Claims

1. A monoclonal antibody or antigen-binding fragment thereof that specifically binds to AXL, comprising:

(a) a light chain variable domain comprising:

CDR1 with the amino acid sequence of SEQ ID NO: 1,

CDR2 with the amino acid sequence of SEQ ID NO: 2 and

CDR3 with the amino acid sequence of SEQ ID NO: 3; and

(b) a heavy chain variable domain comprising:

CDR1 with the amino acid sequence of SEQ ID NO: 7,

CDR2 with the amino acid sequence of SEQ ID NO: 8 and

CDR3 with the amino acid sequence of SEQ ID NO: 9.

2. The monoclonal antibody or antigen-binding fragment thereof according to claim 1, wherein the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 13.

3. The monoclonal antibody or antigen-binding fragment thereof according to claim 1, wherein the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 14.

4. The monoclonal antibody or antigen-binding fragment thereof according to claim 1, wherein:

(a) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 13 and

(b) the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 14.

5. The monoclonal antibody according to any one of claims 1–4, wherein the antibody that specifically binds to AXL is a full-length IgG antibody.

6. The monoclonal antibody according to claim 5, wherein the full-length IgG antibody is of human IgG1, IgG2, IgG3 or IgG4 isotype.

7. The monoclonal antibody according to claim 6, wherein the antibody comprises the mutations S239D and I332E according to the EU numbering scheme for amino acids of antibodies.

8. The monoclonal antibody according to claim 6, wherein the antibody comprises the deletion 446G and 447K according to the EU numbering scheme for amino acids of antibodies in the CH3 region.

9. The monoclonal antibody according to claim 1, comprising a light chain comprising the amino acid sequence of SEQ ID NO: 15.

10. The monoclonal antibody according to claim 1, comprising a heavy chain comprising an amino acid sequence that is selected from the group: SEQ ID NO: 16 or SEQ ID NO: 17.

11. The monoclonal antibody according to claim 1, comprising:

(i) (a) a light chain comprising the amino acid sequence of SEQ ID NO: 15, and

(b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 16; or

(ii) (a) a light chain comprising the amino acid sequence of SEQ ID NO: 15, and

(b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 17.

12. The nucleic acid that encodes the antibody or antigen-binding fragment thereof according to any one of claims 1–11.

13. The nucleic acid according to claim 12, wherein the nucleic acid is DNA.

14. An expression vector comprising the nucleic acid according to any one of claims 12–13.

15. A method for producing a host cell to produce the antibody or antigen-binding fragment thereof according to any one of claims 1–11, comprising cell transformation by the vector according to claim 14.

16. A host cell for producing the antibody or antigen-binding fragment thereof according to any one of claims 1–11, comprising the nucleic acid according to any one of claims 12–13.

17. A method for producing the antibody or antigen-binding fragment thereof according to any one of claims 1-11, comprising culturing the host cell according to claim 16 in a culture medium under conditions sufficient to produce said antibody or antigen-binding fragment thereof, followed by isolation and purification of the resulting antibody or antigen-binding fragment thereof.

18. A pharmaceutical composition for treating an AXL-mediated disease or disorder comprising the antibody or antigen-binding fragment thereof according to any one of claims 1–11 in a therapeutically effective amount in combination with one or more pharmaceutically acceptable excipients.

19. The pharmaceutical composition according to claim 18, wherein the AXL-mediated disease or disorder is selected from the group: non-small cell lung cancer, non-small cell lung cancer with a EGFR mutation, breast carcinoma, HER2-positive breast cancer, four time-negative breast cancer, triple-negative breast cancer (TNBC), ovarian cancer, platinum-resistant ovarian cancer, prostate cancer, docetaxel-resistant prostate cancer, endometrial cancer and uterine sarcoma, endometrioid adenocarcinoma, uterine serous carcinoma, skin melanoma, neuroblastoma, glioblastoma, head and neck squamous cell carcinoma, stomach cancer, renal cell carcinoma, urothelial carcinoma, colorectal cancer, colon cancer, hepatocellular carcinoma, pancreatic cancer, biliary cancer, malignant neoplasm of the extrahepatic bile duct, intrahepatic bile duct cancer, malignant neoplasms of the gallbladder, osteosarcoma, Ewing sarcoma, neoplasms with high-level AXL expression, chronic myeloid leukemia, chronic lymphocytic leukemia, acute myeloid leukemia, acute lymphoblastic leukemia, chronic liver disease, non-alcoholic steatohepatitis, Alzheimer's disease or idiopathic pulmonary fibrosis.

20. A pharmaceutical composition for treating an AXL-mediated disease or disorder, comprising the antibody or antigen-binding fragment thereof according to any one of claims 1–11 and at least one other therapeutically active compound.

21. The pharmaceutical composition according to claim 20, wherein the AXL-mediated disease or disorder is selected from the group: non-small cell lung cancer, non-small cell lung cancer with a EGFR mutation, breast carcinoma, HER2-positive breast cancer, four time-negative breast cancer, triple-negative breast cancer (TNBC), ovarian cancer, platinum-resistant ovarian cancer, prostate cancer, docetaxel-resistant prostate cancer, endometrial cancer and uterine sarcoma, endometrioid adenocarcinoma, uterine serous carcinoma, skin melanoma, neuroblastoma, glioblastoma, head and neck squamous cell carcinoma, stomach cancer, renal cell carcinoma, urothelial carcinoma, colorectal cancer, colon cancer, hepatocellular carcinoma, pancreatic cancer, biliary cancer, malignant neoplasm of the

extrahepatic bile duct, intrahepatic bile duct cancer, malignant neoplasms of the gallbladder, osteosarcoma, Ewing sarcoma, neoplasms with high-level AXL expression, chronic myeloid leukemia, chronic lymphocytic leukemia, acute myeloid leukemia, acute lymphoblastic leukemia, chronic liver disease, non-alcoholic steatohepatitis, Alzheimer's disease or idiopathic pulmonary fibrosis.

22. The pharmaceutical composition according to any one of claims 20–21, wherein the other therapeutically active compound is an antibody, a small molecule, a hormone therapy agent or combination thereof.

23. Use of the antibody or antigen-binding fragment thereof according to any one of claims 1–11 or the pharmaceutical composition according to any one of claims 18–22 for treating an AXL-mediated disease or disorder in a subject in need of such treatment.

24. The use according to claim 23 of the antibody or antigen-binding fragment thereof according to any one of claims 1–11 and at least one other therapeutically active compound for treating an AXL-mediated disease or disorder in a subject in need of such treatment.

25. The use according to claim 24, wherein the AXL-mediated disease or disorder is selected from the group: non-small cell lung cancer, non-small cell lung cancer with a EGFR mutation, breast carcinoma, HER2-positive breast cancer, four time-negative breast cancer, triple-negative breast cancer (TNBC), ovarian cancer, platinum-resistant ovarian cancer, prostate cancer, docetaxel-resistant prostate cancer, endometrial cancer and uterine sarcoma, endometrioid adenocarcinoma, uterine serous carcinoma, skin melanoma, neuroblastoma, glioblastoma, head and neck squamous cell carcinoma, stomach cancer, renal cell carcinoma, urothelial carcinoma, colorectal cancer, colon cancer, hepatocellular carcinoma, pancreatic cancer, biliary cancer, malignant neoplasm of the extrahepatic bile duct, intrahepatic bile duct cancer, malignant neoplasms of the gallbladder, osteosarcoma, Ewing sarcoma, neoplasms with high-level AXL expression, chronic myeloid leukemia, chronic lymphocytic leukemia, acute myeloid leukemia, acute lymphoblastic leukemia, chronic liver disease, non-alcoholic steatohepatitis, Alzheimer's disease or idiopathic pulmonary fibrosis.

26. The use according to claim 24, wherein the other therapeutically active compound is an antibody, small molecule, hormone therapy agent, or any combination thereof.