characterized in that said antibody or epitope-binding fragment thereof is capable of killing more than 11 % of MOLP-8 multiple myeloma cells by apoptosis in the absence of stroma cells or stroma-derived cytokines.

9) An antibody or epitope-binding fragment thereof according to claim 1, characterized in that said antibody or epitope-binding fragment thereof is capable of killing more than 36 % of SU-DHL-8 lymphoma cells by apoptosis in the absence of stroma cells or stroma-derived cytokines.

10) An antibody or epitope-binding fragment thereof according to claim 1, characterized in that said antibody or epitope-binding fragment thereof is capable of killing more than 62 % of DND-41 leukemia cells by apoptosis in the absence of stroma cells or stroma-derived cytokines.

11) An antibody or epitope-binding fragment thereof according to claim 1, characterized in that said antibody or epitope-binding fragment thereof is capable of killing more than 27 % NU-DUL-1 lymphoma cells by apoptosis in the absence of stroma cells or stroma-derived cytokines.

12) An antibody or epitope-binding fragment thereof according to claim 1, characterized in that said antibody or epitope-binding fragment thereof is capable of killing more than 9 % of JVM-13 leukemia cells by apoptosis in the absence of stroma cells or stroma-derived cytokines.

13) An antibody or epitope-binding fragment thereof according to claim 1, characterized in that said antibody or epitope-binding fragment thereof is capable of killing more than 4 % of HC-1 leukemia cells by apoptosis in the absence of stroma cells or stroma-derived cytokines.

14) An antibody or epitope-binding fragment thereof according to any of the previous claims, characterized in that said antibody or epitope-binding fragment thereof binds CD38 with a k_D of 3×10^{-9} M or lower.

~~**15)** An antibody or epitope-binding fragment thereof according to claims 1-14, characterized in that said antibody or epitope-binding fragment thereof comprises one or more complementarity-determining region having an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32,~~

33, 34, 35, and 36.

16) An antibody or epitope-binding fragment thereof according to claim 15, characterized in that said antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain, and said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences selected from the group consisting of SEQ ID NOs:1, 2, 3, 7, 8, 9, 13, 14, 15, 19, 20, 21, 25, 26, 27, 31, 32, and 33, and said light chain comprises three sequential complementarity-determining regions having amino acid sequences selected from the group consisting of SEQ ID NOs: 4, 5, 6, 10, 11, 12, 16, 17, 18, 22, 23, 24, 28, 29, 30, 34, 35, and 36.

17) An antibody or epitope-binding fragment thereof according to claim 16, characterized in that said antibody or epitope-binding fragment thereof comprises a light chain variable region having an amino acid sequence selected from the group consisting of SEQ ID NOS: 38, 40, 42, 44, 46, and 48.

18) An antibody or epitope-binding fragment thereof according to claim 16, characterized in that said antibody or epitope-binding fragment thereof comprises a heavy chain variable region having an amino acid sequence selected from the group consisting of SEQ ID NOS: 50, 52, 54, 56, 58, 60.

19) An antibody or epitope-binding fragment thereof according to claim 16, characterized in that said antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 1, 2, and 3, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 4, 5, and 6.

20) An antibody or epitope-binding fragment thereof according to claim 19, charaterized in that said antibody or epitope-binding fragment thereof comprises a light chain variable region having an amino acid sequence consisting of SEQ ID NO: 38.

21) An antibody or epitope-binding fragment thereof according to claim 19, charaterized in that said antibody or epitope-binding fragment thereof comprises a heavy chain variable region having an amino acid sequence consisting of SEQ ID

NO: 50.

22) An antibody or epitope-binding fragment thereof according to claim 16, characterized in that said antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 7, 8, and 9, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 10, 11, and 12.

23) An antibody or epitope-binding fragment thereof according to claim 22, charaterized in that said antibody or epitope-binding fragment thereof comprises a light chain variable region having an amino acid sequence consisting of SEQ ID NO: 40.

24) An antibody or epitope-binding fragment thereof according to claim 22, charaterized in that said antibody or epitope-binding fragment thereof comprises a heavy chain variable region having an amino acid sequence consisting of SEQ ID NO: 52.

25) An antibody or epitope-binding fragment thereof according to claim 16, characterized in that said antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 13, 14, and 15, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 16, 17, and 18.

26) An antibody or epitope-binding fragment thereof according to claim 25, charaterized in that said antibody or epitope-binding fragment thereof comprises a light chain variable region having an amino acid sequence consisting of SEQ ID NO: 42.

27) An antibody or epitope-binding fragment thereof according to claim 25, charaterized in that said antibody or epitope-binding fragment thereof comprises a heavy chain variable region having an amino acid sequence consisting of SEQ ID NO: 54.

28) An antibody or epitope-binding fragment thereof according to claim 16, characterized in that said antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 19, 20, and 21, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 22, 23, and 24.

29) An antibody or epitope-binding fragment thereof according to claim 28, charaterized in that said antibody or epitope-binding fragment thereof comprises a light chain variable region having an amino acid sequence consisting of SEQ ID NO: 44.

30) An antibody or epitope-binding fragment thereof according to claim 28, charaterized in that said antibody or epitope-binding fragment thereof comprises a heavy chain variable region having an amino acid sequence consisting of SEQ ID NO: 56.

31) An antibody or epitope-binding fragment thereof according to claim 16, characterized in that said antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 25, 26, and 27, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 28, 29, and 30.

32) An antibody or epitope-binding fragment thereof according to claim 31, charaterized in that said antibody or epitope-binding fragment thereof comprises a light chain variable region having an amino acid sequence consisting of SEQ ID NO: 46.

33) An antibody or epitope-binding fragment thereof according to claim 31, charaterized in that said antibody or epitope-binding fragment thereof comprises a heavy chain variable region having an amino acid sequence consisting of SEQ ID NO: 58.

34) An antibody or epitope-binding fragment thereof according to claim 16, characterized in that said antibody or epitope-binding fragment thereof comprises

at least one heavy chain and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 31, 32, and 33, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 34, 35, and 36.

35) An antibody or epitope-binding fragment thereof according to claim 34, charaterized in that said antibody or epitope-binding fragment thereof comprises a light chain variable region having an amino acid sequence consisting of SEQ ID NO: 48.

36) An antibody or epitope-binding fragment thereof according to claim 34, charaterized in that said antibody or epitope-binding fragment thereof comprises a heavy chain variable region having an amino acid sequence consisting of SEQ ID NO: 60.

37) An antibody or epitope-binding fragment thereof according to claim 16, characterized in that said antibody or epitope-binding fragment thereof is produced by a hybridoma cell line selected from the group of hybridoma cell lines deposited at the American Type Culture Collection (10801 University Bld, Manassas, VA, 20110-2209, USA), on June 21, 2006, under the deposit numbers PTA-7667, PTA-7669, PTA-7670, PTA-7666, PTA-7668, and PTA-7671.

38) An antibody or epitope-binding fragment thereof according to claim 16, characterized in that said antibody or epitope-binding fragment thereof comprises at least one human constant region.

39) An antibody or epitope-binding fragment thereof according to claim 38, characterized in that said constant region is the human IgG1/IgKappa constant region.

40) An antibody or epitope-binding fragment thereof according to claim 16, characterized in that said antibody or epitope-binding fragment thereof is a humanized or resurfaced antibody.

41) A humanized or resurfaced antibody or epitope-binding fragment thereof according to claim 40, characterized in that said humanized or resurfaced antibody or epitope-binding fragment thereof comprises at least one heavy chain

and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 1, 2, and 3, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 4, 5, and 6.

42) A humanized or resurfaced antibody or epitope-binding fragment thereof according to claim 40, characterized in that said humanized or resurfaced antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 7, 8, and 9, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 10, 11, and 12.

43) A humanized or resurfaced antibody or epitope-binding fragment thereof according to claim 40, characterized in that said humanized or resurfaced antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 13, 14, and 15, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 16, 17, and 18.

44) A humanized or resurfaced antibody or epitope-binding fragment thereof according to claim 43, characterized in that said humanized or resurfaced antibody or epitope-binding fragment thereof comprises a heavy chain variable region having an amino acid sequence represented by SEQ ID NO: 66.

45) A humanized or resurfaced antibody or epitope-binding fragment thereof according to claim 43, characterized in that said humanized or resurfaced antibody or epitope-binding fragment thereof comprises a light chain variable region having an amino acid sequence selected from the group of SEQ ID NOS: 62 and 64.

46) A humanized or resurfaced antibody or epitope-binding fragment thereof according to claim 40, characterized in that said humanized or resurfaced

antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 19, 20, and 21, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 22, 23, and 24.

47) A humanized or resurfaced antibody or epitope-binding fragment thereof according to claim 40, characterized in that said humanized or resurfaced antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 25, 26, and 27, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 28, 29, and 30.

48) A humanized or resurfaced antibody or epitope-binding fragment thereof according to claim 47, characterized in that said humanized or resurfaced antibody or epitope-binding fragment thereof comprises a heavy chain variable region having an amino acid sequence represented by SEQ ID NO: 72.

49) A humanized or resurfaced antibody or epitope-binding fragment thereof according to claim 47, characterized in that said humanized or resurfaced antibody or epitope-binding fragment thereof comprises a light chain variable region having an amino acid sequence selected from the group of SEQ ID NOS: 68 and 70.

50) A humanized or resurfaced antibody or epitope-binding fragment thereof according to claim 40, characterized in that said humanized or resurfaced antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain, wherein said heavy chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 31, 32, and 33, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 34, 35, and 36.

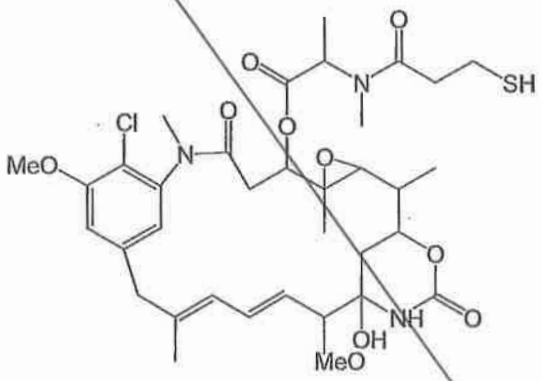
~~**51)** An antibody or epitope-binding fragment thereof according to claim 16,~~

characterized in that said antibody or epitope-binding fragment thereof is a Fab, Fab', F(ab')2 or Fv fragment.

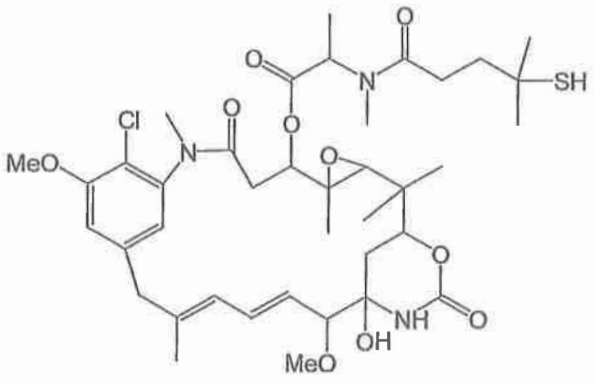
52) A conjugate comprising the antibody or epitope-binding fragment thereof according to any of claims 1 to 51 linked to a cytotoxic agent.

53) The conjugate of claim 52, characterized in that said cytotoxic agent is selected from the group consisting of a maytansinoid, a small drug, a tomaymycin derivative, a leptomycin derivative, a prodrug, a taxoid, CC-1065 and a CC-1065 analog.

54) The conjugate of claim 53, characterized in that said cytotoxic agent is the maytansine DM1 of formula :



55) The conjugate of claim 53, characterized in that said cytotoxic agent is the maytansine DM4 of formula :



56) The conjugate of claim 53, characterized in that said cytotoxic agent is a

tomaymycin derivative selected from the group consisting of:

- 8,8'-[1,3-benzenediylbis(methyleneoxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-methoxy-1,3-benzenediylbis(methyleneoxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[1,5-pentanediylbis(oxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[1,4-butanediylbis(oxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[3-methyl-1,5-pentanediylbis(oxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[2,6-pyridinediylbis(oxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[4-(3-tert-butoxycarbonylaminopropyloxy)-2,6-pyridinediylbis-(methyleneoxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-(3-aminopropyloxy)-1,3-benzenediylbis(methyleneoxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-(N-methyl-3-tert-butoxycarbonylaminopropyl)-1,3-benzenediylbis-(methyleneoxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-{5-[3-(4-methyl-4-methyldisulfanyl-pentanoylamino)propyloxy]-1,3-benzenediylbis(methyleneoxy)}-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-acetylthiomethyl-1,3-benzenediylbis(methyleneoxy)]-bis[(S)-2-methylene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]

- bis-{2-[(S)-2-methylene-7-methoxy-5-oxo-1,3,,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yloxy]-ethyl}-carbamic acid tert-butyl ester
- 8,8'-[3-(2-acetylthioethyl)-1,5-pentanediylbis(oxy)]-bis[(S)-2-methylene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-(N-4-mercapto-4,4-dimethylbutanoyl)amino-1,3-benzenediylbis(methyleneoxy)]-bis[7-methoxy-2-methylene-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-(N-4-methyldithio-4,4-dimethylbutanoyl)-amino-1,3-benzenediylbis(methyleneoxy)]-bis[7-methoxy-2-methylene-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-(N-methyl-N-(2-mercapto-2,2-dimethylethyl)amino-1,3-benzenediyl(methyleneoxy)]-bis[7-methoxy-2-methylene-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-(N-methyl-N-(2-methyldithio-2,2-dimethylethyl)amino-1,3-benzenediyl(methyleneoxy)]-bis[7-methoxy-2-methylene-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(2-(4-mercapto-4-methyl)-pentanamido-ethoxy)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(1-(2-(4-methyl-4-methyldisulfanyl)-pentanamido-ethoxy)-benzene-3,5-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(3-(4-methyl-4-methyldisulfanyl)-pentanamido-propoxy)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4] benzodiazepin-5-one]
- 8,8'-[(4-(4-(4-methyl-4-methyldisulfanyl)-pentanamido-butoxy)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(3-[4-(4-methyl-4-methyldisulfanyl-pentanoyl)-piperazin-1-yl]-propyl)-

pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]

- 8,8'-[(1-(3-[4-(4-methyl-4-methyldisulfanyl-pentanoyl)-piperazin-1-yl]-propyl)-benzene-3,5-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(2-{2-[2-(4-methyl-4-methyldisulfanyl-pentanoylamino)-ethoxy]-ethoxy}-ethoxy)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(1-(2-{2-[2-(2-{2-[2-(4-methyl-4-methyldisulfanyl-pentanoylamino)-ethoxy]-ethoxy}-ethoxy)-ethoxy]-ethoxy}-ethoxy)-benzene-3,5-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(1-(2-{2-[2-(4-methyl-4-methyldisulfanyl-pentanoylamino)-ethoxy]-ethoxy}-ethoxy)-benzene-3,5-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(2-{2-[2-(2-{2-[2-(4-methyl-4-methyldisulfanyl-pentanoylamino)-ethoxy]-ethoxy}-ethoxy)-ethoxy]-ethoxy}-ethoxy)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(1-(2-[methyl-(2-methyl-2-methyldisulfanyl-propyl)-amino]-ethoxy)-benzene-3,5-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(3-[methyl-(4-methyl-4-methyldisulfanyl-pentanoyl)-amino]-propyl)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(3-[methyl-(2-methyl-2-methyldisulfanyl-propyl)-amino]-propyl)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]

8,8'-[(1-(4-methyl-4-methyldisulfanyl)-pentanamido)-benzene-3,5-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-

c][1,4]benzodiazepin-5-one].

57) The conjugate of claim 53, characterized in that the cytotoxic agent is a leptomycin derivative selected from the group consisting of:

- (2-Methylsulfanyl-ethyl)-amid of (2E,10E,12E,16Z,18E)-(R)-6-Hydroxy-3,5,7,9,11,15,17-heptamethyl-19-((2S,3S)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)-8-oxo-nonadeca-2,10,12,16,18-pentaenoic acid (2-methylsulfanyl-ethyl)-amid

- Bis-[(2-mercaptoethyl)-amid of (2E,10E,12E,16Z,18E)-(R)-6-hydroxy-3,5,7,9,11,15,17-heptamethyl-19-((2S,3S)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)-8-oxo-nonadeca-2,10,12,16,18-pentaenoic acid]

- (2-Mercapto-ethyl)-amid of (2E,10E,12E,16Z,18E)-(R)-6-hydroxy-3,5,7,9,11,15,17-heptamethyl-19-((2S,3S)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)-8-oxo-nonadeca-2,10,12,16,18-pentaenoic acid

- (2-Methyldisulfanyl-ethyl)-amid of (2E,10E,12E,16Z,18E)-(R)-6-hydroxy-3,5,7,9,11,15,17-heptamethyl-19-((2S,3S)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)-8-oxo-nonadeca-2,10,12,16,18-pentaenoic acid

- (2-Methyl-2-methyldisulfanyl-propyl)-amid of (2E,10E,12E,16Z,18E)-(R)-6-hydroxy-3,5,7,9,11,15,17-heptamethyl-19-((2S,3S)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)-8-oxo-nonadeca-2,10,12,16,18-pentaenoic acid

(2-Mercapto-2-methyl-propyl)-amid of (2E,10E,12E,16Z,18E)-(R)-6-hydroxy-3,5,7,9,11,15,17-heptamethyl-19-((2S,3S)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)-8-oxo-nonadeca-2,10,12,16,18-pentaenoic acid.

58) An antibody or epitope-binding fragment thereof according to any of claims 1-51, or a conjugate according to any of claims 52-57, for use as a medicament.

59) A pharmaceutical composition containing an antibody or epitope-binding fragment thereof according to any of claims 1-51, or a conjugate according to any of claims 52-57, and a pharmaceutically acceptable carrier or excipients.

60) The pharmaceutical composition of claim 59, characterized in that said composition contains a further therapeutic agent.

61) The pharmaceutical composition of claim 60, characterized in that the further therapeutic agent is an antagonist of epidermal-growth factor (EGF), fibroblast-growth factor (FGF), hepatocyte growth factor (HGF), tissue factor (TF), protein C, protein S, platelet-derived growth factor (PDGF), heregulin, macrophage-stimulating protein (MSP) or vascular endothelial growth factor (VEGF), or an antagonist of a receptor for epidermal-growth factor (EGF), fibroblast-growth factor (FGF), hepatocyte growth factor (HGF), tissue factor (TF), protein C, protein S, platelet-derived growth factor (PDGF), heregulin, macrophage-stimulating protein (MSP), or vascular endothelial growth factor (VEGF), including HER2 receptor, HER3 receptor, c-MET, and other receptor tyrosine kinases.

62) The pharmaceutical composition of claim 60, characterized in that the further therapeutic agent is an antibody directed against a cluster of differentiation antigen selected from a group comprising CD3, CD14, CD19, CD20, CD22, CD25, CD28, CD30, CD33, CD36, CD40, CD44, CD52, CD55, CD59, CD56, CD70, CD79, CD80, CD103, CD134, CD137, CD138, and CD152.

63) The use of an antibody or epitope-binding fragment thereof according to any of claims 1-51, or a conjugate according to any of claims 52-57, to make a medicament to treat cancer or autoimmune disease.

64) The use of claim 63, characterized in that said cancer is selected from the group consisting of carcinoma, including that of the bladder, breast, colon, kidney, liver, lung, ovary, pancreas, stomach, cervix, thyroid and skin; including squamous cell carcinoma ; tumors of mesenchymal origin, including fibrosarcoma and rhabdomyoscarcoma; other tumors, including melanoma, seminoma, tetratocarcinoma, neuroblastoma and glioma; tumors of the central and peripheral nervous system, including astrocytoma, neuroblastoma, glioma, and schwannomas; tumors of mesenchymal origin, including fibrosarcoma, rhabdomyoscarama, and osteosarcoma; and other tumors, including melanoma, xeroderma pigmentosum, keratoactanthoma, seminoma, thyroid follicular cancer and teratocarcinoma.

65) The use of claim 63, characterized in that said cancer is hematopoietic tumors of lymphoid lineage, including leukemia, non-Hodgkin's lymphoma, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Burkitt's lymphoma, Hodgkin's lymphoma, hairy cell leukemia, multiple

myeloma, chronic lymphocytic leukemia; hematopoietic tumors of myeloid lineage, including acute and chronic myeloid leukemias and promyelocytic leukemia.

66) The use of claim 63, characterized in that said autommune or inflammatory disease is selected from the group consisting of systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, Crohn's diasease, ulcerative colitis, gastritis, Hashimoto's thyroiditis, ankylosing spondylitis, hepatitis C-associated cryoglobulinemic vasculitis, chronic focal encephalitis, bullous pemphigoid, hemophilia A, membranoproliferative glomerulnephritis, Sjogren's syndrome, adult and juvenile dermatomyositis, adult polymyositis, chronic urticaria, primary biliary cirrhosis, idiopathic thrombocytopenic purpura, neuromyelitis optica, Graves' dysthyroid disease, bullous pemphigoid, membranoproliferative glonerulonephritis, Churg- Strauss syndrome, and asthma.

67) The use according to claim 63, further comprising the use of a further therapeutic agent in the manufacture of the same or different composition.

68) The use according to claim 67, characterized in that the further therapeutic agent is an antagonist of fibroblast-growth factor (FGF), hepatocyte growth factor (HGF), tissue factor (TF), protein C, protein S, platelet-derived growth factor (PDGF), heregulin, macrophage-stimulating protein (MSP) or vascular endothelial growth factor (VEGF), or an antagonist of a receptor for epidermal-growth factor (EGF), fibroblast-growth factor (FGF), hepatocyte growth factor (HGF), tissue factor (TF), protein C, protein S, platelet-derived growth factor (PDGF), heregulin, macrophage-stimulating protein (MSP), or vascular endothelial growth factor (VEGF), including HER2 receptor, HER3 receptor, c-MET, and other receptor tyrosine kinases.

69) The use according to claim 67, characterized in that the further therapeutic agent is an antibody directed against a cluster of differentiation antigen selected from a group comprising CD3, CD14, CD19, CD20, CD22, CD25, CD28, CD30, CD33, CD36, CD40, CD44, CD52, CD55, CD59, CD56, CD70, CD79, CD80, CD103, CD134, CD137, CD138, and CD152.

70) A method of diagnosing a cancer in a subject known to or suspected to have a cancer, said method comprising:

a) Contacting cells of said patient with an antibody or epitope-binding fragment thereof according to claims 1-51,

b) Measuring the binding of said antibody or epitope-binding fragment thereof to said cells, and

c) comparing the expression in part (b) with that of a normal reference subject or standard.

71) The method of claim 70, characterized in that said cancer is selected from the group consisting of carcinoma, including that of the bladder, breast, colon, kidney, liver, lung, ovary, pancreas, stomach, cervix, thyroid and skin; including squamous cell carcinoma; tumors of mesenchymal origin, including fibrosarcoma and rhabdomyoscarcoma; other tumors, including melanoma, seminoma, tetratocarcinoma, neuroblastoma and glioma; tumors of the central and peripheral nervous system, including astrocytoma, neuroblastoma, glioma, and schwannomas; tumors of mesenchymal origin, including fibrosarcoma, rhabdomyoscarama, and osteosarcoma; and other tumors, including melanoma, xeroderma pigmentosum, keratoactanthoma, seminoma, thyroid follicular cancer and teratocarcinoma.

72) The method of claim 70, wherein said cancer is hematopoietic tumors of lymphoid lineage, including leukemia, non-Hodgkin's lymphoma, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Burkitt's lymphoma, Hodgkin's lymphoma, hairy cell leukemia, multiple myeloma, chronic lymphocytic leukemia; hematopoietic tumors of myeloid lineage, including acute and chronic myeloid leukemias and promyelocytic leukemia.

73) The method of claim 70, characterized in that the said cells are in frozen or fixed tissue or cells from said patient.

74) A polynucleotide encoding a polypeptide selected from the group consisting of SEQ ID NOS: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, and 72.

75) A polynucleotide accroding to claim 74, characterized in that said polynucleotide has a sequence sharing at least 80 % homology with a polynucleotide selected

from the group consisting of SEQ ID NOs: 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, and 71.

76) A recombinant vector comprising a nucleic acid of any of claims 74 or 75.

77) A host cell comprising a vector of claim 76.

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15) An antibody or epitope-binding fragment thereof according to claims 1-14, characterized in that said antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain, wherein said heavy chain comprises an amino acid sequence represented by SEQ ID NO: 66 or comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 13, 14, and 15, and wherein said light chain comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS: 16, 17, and 18.

16) An antibody or epitope-binding fragment thereof according to claim 15, characterized in that said antibody or epitope-binding fragment thereof comprises a light chain variable region having an amino acid sequence represented by SEQ ID NO: 42.

17) An antibody or epitope-binding fragment thereof according to claim 15, characterized in that said antibody or epitope-binding fragment thereof comprises a heavy chain variable region having an amino acid sequence represented by SEQ ID NO: 54.

18) An antibody or epitope-binding fragment thereof according to claim 15, characterized in that said antibody or epitope-binding fragment thereof is produced by a hybridoma cell line selected from the group of hybridoma cell lines deposited at the American Type Culture Collection (10801 University Bld, Manassas, VA, 20110-2209, USA), on June 21, 2006, under the deposit number PTA-7670.

19) An antibody or epitope-binding fragment thereof according to claim 15, characterized in that said antibody or epitope-binding fragment thereof comprises at least one human constant region.

20) An antibody or epitope-binding fragment thereof according to claim 19, characterized in that said constant region is the human IgG1/IgKappa constant region.

21) An antibody or epitope-binding fragment thereof according to claim 15, characterized in that said antibody or epitope-binding fragment thereof is a humanized or resurfaced antibody.

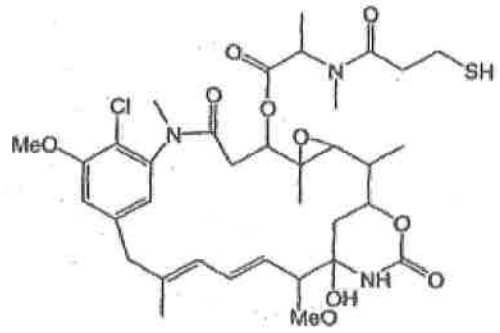
22) A humanized or resurfaced antibody or epitope-binding fragment thereof according to claim 21, characterized in that said humanized or resurfaced antibody or epitope-binding fragment thereof comprises a heavy chain variable region having an amino acid sequence represented by SEQ ID NO: 66.

23) A humanized or resurfaced antibody or epitope-binding fragment thereof according to claim 21, characterized in that said humanized or resurfaced antibody or epitope-binding fragment thereof comprises a light chain variable region having an amino acid sequence represented by SEQ ID NO: 64.

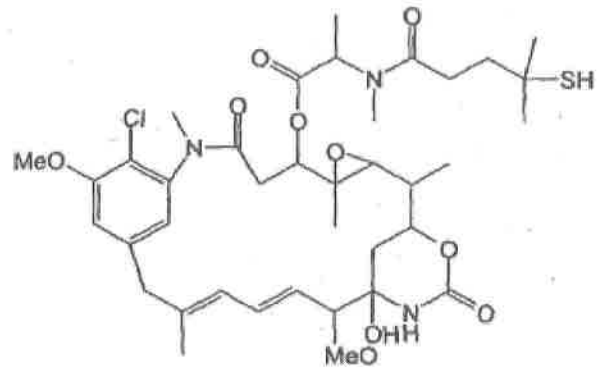
24) A conjugate comprising the antibody or epitope-binding fragment thereof according to any of claims 1 to 23 linked to a cytotoxic agent.

25) The conjugate of claim 24, characterized in that said cytotoxic agent is selected from the group consisting of a maytansinoid, a small drug, a tomaymycin derivative, a leptomycin derivative, a prodrug, a taxoid, CC-1065 and a CC-1065 analog.

26) The conjugate of claim 25, characterized in that said cytotoxic agent is the maytansine DM1 of formula :



27) The conjugate of claim 25, characterized in that said cytotoxic agent is the maytansine DM4 of formula :



28) The conjugate of claim 25, characterized in that said cytotoxic agent is a tomaymycin derivative selected from the group consisting of:

- 8,8'-[1,3-benzenediylbis(methyleneoxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-methoxy-1,3-benzenediylbis(methyleneoxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[1,5-pentanediylbis(oxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[1,4-butanediylbis(oxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[3-methyl-1,5-pentanediylbis(oxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[2,6-pyridinediylbis(oxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[4-(3-tert-butoxycarbonylaminopropyloxy)-2,6-pyridinediylbis-(methyleneoxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-(3-aminopropyloxy)-1,3-benzenediylbis(methyleneoxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-(N-methyl-3-tert-butoxycarbonylaminopropyl)-1,3-benzenediylbis-(methyleneoxy)]-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-{5-[3-(4-methyl-4-methyldisulfanyl-pentanoylamino)propyloxy]-1,3-benzenediylbis(methyleneoxy)}-bis[(S)-2-eth-(E)-ylidene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-acetylthiomethyl-1,3-benzenediylbis(methyleneoxy)]-bis[(S)-2-methylene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]

- bis-{2-[(S)-2-methylene-7-methoxy-5-oxo-1,3,,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yloxy]-ethyl}-carbamic acid tert-butyl ester
- 8,8'-[3-(2-acetylthioethyl)-1,5-pentanediylbis(oxy)]-bis[(S)-2-methylene-7-methoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-(N-4-mercapto-4,4-dimethylbutanoyl)amino-1,3-benzenediylbis(methyleneoxy)]-bis[7-methoxy-2-methylene-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-(N-4-methyldithio-4,4-dimethylbutanoyl)-amino-1,3-benzenediylbis(methyleneoxy)]-bis[7-methoxy-2-methylene-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-(N-methyl-N-(2-mercapto-2,2-dimethylethyl)amino-1,3-benzenediyl(methyleneoxy)]-bis[7-methoxy-2-methylene-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[5-(N-methyl-N-(2-methyldithio-2,2-dimethylethyl)amino-1,3-benzenediyl(methyleneoxy)]-bis[7-methoxy-2-methylene-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(2-(4-mercapto-4-methyl)-pentanamido-ethoxy)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(1-(2-(4-methyl-4-methyldisulfanyl)-pentanamido-ethoxy)-benzene-3,5-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(3-(4-methyl-4-methyldisulfanyl)-pentanamido-propoxy)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4] benzodiazepin-5-one]
- 8,8'-[(4-(4-(4-methyl-4-methyldisulfanyl)-pentanamido-butoxy)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(3-[4-(4-methyl-4-methyldisulfanyl-pentanoyl)-piperazin-1-yl]-propyl)-

pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]

- 8,8'-[(1-(3-[4-(4-methyl-4-methyldisulfanyl-pentanoyl)-piperazin-1-yl]-propyl)-benzene-3,5-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(2-{2-[2-(4-methyl-4-methyldisulfanyl-pentanoylamino)-ethoxy]-ethoxy}-ethoxy)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(1-(2-{2-[2-(2-{2-[2-(4-methyl-4-methyldisulfanyl-pentanoylamino)-ethoxy]-ethoxy}-ethoxy)-ethoxy]-ethoxy}-ethoxy)-benzene-3,5-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(1-(2-{2-[2-(4-methyl-4-methyldisulfanyl-pentanoylamino)-ethoxy]-ethoxy}-ethoxy)-benzene-3,5-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(2-{2-[2-(2-{2-[2-(4-methyl-4-methyldisulfanyl-pentanoylamino)-ethoxy]-ethoxy}-ethoxy)-ethoxy]-ethoxy}-ethoxy)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(1-(2-[methyl-(2-methyl-2-methyldisulfanyl-propyl)-amino]-ethoxy)-benzene-3,5-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(3-[methyl-(4-methyl-4-methyldisulfanyl-pentanoyl)-amino]-propyl)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]
- 8,8'-[(4-(3-[methyl-(2-methyl-2-methyldisulfanyl-propyl)-amino]-propyl)-pyridin-2,6-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]

8,8'-[(1-(4-methyl-4-methyldisulfanyl)-pentanamido)-benzene-3,5-dimethyl)-dioxy]-bis[(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-

c][1,4]benzodiazepine-5-one].

29) The conjugate of claim 25, characterized in that the cytotoxic agent is a leptomycin derivative selected from the group consisting of:

- (2-Methylsulfanyl-ethyl)-amid of (2E,10E,12E,16Z,18E)-(R)-6-Hydroxy-3,5,7,9,11,15,17-heptamethyl-19-((2S,3S)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)-8-oxo-nonadeca-2,10,12,16,18-pentaenoic acid (2-methylsulfanyl-ethyl)-amid
- Bis-[(2-mercaptoethyl)-amid of (2E,10E,12E,16Z,18E)-(R)-6-hydroxy-3,5,7,9,11,15,17-heptamethyl-19-((2S,3S)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)-8-oxo-nonadeca-2,10,12,16,18-pentaenoic acid]
- (2-Mercapto-ethyl)-amid of (2E,10E,12E,16Z,18E)-(R)-6-hydroxy-3,5,7,9,11,15,17-heptamethyl-19-((2S,3S)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)-8-oxo-nonadeca-2,10,12,16,18-pentaenoic acid
- (2-Methyldisulfanyl-ethyl)-amid of (2E,10E,12E,16Z,18E)-(R)-6-hydroxy-3,5,7,9,11,15,17-heptamethyl-19-((2S,3S)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)-8-oxo-nonadeca-2,10,12,16,18-pentaenoic acid
- (2-Methyl-2-methyldisulfanyl-propyl)-amid of (2E,10E,12E,16Z,18E)-(R)-6-hydroxy-3,5,7,9,11,15,17-heptamethyl-19-((2S,3S)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)-8-oxo-nonadeca-2,10,12,16,18-pentaenoic acid

(2-Mercapto-2-methyl-propyl)-amid of (2E,10E,12E,16Z,18E)-(R)-6-hydroxy-3,5,7,9,11,15,17-heptamethyl-19-((2S,3S)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)-8-oxo-nonadeca-2,10,12,16,18-pentaenoic acid.

30) An antibody or epitope-binding fragment thereof according to any of claims 1-24, or a conjugate according to any of claims 25-29, for use as a medicament.

31) A pharmaceutical composition containing an antibody or epitope-binding fragment thereof according to any of claims 1-24, or a conjugate according to any of claims 25-29, and a pharmaceutically acceptable carrier or excipients.

32) The pharmaceutical composition of claim 31, characterized in that said composition contains a further therapeutic agent.

33) The pharmaceutical composition of claim 32, characterized in that the further therapeutic agent is an antagonist of epidermal-growth factor (EGF), fibroblast- growth factor (FGF), hepatocyte growth factor (HGF), tissue factor (TF), protein C, protein S, platelet-derived growth factor (PDGF), heregulin, macrophage- stimulating protein (MSP) or vascular endothelial growth factor (VEGF), or an antagonist of a receptor for epidermal-growth factor (EGF), fibroblast-growth factor (FGF), hepatocyte growth factor (HGF), tissue factor (TF), protein C, protein S, platelet-derived growth factor (PDGF), heregulin, macrophage-stimulating protein (MSP), or vascular endothelial growth factor (VEGF), including HER2 receptor, HER3 receptor, c-MET, and other receptor tyrosine kinases.

34) The pharmaceutical composition of claim 32, characterized in that the further therapeutic agent is an antibody directed against a cluster of differentiation antigen selected from a group comprising CD3, CD14, CD19, CD20, CD22, CD25, CD28, CD30, CD33, CD36, CD40, CD44, CD52, CD55, CD59, CD56, CD70, CD79, CD80, CD103, CD134, CD137, CD138, and CD152.

35) The use of an antibody or epitope-binding fragment thereof according to any of claims 1-24, or a conjugate according to any of claims 25-29, to make a medicament to treat cancer or autoimmune disease.

36) The use of claim 35, characterized in that said cancer is selected from the group consisting of carcinoma, including that of the bladder, breast, colon, kidney, liver, lung, ovary, pancreas, stomach, cervix, thyroid and skin; including squamous cell carcinoma; tumors of mesenchymal origin, including fibrosarcoma and rhabdomyoscarcoma; other tumors, including melanoma, seminoma, tetratocarcinoma, neuroblastoma and glioma; tumors of the central and peripheral nervous system, including astrocytoma, neuroblastoma, glioma, and schwannomas; tumors of mesenchymal origin, including fibrosarcoma, rhabdomyoscarama, and osteosarcoma; and other tumors, including melanoma, xeroderma pigmentosum, keratoactanthoma, seminoma, thyroid follicular cancer and teratocarcinoma.

37) The use of claim 35, characterized in that said cancer is hematopoietic tumors of lymphoid lineage, including leukemia, non-Hodgkin's lymphoma, acute lymphocytic

leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Burkitt's lymphoma, Hodgkin's lymphoma, hairy cell leukemia, multiple myeloma, chronic lymphocytic leukemia; hematopoietic tumors of myeloid lineage, including acute and chronic myeloid leukemias and promyelocyte leukemia.

38) The use of claim 35, characterized in that said autoimmune or inflammatory disease is selected from the group consisting of systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, Crohn's disease, ulcerative colitis, gastritis, Hashimoto's thyroiditis, ankylosing spondylitis, hepatitis C-associated cryoglobulinemic vasculitis, chronic focal encephalitis, bullous pemphigoid, hemophilia A, membranoproliferative glomeruinephritis, Sjogren's syndrome, adult and juvenile dermatomyositis, adult polymyositis, chronic urticaria, primary biliary cirrhosis, idiopathic thrombocytopenic purpura, neuromyelitis optica, Graves' dysthyroid disease, bullous pemphigoid, membranoproliferative glonerulonephritis, Churg-Strauss syndrome, and asthma.

39) The use according to claim 35, further comprising the use of a further therapeutic agent in the manufacture of the same or different composition.

40) The use according to claim 39, characterized in that the further therapeutic agent is an antagonist of fibroblast-growth factor (FGF), hepatocyte growth factor (HGF), tissue factor (TF), protein C, protein S, platelet-derived growth factor (PDGF), heregulin, macrophage-stimulating protein (MSP) or vascular endothelial growth factor (VEGF), or an antagonist of a receptor for epidermal-growth factor (EGF), fibroblast-growth factor (FGF), hepatocyte growth factor (HGF), tissue factor (TF), protein C, protein S, platelet-derived growth factor (PDGF), heregulin, macrophage-stimulating protein (MSP), or vascular endothelial growth factor (VEGF), including HER2 receptor, HER3 receptor, c-MET, and other receptor tyrosine kinases.

41) The use according to claim 39, characterized in that the further therapeutic agent is an antibody directed against a cluster of differentiation antigen selected from a group comprising CD3, CD14, CD19, CD20, CD22, CD25, CD28, CD30, CD33, CD36, CD40, CD44, CD52, CD55, CD59, CD56, CD70, CD79, CD80, CD103, CD134, CD137, CD138, and CD152.

42) A polynucleotide encoding a polypeptide of an antibody or epitope-binding fragment thereof according to any one of claims 1-24 selected from the group consisting of SEQ ID NOS: 13, 14, 15, 16, 17, 18, 42, 54, 64 and 66.

43) A polynucleotide according to claim 42, characterized in that said polynucleotide has a sequence sharing at least 80% homology with a polynucleotide selected from the group consisting of SEQ ID NOs: 41, 53, 61, 63, and 65.

44) A recombinant vector comprising a nucleic acid of any of claims 42 or 43.

45) A host cell comprising a vector of claim 44.

46) A humanized or resurfaced antibody or epitope-binding fragment thereof wherein said humanized or resurfaced antibody or epitope-binding fragment thereof comprises a light chain variable region having an amino acid sequence represented by SEQ ID NO: 62 and a heavy chain variable region having an amino acid sequence represented by SEQ ID NO: 66.