What is claimed is:

1. An anti-GCC antibody molecule, wherein the light chain variable region and the heavy chain variable region of the anti-GCC antibody molecule are selected from: the light and heavy chain sequences disclosed in Table 2 for any one of the following antibodies:

5F9;

Ab 229; or

3G1.

2. The anti-GCC antibody molecule, of claim 1, wherein said anti-GCC antibody molecule is an IgG1 antibody.

3. The anti-GCC antibody molecule of claim 1, wherein said anti-GCC antibodymolecule is not conjugated to a therapeutic agent.

4. The anti-GCC antibody molecule of claim 1, wherein said anti-GCC antibodymolecule is conjugated to a therapeutic agent.

5. The anti-GCC antibody molecule of claim 1, wherein said anti-GCC antibody molecule is conjugated to a detectable label.

6. An anti-GCC antibody molecule, comprising light chain CDR1, CDR2, and CDR3, and heavy chain CDR1, CDR2, and CDR3, disclosed in Table 5 for any one of the following antibodies:

5F9;

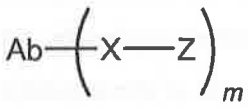
Ab 229; or

3G1.

7. The anti-GCC antibody molecule of claim 6, further comprising human or human derived light and heavy variable region frameworks.

8. The anti-GCC antibody molecule of claim 7, wherein said anti-GCC antibody is an IgG1 antibody.

9. An immunoconjugate of formula (*I*):



(*I*)

or a pharmaceutically acceptable salt thereof, wherein:

Ab is an anti-GCC antibody molecule of claim 1;

X is a linker moiety which connects Ab and Z;

Z is a therapeutic agent or a label; and

m is an integer from 1 to 15.

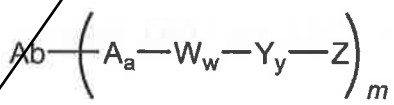
10. The immunoconjugate of claim 9, wherein Z is a detectable label.

11. The immunoconjugate of claim 9, wherein –Z is a maytansine or an auristatin.

12. The immunoconjugate of claim 9, wherein -Z is DM1 or DM4.

13. The immunoconjugate of claim 9, wherein -Z is MMAE or MMAF.

14. The immunoconjugate of claim 9, wherein the linker –X- has the formula $-A_a-W_w-Y_y-$, and the immunoconjugate is characterized by formula (*II*):



(*II*)

or a pharmaceutically acceptable salt thereof, wherein:

-A- is a Stretcher unit;

a is 0 or 1;

each –W- independently is an Amino Acid unit;

w is an integer ranging from 0 to 12;

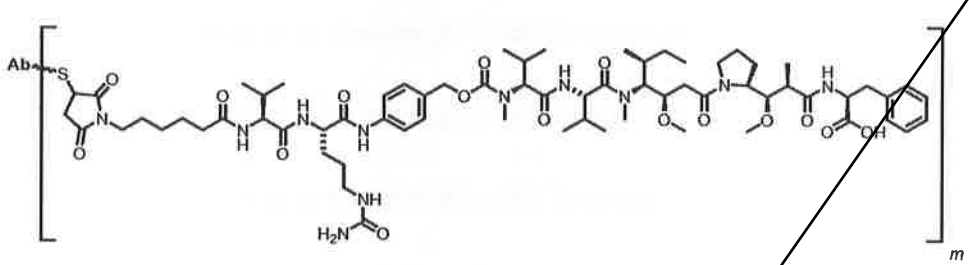
-Y- is a self-immolative Spacer unit;

y is 0, 1, or 2;

Z is a therapeutic agent or label; and

m ranges from about 1 to about 15.

15. An immunoconjugate of formula (*I-4*):



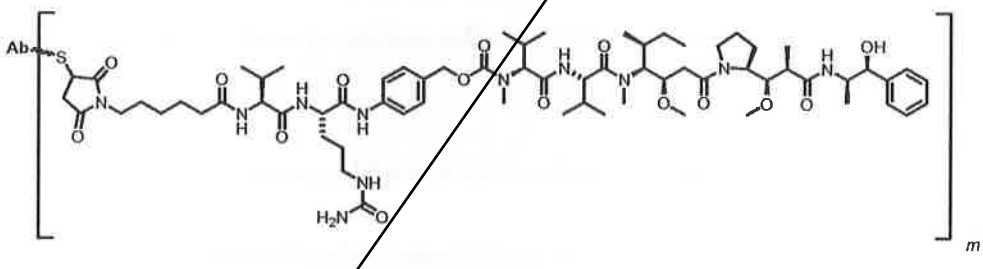
(*I-4*)

or a pharmaceutically acceptable salt thereof, wherein:

Ab is 5F9; and

m is an integer from 1 to 8.

16. An immunoconjugate of formula (*I-5*):



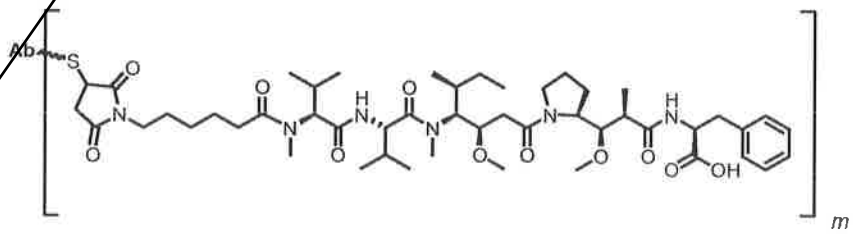
(*I-5*)

or a pharmaceutically acceptable salt thereof, wherein:

Ab is 5F9; and

m is an integer from 1 to 8.

17. An immunoconjugate of formula (*I-7*):



(*I-7*)

or a pharmaceutically acceptable salt thereof, wherein:

Ab is 5F9; and

m is an integer from 1 to 8.

18. The immunoconjugate of claim 15, wherein *m* is from 1 to 3.

19. The immunoconjugate of claim 15, wherein *m* is from 3 to 5.

20. The immunoconjugate of claim 16, wherein *m* is from 3 to 5.

21. The immunoconjugate of claim 18, wherein *m* is from 3 to 5.

22. A method of treating a subject for colon cancer, comprising administering to said subject, a therapeutically effective amount of an antibody molecule of claim 1 or 6, thereby treating said subject.

23. A method of treating a subject for colon cancer, comprising administering to said subject a therapeutically effective amount of an immunoconjugate of any one of claims 9-17.

24. Isolated nucleic acid sequences that encode an antibody molecule of claim 1 or 6.

25. A cell comprising the isolated nucleic acid sequences of claim 24.

26. A method of producing an antibodymolecule of claim 1 or 6, comprising culturing the cell of claim 25under conditions that allow production of an antibody molecule, thereby producing the antibody molecule of claim 1 or 6.

27. A vector comprising one or both of the light chain and heavy chain of an antibody molecule of claim 1 or 6.

28. A method of detecting a GCC molecule comprising contacting the molecule with an antibody molecule of claim 1 or 6 and determining if said antibody molecule, binds to said GCC molecule.

Claims

1. An anti-GCC antibody molecule, comprising a light chain variable region and a heavy chain variable region, wherein the light chain variable region comprises one, two, or three light chain complementarity determining region amino acid sequences (LCDR1, LCDR2, and LCDR3) disclosed in Table 5 for any one of the antibody molecules disclosed in Table 5, and wherein the heavy chain variable region comprises one, two, or three heavy chain complementarity determining region amino acid sequences (HCDR1, HCDR2, and HCDR3) disclosed in Table 5 for any one of the antibody molecule disclosed in Table 5.

2. The anti-GCC antibody molecule of claim 1, further comprising human or human derived light and heavy variable region frameworks.

3. The anti-GCC antibody molecule of claim 1 or 2, wherein the light chain variable region comprises a light chain variable region amino acid sequence from Table 3, and wherein the heavy chain variable region comprises a heavy chain variable region amino acid sequence from Table 3.

4. The anti-GCC antibody molecule of any of claims 1 to 3, wherein the light chain variable region comprises a light chain variable region amino acid sequence encoded by a nucleotide sequence from Table 4, and wherein the heavy chain variable region comprises a heavy chain variable region amino acid sequence encoded by a nucleotide sequence from Table 4.

5. The anti-GCC antibody molecule of any of claims 1 to 4, wherein said anti-GCC antibody molecule is an IgG1 antibody.

6. The anti-GCC antibody molecule of any of claims 1 to 5, wherein the anti-GCC antibody molecule is one of the antibody molecules disclosed in Tables 1 and 2.

7. The anti-GCC antibody molecule of any of claims 1 to 6, wherein the antibody molecule disclosed in Tables 1 and 2 is a 5F9 antibody molecule.

8. The anti-GCC antibody molecule of any of claims 1 to 7, wherein said anti-GCC antibody molecule comprises an Fc region, wherein said Fc region comprises a mutation.

9. The anti-GCC antibody molecule of any of claims 1 to 8, wherein said anti-GCC antibody molecule is a bispecific antibody molecule.

10. The anti-GCC antibody molecule of claim 9, comprising two antibody molecules, one with binding specificity to GCC and another with binding specificity to a second molecule.

11. The anti-GCC antibody molecule of claim 10, wherein the two antibody molecules are conjugated together.

12. The anti-GCC antibody molecule of claim 9, comprising a single antibody molecule that comprises one chain with binding specificity to GCC and a second chain with binding specificity to a second molecule.

13. The anti-GCC antibody molecule of claim 9, comprising a single chain antibody molecule that has binding specificity to GCC and a second molecule.

14. The anti-GCC antibody molecule of any of claims 1 to 13, wherein said anti-GCC antibody molecule is not conjugated to a therapeutic agent.

15. The anti-GCC antibody molecule of any of claims 1 to 13, wherein said anti-GCC antibody molecule is conjugated to a therapeutic agent.

16. The anti-GCC antibody molecule of any of claims 1 to 13, wherein said anti-GCC antibody molecule is conjugated to a detectable label.

17. The anti-GCC antibody molecule of any of claims 1 to 13, 15, and 16, wherein said anti-GCC antibody molecule is conjugated to a therapeutic radiolabel.

18. The anti-GCC antibody molecule of claim 17, wherein the therapeutic radiolabel comprises an α-emitter.

19. The anti-GCC antibody molecule of claim 18, wherein the α-emitter is ^{213}Bi or ^{225}Ac.

20. The anti-GCC antibody molecule of claim 17, wherein the therapeutic radiolabel comprises a β-emitter.

21. The anti-GCC antibody molecule of claim 20, wherein the β-emitter is ^{90}Y or ^{177}Lu.

22. An antibody molecule that binds to the same, or substantially the same, epitope on GCC as any one of the antibody molecules disclosed in Tables 1 and 2.

23. The antibody molecule of claim 22, wherein the antibody molecule disclosed in Tables 1 and 2 is a 5F9 antibody molecule.

24. The antibody molecule of claim 23, wherein the epitope resides within, or comprises one or more amino acid residues from, amino acid residues 1-50 of SEQ ID NO: 228.

25. The antibody molecule of claim 23 or 24, wherein the epitope resides within, or comprises one or more amino acid residues from, amino acid residues 25-50 of SEQ ID NO: 228.

26. The antibody molecule of any of claims 23 to 25, wherein the epitope resides within, or comprises one or more amino acid residues from, amino acid residues 33-50 of SEQ ID NO: 228.

27. The antibody molecule of any of claims 24 to 26, wherein the epitope further comprises one or more amino acid residues from amino acid residues 50-1073 of SEQ ID NO: 228.

28. The antibody molecule of claim 23, wherein the epitope resides within, or comprises one or more amino acid residues, from amino acid residues 24-75 of SEQ ID NO: 228.

29. The antibody molecule of any of claims 22 to 28, wherein the epitope is a conformational epitope.

30. The antibody molecule of claim 23, wherein the antibody molecule binds a fragment comprising amino acid residues 1-50 of SEQ ID NO: 228.

31. The antibody molecule of claim 23 or 30, wherein the antibody molecule binds a fragment comprising amino acid residues 25-50 of SEQ ID NO: 228.

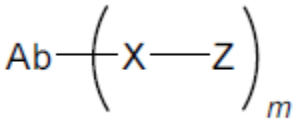
32. The antibody molecule of any of claims 23, 30, and 31, wherein the antibody molecule binds a fragment comprising amino acid residues 33-50 of SEQ ID NO: 228.

33. The antibody molecule of claim 23, wherein the antibody molecule binds a fragment comprising amino acid residues 24-420 of SEQ ID NO: 228.

34. The antibody molecule of claim 23 or 33, wherein the antibody molecule binds a fragment comprising amino acid residues 24-75 of SEQ ID NO: 228.

35. An antibody molecule that competes for binding to GCC with any one of the anti-GCC antibody molecules disclosed in Tables 1 and 2.

36. An immunoconjugate of formula (***I***):



(*I*)

or a pharmaceutically acceptable salt thereof, wherein:

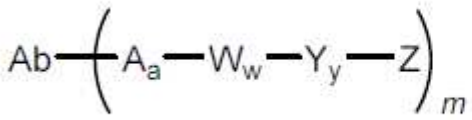
Ab is the anti-GCC antibody molecule of any of claims 1-13;

X is a linker moiety which connects Ab and Z;

Z is a therapeutic agent or a label; and

m is the number of –X-Z moieties per anti-GCC antibody molecule in the immunoconjugate of formula (***I***), and *m* is an integer from about 1 to about 15.

37. The immunoconjugate of claim 36, wherein the linker –X- has the formula -Aa-Ww-Yy-, and the immunoconjugate is characterized by formula (***II***):



(*II*)

or a pharmaceutically acceptable salt thereof, wherein:

-A- is a Stretcher unit;

a is 0 or 1;

each –W- independently is an Amino Acid unit;

w is an integer ranging from 0 to 12;

-Y- is a self-immolative Spacer unit;

y is 0, 1, or 2;

Z is a therapeutic agent or label; and

m is an integer from about 1 to about 15.

38. The immunoconjugate of claim 36 or 37, wherein Z is a detectable label.

39. The immunoconjugate of any of claims 36 to 38, wherein said anti-GCC antibody molecule is conjugated to a therapeutic radiolabel.

40. The immunoconjugate of claim 39, wherein the therapeutic radiolabel comprises an α-emitter.

41. The immunoconjugate of claim 40, wherein the α-emitter is ^{213}Bi or ^{225}Ac.

42. The immunoconjugate of claim 39, wherein the therapeutic radiolabel comprises a β-emitter.

43. The immunoconjugate of claim 42, wherein the β-emitter is ^{90}Y or ^{177}Lu.

44. The immunoconjugate of claim 36 or 37, wherein Z is a cytostatic or cytotoxic agent.

45. The immunoconjugate of claim 44, wherein the cytostatic or cytotoxic agent is selected from antimetabolites; alkylating agents; anthracyclines; antibiotics; antimitotic agents; topoisomerase inhibitors; or proteasome inhibitors.

46. The immunoconjugate of claim 45, wherein the antimetabolite is selected from azathioprine, 6-mercaptopurine, 6-thioguanine, fludarabine, pentostatin, cladribine, 5-fluorouracil (5FU), floxuridine (FUDR), cytosine arabinoside (cytarabine), methotrexate, trimethoprim, pyrimethamine, or pemetrexed.

47. The immunoconjugate of claim 45, wherein the alkylating agent is selected from cyclophosphamide, mechlorethamine, uramustine, melphalan, chlorambucil, thiotepa/chlorambucil, ifosfamide, carmustine, lomustine, streptozocin, busulfan, dibromomannitol, cisplatin, carboplatin, nedaplatin, oxaliplatin, satraplatin, triplatin tetranitrate, procarbazine, altretamine, dacarbazine, mitozolomide, or temozolomide.

48. The immunoconjugate of claim 45, wherein the anthracycline is selected from daunorubicin, doxorubicin, epirubicin, idarubicin, or valrubicin.

49. The immunoconjugate of claim 45, wherein the antibiotic is selected from dactinomycin, bleomycin, mithramycin, anthramycin, streptozotocin, gramicidin D, mitomycins, duocarmycins, or calicheamicins.

50. The immunoconjugate of claim 49, wherein the mitomycin is mitomycin C.

51. The immunoconjugate of claim 49, wherein the duocarmycin is CC-1065.

52. The immunoconjugate of claim 45, wherein the antimitotic agent is selected from maytansinoids, auristatins, dolastatins, cryptophycins, vinca alkaloids, taxanes, or colchicines.

53. The immunoconjugate of claim 52, wherein the vinca alkaloid is selected from vincristine, vinblastine, vindesine, or vinorelbine.

54. The immunoconjugate of claim 52, wherein the taxane is paclitaxel or docetaxel.

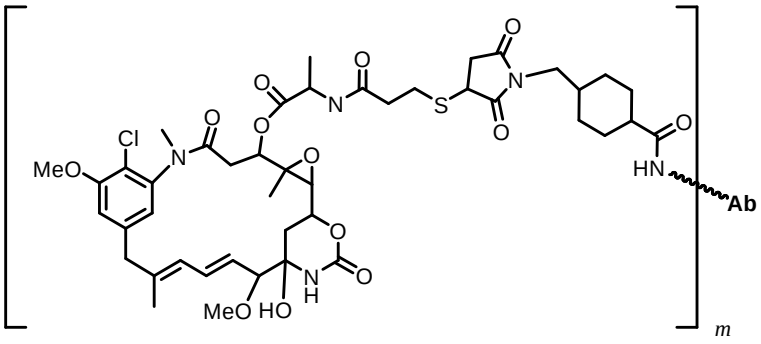
55. The immunoconjugate of claim 45, wherein the topoisomerase inhibitor is selected from irinotecan, topotecan, amsacrine, etoposide, teniposide, or mitoxantrone.

56. The immunoconjugate of claim 45, wherein the proteasome inhibitors is a peptidyl boronic acid.

57. The immunoconjugate of claim 36 or 37, wherein Z is a maytansinoid.

58. The immunoconjugate of claim 57, wherein the maytansinoid is $N^{2'}$-deacetyl-$N^{2'}$-(4-mercapto-1-oxopentyl)maytansine (DM3), $N^{2'}$-deacetyl-$N^{2'}$-(3-mercapto-1-oxopropyl)-maytansine (DM1), or $N^{2'}$-deacetyl-$N^{2'}$-(4-mercapto-4-methyl-1-oxopentyl)maytansine (DM4).

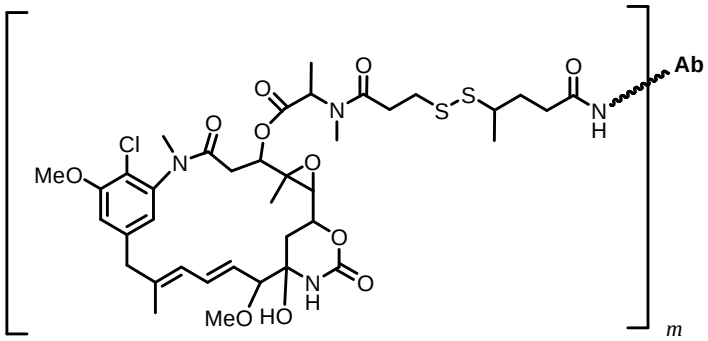
59. The immunoconjugate of claim 57 or 58, having formula (***I-1***):



(***I-1***)

or a pharmaceutically acceptable salt thereof.

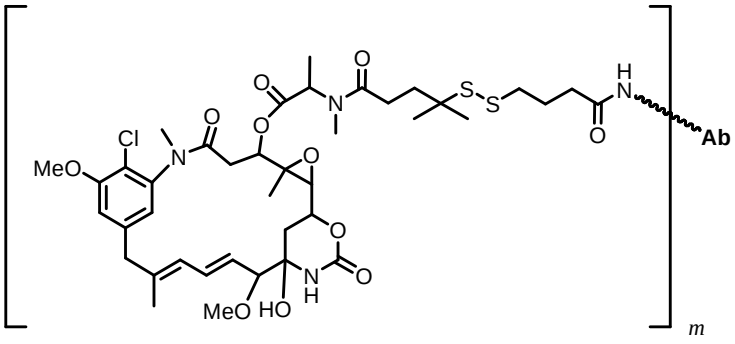
60. The immunoconjugate of claim 57 or 58, having formula (***I-2***):



(***I-2***)

or a pharmaceutically acceptable salt thereof.

61. The immunoconjugate of claim 57 or 58, having the formula (***I-3***):



(***I-3***)

or a pharmaceutically acceptable salt thereof.

62. The immunoconjugate of any of claims 57 to 61, wherein *m* is an integer from about 1 to about 10.

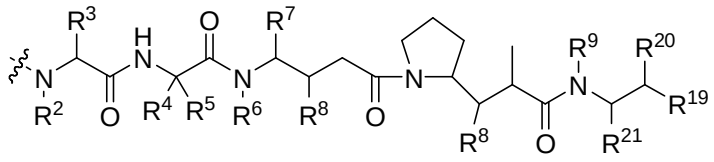
63. The immunoconjugate of any of claims 57 to 62, wherein *m* is an integer from about 3 to about 7.

64. The immunoconjugate of any of claims 57 to 63, wherein *m* is an integer from about 3 to about 5.

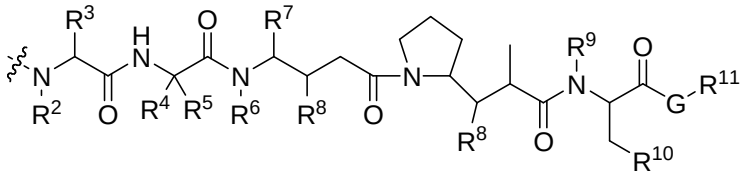
65. The immunoconjugate of any of claims 57 to 64, wherein *m* is about 4.

66. The immunoconjugate of claim 36 or 37, wherein Z is a dolastatin or auristatin.

67. The immunoconjugate of claim 66, wherein Z is an auristatin moiety of formula (***X-A***) or formula (***X-B***):



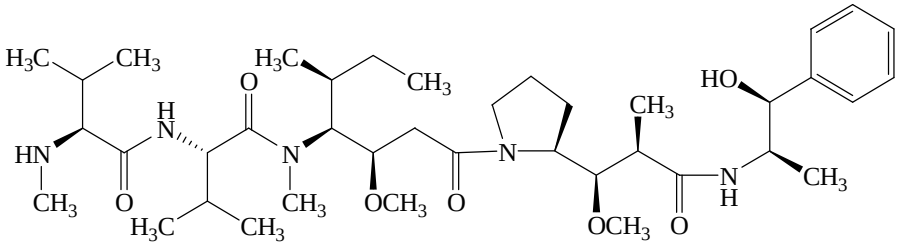
(***X-A***)



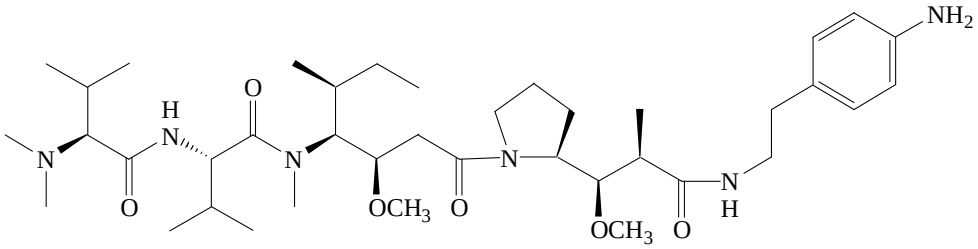
(***X-B***)

.

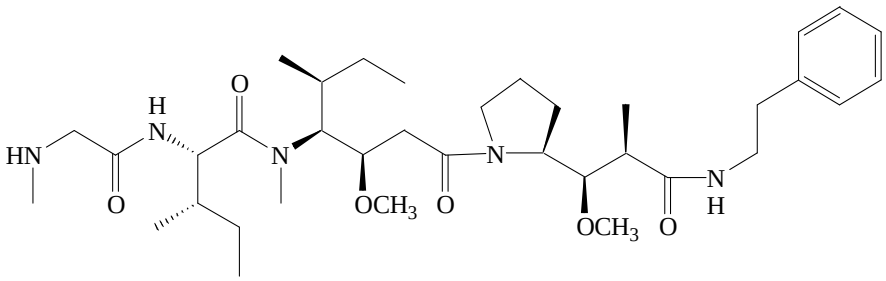
68. The immunoconjugate of claim 66 or 67, wherein Z is selected from compounds of formulae (***XIII***)-(***XXIII***):



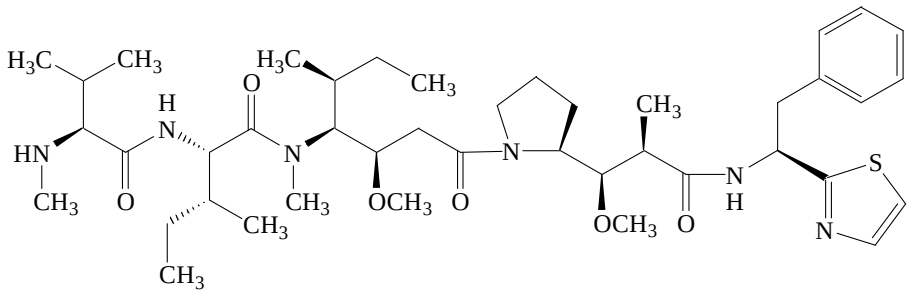
(***XIII***)



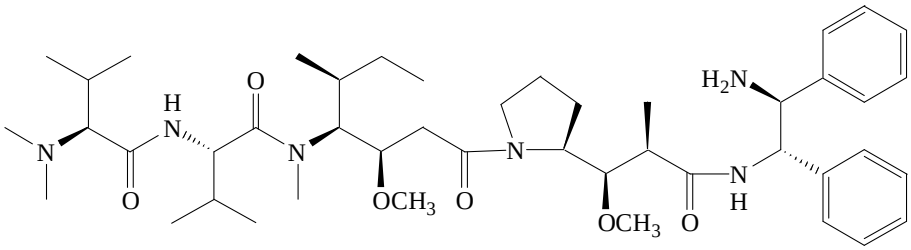
(***XIV***)



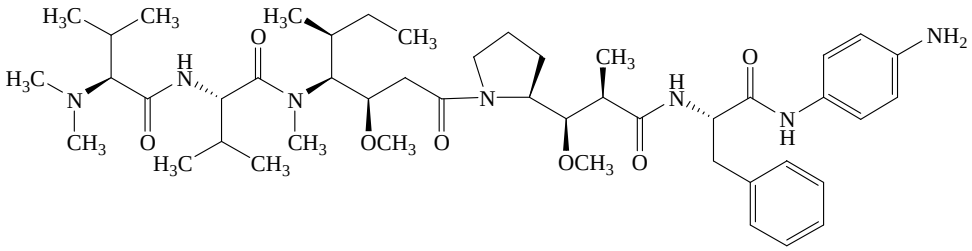
(***XV***)



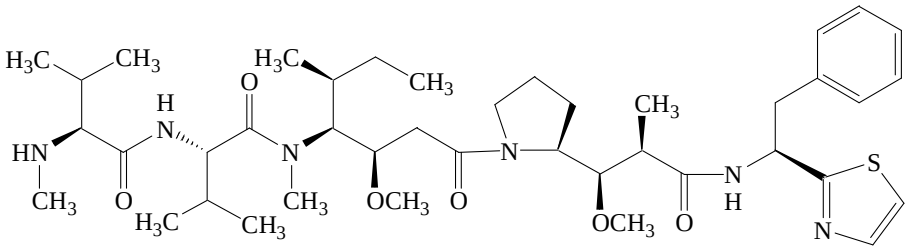
(***XVI***)



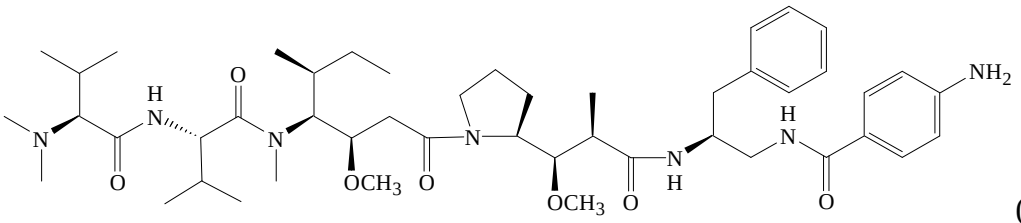
(***XVII***)



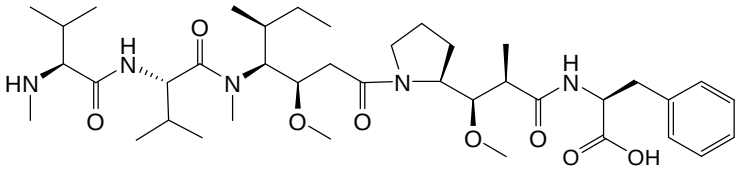
(***XVIII***)



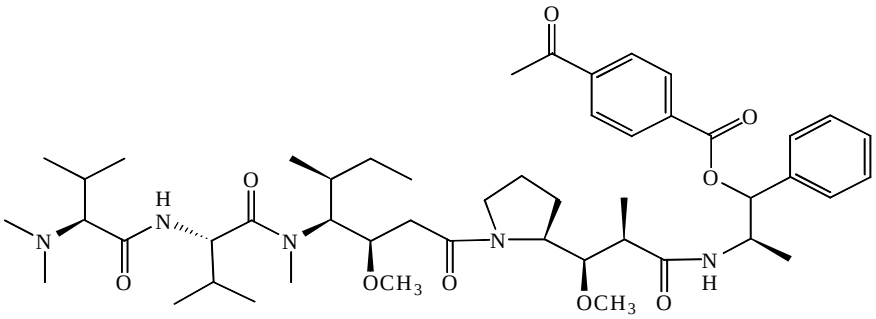
(*XIX*)



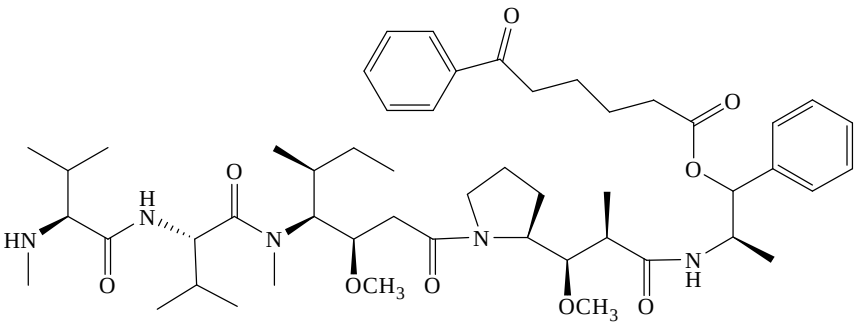
(***XX***)



(***XXI***)



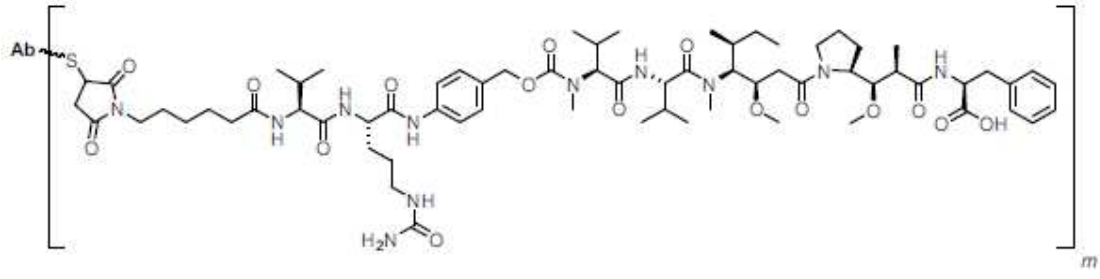
(***XXII***)



(***XXIII***).

69. The immunoconjugate of any of claims 66 to 68, wherein Z is selected from AEB, AEVB, AFP, MMAE, or MMAF.

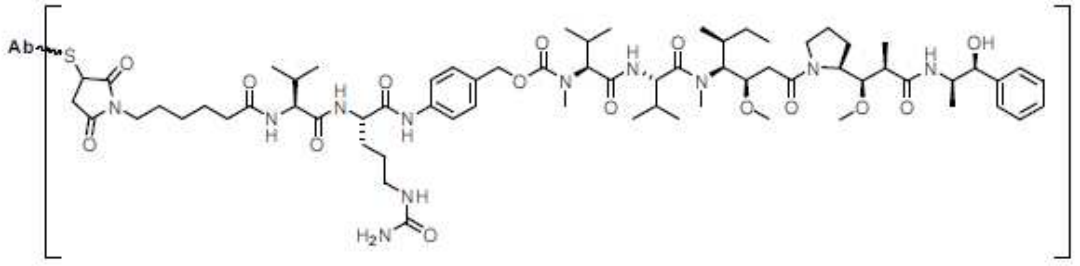
70. The immunoconjugate of any of claims 66 to 69, having formula (***I-4***):



(***I-4***)

or a pharmaceutically acceptable salt thereof.

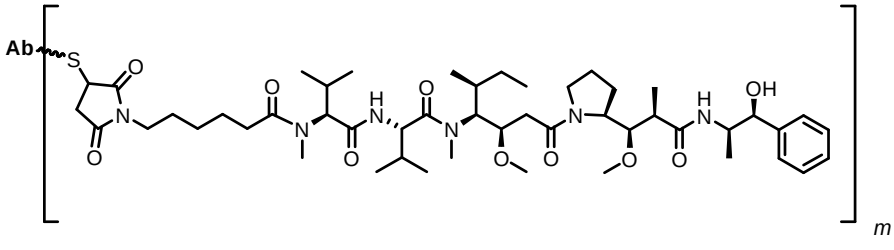
71. The immunoconjugate of any of claims 66 to 69, having formula (***I-5***):



(***I-5***)

or a pharmaceutically acceptable salt thereof.

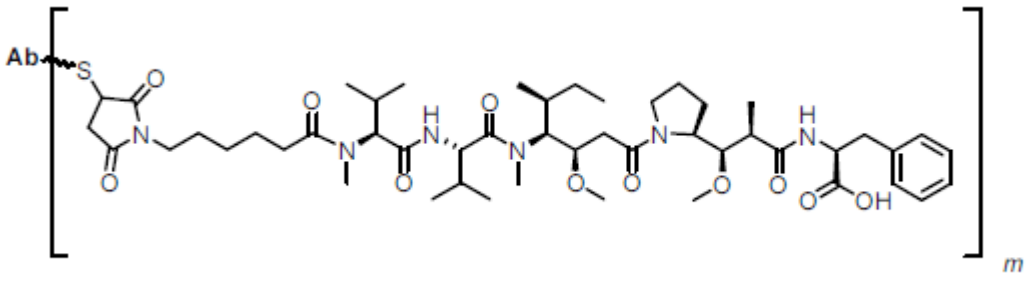
72. The immunoconjugate of any of claims 66 to 69, having formula (***I-6***):



(***I-6***)

or a pharmaceutically acceptable salt thereof.

73. The immunoconjugate of any of claims 66 to 69, having formula (***I-7***):



(*I-7*)

or a pharmaceutically acceptable salt thereof.

74. The immunoconjugate of any one of claims 66 to 73, wherein *m* is from about 1 to about 5.

75. The immunoconjugate of any one of claims 66 to 73, wherein *m* is from about 2 to about 10.

76. The immunoconjugate of any one of claims 66 to 75, wherein *m* is about 4.

77. An antibody molecule of any one of claims 1 to 35 or an immunoconjugate of any of claims 36 to 76 for use in a method of treating a subject for a disorder.

78. The antibody molecule or immunoconjugate of claim 77, wherein the disorder is a cancer.

79. The antibody molecule or immunoconjugate of claim 78, wherein the cancer is a cancer of the gastrointestinal system, or a metastatic lesion thereof.

80. The antibody molecule or immunoconjugate of claim 78, wherein the cancer is primary or metastatic colorectal cancer, gastric cancer, esophageal cancer, pancreatic cancer, or lung cancer.

81. Use of the antibody molecule of any of claims 1 to 35 or an immunoconjugate of any of claims 36 to 76 in the manufacture of a medicament for the treatment of a disorder.

82. The use of claim 81, wherein the disorder is a cancer.

83. The use of claim 82, wherein the cancer is a cancer of the gastrointestinal system, or a metastatic lesion thereof.

84. The use of claim 82, wherein the cancer is primary or metastatic colorectal cancer, gastric cancer, esophageal cancer, pancreatic cancer, or lung cancer.

85. The use of any of claims 81 to 84 for use in combination with one or more additional therapeutic agents.

86. The use of claim 85, wherein the one or more additional therapeutic agents comprise 5-fluorouricil (5-FU), capecitibine, leucovorin, irinotecan, oxaliplatin, bevacizumab cetuximab, panitumum, or any combination thereof.

87. The use of claim 86, wherein the combination thereof is selected from oxaliplatin/capecitibine (XELOX), 5-FU/leucovorin/oxaliplatin (FOLFOX), 5-FU/leucovorin/irinotecan (FOLFIRI), FOLFOX plus bevacizumab, or FOLOFIRI plus bevacizumab.

88. The use of claim 85, wherein the one or more additional therapeutic agents comprise a chemotherapeutic agent.

89. The use of claim 88, wherein the chemotherapeutic agent is a DNA damaging agent.

90. The use of claim 89, wherein the DNA damaging agent is selected from topoisomerase I inhibitors; topoisomerase II inhibitors; alkylating agents; DNA intercalators; free radical generators; and nucleoside mimetics.

91. The use of claim 90, wherein the topoisomerase I inhibitor is selected from irinotecan, topotecan, camptothecin and analogs or metabolites thereof, or doxorubicin.

92. The use of claim 90, wherein the topoisomerase II inhibitor is selected from etoposide, teniposide, or daunorubicin.

93. The use of claim 90, wherein the alkylating agent is selected from melphalan, chlorambucil, busulfan, thiotepa, ifosfamide, carmustine, lomustine, semustine, streptozocin, decarbazine, methotrexate, mitomycin C, or cyclophosphamide.

94. The use of claim 90, wherein the DNA intercalator is selected from cisplatin, oxaliplatin, or carboplatin.

95. The use of claim 90, wherein the free radical generator is bleomycin.

96. The use of claim 90, wherein the nucleoside mimetic is selected from 5-fluorouracil, capecitibine, gemcitabine, fludarabine, cytarabine, mercaptopurine, thioguanine, pentostatin, or hydroxyurea.

97. The use of claim 88, wherein the chemotherapeutic agent is an agent that disrupts cell replication.

98. The use of claim 97, wherein the chemotherapeutic agent is selected from paclitaxel, docetaxel, and related analogs; vincristine, vinblastine, and related analogs; thalidomide, lenalidomide, and related analogs; protein tyrosine kinase inhibitors; proteasome inhibitors; NF-KB inhibitors, including inhibitors of IκB kinase; antibodies which bind to proteins overexpressed in cancers and thereby downregulate cell replication; and other inhibitors of proteins or enzymes known to be upregulated, over-expressed or activated in cancers, the inhibition of which downregulates cell replication.

99. The use of claim 98, wherein the related analog of thalidomide or lenalidomide is CC-5013 or CC-4047.

100. The use of claim 98, wherein the protein tyrosine kinase inhibitor is imatinib mesylate or gefitinib.

101. The use of claim 98, wherein the proteasome inhibitor is bortezomib.

102. The use of claim 98, the antibody which binds to proteins overexpressed in cancers and thereby downregulate cell replication is selected from trastuzumab, rituximab, cetuximab, or bevacizumab.

103. The use of any of claims 81 to 102, wherein the disorder has been determined to express a GCC molecule.

104. An isolated nucleic acid encoding an antibody molecule of any of claims 1 to 8.

105. An isolated nucleic acid encoding a variable region of an antibody molecule of any one of claims 1 to 8.

106. The isolated nucleic acid of claim 105, wherein the variable region is encoded by a nucleic acid sequence from Table 4.

107. A cell comprising the isolated nucleic acid of any of claims 104 to 106.

108. A method of producing an antibody molecule of any of claims 1 to 8, comprising culturing the cell of claim 107 under conditions that allow production of an antibody molecule, thereby producing the antibody molecule of any of claims 1 to 8.

109. A vector comprising one or both of the light chain and heavy chain variable regions of an antibody molecule of any of claims 1 to 8.

110. A method of detecting a GCC molecule comprising contacting the molecule with an antibody molecule of any of claims 1 to 35 and determining if said antibody molecule binds to said GCC molecule.

111. A pharmaceutical composition comprising the antibody molecule of any of claims 1 to 35 and a pharmaceutically acceptable carrier.

112. A pharmaceutical composition comprising the immunoconjugate of claim 36 to 76 and a pharmaceutically acceptable carrier.

113. The pharmaceutical composition of claim 112, comprising a plurality of immunoconjugates of formula (*I*), wherein two or more than two of the immunoconjugates have a different *m* value.

114. The pharmaceutical composition of claim 112, comprising a plurality of immunoconjugates of formula (*I*), wherein *m* is the average number of –X-Z moieties per anti-GCC antibody molecule.

115. The pharmaceutical composition of claim 114, wherein *m* is the integer 4.

116. The pharmaceutical composition of any of claims 112 to 115, comprising a plurality of immunoconjugates of formula (*I-5*).

117. A container comprising the pharmaceutical composition of any of claims 111 to 116.

118. A kit comprising the anti-GCC antibody molecule of any of claims 1 to 35 or the immunoconjugate of any of claims 36 to 76.

119. A method of producing an immunoconjugate, the method comprising: providing the antibody molecule of any of claims 1 to 35; and contacting the antibody molecule with a non-antibody moiety comprising a therapeutic agent or label under conditions that allow the production of an immunoconjugate, thereby producing the immunoconjugate.