C L A I M S

1) An antibody or epitope-binding fragment thereof that specifically binds CD38, characterized in that said antibody or epitope-binding fragment thereof comprises at least one heavy chain and at least one light chain wherein:

(i) said heavy chain comprises three sequential complementarity-determining regions (CDRs) having amino acid sequences represented by SEQ ID NOs: 13, 14, and 15, and said light chain comprises three sequential CDRs having amino acid sequences represented by SEQ ID NOs: 16, 17, and 18;

(ii) said heavy chain comprises a variable region hawng an amino acid sequence represented by SEQ ID NO: 54 and said light chain comprises a variable region having an amino acid sequence represented by SEQ ID NO: 42; or

(iii) said heavy chain comprises a variable region having an amino acid sequence represented by SEQ ID NO: 66 and said light chain comprises a variable region having an amino acid sequence represented by SEQ ID NO: 62 or SEQ ID NO: 64.

2) The antibody or epitope-binding fragment thereof according to claim 1, characterized in that said antibody or epitope-binding fragment thereof is capable of killing a $CD38^+$ cell by apoptosis in the absence of stroma cells or stroma-derived cytokines, antibody-dependent cell-mediated cytotoxicity (ADCC), and complement-dependent cytotoxicity (CDC).

3) The antibody or epitope-binding fragment thereof according to any of claims 1-2, characterized in that said antibody or epitope-binding fragment thereof is a monoclonal antibody.

4) The antibody or epitope-binding fragment thereof according to any of claims 1-3, characterized in that said $CD38^+$ cell is a lymphoma cell, a leukemia cell, or a multiple myeloma cell.

5) The antibody or epitope-binding fragment thereof of claim 4, characterized in that said $CD38^+$ cell is a non-Hodgkin's lymphoma (NHL) cell, a Burkitt's lymphoma (BL) cell, a multiple myeloma (MM) cell, a B chronic lymphocytic leukemia (B-CLL) cell, a B and T acute lymphocytic leukemia (ALL) cell, a T cell lymphoma

(TCL) cell, an acute myeloid leukemia (AML) cell, a hairy cell leukemia (HCL) cell, a Hodgkin's Lymphoma (HL) cell, or a chronic myeloid leukemia (CML) cell.

6) The antibody or epitope-binding fragment thereof according to claim 1, characterized in that said antibody or epitope-binding fragment thereof is capable of killing at least 24 % of Daudi lymphoma cells by apoptosis in the absence of stroma cells or stroma-derived cytokines.

7) The 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 7 % of Ramos lymphoma cells by apoptosis in the absence of stroma cells or stroma-derived cytokines.

8) The 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 11 % of MOLP-8 multiple myeloma cells by apoptosis in the absence of stroma cells or stroma-derived cytokines.

9) The 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) The 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) The 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) The 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) The 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) The 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) The antibody or epitope-binding fragment thereof according to claims 1-14, 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.

16) The 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) The 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 represented by SEQ ID NO: 54.

18) The 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 Bid, Manassas, VA, 20110-2209, USA), on June 21 , 2006, under the deposit number PTA-7670.

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

21) The antibody or epitope-binding fragment thereof according to claim 1, characterized in that said antibody or epitope-binding fragment thereof is a humanized or resurfaced antibody.

22) The 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) The 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: 62 or 64.

24) The antibody or epitope-binding fragment thereof according to claim 28, 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: 62.

25) A humanized or resurfaced antibody, characterized in that said antibody comprises:

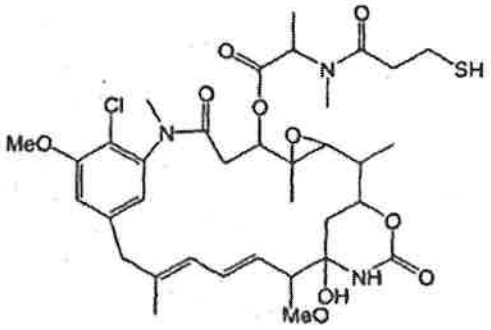
a light chain variable region comprising an amino acid sequence represented by SEQ ID NO: 62, and

a heavy chain variable region comprising an amino acid sequence represented by SEQ ID NO: 66.

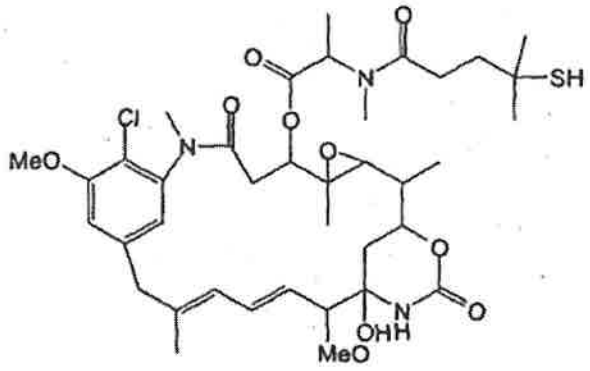
26) A conjugate comprising the antibody or epitope-binding fragment thereof according to any of claims 1 to 25 linked to a cytotoxic agent.

27) The conjugate of claim 26, 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.

28) The conjugate of claim 27, characterized in that said cytotoxic agent is the maytansine DM1 of formula :



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



30) The conjugate of claim 27, 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, 11 a-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-1,2,3,11 a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]

• 8,8'-[5-(3-aminopropyloxy)-1,3-benzenediylbis(methy!eneoxy)]-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-1,2,3,11 a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one]

• 8,8'-{5-[3-(4-ιτιethyl-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-1,2,3,11 a-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-2ı2-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-1,2,3,11 a-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-dinnethoxy-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]-bist(S)-2-eth-(E)-ylidene-7-dimethoxy-1,2,3,11a-tetrahydro-pyrrolo[2,1-c][1,4]benzodiazepin-5-one].

31) The conjugate of claim 27, 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)18EHR)-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.

32) An antibody or epitope-binding fragment thereof according to any of claims 1-26, or a conjugate according to any of claims 27-31, for use as a medicament.

33) A pharmaceutical composition containing an antibody or epitope-binding fragment thereof according to any of claims 1-26, or a conjugate according to any of claims 27-31, and a pharmaceutically acceptable carrier or excipients.

34) The pharmaceutical composition of claim 33, characterized in that said composition contains a further therapeutic agent.

35) The pharmaceutical composition of claim 34, 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)$_1$ 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)$_1$ hepatocyte growth factor (HGF), tissue factor (TF), protein C$_1$ protein S$_1$ 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.

36) The pharmaceutical composition of claim 34, 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.

37) The use of an antibody or epitope-binding fragment thereof according to any of claims 1-26, or a conjugate according to any of claims 27-31, to make a medicament to treat cancer or autoimmune disease.

38) The use of claim 37, 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.

39) The use of claim 37, 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.

40) The use of claim 37, 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.

41) The use according to claim 37, further comprising the use of a further therapeutic agent in the manufacture of the same or different composition.

42) The use according to claim 41, 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.

43) The use according to claim 41, 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.

44) A polynucleotide encoding a polypeptide of an antibody or epitope-binding fragment thereof according to any one of claims 1-26 selected from the group consisting of SEQ ID NOS: 13, 14, 15, 16, 17, 18, 42, 54, 62, 64 and 66.