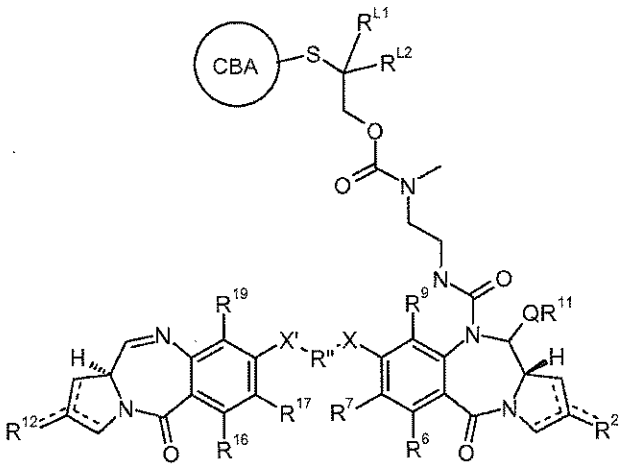
(a2);

wherein N shows where the group binds to the N10 of the PBD moiety.

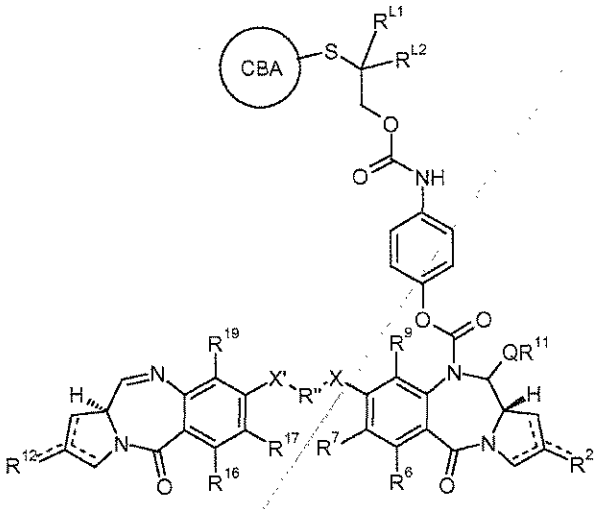
21. The immunoconjugate of claim 20, comprising a structure selected from:



D-I ;

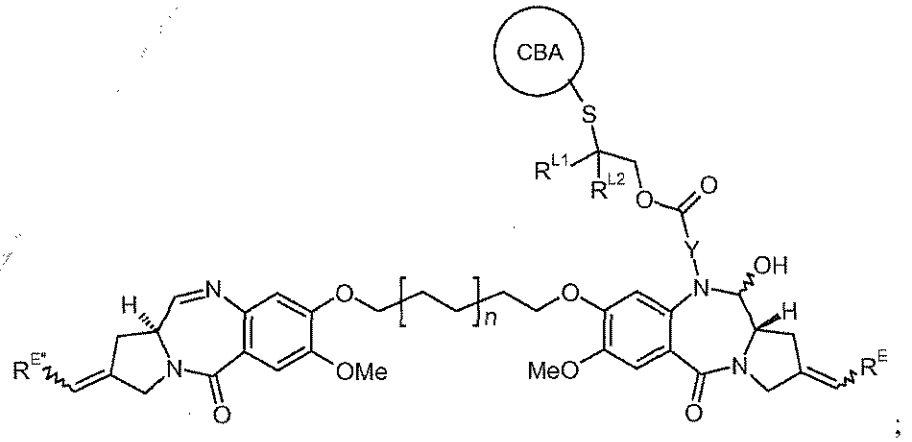


D-II ; and



D-III

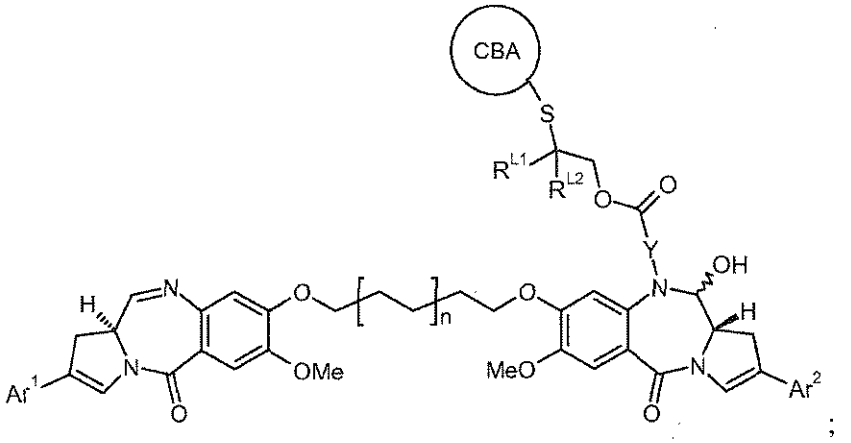
22. The immunoconjugate of claim 20 or claim 21, comprising the structure:



;

wherein R^E and $R^{E''}$ are each independently selected from H and R^D.

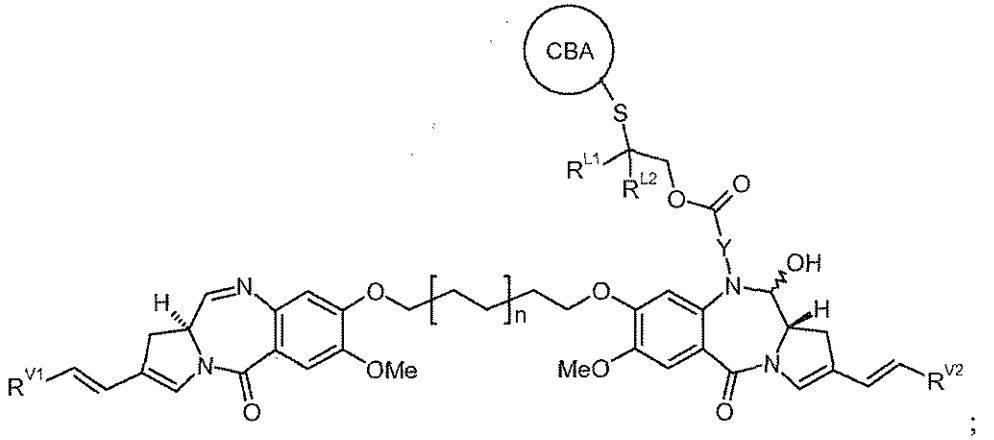
23. The immunoconjugate of claim 20 or claim 21, comprising the structure:



wherein Ar^1 and Ar^2 are each independently optionally substituted C_{5-20} aryl.

24. The immunoconjugate of claim 23, wherein Ar^1 and Ar^2 are each independently selected from optionally substituted phenyl, furanyl, thiophenyl and pyridyl.

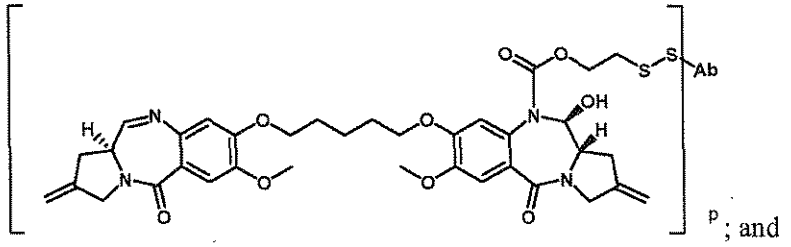
25. The immunoconjugate of claim 20 or claim 21, comprising the structure:



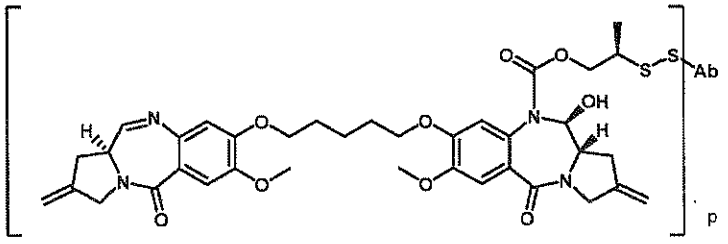
wherein R^{V1} and R^{V2} are each independently selected from H, methyl, ethyl, optionally substituted phenyl, and C_{5-6} heterocyclyl.

26. The immunoconjugate of claim 25, wherein R^{V1} and R^{V2} are each independently selected from H, phenyl, and 4-fluorophenyl.

27. An immunoconjugate having a formula selected from:

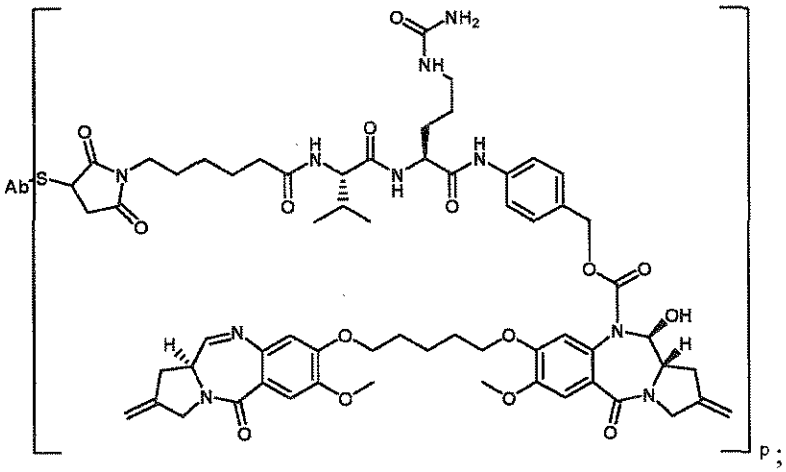


; and



wherein Ab is an antibody comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 15, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14; and wherein p ranges from 1 to 3.

28. An immunoconjugate having the formula:



wherein Ab is an antibody comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 15, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14; and wherein p ranges from 1 to 3.

29. The immunoconjugate of claim 27 or 28, wherein the antibody comprises a VH sequence of SEQ ID NO: 7 and a VL sequence of SEQ ID NO: 8.

30. The immunoconjugate of claim 29, wherein the antibody comprises a heavy chain of SEQ ID NO: 26 and a light chain of SEQ ID NO: 23.

31. The immunoconjugate of any one of the preceding claims, wherein the antibody is a monoclonal antibody.

32. The immunoconjugate of any one of the preceding claims, wherein the antibody is a human, humanized, or chimeric antibody.

33. The immunoconjugate of any one of the preceding claims, wherein the antibody is an antibody fragment that binds CD22.

34. The immunoconjugate of claim any one of the preceding claims, wherein the antibody binds human CD22.

35. The immunoconjugate of claim 34, wherein human CD22 has the sequence of SEQ ID NO: 28 or SEQ ID NO: 29.

36. A pharmaceutical formulation comprising the immunoconjugate of any one of the preceding claims and a pharmaceutically acceptable carrier.

37. The pharmaceutical formulation of claim 36, further comprising an additional therapeutic agent.

38. Use of the immunoconjugate of any one of claims 1 to 35 in the manufacture of a medicament for the treatment of an individual having a CD22-positive cancer.

39. The use of claim 38, wherein the CD22-positive cancer is selected from - lymphoma, non-Hogkins lymphoma (NHL), aggressive NHL, relapsed aggressive NHL, relapsed indolent NHL, refractory NHL, refractory indolent NHL, chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma, leukemia, hairy cell leukemia (HCL), acute lymphocytic leukemia (ALL), Burkitt's lymphoma, and mantle cell lymphoma.

40. The use of claim 39, wherein the immunoconjugate is to be administered with an additional therapeutic agent to the individual.

41. The use of claim 40, wherein the additional therapeutic agent comprises an antibody that binds CD79b.

42. The use of claim 41, wherein the additional therapeutic agent is an immunoconjugate comprising an antibody that binds CD79b covalently attached to a cytotoxic agent.

43. Use of the immunoconjugate of any one of claims 1 to 35 in the manufacture of a medicament for the inhibition of proliferation of a CD22-positive cell, wherein the cell is to be exposed to the immunoconjugate under conditions permissive for binding of the immunoconjugate to CD22 on the surface of the cell, thereby inhibiting proliferation of the cell.

44. The use of claim 43, wherein the cell is a neoplastic B cell.

45. The use of claim 44, wherein the cell is a lymphoma cell.

46. An *in vitro* method of inhibiting proliferation of a CD22-positive cell, the method comprising exposing the cell to the immunoconjugate of any one of claims 1 to 35 under conditions permissive for binding of the immunoconjugate to CD22 on the surface of the cell, thereby inhibiting proliferation of the cell.

47. The method of claim 46, wherein the cell is a neoplastic B cell.

48. The method of claim 47, wherein the cell is a lymphoma cell.

WHAT IS CLAIMED IS:

1. An immunoconjugate of formula Ab-(L-D)p, wherein:

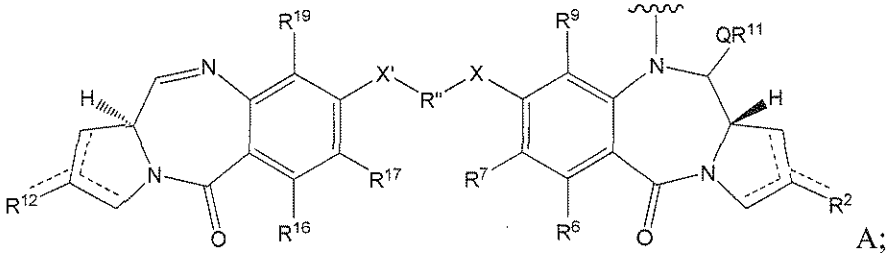
(a) Ab is an antibody that binds CD22;

(b) L is a linker;

(c) D is a cytotoxic agent; and

(d) p ranges from 1-8;

wherein D is a pyrrolobenzodiazepine of Formula A:



A;

wherein the wavy line indicates the covalent attachment site to the linker;

the dotted lines indicate the optional presence of a double bond between C1 and C2 or C2 and C3;

R^2 is independently selected from H, OH, =O, $=CH_2$, CN, R, OR, $=CH\text{-}R^D$, $=C(R^D)_2$, $O\text{-}SO_2\text{-}R$, CO_2R and COR, and optionally further selected from halo or dihalo, wherein R^D is independently selected from R, CO_2R, COR, CHO, CO_2H, and halo;

R^6 and R^9 are independently selected from H, R, OH, OR, SH, SR, NH_2, NHR, NRR', NO_2, Me_3Sn and halo;

R^7 is independently selected from H, R, OH, OR, SH, SR, NH_2, NHR, NRR', NO_2, Me_3Sn and halo;

Q is independently selected from O, S and NH;

R^{11} is either H, or R or, where Q is O, SO_3M, where M is a metal cation;

R and R' are each independently selected from optionally substituted C_{1-12} alkyl, C_{3-20} heterocyclyl and C_{5-20} aryl groups, and optionally in relation to the group NRR', R and R' together with the nitrogen atom to which they are attached form an optionally substituted 4-, 5-, 6- or 7-membered heterocyclic ring;

R^{12}, R^{16}, R^{19} and R^{17} are as defined for R^2, R^6, R^9 and R^7 respectively;

R'' is a C_{3-12} alkylene group, which chain may be interrupted by one or more heteroatoms and/or aromatic rings that are optionally substituted; and

X and X' are independently selected from O, S and N(H); and wherein the antibody binds an epitope within amino acids 20 to 240 of SEQ ID NO: 28.

2. The immunoconjugate of claim 1, wherein the antibody comprises (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10.

3. The immunoconjugate of claim 1 or claim 2, wherein the antibody comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11.

4. The immunoconjugate of claim 1, wherein the antibody comprises:

a) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (iv) HVR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 12 and 15 to 22, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14; or

b) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 15, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14.

5. The immunoconjugate of any one of claims 1 to 3, wherein the antibody comprises:

a) (i) HVR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 12 and 15 to 22, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14; or

b) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 15, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14.

6. The immunoconjugate of any one of claims 1 to 5, wherein the antibody comprises:

a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 7; or

b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 8; or

c) a VH sequence as in (a) and a VL sequence as in (b).

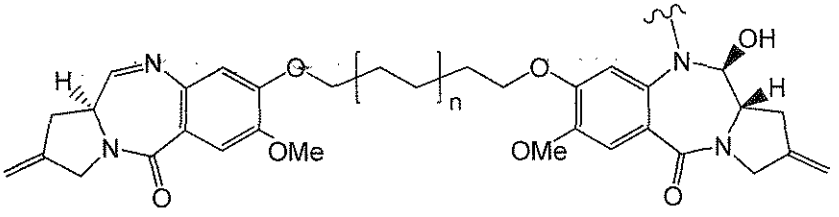
7. The immunoconjugate of claim 6, comprising a VH sequence having the amino acid sequence of SEQ ID NO: 7.

8. The immunoconjugate of claim 6, comprising a VL sequence having the amino acid sequence of SEQ ID NO: 6 or a VL sequence having the amino acid sequence of SEQ ID NO:8.

9. An immunoconjugate comprising an antibody that binds CD22 covalently attached to a cytotoxic agent, wherein the antibody comprises (a) a VH sequence having the amino acid sequence of SEQ ID NO: 7 and a VL sequence having the amino acid sequence of SEQ ID NO: 8, and wherein the cytotoxic agent is a pyrrolobenzodiazepine.

10. The immunoconjugate of any one of claims 1 to 9, wherein the antibody is an IgG1, IgG2a or IgG2b antibody.

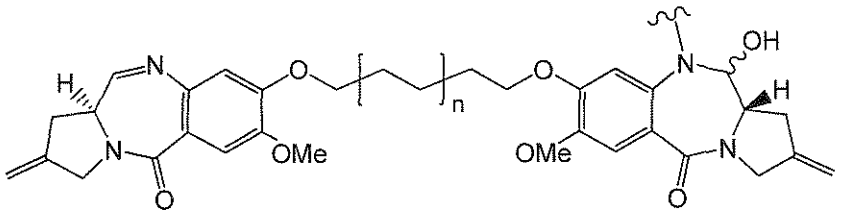
11. The immunoconjugate of any one of claims 1 to 10, wherein D has the structure:



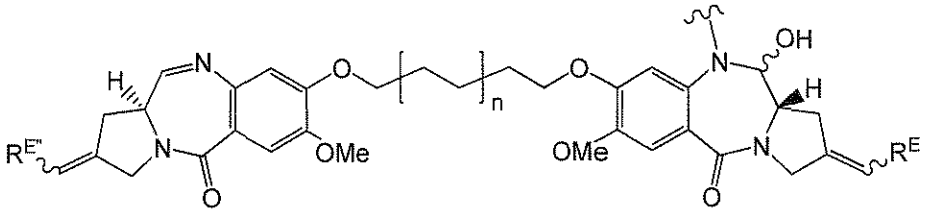
A(II);

wherein n is 0 or 1.

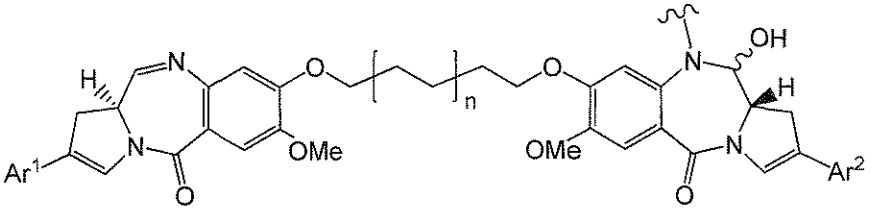
12. The immunoconjugate of any one of claims 1 to 10, wherein D has a structure selected from:



A(I);

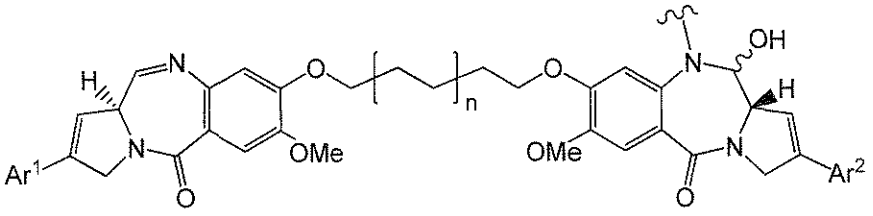


A(III);



A(IV);

and



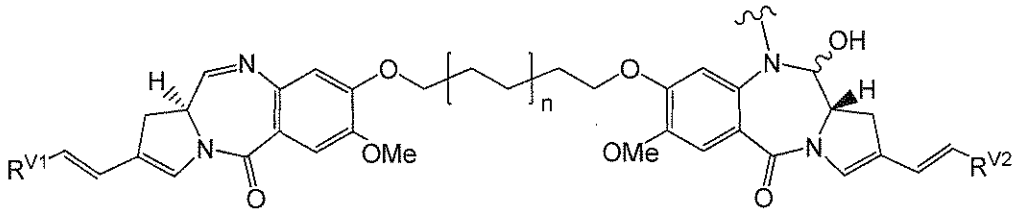
A(V);

wherein R^E and $R^{E''}$ are each independently selected from H or R^D, wherein R^D is independently selected from R, CO_2R, COR, CHO, CO_2H, and halo;

wherein Ar^1 and Ar^2 are each independently optionally substituted C_{5-20} aryl; and

wherein n is 0 or 1.

13. The immunoconjugate of any one of claims 1 to 10, wherein D is a pyrrolobenzodiazepine of Formula B:



wherein the horizontal wavy line indicates the covalent attachment site to the linker;

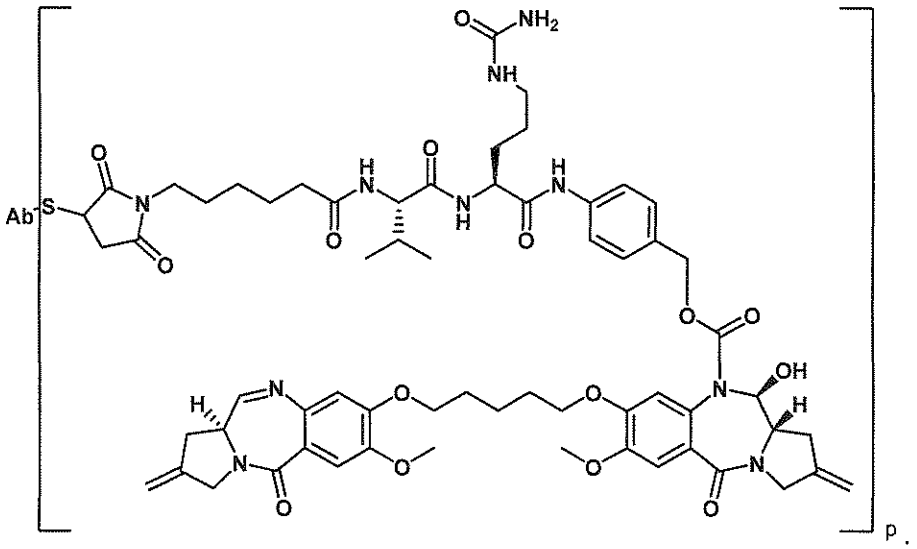
R^{V1} and R^{V2} are independently selected from H, methyl, ethyl, phenyl, fluoro-substituted phenyl, and C_{5-6} heterocyclyl; and

n is 0 or 1.

14. The immunoconjugate of any one of claims 1 to 13, wherein the linker is cleavable by a protease.

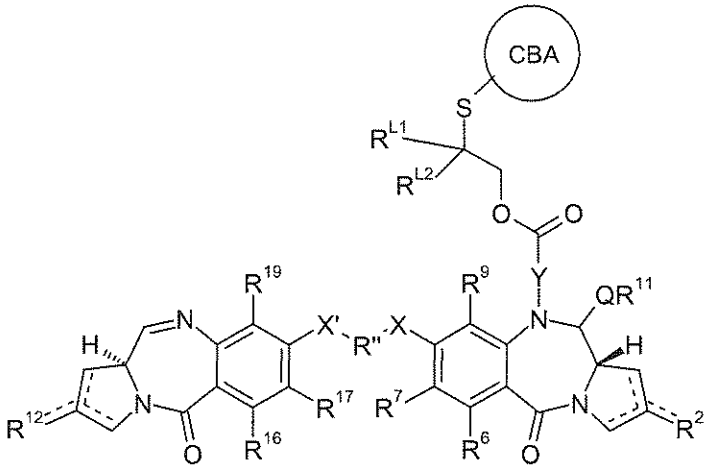
15. The immunoconjugate of claim 14, wherein the linker comprises a val-cit dipeptide or a Phe-Lys dipeptide.

16. The immunoconjugate of any one of claims 1 to 10having the formula



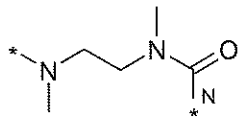
17. The immunoconjugate of any one of claims 1 to 16, wherein p ranges from 1-3.

18. The immunoconjugate of any one of claims 1 to 10, comprising the structure:

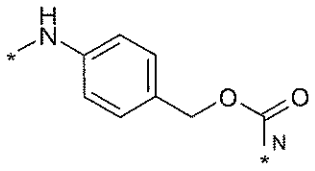


D ;

wherein CBA represents the antibody (Ab); R^{L1} and R^{L2} are each independently selected from H and methyl, or together with the carbon atom to which they are bound form a cyclopropylene group; and Y is selected from a single bond, (a1), and (a2):



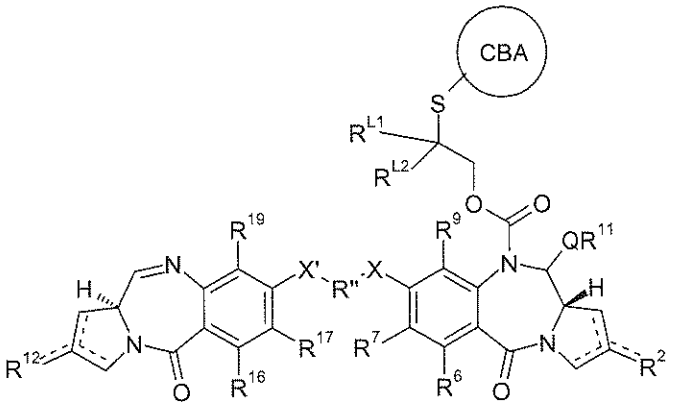
(a1)



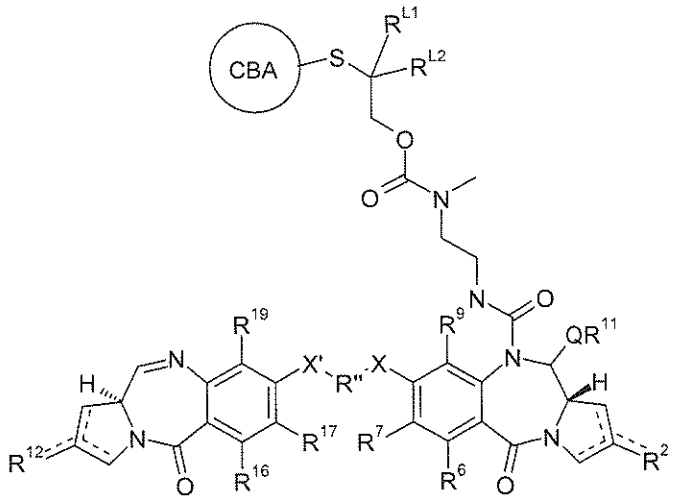
(a2);

wherein N shows where the group binds to the N10 of the PBD moiety.

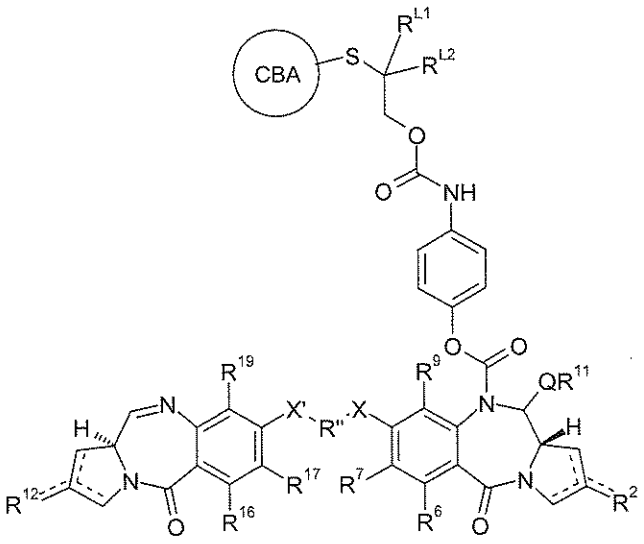
19. The immunoconjugate of claim 18, comprising a structure selected from:



D-I ;

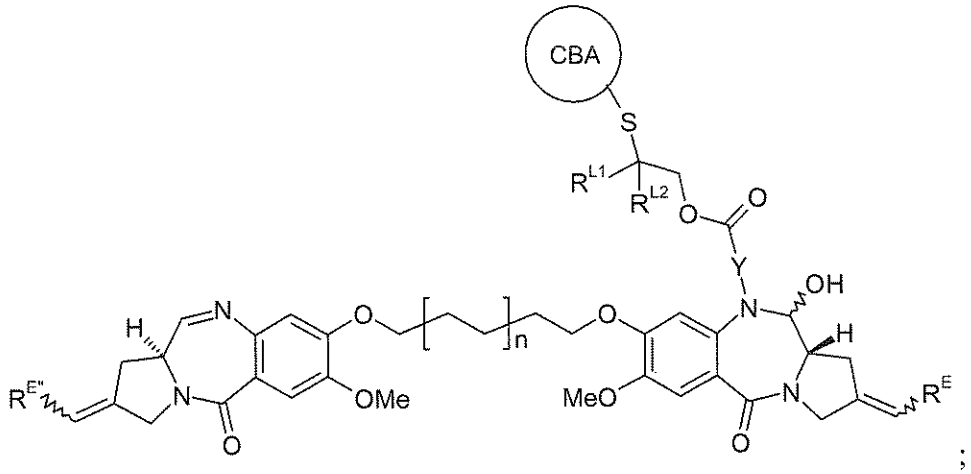


D-II ; and



D-III

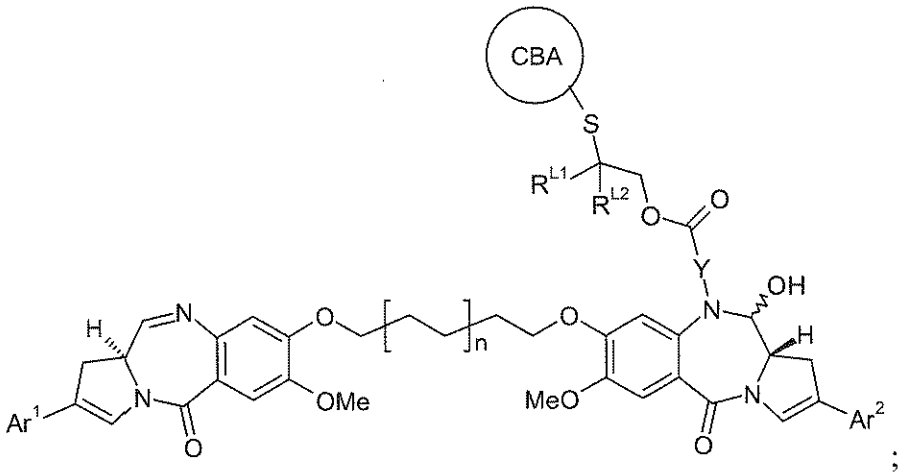
20. The immunoconjugate of claim 18 or claim 19, comprising the structure:



;

wherein R^E and $R^{E''}$ are each independently selected from H and R^D.

21. The immunoconjugate of claim 18 or claim 19, comprising the structure:

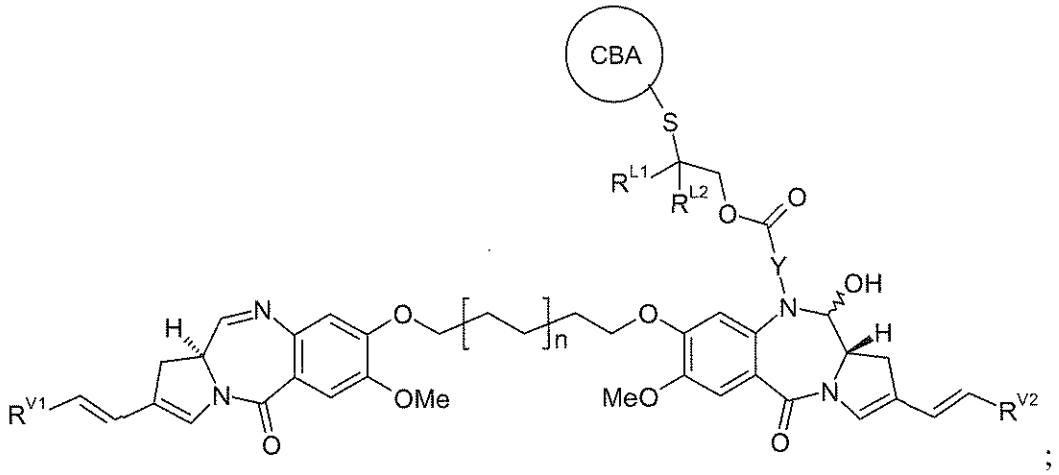


;

wherein Ar^1 and Ar^2 are each independently optionally substituted C_{5-20} aryl.

22. The immunoconjugate of claim 21, wherein Ar^1 and Ar^2 are each independently selected from optionally substituted phenyl, furanyl, thiophenyl and pyridyl.

23. The immunoconjugate of claim 18 or claim 19, comprising the structure:

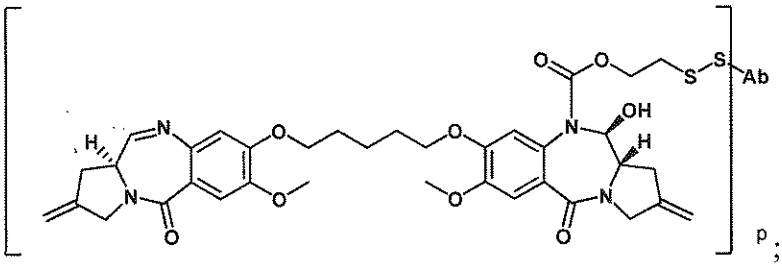


;

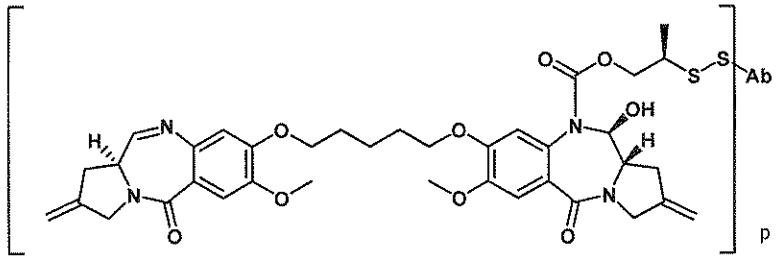
wherein R^{V1} and R^{V2} are each independently selected from H, methyl, ethyl, optionally substituted phenyl, and C_{5-6} heterocyclyl.

24. The immunoconjugate of claim 23, wherein R^{V1} and R^{V2} are each independently selected from H, phenyl, and 4-fluorophenyl.

25. An immunoconjugate having a formula selected from:



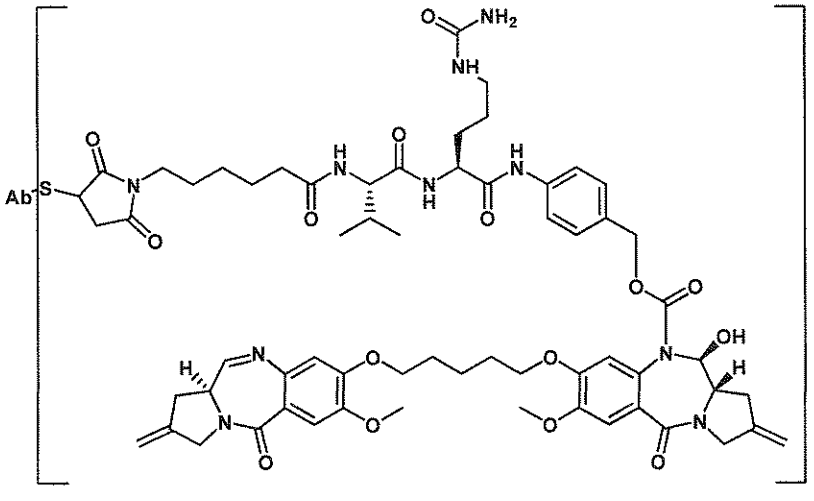
; and



;

wherein Ab is an anti-CD22 antibody comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 15, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14; and wherein p ranges from 1 to 3.

26. An immunoconjugate having the formula:



;

wherein Ab is an anti-CD22 antibody comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (iv) HVR-L1

comprising the amino acid sequence of SEQ ID NO: 15, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14; and wherein p ranges from 1 to 3.

27. The immunoconjugate of claim 25 or 26, wherein the antibody comprises a VH sequence of SEQ ID NO: 7 and a VL sequence of SEQ ID NO: 8.

28. The immunoconjugate of claim 27, wherein the antibody comprises a heavy chain of SEQ ID NO: 26 and a light chain of SEQ ID NO: 23.

29. The immunoconjugate of any one of the preceding claims, wherein the antibody is a monoclonal antibody.

30. The immunoconjugate of any one of the preceding claims, wherein the antibody is a human, humanized, or chimeric antibody.

31. The immunoconjugate of any one of the preceding claims, wherein the antibody is an antibody fragment that binds CD22.

32. The immunoconjugate of claim any one of the preceding claims, wherein the antibody binds human CD22.

33. The immunoconjugate of claim 32, wherein human CD22 has the sequence of SEQ ID NO: 28 or SEQ ID NO: 29.

34. A pharmaceutical formulation comprising the immunoconjugate of any one of the preceding claims and a pharmaceutically acceptable carrier.

35. The pharmaceutical formulation of claim 34, further comprising an additional therapeutic agent.

36. Use of the immunoconjugate of any one of claims 1 to 33 in the manufacture of a medicament for the treatment of an individual having a CD22-positive cancer.

37. The use of claim 36, wherein the CD22-positive cancer is selected from - lymphoma, non-Hogkins lymphoma (NHL), aggressive NHL, relapsed aggressive NHL, relapsed indolent NHL, refractory NHL, refractory indolent NHL, chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma, leukemia, hairy cell leukemia (HCL), acute lymphocytic leukemia (ALL), Burkitt's lymphoma, and mantle cell lymphoma.

38. The use of claim 37, wherein the immunoconjugate is to be administered with an additional therapeutic agent to the individual.

39. The use of claim 38, wherein the additional therapeutic agent comprises an antibody that binds CD79b.

40. The use of claim 39, wherein the additional therapeutic agent is an immunoconjugate comprising an antibody that binds CD79b covalently attached to a cytotoxic agent.

41. Use of the immunoconjugate of any one of claims 1 to 33 in the manufacture of a medicament for the inhibition of proliferation of a CD22-positive cell in a condition characterized by unregulated cell growth or proliferation, wherein the cell is to be exposed to the immunoconjugate under conditions permissive for binding of the immunoconjugate to CD22 on the surface of the cell, thereby inhibiting proliferation of the cell.

42. The use of claim 41, wherein the cell is a neoplastic B cell.

43. The use of claim 42, wherein the cell is a lymphoma cell.

44. An *in vitro* method of inhibiting proliferation of a CD22-positive cell, the method comprising exposing the cell to the immunoconjugate of any one of claims 1 to 35 under conditions permissive for binding of the immunoconjugate to CD22 on the surface of the cell.

45. The method of claim 44, wherein the cell is a neoplastic B cell.

46. The method of claim 45, wherein the cell is a lymphoma cell.

enhanced apoptosis, which suggests a role of this antigen in B-cell survival (Otipoby, K.L. et al., Nature (Lond) 384:634-637 (1996)). After binding with its natural ligand(s) or antibodies, CD22 is rapidly internalized, providing a costimulatory signal in primary B cells and proapoptotic signals in neoplastic B cells (Sato, S. et al., Immunity 5:551-562 (1996)).

[005] There is a need in the art for agents that target CD22 for the diagnosis and treatment of CD22-associated conditions, such as cancer. The invention fulfills that need and provides other benefits.

SUMMARY

[006] The disclosure provides anti-CD22 antibodies and immunoconjugates and methods of using the same.

[007] In one aspect, there is provided an immunoconjugate of formula Ab-(L-D)p, wherein: ~~comprising an antibody that binds CD22 covalently attached to a cytotoxic agent, wherein the antibody binds an epitope within amino acids 20 to 240 of SEQ ID NO: 28, and wherein the cytotoxic agent is a pyrrolobenzodiazepine.~~

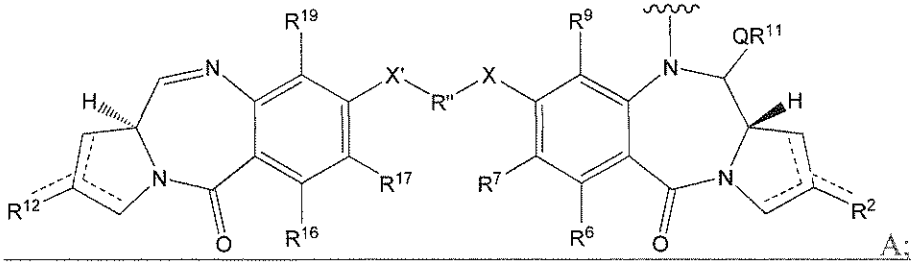
(a) Ab is an antibody that binds CD22;

(b) L is a linker;

(c) D is a cytotoxic agent; and

(d) p ranges from 1-8;

wherein D is a pyrrolobenzodiazepine of Formula A:



A;

wherein the wavy line indicates the covalent attachment site to the linker;

the dotted lines indicate the optional presence of a double bond between C1 and C2 or C2 and C3;

R^2 is independently selected from H, OH, =O, $=CH_2$, CN, R, OR, $=CH\text{-}R^D$, $=C(R^D)_2$, $O\text{-}SO_2\text{-}R$, CO_2R and COR, and optionally further selected from halo or dihalo, wherein R^D is independently selected from R, CO_2R, COR, CHO, CO_2H, and halo;

R^6 and R^9 are independently selected from H, R, OH, OR, SH, SR, NH_2, NHR, NRR', NO_2, Me_3Sn and halo;

R^7 is independently selected from H, R, OH, OR, SH, SR, NH_2, NHR, NRR', NO_2, Me_3Sn and halo;

Q is independently selected from O, S and NH;

R^{11} is either H, or R or, where Q is O, SO_3M, where M is a metal cation;

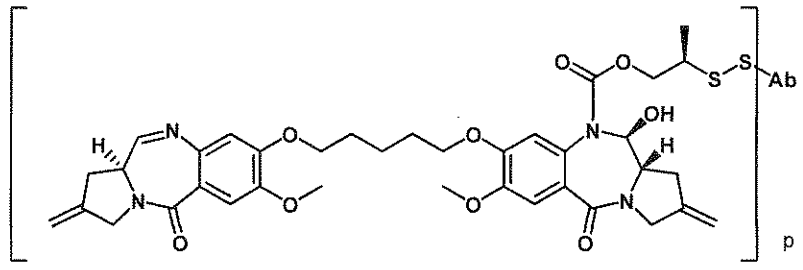
R and R' are each independently selected from optionally substituted C_{1-12} alkyl, C_{3-20} heterocyclyl and C_{5-20} aryl groups, and optionally in relation to the group NRR', R and R' together with the nitrogen atom to which they are attached form an optionally substituted 4-, 5-, 6- or 7-membered heterocyclic ring;

R^{12}, R^{16}, R^{19} and R^{17} are as defined for R^2, R^6, R^9 and R^7 respectively;

R'' is a C_{3-12} alkylene group, which chain may be interrupted by one or more heteroatoms and/or aromatic rings that are optionally substituted; and

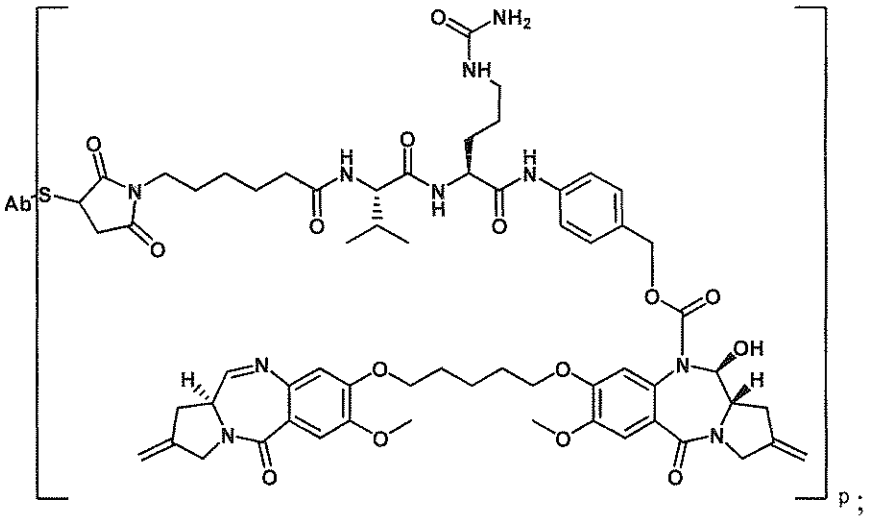
X and X' are independently selected from O, S and N(H); and wherein the antibody binds an epitope within amino acids 20 to 240 of SEQ ID NO: 28.

[008] In some embodiments, the antibody comprises (i) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (ii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14, and (iii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10. In some embodiments, the antibody comprises (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, and (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11. In some embodiments, the antibody comprises: a) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (iv) HVR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 12 and 15 to 22, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14; or b) (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 15, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14. In some embodiments, the antibody comprises: a) (i) HVR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 12 and 15 to 22, (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14; or b) (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 15, (ii) HVR-L2 comprising the amino



wherein Ab is an anti-CD22 antibody comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 15, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14; and wherein p ranges from 1 to 3.

[021] In one aspect, there is provided an immunoconjugate having the formula:



wherein Ab is an anti-CD22 antibody comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 9, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 10, (iii) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 11, (iv) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 15, (v) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and (vi) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14; and wherein p ranges from 1 to 3. In some such embodiments, the antibody comprises a VH sequence of SEQ ID NO: 7 and a VL sequence of SEQ ID NO: 8. In some embodiments, the antibody comprises a heavy chain of SEQ ID NO: 26 and a light chain of SEQ ID NO: 23.

[022] In any of the embodiments discussed herein, the antibody may be a monoclonal antibody. In some embodiments, the antibody may be a human, humanized, or chimeric antibody. In some embodiments, the antibody is an antibody fragment that binds CD22. In

some embodiments, the antibody binds human CD22. In some such embodiments, human CD22 has the sequence of SEQ ID NO: 28 or SEQ ID NO: 29.

[023] In one aspect, there is provided a pharmaceutical formulation comprising the immunoconjugate as described herein and a pharmaceutically acceptable carrier. In some embodiments, the pharmaceutical formulation comprises an additional therapeutic agent.

[0023a] In one aspect, there is provided the use of the immunoconjugate as described herein in the manufacture of a medicament for the treatment of an individual having a CD22-positive cancer.

[024] In some embodiments, methods of treating an individual with a CD22-positive cancer are provided. In some embodiments, a method comprises administering to the individual an effective amount of an immunoconjugate described herein. In some embodiments, the CD22-positive cancer is selected from lymphoma, non-Hogkins lymphoma (NHL), aggressive NHL, relapsed aggressive NHL, relapsed indolent NHL, refractory NHL, refractory indolent NHL, chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma, leukemia, hairy cell leukemia (HCL), acute lymphocytic leukemia (ALL), Burkitt's lymphoma, and mantle cell lymphoma. In some embodiments, the method further comprises administering an additional therapeutic agent to the individual. In some such embodiments, the additional therapeutic agent comprises an antibody that binds CD79b. In some embodiments, the additional therapeutic agent is an immunoconjugate comprising an antibody that binds CD79b covalently attached to a cytotoxic agent.

[0024a] In one aspect, there is provided the use of the immunoconjugate as described herein in the manufacture of a medicament for the inhibition of proliferation of a CD22-positive cell in a condition characterized by unregulated cell growth or proliferation, wherein the cell is to be exposed to the immunoconjugate under conditions permissive for binding of the immunoconjugate to CD22 on the surface of the cell, thereby inhibiting proliferation of the cell.

[025] In one aspect, there is provided an *in vitro* method of inhibiting proliferation of a CD22-positive cell, the method comprising exposing the cell to the immunoconjugate described herein under conditions permissive for binding of the immunoconjugate to CD22 on the surface of the cell~~, thereby inhibiting proliferation of the cell~~. In some embodiments, the cell is a neoplastic B cell. In some embodiments, the cell is a lymphoma cell.