

WHAT IS CLAIMED IS:

1. An isolated or purified antibody that specifically binds to an epitope in an immunoglobulin-like (IgL) domain of human AXL ectodomain (ECD).
2. The antibody of claim 1, wherein the AXL ECD has the amino acid sequence of SEQ ID NO:71.
3. The antibody of claim 1, wherein the epitope is located in IgL1 or IgL2 of AXL.
4. The antibody of claim 1, capable of internalization into AXL expressing tumor cells.
5. The antibody of claim 1, which is a single domain antibody, a monoclonal antibody, a humanized antibody, a chimeric antibody, a biparatopic antibody, a bispecific antibody, or an AXL-binding antibody fragment thereof.
6. The antibody of claim 5, wherein the chimeric antibody comprises framework regions from human IgG1.
7. The antibody of claim 6, wherein the chimeric antibody comprises framework regions from human kappa light chain and human IgG heavy chain.
8. The antibody of claim 1, comprising framework regions from IgA, IgD, IgE, IgG, or IgM.
9. The antibody of claim 1, comprising a full-length IgG, Fv, scFv, Fab, or F(ab')₂, VHH, VL, or VH.
10. The antibody of claim 1, having an equilibrium dissociation constant (K_D) of $\leq$ 50 nM to human AXL ectodomain.
11. The antibody of claim 1, wherein the binding to the epitope in an IgL domain of AXL ECD does not compete with the binding of Growth arrest-specific 6 (Gas6) ligand to AXL.
12. An antibody or fragment thereof comprising variable light chain (VL) CDR1, CDR2, and CDR3 sequences selected from the group consisting of:
SEQ ID NO:98, 99, and 100;

SEQ ID NO:92, 93 and 94;
SEQ ID NO:110, 111, and 112;
SEQ ID NO:86, 87, and 88;
SEQ ID NO:80, 81, and 82;
SEQ ID NO:104, 105, and 106;
SEQ ID NO:116, 117, and 118; and
sequences substantially identical thereto.

13. An antibody or fragment thereof comprising a variable light chain (VL) sequence selected from the group consisting of:

SEQ ID NO:38;
SEQ ID NO:40;
SEQ ID NO:42;
SEQ ID NO:44;
SEQ ID NO:46;
SEQ ID NO:74;
SEQ ID NO:76; and
a sequence substantially identical thereto.

14. An antibody or fragment thereof comprising variable heavy chain (VH) CDR1, CDR2, and CDR3 sequences selected from the group consisting of:

SEQ ID NO:95, 96, and 97;
SEQ ID NO:89, 90 and 91;
SEQ ID NO:107, 108, and 109;
SEQ ID NO:83, 84, and 85;
SEQ ID NO:77, 78, and 79;
SEQ ID NO:101, 102, and 103;
SEQ ID NO:113, 114, and 115; and
sequences substantially identical thereto.

15. An antibody or fragment thereof comprising a variable heavy chain (VH) sequence selected from the group consisting of:

SEQ ID NO:39;

SEQ ID NO:41;
SEQ ID NO:43;
SEQ ID NO:45;
SEQ ID NO:47;
SEQ ID NO:73;
SEQ ID NO:75; and
a sequence substantially identical thereto.

16. The antibody according to any one of claims 1 to 4, or a fragment thereof, comprising variable heavy chain (VL) CDR1, CDR2, and CDR3 sequences; and (VH) CDR1, CDR2, and CDR3 sequences selected from the group consisting of:

VL, SEQ ID NO:98-100; and VH, SEQ ID NO:95-97;
VL, SEQ ID NO:92-94; and VH, SEQ ID NO:89-91;
VL, SEQ ID NO:110-112; and VH, SEQ ID NO:107-109;
VL, SEQ ID NO:86-88; and VH, SEQ ID NO:83-85;
VL, SEQ ID NO:80-82; and VH, SEQ ID NO:77-79;
VL, SEQ ID NO:104-106; and VH, SEQ ID NO:101-103;
VL, SEQ ID NO:116-118; and VH, SEQ ID NO:113-115; and
sequences substantially identical thereto.

17. The antibody according to any one of claims 1 to 4, or a fragment thereof comprising single domain (sd) heavy chain variable (VHH) domain CDR1, CDR2, and CDR3 sequences selected from the group consisting of:

SEQ ID NO:127, 128, and 129;
SEQ ID NO:130, 131, and 132;
SEQ ID NO:133, 134, and 135;
SEQ ID NO:136, 137, and 138;
SEQ ID NO:139, 140, and 141;
SEQ ID NO:142, 143, and 144;
SEQ ID NO:145, 146, and 147;
SEQ ID NO:148, 149, and 150; and
sequences substantially identical thereto.

18. An antibody or fragment thereof comprising a single domain (sd) heavy chain variable (VHH) domain sequence selected from the group consisting of:

QVKLEESGGGLVQAGGSLRLSCTASASISSFDIMGWYRQAPGKQRELVAAI
TTLDIANYRDSVKGRFTISRDNANTVYLQMDSLKPEDTARYHCAAFQSDQN
YWGQGTQVTVSS (SEQ ID NO:119);

QVQLVDSGGGLVQAGGSLRLSCATSTRTVSSAVMAWFRQAPEKVRDFVGF
ITNSGNILYDDSVKGRFTISRDNANTVYLQMNSLKPEDTAVYYCAAKWSFS
SGYGDLRRAAMYDYWGQGTQVTVSS (SEQ ID NO:120);

QVQLVESGGGLVQAGGSLRLSCAASGVTLDYTAIGWFRQAPGKERELVAAI
TSGGNTDYAESAKGRFRISRDNANKNTIYLQMNSLKPEDTGVIYCAARRGGA
RGEYDYWDQGTQVTVSS (SEQ ID NO:121);

QVQLVESGGGVVQAGGSLRLSCAFSRGAFDYEIGWFRQAPGKEREFVAA
VTRNGDSVYADSLKARFTASRNNAVNTAYLHMNILQPEDTATYYCAANWR
PLRTSSGADDYADWGQGTQVTVSS (SEQ ID NO:122);

QVKLEESGGGLAQAGGSLRLSCAASGSISSINTIGWFRQAPGKQRELVAAS
DSGANRNYADSVKGRFTISRDNANTVYLQMNNLKPEDTAIYYCRAWGTGT
ISTMYWGQGTQVTVSS (SEQ ID NO:123);

QVKLEESGGGLVQAGASLRLSCVASESIFGFNTMGWYRQAPGNERELVASI
SNSKRTMYADSVKGRFTISRDNANTVNLQMNNLKPEDTAVYYCRAWGIITS
ATVYWGQGTQVTVSS (SEQ ID NO:124);

QVKLEESGGGLVQAGGSLRLSCATSTRTVSSAVMAWFRQAPEKERDFVGF
SNSGSVYYDDSVKGRFTISRDNANTVYLQMNSLKPEDTAVYYCAIIWRTSD
LTGRFNTWGQGTQVTVSS (SEQ ID NO:125);

QVKLEESGGGLVQAGGSLRLSCAASGSSGMINTMGWYRQAPGKQRELVA
RRSTGGTTNYADSVKGRFTISRDDANNTVYLQMNSLKPEDTAVYYCAIIWRT
SDLTGRFNTWGQGTQVTVSS (SEQ ID NO:126); and

a sequence substantially identical thereto.

19. An antibody or fragment thereof selected from the group consisting of:
VH of SEQ ID NO:39, and VL of SEQ ID NO:38;
VH of SEQ ID NO:41, and VL of SEQ ID NO:40;
VH of SEQ ID NO:43, and VL of SEQ ID NO:42;
VH of SEQ ID NO:45, and VL of SEQ ID NO:44;
VH of SEQ ID NO:47, and VL of SEQ ID NO:46;
VH of SEQ ID NO:73, and VL of SEQ ID NO:74;
VH of SEQ ID NO:75, and VL of SEQ ID NO:76;
VHH of SEQ ID NO:119;
VHH of SEQ ID NO:120;
VHH of SEQ ID NO:121;
VHH of SEQ ID NO:122;
VHH of SEQ ID NO:123;
VHH of SEQ ID NO:124;
VHH of SEQ ID NO:125;
VHH of SEQ ID NO:126; and
sequences having 85% or greater identity thereto.
20. The antibody or fragment of claim 19, wherein the sequence identity is $\geq 90\%$, $\geq 95\%$, or $\geq 98\%$.
21. The antibody of claim 1, comprising light chain CDR1, CDR2 and CDR3 sequences of SEQ ID NO:1, 2, and 11; and heavy chain CDR1, CDR2 and CDR3 sequence of SEQ ID NO:3, 4, and 5; wherein the antibody binds an epitope in the IgL1 domain and not in the IgL2 domain of AXL.
22. The antibody of claim 1, comprising light chain CDR1, CDR2 and CDR3 sequences of SEQ ID NO:1, 6, and 11; and heavy chain CDR1, CDR2 and CDR3 sequence of SEQ ID NO:7, 8, and 5; wherein the antibody binds an epitope in the IgL1 domain and not in the IgL2 domain of AXL.

23. The antibody of claim 1, comprising light chain CDR1, CDR2 and CDR3 sequences of SEQ ID NO:9, 10, and 11; and heavy chain CDR1, CDR2 and CDR3 sequence of SEQ ID NO:12, 13, and 14.
24. The antibody of claim 1, comprising light chain CDR1, CDR2 and CDR3 sequences of SEQ ID NO:15, 16, and 11; and heavy chain CDR1, CDR2 and CDR3 sequence of SEQ ID NO:17, 18, and 19.
25. The antibody of any one of claims 1 to 24, which does not compete with Gas6 for AXL binding.
26. The antibody of claim 5, wherein the antibody is biparatopic and comprises sdAb001/005 or sd Ab 001/006.
27. An antibody drug conjugate (ADC) comprising the antibody of any one of claims 1 to 24, conjugated to a drug moiety.
28. The antibody drug conjugate of claim 27, wherein the drug moiety is an anti-cancer drug.
29. The antibody drug conjugate of claim 27, wherein the drug moiety is DM1.
30. A pharmaceutical composition comprising the ADC of claim 22 and a pharmaceutically acceptable excipient.
31. A fusion protein comprising the antibody according to claim 1, and human IgG1 Fc.
32. A nucleic acid molecule encoding the antibody of any one of claims 1 to 24.
33. A vector comprising the nucleic acid molecule of claim 32.
34. A host cell comprising the vector of claim 33.

35. The host cell of claim 34, which is a recombinant microbial host cell or is a mammalian cell.
36. The host cell of claim 32 or 33, wherein said cell produces the antibody of claim 1.
37. A hybridoma or an organism that produces the antibody of claim 1.
38. The antibody of any one of claims 1 to 24, wherein the antibody is immobilized onto a surface.
39. The antibody of any one of claims 1 to 24, wherein the antibody is linked to a cargo molecule.
40. The antibody of claim 39, wherein the cargo molecule is a detectable agent, a therapeutic agent, a drug, a peptide, an enzyme, a growth factor, a cytokine, a receptor trap, an antibody thereof, a chemical compound, a carbohydrate moiety, a DNA-based molecule, a cytotoxic agent, or a viral vector.
41. The antibody of claim 39, wherein the cargo molecule is from about 1 kDa to about 500 kDa in size.
42. The antibody of claim 40, wherein the cargo molecule is loaded in one or more liposome or nanocarrier.
43. The antibody of claim 42, wherein the nanocarrier comprises one or more nanoparticle, nanowire, nanotube, or quantum dots.
44. The antibody of claim 40 wherein the viral vector is adenoviral, lentiviral or retroviral.
45. The antibody of claim 40, wherein the DNA-based molecule comprises an anti-sense oligonucleotide, microRNA, siRNA, or a plasmid.

46. The antibody of any one of claims 39 to 42, wherein the cargo molecule is a cytotoxic agent.
47. An *in vitro* method of detecting AXL, comprising:
- a) contacting a sample with one or more than one isolated or purified antibody of any one of claims 1 to 24 linked to a detectable agent; and
 - b) detecting the detectable agent linked to the antibody thereof bound to AXL in the sample.
48. The method of claim 47, wherein method detects AXL in circulating cells and the sample is a serum sample.
49. The method of claim 47 or 48, wherein the step of detecting is performed using optical imaging, immunohistochemistry, molecular diagnostic imaging, or ELISA.
50. Use of one or more antibody of any one of claims 1 to 24 in the manufacture of a composition for *in vivo* detection of AXL expression in a subject, wherein the antibody is linked to a detectable agent wherein the composition is to be administered to the subject and the detectable agent linked to the antibody thereof bound to AXL is to be detected.
51. The use of claim 50, wherein the detecting is to be performed using PET, SPECT, or fluorescence imaging.
52. Use of one or more antibody of claim 1 in the manufacture of a medicament for transporting a molecule of interest into a subject's cells expressing AXL, wherein the antibody is linked to the molecule of interest, and wherein the antibody delivers the molecule of interest to the subject's cells expressing AXL.
53. The use of claim 52, wherein the molecule of interest is a detectable agent, a therapeutic agent, a drug, a peptide, an enzyme, a growth factor, a cytokine, a receptor trap, an antibody thereof, a chemical compound, a carbohydrate moiety, a DNA-based molecule, a cytotoxic agent, or a viral vector.

54. The use of claim 52, wherein the molecule of interest is loaded on one or more liposome or nanocarrier.
55. The use of claim 54, wherein the nanocarrier comprises one or more nanoparticle, nanowire, nanotube, or quantum dots.
56. The use of any one of claims 52 to 55, wherein the molecule of interest comprises a cytotoxic agent.
57. The use of claim 56, wherein the cytotoxic agent is for use in treating cancer.
58. Use of an anti-cancer antibody drug conjugate comprising the antibody of any one of claims 1 to 24 in the manufacture of a medicament for treating cancer in a subject in need thereof.
59. Use of the antibody of any one of claims 1 to 24 in the manufacture of a cellular therapy, a chimeric antigen receptor (CAR-T cell) therapy, or an oncolytic virus for treating cancer.
60. Use of the antibody of any one of claims 1 to 24 for preparation of a medicament comprising an anti-cancer antibody drug conjugate, for treating cancer in a subject in need thereof.
61. Use of the antibody of any one of claims 1 to 24 for preparation of a cellular therapy, a chimeric antigen receptor (CAR-T cell) therapy, or an oncolytic virus.