

CLAIMS

1. An anti-AXL antibody or an antigen-binding portion thereof, wherein said antibody comprises the H-CDR1-3 and L-CDR1-3 amino acid sequences of:
 - a) SEQ ID NOs: 15-20, respectively;
 - b) SEQ ID NOs: 5-10, respectively;
 - c) SEQ ID NOs: 25-30, respectively; or
 - d) SEQ ID NOs: 35-40, respectively.
2. The anti-AXL antibody or antigen-binding portion of claim 1, wherein said antibody comprises a heavy chain variable domain amino acid sequence and a light chain variable domain amino acid sequence that are at least 90% identical to the amino acid sequences of:
 - a) SEQ ID NOs: 13 and 14, respectively;
 - b) SEQ ID NOs: 3 and 4, respectively;
 - c) SEQ ID NOs: 23 and 24, respectively; or
 - d) SEQ ID NOs: 33 and 34, respectively.
3. The anti-AXL antibody or antigen-binding portion of claim 1, wherein said antibody comprises a heavy chain variable domain and a light chain variable domain comprising the amino acid sequences of:
 - a) SEQ ID NOs: 13 and 14, respectively;
 - b) SEQ ID NOs: 3 and 4, respectively;
 - c) SEQ ID NOs: 23 and 24, respectively; or
 - d) SEQ ID NOs: 33 and 34, respectively.
4. The anti-AXL antibody of any one of claims 1-3, wherein the antibody is an IgG.
5. The anti-AXL antibody of claim 4, wherein the antibody is an IgG₁.
6. The anti-AXL antibody of any one of claims 1-3, wherein the antibody comprises at least one mutation in the F_C region.

7. The anti-AXL antibody of any one of claims 1-3, wherein the antibody is an IgG₁ and comprises a mutation in either or both of heavy chain amino acid positions 234 and 235, which are numbered according to the IMGT[®] numbering scheme.
8. The anti-AXL antibody of claim 7, wherein either or both of the amino acid residues at positions 234 and 235 are mutated from Leu to Ala.
9. An anti-AXL antibody that comprises:
 - a) an HC comprising the amino acid sequences of SEQ ID NOs: 13 and 61 and an LC comprising the amino acid sequences of SEQ ID NOs: 14 and 62;
 - b) an HC comprising the amino acid sequences of SEQ ID NOs: 3 and 61 and an LC comprising the amino acid sequences of SEQ ID NOs: 4 and 62;
 - c) an HC comprising the amino acid sequences of SEQ ID NOs: 23 and 61 and an LC comprising the amino acid sequences of SEQ ID NOs: 24 and 62; or
 - d) an HC comprising the amino acid sequences of SEQ ID NOs: 33 and 61 and an LC comprising the amino acid sequences of SEQ ID NOs: 34 and 62.
10. The anti-AXL antibody or antigen-binding portion of any one of claims 1-3, wherein the antibody or antigen-binding portion has at least one property selected from:
 - a) binds to human AXL with a K_D of 3×10^{-8} M or less;
 - b) binds to cynomolgus AXL with a K_D of 8×10^{-8} M or less;
 - c) does not bind to mouse AXL;
 - d) binds to the Ig1 or Ig2 domain of human AXL;
 - e) inhibits binding of GAS6 to human AXL;
 - f) inhibits proliferation of H1299 cells *in vitro* in the presence of GAS6;
 - g) does not exhibit agonistic activity in the absence of GAS6;
 - h) inhibits GAS6-induced uptake of phosphatidylserine-containing

liposomes in MDA-MB-468-AXL cells stably expressing exogenous AXL; and

- i) inhibits tumor growth *in vivo*.
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- 11. The anti-AXL antibody or antigen-binding portion of claim 10, wherein the antibody or antigen-binding portion has at least two, three, four, five, six, seven, eight, or all of said properties.
 - 12. A pharmaceutical composition comprising an anti-AXL antibody or antigen-binding portion of any one of claims 1-3 and a pharmaceutically acceptable excipient.
 - 13. The pharmaceutical composition of claim 12, further comprising an immunostimulatory agent, a vaccine, a chemotherapeutic agent, an anti-neoplastic agent, an anti-angiogenic agent, or a tyrosine kinase inhibitor.
 - 14. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the heavy chain or an antigen-binding portion thereof, or a nucleotide sequence that encodes the light chain or an antigen-binding portion thereof, or both, of the anti-AXL antibody of any one of claims 1-3.
 - 15. The isolated nucleic acid molecule of claim 14, wherein said nucleic acid molecule comprises the nucleotide sequence of any one of SEQ ID NOs: 11, 12, 1, 2, 21, 22, 31, and 32.
 - 16. A vector comprising the isolated nucleic acid molecule of claim 14 or 15, wherein said vector further comprises an expression control sequence operably linked to the nucleotide sequence.
 - 17. A host cell comprising a nucleotide sequence that encodes the heavy chain or an antigen-binding portion thereof, and a nucleotide sequence that encodes the light chain or an antigen-binding portion thereof, of the anti-AXL antibody of any one of claims 1-3.

18. A method for producing an anti-AXL antibody or an antigen-binding portion thereof, comprising providing a host cell according to claim 17, culturing said host cell under conditions suitable for expression of the antibody or portion, and isolating the resulting antibody or portion.
19. A bi-specific binding molecule comprising the antigen-binding portion of one or two distinct anti-AXL antibodies according to any one of claims 1-3.
20. Use of the anti-AXL antibody or antigen-binding portion of any one of claims 1-11, the pharmaceutical composition of claim 12 or 13, or the bi-specific binding molecule of claim 19 in the manufacture of a medicament for treating cancer in a patient.
21. The use of claim 20, wherein the cancer is in a tissue selected from the group consisting of breast.
22. The use of claim 20, wherein the cancer is breast cancer (e.g., triple negative breast cancer).
23. The use of any one of claims 20-22, further comprising administering to the patient an immunostimulatory agent, a vaccine, a chemotherapeutic agent, an anti-neoplastic agent, an anti-angiogenic agent, a tyrosine kinase inhibitor, or radiation therapy.
24. Use of the anti-AXL antibody or antigen-binding portion of any one of claims 1-11, the pharmaceutical composition of claim 12 or 13, or the bi-specific binding molecule of claim 19 in the manufacture of a medicament for treating cancer in a patient in a method of any one of claims 20-22.
25. The antibody or antigen-binding portion of any one of claims 1-11, the pharmaceutical composition of claim 12 or 13, or the bi-specific binding molecule of claim 19, for use in treating cancer in a patient in a method of any one of claims 20-22.

26. The use of claim 24, or the antibody or antigen-binding portion for use, pharmaceutical composition for use, or bi-specific binding molecule for use of claim 25, wherein the patient is human.