CLAIMS

1. An antibody or an antigen binding fragment thereof that specifically binds to L1-CAM (CD171), the antibody or the antigen binding fragment thereof comprising:
a variable heavy chain region comprising:
CDR-H1 characterized by a sequence selected from
a sequence according to SEQ ID NO.:1 (GYWMH),
a sequence according to SEQ ID NO.: 2 (GYYMH),
a sequence according to SEQ ID NO.: 3 (GYFMH), and
a sequence according to SEQ ID NO.: 4 (GYLMH); and
CDR-H2 characterized by a sequence selected from
a sequence according to SEQ ID NO.: 5 (EINPSNGRTNYNERFQG),
a sequence according to SEQ ID NO.: 6 (EINPSNGRTNYNEKFQG),
a sequence according to SEQ ID NO.: 7 (EINPSNGRTNYNERFKS),
a sequence according to SEQ ID NO.: 8 (EINPSNGRTNYNERLKS),
a sequence according to SEQ ID NO.: 9 (EINPSNARTNYNERFQG),
a sequence according to SEQ ID NO.: 10 (EINPSNARTNYNEKFQG)
a sequence according to SEQ ID NO.: 11 (EINPSNARTNYNERFKS) and
a sequence according to SEQ ID NO.: 12 (EINPSNARTNYNERLKS); and
CDR-H3 characterized by a sequence according to SEQ ID NO.: 13 (DYYGTSYNFDY); and
a variable light chain region comprising:
CDR-L1 characterized by a sequence selected from
a sequence according to SEQ ID NO.: 14 (RANEDINNRLA),
a sequence according to SEQ ID NO.: 15 (KANEDINNRLA),
a sequence according to SEQ ID NO.: 16 (QANEDINNRLA),
a sequence according to SEQ ID NO.: 17 (RANEDINARLA),
a sequence according to SEQ ID NO.: 18 (KANEDINARLA),

a sequence according to SEQ ID NO.: 19 (QANEDINARLA),
a sequence according to SEQ ID NO.: 20 (RANEDINLRLA),
a sequence according to SEQ ID NO.: 21 (KANEDINLRLA), and
a sequence according to SEQ ID NO.: 22 (QANEDINLRLA); and
CDR-L2 characterized by a sequence selected from
a sequence according to SEQ ID NO.: 23 (GATNLVT) and
a sequence according to SEQ ID NO.: 24 (GASNLVS); and
CDR-L3 characterized by a sequence selected from
a sequence according to SEQ ID NO.: 25 (QQYWSTPFT),
a sequence according to SEQ ID NO.: 26 (QQYYSTPFT) and
a sequence according to SEQ ID NO.: 27 (QQYFSTPFT),

2. The antibody or the antigen-binding fragment thereof of claim 1, wherein the antibody or the antigen binding fragment thereof is a monoclonal antibody, a chimeric antibody, a recombinant antibody, an antigen-binding fragment of a recombinant antibody, a single chain antibody, a humanized antibody, a bispecific antibody, a multi-specific antibody, or an antibody displayed upon the surface of a phage or displayed upon the surface of a chimeric antigen receptor (CAR) T cell, preferably wherein the antibody or the antigen binding fragment thereof is a monoclonal antibody, more preferably wherein the antibody or the antigen binding fragment thereof is an IgG1 antibody.

3. The antibody or the antigen-binding fragment thereof of claim 1 or 2, wherein the variable heavy chain region comprises CDR-H1 characterized by a sequence according to SEQ ID NO.: 1.

4. The antibody or the antigen-binding fragment thereof of any one of claims 1 to 3, wherein the variable heavy chain region comprises CDR-H2 characterized by a sequence according to SEQ ID NO.: 5, 6, 9 or 10, preferably wherein the variable heavy chain region comprises CDR-H2 characterized by a sequence according to SEQ ID NO.: 5 or 6.

5. The antibody or the antigen-binding fragment thereof of any one of claims 1 to 4, wherein the variable light chain region comprises CDR-L1 characterized by a

sequence according to SEQ ID NO.: 14, 15, 17, 18, or 21, preferably wherein the variable light chain region comprises CDR-L1 characterized by a sequence according to SEQ ID NO.: 14 or 15.

6. The antibody or the antigen-binding fragment thereof of any one of claims 1 to 5, wherein the variable light chain comprises CDR-L2 characterized by a sequence according to SEQ ID NO.: 23.

7. The antibody or the antigen-binding fragment thereof of any one of claims 1 to 6, wherein the variable light chain comprises CDR-L3 characterized by a sequence according to SEQ ID NO.: 25.

8. The antibody or the antigen-binding fragment thereof of any one of claims 1 to 7, wherein the variable heavy chain region is characterized by a sequence at least 90% identical to, preferably at least 95% identical to, more preferably identical to a sequence selected from

a sequence according to SEQ ID NO.: 28 (QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYWMHWVRQAPGQGLEWIGE INPSNGRTNYNERFQGRVTLTVDKSISTAYMELSRLRSDDTAVYYCARDYYGT SYNFDYWGQGTLVTVSS),

a sequence according to SEQ ID NO.: 29 (QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYWMHWVRQAPGQGLEWIGE INPSNGRTNYNERFKSRVTLTVDKSISTAYMELSRLRSDDTAVYFCARDYYGT SYNFDYWGQGTLVTVSS),

a sequence according to SEQ ID NO.: 30 (QVQLQQWGAGLLKPSETLSLTCAAYGYTFTGYWMHWIRQPPGKGLEWIGEI NPSNGRTNYNERLKSRVTLSVDKSKNQASLKLSSVTAADTAVYFCARDYYGT SYNFDYWGQGTLVTVSS),

a sequence according to SEQ ID NO.: 31 (QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYWMHWVRQAPGQGLEWIGE INPSNGRTNYNEkFQGRVTLTVDKSISTAYMELSRLRSDDTAVYYCARDYYGT SYNFDYWGQGTLVTVSS), and

a sequence according to SEQ ID NO.: 32 (QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYWMHWVRQAPGQGLEWmG

EINPSNGRTNYNEkFQGRVTLTVDKSISTAYMELSRLRSDDTAVYYCARDYYG TSYNFDYWGQGTLVTVSS),

preferably wherein the variable heavy chain region is characterized by a sequence according to SEQ ID NO.: 28 or a sequence according to SEQ ID NO.: 32.

9. The antibody or the antigen-binding fragment thereof of any one of claims 1 to 8, wherein the variable light chain region is characterized by a sequence at least 90% identical to, preferably at least 95% identical to, more preferably identical to a sequence selected from

a sequence according to SEQ ID NO.: 33 (DIQMTQSPSSLSASVGDRVTITCKANEDINNRLAWYQQKPGKAPKLLISGATN LVTGVPSRFSGSGSGKDYTLTISSLQPEDFATYYCQQYWSTPFTFGQGTKLEI K),

a sequence according to SEQ ID NO.: 34 (DIQMTQSPSSLSASVGDRVTITCKANEDINNRLAWYQQKPGKAPKLLISGATN LVTGVPSRFSGSGSGKDYTLTISSLQPEDIATYYCQQYWSTPFTFGQGTKLEI K),

a sequence according to SEQ ID NO.: 35 (EIVMTQSPATLSVSPGERATLSCRANEDINNRLAWYQQKPGQAPRLLISGAT NLVTGIPARFSGSGSGKEFTLTISSLQSEDFAVYYCQQYWSTPFTFGQGTKLEI K),

a sequence according to SEQ ID NO.: 36 (DIQMTQSPSSLSASVGDRVTITCRANEDINNRLAWYQQKPGKAPKLLISGATN LVTGVPSRFSGSGSGKDYTLTISSLQPEDFATYYCQQYWSTPFTFGQGTKLEI K), and

a sequence according to SEQ ID NO.: 37 (DIQMTQSPSSLSASVGDRVTITCRANEDINNRLAWYQQKPGKAPKLLISGAsN LVsGVPSRFSGSGSGKDYTLTISSLQPEDFATYYCQQYWSTPFTFGQGTKLEI K),

preferably wherein the variable light chain region is characterized by a sequence selected from a sequence according to SEQ ID NO.: 33, a sequence according to SEQ ID NO.: 36 and a sequence according to SEQ ID NO. 37.

10. The antibody or the antigen-binding fragment thereof of any one of claims 1 to 9, wherein the variable heavy chain region is characterized by a sequence according to SEQ ID NO.: 28 and the variable light chain region is characterized by a sequence according to SEQ ID NO.: 33; or
wherein the variable heavy chain region is characterized by a sequence according to SEQ ID NO.: 32 and the variable light chain region is characterized by a sequence according to SEQ ID NO.: 36; or
wherein the variable heavy chain region is characterized by a sequence according to SEQ ID NO.: 14 and the variable light chain region is characterized by a sequence according to SEQ ID NO.: 37.

11. The antibody or the antigen-binding fragment thereof of claims 1 or 2,
wherein the variable heavy chain region is characterized by a sequence at least 90% identical to, preferably at least 95% identical to, more preferably identical to a sequence:

FH0 – CDR-H1 – FH1 – CDR-H2 – FH2 – CDR-H3 – FH3

wherein CDR-H1, CDR-H2 and CDR-H3 are as defined in claim 1, wherein:
FH0 is characterized by a sequence according to SEQ ID NO: 38 (QVQLVQSGAEVKKPGASVKVSCKASGYTFT) or a sequence according to SEQ ID NO: 39 (QVQLQQWGAGLLKPSETLSLTCAAYGYTFT),
FH1 is characterized by a sequence according to SEQ ID NO: 40 (WVRQAPGQGLEWIG) or a sequence according to SEQ ID NO.: 41 (WIRQPPGKGLEWIG)
FH2 is characterized by a sequence according to SEQ ID NO: 42 (RVTLTVDKSISTAYMELSRLRSDDTAVYFCAR) or a sequence according to SEQ ID NO.: 43 (RVTLSVDKSKNQASLKLSSVTAADTAVYFCAR), and
FH3 is characterized by a sequence according to SEQ ID NO:44 (WGQGTLVTVSS),
and
wherein the variable light chain region is characterized by a sequence at least 90% identical to, preferably at least 95% identical to, more preferably identical to a sequence:

FL0 – CDR-L1 – FL1 – CDR-L2 – FL2 – CDR-L3 – FL3

wherein CDR-L1, CDR-L2 and CDR-L3 are as defined in claim 1, wherein:

FL0 is characterized by a sequence according to SEQ ID NO: 45 (DIQMTQSPSSLSASVGDRVTITC) or a sequence according to SEQ ID NO: 46 (EIVMTQSPATLSVSPGERATLSC),

FL1 is characterized by a sequence according to SEQ ID NO: 47 (WYQQKPGKAPKLLIS) or a sequence according to SEQ ID NO.: 48 (WYQQKPGQAPRLLIS),

FL2 is characterized by a sequence according to SEQ ID NO: 49 (GVPSRFSGSGSGKDYTLTISSLQPEDIATYYC) or a sequence according to SEQ ID NO.: 50 (GIPARFSGSGSGKEFTLTISSLQSEDFAVYYC), and

FL3 is characterized by a sequence according to SEQ ID NO:51 (FGQGTKLEIK).

12. The antibody or the antigen-binding fragment thereof of claim 1 or 2, wherein the heavy chain of the antibody or the antigen-binding fragment thereof comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence selected from sequences according to SEQ ID NO.: 110, 142, 155 to 163, preferably identical to a sequence according to SEQ ID NO.: 110, 142, 155, 160 or 162, and wherein the light chain of the antibody or the antigen-binding fragment thereof comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence according to SEQ ID NO.: 97 or 143;

or

wherein the heavy chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably identical to a sequence according to SEQ ID NO.: 155, and wherein the light chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence according to SEQ ID NO.: 143;

or

wherein the heavy chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence according to SEQ ID NO. 110, 142, 155 to 163,

and

wherein the light chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence according to SEQ ID NO.: 97 or 143;

or

wherein the heavy chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence selected from sequences according to SEQ ID NO. 95 or 164 to 172,

and

wherein the light chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence according to SEQ ID NO.: 97 or 143;

or

wherein the heavy chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence selected from sequences according to SEQ ID NO. 173 to 183,

and

wherein the light chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence according to SEQ ID NO.: 193;

or

wherein the heavy chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a

sequence selected from sequences according to SEQ ID NO. 173 to 183,
and
wherein the light chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence according to SEQ ID NO.: 194;
or
wherein the heavy chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence selected from sequences according to SEQ ID NO. 184 to 192,
and
wherein the light chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence according to SEQ ID NO.: 193;
or
wherein the heavy chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence selected from sequences according to SEQ ID NO. 184 to 192,
and
wherein the light chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence according to SEQ ID NO.: 194;
or
wherein the heavy chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably identical to a sequence according to SEQ ID NO.: 175, and wherein the light chain comprises a sequence at least 90% identical to, preferably at least 95% identical to, more preferably at least 98% identical to, even more preferably at least 99% identical to, still more preferably identical to a sequence according to SEQ ID NO.: 194.

13. The antibody or an antigen binding fragment thereof of claim 1 or 2, wherein the heavy chain comprises a sequence at least 90% identical to a sequence according to SEQ ID NO. 110, or a sequence according to SEQ ID NO. 110 wherein the mutation N297A has been reversed; and wherein the light chain comprises a sequence at least 90% identical to a sequence according to SEQ ID NO.: 97;

    or

    wherein the heavy chain comprises a sequence at least 90% identical to a sequence according to SEQ ID NO. 173, or a sequence according to SEQ ID NO. 173 wherein mutation N297A is further present; and wherein the light chain comprises a sequence at least 90% identical to a sequence according to SEQ ID NO.: 193.

14. The antibody or the antigen-binding fragment thereof of any one of claims 1 to 13, wherein the heavy chain further comprises at least one point mutation in Fc part that influences antibody-dependent cell-mediated cytotoxicity (ADCC), complement-dependent cytotoxicity (CDC), serum half-life and/or glycosylation status of the antibody, preferably wherein the at least one point mutation is selected from L234A, L234F, L235A, L235E, L235Q, G236A, M252Y, S254T, T256E, S267E, H268F, N297A, K322A, K322Q, S324T, P331S, and I332E, more preferably wherein the at least one point mutation is selected from L234A, L235A, P331S and N297A,

    and/ or

    wherein the antibody or the antigen-binding fragment thereof is characterized by a dissociation constant K_D to L1-CAM (CD171) not exceeding 10^{-11} M, as measured in a Biacore-based assay.

15. A polynucleotide encoding at least one variable heavy chain sequence and/or at least one variable light chain sequence as described in any one of claims 1 to 14.

16. A host cell comprising the polynucleotide of claim 15.

17. An immunoconjugate comprising an antibody or an antigen-fragment binding thereof of any one of claims 1 to 14 and an active agent, preferably wherein the

active agent is a cytotoxic agent or a prodrug thereof.

18. The immunoconjugate of claim 17, wherein the antibody or the antigen-binding fragment thereof is linked to the active agent through a linker moiety, preferably wherein said linker moiety comprises a polymer carrier, to which at least one active agent is attached.

19. The immunoconjugate of claim 17 or 18, wherein the active agent is a radionuclide, preferably a radionuclide useful for therapeutic application, preferably selected from copper-67, strontium-89, yttrium-90, iodine-131, samarium-153, terbium-161, lutetium-177, astatine-211, radium-223 and actinium 225, and/or a radionuclide useful in diagnosis, preferably selected from fluorine-18, scandium-43, scandium-44, copper-61, copper-64, gallium-68, zirconium-89, indium-111, iodine-123, terbium-152, and terbium-155.

20. The immunoconjugate of claim 17 or 18, wherein the active agent is selected from maytansinoid, calicheamicin, pyrrolobenzodiazepine (PBD), nemorubicin and its derivatives, PNU-159682, anthracycline, duocarmycin, vinca alkaloid, taxane, trichothecene, CC1065, camptothecin, elinafide, Exatecan, Deruxtecan, topotecan, irinotecan, SN38, and belotecan.

21. A pharmaceutical composition comprising the antibody or the antigen-binding fragment thereof of any one of claims 1 to 14 or the immunoconjugate of any one of claims 17 to 20, and a pharmaceutically acceptable carrier.

22. Use of the antibody or the antigen-binding fragment thereof of any one of claims 1 to 14 or the immunoconjugate of any one of claims 17 to 20, in the manufacture of a medicament for the treatment of an L1-CAM (CD171) associated cancer.

23. The use of claim 22, wherein the L1-CAM (CD171) associated cancer is selected from leukemia, Ewing's sarcoma, neuroblastoma, osteosarcoma, glioblastoma multiforme, ovarian cancer, endometrial cancer, uterine cancer, triple negative breast cancer, quadruple-negative breast cancer, melanoma, clear cell renal cell cancer, pheochromacytoma and paraganglioma, mesothelioma, small cell lung

cancer (SCLC), non-small cell lung cancer, NSCLC, pancreatic ductal cancer, colon cancer, pancreatic cancer, hepatocellular carcinoma, gastric cancer, cholangiocarcinoma, carcinoid, neuroendocrine tumors, gastrointestinal stromal tumor (GIST), pheochromocytoma, glioma, pancreatic neuroectodermal cancer, pancreatic adenocarcinoma, colorectal cancer, renal cell carcinoma, tumor blood vessels, chondrosarcoma, esophageal adenocarcinoma, oligodendroglioma, astrocytoma, ependymoma, pancreatic neuroendocrine carcinoma, adrenal adenoma, leiomyosarcoma, liposarcoma, granular cell tumor of the ovary, schwannoma, primitive neuroectodermal tumor (PNET), epitheliod sarcoma, esthesioneuroblastoma, medulloblastoma, capillary hemangioma, Kaposi sarcoma, rhabdomyosarcoma, submaxillary salivary gland cancer, prostate cancer and head and neck squamous cell carcinoma.

24. The use of claim 22 or 23, wherein said antibody or the antigen-binding fragment thereof or the immunoconjugate is to be administered to a subject with an additional therapeutic agent, selected from alkylating agents, platinum agents, taxanes, vinca agents, anti-estrogen drugs, aromatase inhibitors, ovarian suppression agents, VEGF/VEGFR inhibitors, EGF/EGFR inhibitors, PARP inhibitors, cytostatic alkaloids, cytotoxic antibiotics, antimetabolites, endocrine/hormonal agents, immune checkpoint inhibitors and bisphosphonate therapy agent.

25. Use of the antibody or the antigen-binding fragment thereof of any one of claims 1 to 14 or the immunoconjugate of any one of claims 17 to 20 in the manufacture of a reagent for diagnosis of L1-CAM (CD171) associated cancer.

26. The use of claim 25, wherein the L1-CAM (CD171) associated cancer is selected from leukemia, Ewing's sarcoma, neuroblastoma, osteosarcoma, glioblastoma multiforme, ovarian cancer, endometrial cancer, uterine cancer, triple negative breast cancer, quadruple-negative breast cancer, melanoma, clear cell renal cell cancer, pheochromacytoma and paraganglioma, mesothelioma, small cell lung cancer (SCLC), non-small cell lung cancer, NSCLC, pancreatic ductal cancer, colon cancer, pancreatic cancer, hepatocellular carcinoma, gastric cancer, cholangiocarcinoma, carcinoid, neuroendocrine tumors, gastrointestinal stromal

tumor (GIST), pheochromocytoma, glioma, pancreatic neuroectodermal cancer, pancreatic adenocarcinoma, colorectal cancer, renal cell carcinoma, tumor blood vessels, chondrosarcoma, esophageal adenocarcinoma, oligodendroglioma, astrocytoma, ependymoma, pancreatic neuroendocrine carcinoma, adrenal adenoma, leiomyosarcoma, liposarcoma, granular cell tumor of the ovary, schwannoma, primitive neuroectodermal tumor (PNET), epitheliod sarcoma, esthesioneuroblastoma, medulloblastoma, capillary hemangioma, Kaposi sarcoma, rhabdomyosarcoma, submaxillary salivary gland cancer, prostate cancer, and head and neck squamous cell carcinoma.