

What is claimed is

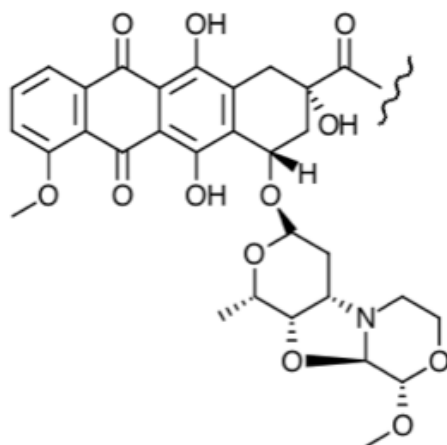
1. An antibody drug conjugate (ADC) comprising:

- an antibody, or antibody fragment or derivative retaining target binding properties, comprising at least one light chain constant region C-terminus, and
- an anthracycline-based small molecule,

wherein the anthracycline-based small molecule(s) is/are exclusively linked to the light chain constant region C-terminus/i of the antibody, fragment or derivative, and

wherein the anthracycline-based small molecule is linked, via a linker comprising a peptidic sequence, to said antibody, fragment or derivative,

wherein the anthracycline-based small molecule is selected from PNU-159682, or from derivatives thereof, comprising the structure of formula (i)



formula (i)

2. The antibody drug conjugate according to claim 1, wherein the antibody or fragment or derivative binds to an antigen that

- is tumor specific or
- is expressed at a higher rate on tumor tissue than on healthy tissue.

3. The antibody drug conjugate according to claim 1 or 2, wherein the antibody or fragment or derivative does not bind to human and/or mouse CS1.

4. The antibody drug conjugate according to any one of claims 1-3, wherein the antibody or fragment or derivative comprises the CDRs of hu4-2-17 (based on Kabat numbering)

- HC CDR1 SYYMS
- HC CDR2 AIGISGNAYYASWAKS
- HC CDR3 DHPTYGMDL
- LC CDR1 EGNNIGSKAVH
- LC CDR2 DDDERPS, and
- LC CDR3 QVWDSSAYV

and wherein the CDRs are comprised in a suitable protein framework so as to be capable to bind to the antibody's target.

5. The antibody drug conjugate according to any one of claims 1-3, wherein the antibody or fragment or derivative comprises the CDRs of huERCs-409 (based on Kabat numbering)

- HC CDR1 SYGVI
- HC CDR2 IIGSSGNTYYASSVKG
- HC CDR3 YYGDSGFDS
- LC CDR1 RASQSIGSWLS
- LC CDR2 GASNLAS, and
- LC CDR3 LGASPNGWA

and wherein the CDRs are comprised in a suitable protein framework so as to be capable to bind to the antibody's target.

6. The antibody drug conjugate according to any one of claims 1-5, wherein the antibody or fragment or derivative comprises at least one of the list consisting of:

- the variable domains of trastuzumab (variable domains of SEQ ID NO. 1 or 2)
- the variable domains of hu4-2-17 (variable domains of SEQ ID NO. 4 or 5), and/or
- the variable domains of huERCS-409 (variable domains of SEQ ID NO. 7 or 8).

7. The antibody drug conjugate according to any one of claims 1-6, wherein the peptidic sequence of said linker comprises or consists of a peptidic motif resulting from specific cleavage of a sortase enzyme recognition motif.

8. The antibody drug conjugate according to claim 7, wherein said sortase enzyme recognition motif is selected from the group consisting of LPXTG, LPQTG, LPETG, LPXAG, LPXSG, LAXTG, LPXTA, NPQTG, NPQTN, LPLTG, LAFTG, and LPNTA, preferably wherein said linker comprises or consists of the sequence LPETG or LPQTG.

9. The antibody drug conjugate according to any one of claims 1-6, wherein said peptidic sequence of said linker comprises or consists of an oligoglycine sequence ("tag"), denoted G_n or Gly_n , where n is from 1 to 21 and preferably n is 1, 2, 3, 4 or 5, and most preferably n is 2.

10. The antibody drug conjugate according to any one of claims 1-9, wherein the linker additionally comprises an alkyldiamino group of the form $NH_2-(CH_2)_m-NH_2$, where $m \geq 1$ and ≤ 11 , preferably $m=2$.

11. The antibody drug conjugate according to any one of claims 1-10, wherein the linker further comprises at least one further cleavable or non cleavable linker, which linker is preferably selected from the group consisting of: a hydrazine linker, a thiourea linker, a self-immolative linker, a succinimidyl trans-4-(maleimidylmethyl)cyclohexane-1-carboxylate (SMCC) linker, a disulfide linker, a selenoether linker, an amide linker, a thioether linker, and/or a maleimide linker.

12. The antibody drug conjugate according to any one of claims 1-11, wherein the peptidic linker comprises a spacer sequence, preferably wherein the peptidic linker comprises a spacer

sequence consisting of, from N- to C-terminus, four glycine residues and one serine residue, denoted G4S.

13. The antibody drug conjugate according to any one of claims 1-12, which has a stoichiometric ratio between (i) antibody, fragment or derivative and (ii) anthracycline-based small molecule of any value between ≥ 1 and ≤ 2 .

14. An antibody drug conjugate (ADC) comprising
an antibody consisting of two heavy chains, wherein each heavy chain consists of an amino acid sequence according to SEQ ID NO. 4 (hu4-2-17 HC), and two light chains, wherein each light chain comprises an amino acid sequence according to SEQ ID NO. 5 (hu4-2-17 LC), wherein the antibody binds to human ROR1; and
an anthracycline-based small molecule,
wherein the anthracycline-based small molecule is exclusively linked via a linker comprising a peptidic sequence to the light chain constant region C-terminus/i of the antibody,
wherein said anthracycline-based small molecule consists of the PNU-159682 derivative of formula (i), and
wherein said linker is consisting of a peptidic spacer sequence consisting of, from N- to C-terminus, four glycine residues and one serine residue, denoted G4S, the peptidic motif LPQT resulting from sortase-specific cleavage, two glycine residues denoted G2, and an alkyl-diamino group of the form $\text{NH}_2\text{-(CH}_2\text{)}_2\text{-NH}_2$.

15. An antibody drug conjugate (ADC) comprising
an antibody consisting of two heavy chains, wherein each heavy chain consists of an amino acid sequence according to SEQ ID NO. 7 (huERCS-409 HC), and two light chains, wherein each light chain comprises an amino acid sequence according to SEQ ID NO. 8 (huERCS-409 LC), wherein the antibody binds to human ROR1; and
an anthracycline-based small molecule,
wherein the anthracycline-based small molecule is exclusively linked via a linker comprising a peptidic sequence to the light chain constant region C-terminus/i of the antibody,
wherein said anthracycline-based small molecule consists of the PNU-159682 derivative of formula (i), and

wherein said linker is consisting of a peptidic spacer sequence consisting of, from N- to C-terminus, four glycine residues and one serine residue, denoted G₄S, the peptidic motif LPQT or LPET resulting from sortase-specific cleavage, two glycine residues denoted G₂, and an alkyl-diamino group of the form NH₂-(CH₂)₂-NH₂.

16. The antibody drug conjugate (ADC) according to any of claims 14 to 15, wherein the ratio between said PNU-159682 derivative and said antibody is about 2.

17. A pharmaceutical composition comprising a therapeutically effective amount of the antibody drug conjugate according to any one of claims 1-16, and a pharmaceutically acceptable carrier.

18. An antibody drug conjugate which is obtainable by means of site-specific sortase-enzyme mediated conjugation of:

- a) an antibody or fragment or derivative carrying a sortase enzyme recognition motif at the light chain C-terminus/i, and
- b) one or more anthracycline-based small molecules, each carrying an oligoglycine tag.

19. A method of producing an antibody drug conjugate according to any one of claims 1-16, which method comprises the following steps:

- a) providing an antibody or fragment or derivative carrying a sortase enzyme recognition motif at the light chain C-terminus/i,
- b) providing one or more anthracycline-based small molecules each carrying an oligoglycine tag, and
- c) conjugating the antibody or fragment or derivative and the one or more anthracycline-based small molecules by means of sortase-mediated conjugation using a sortase enzyme that recognizes said sortase enzyme recognition motif.

20. The pharmaceutical composition according to claim 17 for use in the treatment of a subject that is suffering from, and/or diagnosed with, a neoplastic disease.