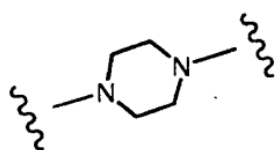


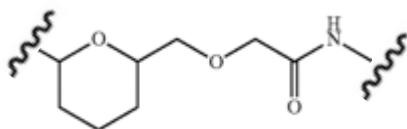
CLAIMS

1. An antibody-drug conjugate having the general formula $A - (L-T)_n$, wherein
- a. A is an antibody or fragment thereof binding to CLDN18.2 comprising the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 21, SEQ ID NO: 22 and SEQ ID NO: 23 respectively, and the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 24, SEQ ID NO: 25 and SEQ ID NO: 26 respectively,
 - b. L is a linker, and
 - c. T is a toxin,
- wherein the toxin is an anthracycline,
- wherein n is an integer between ≥ 1 and ≤ 10 ;
- or a pharmaceutically acceptable salt or ester thereof.
2. The antibody-drug conjugate of claim 1, wherein the linker L comprises at least one a non-cleavable linker element, preferably wherein the non-cleavable linker element is selected from the group consisting of
- a. ethylenediamine (EDA),
 - b. N-formyl-N,N'-dimethylethylenediamine,
 - c. diethylamine (DEA),
 - d. a piperazine-derived compound of the following formula:



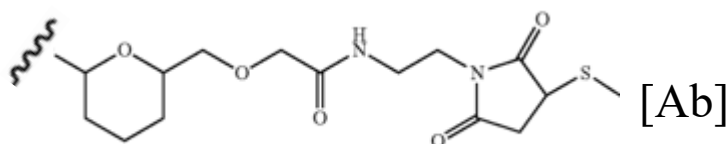
wherein the wavy lines indicate attachments to the toxin and another linker element,

- e. the compound of the following formula:



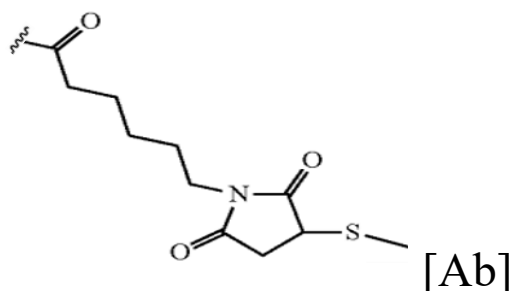
wherein the wavy lines indicate attachments to the toxin and another linker element,

- f. the compound of the following formula:



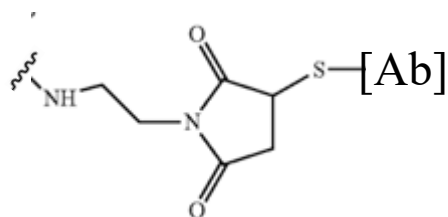
wherein the wavy lines indicate attachments to the toxin and [Ab] indicates the antibody or fragment thereof,

g. a maleimidocaproyl compound of the following formula:



wherein the wavy lines indicate attachments to another linker element and [Ab] indicates the antibody or fragment thereof,

h. the compound of the following formula:



wherein the wavy lines indicate attachments to a toxin and [Ab] indicates the antibody or fragment thereof,

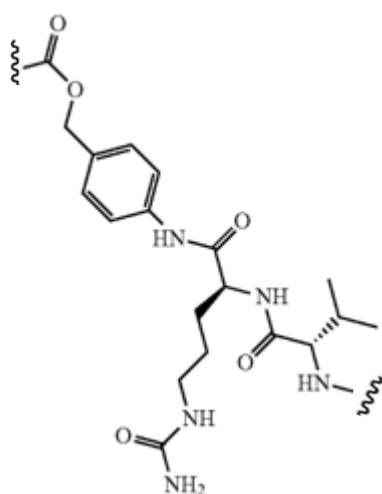
and wherein the non-cleavable linker element is conjugated to the toxin by means of an amide bond or an ether bond.

3. The antibody-drug conjugate of claim 2, wherein the linker further comprises an oligopeptide linker element and/or enzyme-cleavable linker element and/or a spacer element.
4. The antibody-drug conjugate of claim 3, wherein one oligopeptide linker element comprises a sortase recognition motif oligopeptide selected from: -LPXTG_m-, -LPXAG_m-, -LPXSG_m-, -LAXTG_m-, -LPXTG_m-, -LPXTA_m-, -NPQTG_m- or -NPQTN_m-, with G_m being an oligoglycine with m being an integer between ≥ 1 and ≤ 21 , A_m being an oligoalanine with m being an integer between ≥ 1 and ≤ 21 , N_m being an oligoasparagine with m being an integer between ≥ 1 and ≤ 21 and X being any

conceivable amino acid, preferably the sortase recognition motif oligopeptide being -LPQTGG- or -LPETGG-, preferably wherein the oligopeptide linker element comprises:

- a. the sequence SEQ ID NO: 131, or
- b. the sequence SEQ ID NO: 132.

5. The antibody-drug conjugate of any of claim 3 or claim 4, wherein the enzyme-cleavable linker element comprises a val-cit-PAB linker according to the compound of the following formula:

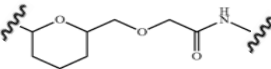


wherein the wavy lines indicate attachments to other linker elements.

6. The antibody-drug conjugate of any of claims 3 to 5, wherein the spacer element comprises a peptidic flexible oligopeptide, preferably wherein the peptidic flexible oligopeptide consists of G and S, more preferably wherein the peptidic flexible oligopeptide is (GGGS)_o with o being 1, 2, 3, 4 or 5.
7. The antibody-drug conjugate of any of claims 1 to 6, wherein the antibody drug conjugate has the following structure:

- a. $A - ([\text{oligopeptide linker element} - \text{non-cleavable linker element}] - T)_n$ and preferably wherein the linker is selected from:

- i. [LPXTGG]-[ethylenediamine], and

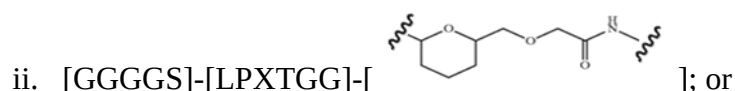
- ii. [LPXTGG]-[];

b. A – ([oligopeptide linker element – enzyme cleavable linker element – non-cleavable linker element] – T)_n and preferably wherein the linker is selected from:

- i. [LPXTGG]-[vc-PAB]-[N-formyl-N,N'-dimethylethylenediamine], and
- ii. [LPXTGG]-[vc-PAB]-[piperazine];

c. A – ([spacer element – oligopeptide linker element – non-cleavable linker element] – T)_n and preferably wherein the linker is selected from:

- i. [GGGGS]-[LPXTGG]-[ethylenediamine], and



d. A – ([spacer element – oligopeptide linker element – enzyme cleavable linker element – non-cleavable element] – T)_n and preferably wherein the linker is selected from:

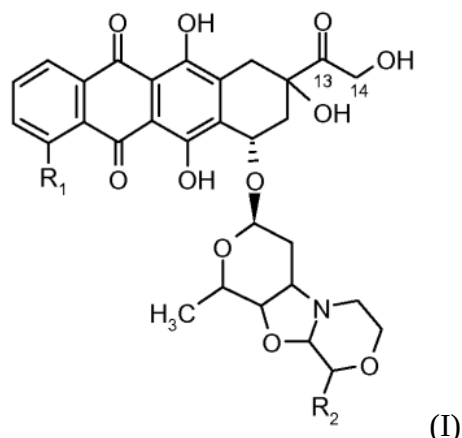
- i. [GGGGS]-[LPXTGG]-[vc-PAB]-[N-formyl-N,N'-dimethylethylenediamine], and
- ii. [GGGGS]-[LPXTGG]-[vc-PAB]-[piperazine].

8. The antibody-drug conjugate of claim 7, wherein the non-cleavable linker element is ethylenediamine and wherein the oligopeptide linker element is LPXTGG wherein X is Q or E, preferably wherein X is Q.

9. The antibody-drug conjugate of any of claims 1 to 8, wherein

- a. (L-T) is covalently linked to both light chains of the antibody,
- b. (L-T) is covalently linked to both heavy chains of the antibody, or
- c. (L-T) is covalently linked to both light chains and both heavy chains of the antibody.

10. The antibody-drug conjugate of any of claims 1 to 9, wherein the anthracycline derivative has the following formula (I), and is covalently linked to the non-cleavable linker element by the C₁₃ resulting in the loss of the C₁₄ and the hydroxyl group, or is covalently linked to the non-cleavable linker element by the hydroxyl group on C₁₄:



and wherein R₁ is a hydrogen atom, a hydroxy or methoxy group,
 and wherein R₂ is a C₁-C₅ alkoxy group, preferably wherein the anthracycline
 derivative is a derivative of 3'-deamino-3'',4'-anhydro-[2''(S)-methoxy-3''(R)-oxy-
 4''-morpholinyl]doxorubicin (PNU-159682).

11. The antibody-drug conjugate of any of claims 1 to 10, wherein A, the antibody or
 fragment thereof, comprises:

- a. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 1, SEQ ID NO: 15
 and SEQ ID NO: 3, respectively, and the LCDR1, LCDR2 and LCDR3 sequences
 of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6, respectively;
- b. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 1, SEQ ID NO: 16
 and SEQ ID NO: 3, respectively, and the LCDR1, LCDR2 and LCDR3 sequences
 of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6, respectively;
- c. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 1, SEQ ID NO: 16
 and SEQ ID NO: 3, respectively, and the LCDR1, LCDR2 and LCDR3 sequences
 of SEQ ID NO: 17, SEQ ID NO: 14 and SEQ ID NO: 11, respectively;
- d. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 1, SEQ ID NO: 16
 and SEQ ID NO: 3, respectively, and the LCDR1, LCDR2 and LCDR3 sequences
 of SEQ ID NO: 18, SEQ ID NO: 19 and SEQ ID NO: 11, respectively;
- e. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 12, SEQ ID NO: 15
 and SEQ ID NO: 3, respectively, and the LCDR1, LCDR2 and LCDR3 sequences
 of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6, respectively;

- f. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 1, SEQ ID NO: 20 and SEQ ID NO: 3, respectively, and the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6, respectively;
 - g. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 1, SEQ ID NO: 20 and SEQ ID NO: 3, respectively, and the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 18, SEQ ID NO: 19 and SEQ ID NO: 11, respectively;
 - h. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 12, SEQ ID NO: 20 and SEQ ID NO: 8, respectively, and the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6, respectively; or
 - i. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 12, SEQ ID NO: 20 and SEQ ID NO: 8, respectively, and the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 17, SEQ ID NO: 14 and SEQ ID NO: 11, respectively.
12. The antibody-drug conjugate of any of claims 1 to 10, wherein A, the antibody or fragment thereof comprises:
- a. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, respectively, and the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6, respectively;
 - b. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 1, SEQ ID NO: 7 and SEQ ID NO: 8, respectively, and the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 9, SEQ ID NO: 10 and SEQ ID NO: 11, respectively; or
 - c. the HCDR1, HCDR2 and HCDR3 sequences of SEQ ID NO: 12, SEQ ID NO: 2 and SEQ ID NO: 3, respectively, and the LCDR1, LCDR2 and LCDR3 sequences of SEQ ID NO: 13, SEQ ID NO: 14 and SEQ ID NO: 11, respectively,
- preferably wherein A, the antibody or fragment thereof comprises:
- a. a VH sequence of SEQ ID NO: 27 and a VL sequence of SEQ ID NO: 28;
 - b. a VH sequence of SEQ ID NO: 29 and a VL sequence of SEQ ID NO: 30; or
 - a VH sequence of SEQ ID NO: 31 and a VL sequence of SEQ ID NO: 32.

13. The antibody-drug conjugate of any of claims 1 to 11, wherein A, the antibody or fragment thereof comprises:

- a. a VH sequence of SEQ ID NO: 33 and a VL sequence of SEQ ID NO: 38;
- b. a VH sequence of SEQ ID NO: 34 and a VL sequence of SEQ ID NO: 38;
- 5 c. a VH sequence of SEQ ID NO: 34 and a VL sequence of SEQ ID NO: 39;
- d. a VH sequence of SEQ ID NO: 34 and a VL sequence of SEQ ID NO: 40;
- e. a VH sequence of SEQ ID NO: 35 and a VL sequence of SEQ ID NO: 38;
- f. a VH sequence of SEQ ID NO: 36 and a VL sequence of SEQ ID NO: 41;
- g. a VH sequence of SEQ ID NO: 36 and a VL sequence of SEQ ID NO: 40;
- 10 h. a VH sequence of SEQ ID NO: 37 and a VL sequence of SEQ ID NO: 41;
- i. a VH sequence of SEQ ID NO: 37 and a VL sequence of SEQ ID NO: 38; or
- j. a VH sequence of SEQ ID NO: 37 and a VL sequence of SEQ ID NO: 39,

preferably wherein A, the antibody or fragment thereof, comprises:

- 15 a. the heavy chain sequence of SEQ ID NO: 46 and light chain sequence of SEQ ID NO: 51;
- b. the heavy chain sequence of SEQ ID NO: 47 and light chain sequence of SEQ ID NO: 51;
- c. the heavy chain sequence of SEQ ID NO: 47 and light chain sequence of SEQ ID NO: 52;
- 20 d. the heavy chain sequence of SEQ ID NO: 47 and light chain sequence of SEQ ID NO: 53;
- e. the heavy chain sequence of SEQ ID NO: 48 and light chain sequence of SEQ ID NO: 51;
- 25 f. the heavy chain sequence of SEQ ID NO: 47 and light chain sequence of SEQ ID NO: 54;

- g. the heavy chain sequence of SEQ ID NO: 49 and light chain sequence of SEQ ID NO: 53;
 - h. the heavy chain sequence of SEQ ID NO: 50 and light chain sequence of SEQ ID NO: 54;
 - 5 i. the heavy chain sequence of SEQ ID NO: 50 and light chain sequence of SEQ ID NO: 51; or
 - j. the heavy chain sequence of SEQ ID NO: 50 and light chain sequence of, SEQ ID NO: 52
- or versions thereof with an engineered Fc domain.
- 10 14. A method of producing an antibody-drug conjugate according to any of claims 1 to 13, wherein the method comprises the following steps:
- a. providing A, an antibody or fragment thereof with an oligopeptide linker element preferably at its C-terminus, optionally preceded by a spacer element at the antibody light and/or heavy chains,
 - 15 b. providing one or more toxins T with a non-cleavable linker element, and
 - c. conjugating the antibody and the toxin resulting in the antibody-drug conjugate.
15. An antibody-drug conjugate consisting of:
- the antibody consisting of two heavy chains of the amino acid sequence according to SEQ ID NO: 46, and two light chains of the amino acid sequence
 - 20 according to SEQ ID NO: 51, wherein the antibody binds to CLDN18.2,
 - the linker [GGGGS]-[LPQTGG]-[ethylenediamine] at the C-terminus of the light chains, and
 - the anthracycline-based small molecule toxin 3'-deamino-3'',4'-anhydro-[2''(S)-methoxy-3''(R)-oxy-4''-morpholinyl]doxorubicin (PNU-159682),
 - 25 linked covalently to the ethylenediamine of the linker at C₁₃, resulting in the loss of C₁₄ and of the hydroxyl group; or
 - the antibody consisting of two heavy chains of the amino acid sequence according to SEQ ID NO: 133, and two light chains of the amino acid sequence according to SEQ ID NO: 51, wherein the antibody binds to CLDN18.2,

- the linker [GGGGS]-[LPQTGG]-[ethylenediamine] at the C-terminus of the light chains, and
 - the anthracycline-based small molecule toxin 3'-deamino-3'',4'-anhydro-[2''(S)-methoxy-3''(R)-oxy-4''-morpholinyl]doxorubicin (PNU-159682),
5 linked covalently to the ethylenediamine of the linker at C₁₃, resulting in the loss of C₁₄ and of the hydroxyl group; or
 - the antibody consisting of two heavy chains of the amino acid sequence according to SEQ ID NO: 134 and two light chains of the amino acid sequence according to SEQ ID NO: 51, wherein the antibody binds to CLDN18.2,
 - the linker [GGGGS]-[LPQXTGG]-[ethylenediamine] at the C-terminus of the light chains, and
 - the anthracycline-based small molecule toxin 3'-deamino-3'',4'-anhydro-[2''(S)-methoxy-3''(R)-oxy-4''-morpholinyl]doxorubicin (PNU-159682),
10 linked covalently to the ethylenediamine of the linker at C₁₃, resulting in the loss of C₁₄ and of the hydroxyl group.
- 15
16. A pharmaceutical composition comprising the antibody-drug conjugate of any of claims 1 to 15 and an excipient.
17. The antibody-drug conjugate of any of claims 1 to 15 for use in therapy.
18. Use of the antibody-drug conjugate of any of claims 1 to 15 in the manufacture of a
20 medicament for the treatment of cancer, preferably wherein the cancer is selected from pancreatic, gastric, esophageal, ovarian, and lung cancer.