CLAIMS

1. A lyophilized formulation of an anti-AXL antibody-drug conjugate (AXL-ADC), the lyophilized formulation obtainable or obtained by lyophilizing an aqueous formulation comprising the AXL-ADC and one or more excipients, wherein the pH of the aqueous formulation in a range from 5.5 to 6.5, the aqueous formulation comprises a non-reducing sugar at a concentration of 0.5% (w/v) to 7% (w/v) or 15 mM to 200 mM; and the aqueous formulation is free of any surfactant and wherein the anti-AXL antibody or the AXL-ADC comprises at least one binding region comprising a VH region and a VL region selected from the group consisting of:

   (a) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 36, 37, and 38, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 39, GAS, and 40, respectively, [107];

   (b) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 46, 47, and 48, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 49, AAS, and 50, respectively, [148];

   (c) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 114, 115, and 116, respectively, and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 117, DAS, and 118, respectively [733];

   (d) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 51, 52, and 53, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 55, GAS, and 56, respectively [154];

   (e) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 51, 52, and 54, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 55, GAS, and 56, respectively [154-M103L];

   (f) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 57, 58, and 59, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 60, GAS, and 61, respectively, [171];

   (g) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 62, 63, and 64, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 65, GAS, and 66, respectively, [172];

(h) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 67, 68, and 69, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 70, GAS, and 71, respectively, [181];

(i) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 72, 73, and 75, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 76, ATS, and 77, respectively, [183];

(j) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 72, 74, and 75, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 76, ATS, and 77, respectively, [183-N52Q];

(k) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 78, 79, and 80, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 81, AAS, and 82, respectively, [187];

(l) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 83, 84, and 85, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 86, GAS, and 87, respectively, [608-01];

(m) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 88, 89, and 90, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 91, GAS, and 92, respectively, [610-01];

(n) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 93, 94, and 95, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 96, GAS, and 97, respectively, [613];

(o) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 98, 99, and 100, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 101, DAS, and 102, respectively, [613-08];

(p) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 103, 104, and 105, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 106, GAS, and 107, respectively, [620-06];

(q) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 108, 109, and 110, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 112, AAS, and 113, respectively, [726];

(r) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 108, 109, and 111, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 112, AAS, and 113, respectively, [726-M101L];

(s) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 41, 42, and 43, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 44, AAS, and 45, respectively, [140];

(t) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 93, 94, and 95, respectively, and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 128, XAS, wherein X is D or G, and 129, respectively, [613 / 613-08];

(u) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 46, 119, and 120, respectively; and a VL region comprising CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 49, AAS, and 50, respectively, [148 / 140];

(v) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 123, 124, and 125, respectively; and a VL region comprising CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 60, GAS, and 61, respectively [171 / 172 / 181]; and

(w) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 121, 109, and 122, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 112, AAS, and 113, respectively [726 / 187]; and

(x) a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.:93, 126, and 127, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 96, GAS, and 97, respectively [613 / 608-01 / 610-01 / 620-06].

2. The lyophilized formulation according to claim 1, the lyophilized formulation being obtainable or obtained by lyophilizing an aqueous formulation comprising the AXL-ADC and

(a) a buffer providing for a pH 5.5 to 6.5 in the aqueous formulation;
(b) at least one bulking agent; and
(c) at least one non-reducing sugar which forms an amorphous phase with the ADC in solid state, the non-reducing sugar being present at a concentration of 0.5% (w/v) to 7% (w/v) or 15 mM to 200 mM; and
wherein the aqueous formulation is free of any surfactant.

3. The lyophilized formulation of any one of the preceding claims,

wherein the aqueous formulation comprises a buffer selected from the group consisting of histidine, citrate, 2-(N-morpholino)ethanesulfonic acid (MES), succinate, glycolate, carbonic acid and phosphate, or a combination of any thereof;

and

wherein the aqueous formulation comprises a buffer at a concentration of 5 mM to 100 mM, such as from 10 mM to 50 mM buffer, such as from 20 mM to 40 mM, such as from 28 mM to 32 mM, such as 30 mM buffer.

4. The lyophilized formulation of any one of the preceding claims, comprising a bulking agent selected from mannitol, glycine, and a combination thereof.

5. The lyophilized formulation of any one of the preceding claims, wherein

the aqueous formulation comprises a bulking agent
at a concentration of 1% (w/v) to 5% (w/v), such as 2% (w/v) to 4% (w/v), such as from 2.5% (w/v) to 3.5% (w/v), such as 3% (w/v), or
at a concentration of 50 mM to 300 mM, such as from 100 mM to 225 mM, such as from 150 mM to 180 mM, such as 165 mM.

6. The lyophilized formulation of any one of the preceding claims, comprising a non-reducing sugar selected from sucrose, trehalose, and a combination thereof.

7. The lyophilized formulation of any one of the preceding claims, wherein the aqueous formulation comprises a non-reducing sugar at

a concentration from 0.5% (w/v) to 4% (w/v), such as from 1% (w/v) to 3% (w/v) or from 2.5% to 3.5%, such as 3% (w/v) or

a concentration from 15 mM to 120 mM, such as from 30 mM to 90 mM, such as 80 mM to 100 mM, such as from 84 mM to 92 mM sucrose, such as 88 mM.

8. The lyophilized formulation of any one of the preceding claims, wherein the AXL-ADC concentration in the aqueous formulation is from 5 mg/mL to 30 mg/mL, such as from 7 mg/mL to 20 mg/mL, such as from 8 mg/mL to 15 mg/mL, such as from 9 mg/mL to 11 mg/mL, such as 10 mg/mL.

9. The lyophilized formulation of any one of the preceding claims, wherein the pH of the aqueous formulation is in a range from 5.8 to 6.2, such as 6.

10. The lyophilized formulation of any one of the preceding claims, wherein the AXL-ADC comprises a cytotoxic agent linked to the antibody with a cleavable linker, such as *N*-succinimydyl 4-(2-pyridyldithio)-pentanoate (SSP), maleimidocaproyl-valine-citrulline-*p*-aminobenzyloxycarbonyl (mc-vc-PAB) or AV-1 K-lock valine-citrulline.

11. The lyophilized formulation of any one of the preceding claims, wherein the AXL-ADC comprises a cytotoxic agent selected from the group consisting of DNA-targeting agents, e.g. DNA alkylators and cross-linkers, such as calicheamicin, duocarmycin, rachelmycin (CC-1065), pyrrolo[2,1-c][1,4] benzodiazepines (PBDs), and indolinobenzodiazepine (IGN); microtubule-targeting agents, auristatin, such as monomethylauristatin E (MMAE) and monomethylauristatin F (MMAF), dolastatin, maytansine, *N*(2')-deacetyl-*N*(2')-(3-marcapto-1-oxopropyl)-maytansine (DM1), and tubulysin; and nucleoside analogs; or an analogs, derivatives, or prodrugs thereof.

12. The lyophilized formulation of any one of claims 1 to 9, wherein AXL-ADC comprises a linker, which is mc-vc-PAB and a cytotoxic agent, which is MMAE.

13. A pharmaceutical formulation of an AXL-ADC obtained or obtainable by reconstituting the lyophilized formulation of any one of the preceding claims in a sterile aqueous diluent.

14. The lyophilized formulation of any one of the preceding claims, wherein the AXL-ADC concentration in the aqueous formulation is from 5 mg/mL to 30 mg/mL, such as from 7 mg/mL to 20 mg/mL, such as from 8 mg/mL to 15 mg/mL, such as from 9 mg/mL to 11 mg/mL, such as 10 mg/mL.

15. The lyophilate or formulation of any one of the preceding claims, wherein the anti-AXL antibody or the AXL-ADC comprises at least one binding region comprising a VH region and a VL region selected from the group consisting of VH and VL sequences at least 90%, such as at least 95%, such as at least 97%, such as at least 99%, such as 100% identical to:

(a) a VH region comprising SEQ ID No: 1 and a VL region comprising SEQ ID No: 2 [**107**];

(b) a VH region comprising SEQ ID No: 5 and a VL region comprising SEQ ID No: 6 [**148**];

(c) a VH region comprising SEQ ID No: 34 and a VL region comprising SEQ ID No: 35 [**733**]

(d) a VH region comprising SEQ ID No: 7 and a VL region comprising SEQ ID No: 9 [**154**];

(e) a VH region comprising SEQ ID No: 10 and a VL region comprising SEQ ID No: 11 [**171**];

(f) a VH region comprising SEQ ID No: 16 and a VL region comprising SEQ ID No: 18 [**183**];

(g) a VH region comprising SEQ ID No: 25 and a VL region comprising SEQ ID No: 26 [**613**];

(h) a VH region comprising SEQ ID No: 31 and a VL region comprising SEQ ID No: 33 [**726**];

(i) a VH region comprising SEQ ID No: 3 and a VL region comprising SEQ ID No: 4 [**140**];

(j) a VH region comprising SEQ ID No:8 and a VL region comprising SEQ ID No:9 [**154-M103L**];

(k) a VH region comprising SEQ ID No:12 and a VL region comprising SEQ ID No:13 [**172**];

(l) a VH region comprising SEQ ID No:14 and a VL region comprising SEQ ID No:15 [**181**];

(m) a VH region comprising SEQ ID No:17 and a VL region comprising SEQ ID No:18 [**183-N52Q**];

(n) a VH region comprising SEQ ID No:19 and a VL region comprising SEQ ID No:20 [**187**];

(o) a VH region comprising SEQ ID No:21 and a VL region comprising SEQ ID No:22 [**608-01**];

(p) a VH region comprising SEQ ID No:23 and a VL region comprising SEQ ID No:24 [**610-01**];

(q) a VH region comprising SEQ ID No:27 and a VL region comprising SEQ ID No:28 [**613-08**];

(r) a VH region comprising SEQ ID No:29 and a VL region comprising SEQ ID No:30 [**620-06**]; and

(s) a VH region comprising SEQ ID No:32 and a VL region comprising SEQ ID No:33 [**726-M101L**].

16. The lyophilate or formulation according to any one of claims 14 and 15, wherein the anti-AXL antibody or the AXL-ADC comprises a VH region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 36, 37, and 38, respectively; and a VL region comprising the CDR1, CDR2, and CDR3 sequences of SEQ ID Nos.: 39, GAS, and 40, respectively [**107**].

17. The lyophilate or formulation according to claim 16, wherein the anti-AXL antibody or the AXL-ADC comprises a VH region comprising SEQ ID No: 1 and a VL region comprising SEQ ID No: 2 **[107]**.

18. The lyophilate or formulation according to any one of claims 1 to 13, wherein the anti-AXL antibody or the AXL-ADC binds to

    an epitope within the Ig1-like domain of AXL, the epitope comprising or requiring one or more amino acids corresponding to positions L121 to Q129 or T112 to Q124 of human AXL,

    an epitope within the Ig2-like domain of AXL, the epitope comprising or requiring the amino acids corresponding to position D170 or the combination of D179 and one or more amino acids corresponding to positions T182 to R190 of human AXL, or

    an epitope within the FN1-like domain of human AXL, the epitope comprises or requires one or more amino acids corresponding to positions Q272 to A287 and G297 to P301 of human AXL.

19. The lyophilate or formulation of any one of the preceding claims, wherein the anti-AXL antibody or the antibody-moiety of the AXL-ADC comprises a heavy chain of an isotype selected from the group consisting of IgG1, IgG2, IgG3, and IgG4.

20. The lyophilate or formulation of claim 19, wherein the isotype of the anti-AXL antibody or the antibody-moiety of the AXL-ADC is IgG1, optionally allotype IgG1m(f).

21. The lyophilate or formulation of any one of the preceding claims, wherein the anti-AXL antibody or the antibody moiety of the AXL-ADC is a full-length monoclonal antibody, such as a full-length monoclonal IgG1,κ antibody.