

CLAIMS

1. A method for producing an antibody-linker conjugate by means of a microbial transglutaminase (MTG), the method comprising a step of conjugating a linker comprising the structure (shown in N -> C direction)

(Sp₁)-RK-(Sp₂)-B-(Sp₃) or (Sp₁)-B-(Sp₂)-RK-(Sp₃)

to a Gln residue comprised in an antibody, wherein

- (Sp₁) is a chemical spacer or is absent;
- (Sp₂) is a chemical spacer or is absent;
- (Sp₃) is a chemical spacer or is absent;
- R is arginine or an arginine derivative or an arginine mimetic;
- K is lysine or a lysine derivative or a lysine mimetic;
- B is a linking moiety or a payload;

and wherein the linker is conjugated to the Gln residue comprised in the antibody via a primary amine comprised in the side chain of the lysine residue, the lysine derivative or the lysine mimetic.

2. The method according to claim 1, wherein the chemical spacers (Sp₁), (Sp₂) and (Sp₃) each independently comprise between 0 and 12 amino acid residues; ~~and/or-~~

~~3. The method according to claim 1 or 2,~~ wherein the linker comprises not more than 25, 20, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4 amino acid residues; ~~and/or-~~

~~4. The method according to any one of claims 1 to 3,~~ wherein the net charge of the linker is neutral or positive; ~~and/or-~~

~~5. The method according to any one of claims 1 to 4,~~ wherein the linker comprises no negatively-charged amino acid residues.

~~6~~3. The method according to ~~any one of claims 1~~ ~~orto~~ 25, wherein the linker comprises the amino acid sequence RKAA (SEQ ID NO:1), RKA (SEQ ID NO:2), ARK (SEQ ID NO:3), RKR (SEQ ID NO:4) or RK-Val-Cit (SEQ ID NO:54), ~~in particular -~~

~~7. The method according to any one of claims 1 to 6,~~ wherein the linker comprises the amino acid sequence RKAA (SEQ ID NO:1), RKA (SEQ ID NO:2), ARK (SEQ ID NO:3), or RK-Val-Cit (SEQ ID NO:54), in particular.

~~8. The method according to any one of claims 1 to 7,~~ wherein the linker comprises the amino acid sequence RKAA (SEQ ID NO:1).

~~49.~~ The method according to any one of claims 1 to ~~83~~, wherein B is a linking moiety, in particular.

~~10. The method according to claim 9,~~ wherein the linking moiety B comprises

- a bioorthogonal marker group, or
- a non-bio-orthogonal entity for crosslinking; in particular.

~~11. The method according to claim 10,~~ wherein the bioorthogonal marker group or the non-bio-orthogonal entity for crosslinking consists of or comprises at least one molecule or moiety selected from the group consisting of:

- $-N-N\equiv N$, or $-N_3$;
- Lys(N_3);
- a tetrazine;
- an alkyne;
- a strained cyclooctyne;
- BCN;
- a strained alkene;
- a photoreactive group;
- an aldehyde;
- an acyltrifluoroborate;
- a protein degradation agent ('PROTAC');
- a cyclopentadiene/spirolodocyclopentadiene;
- a thio-selective electrophile;
- $-SH$; and
- cysteine.

~~125.~~ The method according to ~~any one of claims 9 to 114~~, the method comprising a further step of conjugating one or more payloads to the linking moiety B, in particular.

~~13. — The method according to claim 12,~~ wherein the one or more payload is conjugated to the linking moiety B via a click-reaction.

~~14.6.~~ The method according to any one of claims 1 to ~~38~~, wherein B is a payload, in particular-

~~15. — The method according to any one of claims 12 to 14,~~ wherein the payload comprises at least one of:

- a toxin;
- a cytokine;
- a growth factor;
- a radionuclide;
- a hormone;
- an anti-viral agent;
- an anti-bacterial agent;
- a fluorescent dye;
- an immunoregulatory/immunostimulatory agent;
- a half-life increasing moiety;
- a solubility increasing moiety;
- a polymer-toxin conjugate;
- a nucleic acid;
- a biotin or streptavidin moiety;
- a vitamin;
- a protein degradation agent ('PROTAC');
- a target binding moiety; and/or
- an anti-inflammatory agent; in particular-

~~16. — The method according to claims 15,~~ wherein the toxin is at least one selected from the group consisting of

- a pyrrolobenzodiazepine (e.g., PBD);
- an auristatin (e.g., MMAE, MMAF);
- a maytansinoid (e.g., maytansine, DM1, DM4, DM21);
- a duocarmycin;
- a nicotinamide phosphoribosyltransferase (NAMPT) inhibitor;
- a tubulysin;
- an enediyne (e.g., calicheamicin);

- an anthracycline derivative (PNU) (e.g., doxorubicin);
- a pyrrole-based kinesin spindle protein (KSP) inhibitor;
- a cryptophycin;
- a drug efflux pump inhibitor;
- a sandramycin;
- an amanitin (e.g., α -amanitin); and
- a camptothecin (e.g., exatecans, deruxtecans).

~~177.~~ The method according to ~~any one of claim s 14 to 16~~, wherein the chemical spacer (Sp₂) comprises a self-immolative moiety, in particular -

~~18.~~ ~~The method according to claim 17,~~ wherein the self-immolative moiety is directly attached to the payload B, and/or -

~~19.~~ ~~The method according to claim 17 or 18,~~ wherein the self-immolative moiety comprises a p-aminobenzyl carbamoyl (PABC) moiety.

~~208.~~ The method according to any one of claims 1 to ~~197~~, wherein the antibody is an IgG antibody, in particular an IgG1 antibody, in particular -

~~21.~~ ~~The method according to claim 20,~~ wherein the Gln residue to which the linker is conjugated is comprised in an Fc domain of the antibody, in particular wherein the Gln residue to which the linker is conjugated is Gln residue Q295 (EU numbering) of the C_H2 domain of an IgG antibody; or -

~~22.~~ ~~The method according to claim 20,~~
wherein the Gln residue to which the linker is conjugated has been introduced into the heavy or light chain of the antibody by molecular engineering, in particular -

~~23.~~ ~~The method according to claim 22,~~ wherein the Gln residue that has been introduced into the heavy or light chain of the antibody by molecular engineering is N297Q (EU numbering) of the C_H2 domain of an aglycosylated IgG antibody or -

~~24.~~ ~~The method according to claim 22,~~ wherein the Gln residue that has been introduced into the heavy or light chain of the antibody by molecular engineering is comprised in a peptide that has been (a) integrated into the heavy or light chain of the antibody or (b) fused to the N- or C-terminal end of the heavy or light chain of the antibody, in particular -

~~25. The method according to claim 24,~~ wherein the peptide comprising the Gln residue has been fused to the C-terminal end of the heavy chain of the antibody.

~~269.~~ The method according to ~~any one of claims 20 to 22 or 24 to 25~~8, wherein the IgG antibody is a glycosylated IgG antibody, in particular wherein the IgG antibody is glycosylated at residue N297 (EU numbering) of the C_H2 domain, and/or:-

~~27. The method according to any one of claims 1 to 26,~~ wherein the antibody is selected from the group consisting of: Brentuximab, Trastuzumab, Gemtuzumab, Inotuzumab, Avelumab, Cetuximab, Rituximab, Daratumumab, Pertuzumab, Vedolizumab, Ocrelizumab, Tocilizumab, Ustekinumab, Golimumab, Obinutuzumab, Sacituzumab, Belantamab, Polatuzumab and Enfortumab, in particular:-

~~28. The method according to any one of claims 1 to 27,~~ wherein the antibody is selected from the group consisting of: Brentuximab, Gemtuzumab, Trastuzumab, Inotuzumab, Polatuzumab, Enfortumab, Sacituzumab and Belantamab, in particular:-

~~29. The method according to any one of claims 1 to 28,~~ wherein the antibody is Polatuzumab or Trastuzumab or Enfortumab.

~~30~~10. The method according to any one of claims 1 to ~~299~~9, wherein the linker is conjugated to the γ -carboxamide group of the Gln residue comprised in the antibody; and/or:-

~~31. The method according to any one of claims 1 to 30,~~ wherein the linker is suitable for conjugation to a glycosylated antibody with a conjugation efficiency of at least 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90% or 95%; and/or:-

~~32. The method according to any one of claims 1 to 31,~~ wherein the microbial transglutaminase is derived from a *Streptomyces* species, in particular *Streptomyces mobaraensis*.

~~33~~11. An antibody-linker conjugate which has been produced with a method according to any one of claims 1 to ~~32~~10.

~~34~~12. An antibody-linker conjugate comprising:

a) an antibody; and

b) a linker comprising the structure:

(Sp₁)-RK-(Sp₂)-B-(Sp₃) or

(Sp₁)-B-(Sp₂)-RK-(Sp₃); wherein

- (Sp₁) is a chemical spacer or is absent;
- (Sp₂) is a chemical spacer or is absent;
- (Sp₃) is a chemical spacer or is absent;
- R is arginine or an arginine derivative or an arginine mimetic;
- K is lysine or a lysine derivative or a lysine mimetic;
- B is a linking moiety or a payload;

wherein the linker is conjugated to the antibody via an isopeptide bond formed between a γ -carboxamide group of a glutamine residue comprised in the antibody and a primary amine comprised in the side chain of the lysine residue, the lysine derivative or the lysine mimetic comprised in the RK motif comprised in the linker.

~~35~~13. The antibody-linker conjugate according to claim ~~34~~12, wherein the chemical spacers (Sp₁), (Sp₂) and (Sp₃) each independently comprise between 0 and 12 amino acid residues; ~~and/or~~

~~36. The antibody linker conjugate according to claim 34 or 35,~~ wherein the linker comprises not more than 25, 20, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4 amino acid residues; ~~and/or~~

~~37. The antibody linker conjugate according to any one of claims 34 to 36,~~ wherein the net charge of the linker is neutral or positive; ~~and/or~~

~~38. The antibody linker conjugate according to any one of claims 34 to 37,~~ wherein the linker comprises no negatively-charged amino acid residues.

~~39~~14. The antibody-linker conjugate according to ~~any one of claims 34-12 to or 13~~38, wherein the linker comprises an amino acid sequence selected from the group consisting of: RKAA (SEQ ID NO:1), RKA (SEQ ID NO:2), ARK (SEQ ID NO:3), RKR (SEQ ID NO:4) and RK-Val-Cit (SEQ ID NO:54), ~~in particular~~

~~40. The antibody linker conjugate according to any one of claims 34 to 39,~~ wherein

the linker comprises an amino acid sequence selected from the group consisting of: RKAA (SEQ ID NO:1), RKA (SEQ ID NO:2), ARK (SEQ ID NO:3) and RK-Val-Cit (SEQ ID NO:54), in particular:-

~~41. The antibody-linker conjugate according to any one of claims 34 to 40,~~ wherein the linker comprises the amino acid sequence RKAA (SEQ ID NO:1).

~~42~~15. The antibody-linker conjugate according to any one of claims ~~34-12~~ to ~~41~~14, wherein B is a linking moiety, in particular:-

~~43. The antibody-linker conjugate according to claim 42,~~ wherein the linking moiety B comprises

- a ~~bioorthogonal~~177iorthogonal marker group, or
- a non-bio-orthogonal entity for crosslinking; in particular:-

~~44. The antibody-linker conjugate according to claim 43,~~ wherein the ~~bioorthogonal~~177iorthogonal marker group or the non-bio-orthogonal entity for crosslinking consists of or comprises at least one molecule or moiety selected from the group consisting of:

- $-N-N\equiv N$, or $-N_3$;
- Lys(N_3);
- a tetrazine;
- an alkyne;
- a strained cyclooctyne;
- BCN;
- a strained alkene;
- a photoreactive group;
- an aldehyde;
- an acyltrifluoroborate;
- a protein degradation agent ('PROTAC');;
- a cyclopentadiene/spirolodicyclopentadiene;
- a thio-selective electrophile;
- -SH; and
- cysteine.

~~45~~16. The antibody-linker conjugate according to ~~any one of claims 42-15~~ to ~~44~~, wherein one or more payloads have been conjugated to the linking moiety B, in particular:-

~~46. The antibody-linker conjugate according to claim 45,~~ wherein one or more payloads have been conjugated to the linking moiety B via a click-reaction.

~~47~~17. The antibody-linker conjugate according to any one of claims ~~34-12~~ to ~~41~~16, wherein B is a payload, in particular.

~~48. The antibody-linker conjugate according to any one of claims 45 to 47,~~ wherein the payload comprises at least one of:

- a toxin;
- a cytokine;
- a growth factor;
- a radionuclide;
- a hormone;
- an anti-viral agent;
- an anti-bacterial agent;
- a fluorescent dye;
- an immunoregulatory/immunostimulatory agent;
- a half-life increasing moiety;
- a solubility increasing moiety;
- a polymer-toxin conjugate;
- a nucleic acid;
- a biotin or streptavidin moiety;
- a vitamin;
- a protein degradation agent ('PROTAC');
- a target binding moiety; and/or
- an anti-inflammatory agent; in particular.

~~49. The antibody-linker conjugate according to claim 48,~~ wherein the toxin is at least one selected from the group consisting of

- a pyrrolobenzodiazepine (e.g., PBD);
- an auristatin (e.g., MMAE, MMAF);
- a maytansinoid (e.g., maytansine, DM1, DM4, DM21);
- a duocarmycin;
- a nicotinamide phosphoribosyltransferase (NAMPT) inhibitor;
- a tubulysin;

- an enediyne (e.g., calicheamicin);
- an anthracycline derivative (PNU) (e.g., doxorubicin);
- a pyrrole-based kinesin spindle protein (KSP) inhibitor;
- a cryptophycin;
- a drug efflux pump inhibitor;
- a sandramycin;
- an amanitin (e.g., α -amanitin); and
- a camptothecin (e.g., exatekans, deruxtecans).

~~50~~18. The antibody-linker conjugate according to ~~any one of~~ claims ~~47 to 49~~17, wherein the chemical spacer (Sp₂) comprises a self-immolative moiety, in particular:-

~~51. The antibody linker conjugate according to claim 50~~, wherein the self-immolative moiety is directly attached to the payload B, and/or:-

~~52. The antibody linker conjugate according to claim 50 or 51~~, wherein the self-immolative moiety comprises a p-aminobenzyl carbamoyl (PABC) moiety.

~~53~~19. The antibody-linker conjugate according to any one of claims ~~34 12~~ to ~~52~~18, wherein the antibody is an IgG antibody, in particular an IgG1 antibody, in particular:-

~~54. The antibody linker conjugate according to claim 53~~,

wherein the Gln residue to which the linker is conjugated is comprised in an Fc domain of the antibody, in particular wherein the Gln residue to which the linker is conjugated is Gln residue Q295 (EU numbering) of the C_H2 domain of an IgG antibody, or:-

~~55. The antibody linker conjugate according to claim 53~~, wherein the Gln residue to which the linker is conjugated has been introduced into the heavy or light chain of the antibody by molecular engineering, in particular:-

~~56. The antibody linker conjugate according to claim 55~~, wherein the Gln residue that has been introduced into the heavy or light chain of the antibody by molecular engineering is N297Q (EU numbering) of the C_H2 domain of an aglycosylated IgG antibody or:-

~~57. The antibody linker conjugate according to claim 55~~, wherein the Gln residue that has been introduced into the heavy or light chain of the antibody by molecular engineering is

comprised in a peptide that has been (a) integrated into the heavy or light chain of the antibody or (b) fused to the N- or C-terminal end of the heavy or light chain of the antibody, in particular:-

~~58.~~ The antibody-linker conjugate according to ~~claim 57~~, wherein the peptide comprising the Gln residue has been fused to the C-terminal end of the heavy chain of the antibody.

~~59~~20. The antibody-linker conjugate according to ~~any one of claims 53 to 55 or 57 to 58~~19, wherein the IgG antibody is a glycosylated IgG antibody, in particular wherein the IgG antibody is glycosylated at residue N297 (EU numbering) of the C_H2 domain, and/or -

~~60.~~ The antibody-linker conjugate according to ~~any one of claims 34 to 59~~, wherein the antibody is selected from the group consisting of: Brentuximab, Trastuzumab, Gemtuzumab, Inotuzumab, Avelumab, Cetuximab, Rituximab, Daratumumab, Pertuzumab, Vedolizumab, Ocrelizumab, Tocilizumab, Ustekinumab, Golimumab, Obinutuzumab, Sacituzumab, Belantamab, Polatuzumab and Enfortumab, in particular -

~~61.~~ The antibody-linker conjugate according to ~~any one of claims 34 to 60~~, wherein the antibody is selected from the group consisting of: Brentuximab, Gemtuzumab, Trastuzumab, Inotuzumab, Polatuzumab, Enfortumab, Sacituzumab and Belantamab, in particular -

~~62.~~ The antibody-linker conjugate according to ~~any one of claims 34 to 61~~, wherein the antibody is Polatuzumab or Trastuzumab or Enfortumab.

~~63~~21. An antibody-drug conjugate comprising:

- a) an IgG antibody; and
- b) a linker comprising a drug moiety B, wherein the drug moiety B is covalently linked to an amino acid sequence selected from the group consisting of: RKAA (SEQ ID NO:1), RKA (SEQ ID NO:2), ARK (SEQ ID NO:3), RKR (SEQ ID NO:4) or RK-Val-Cit (SEQ ID NO:54);

wherein the linker is conjugated to the IgG antibody via an isopeptide bond formed between the γ -carboxamide group of glutamine residue Q295 (EU numbering) of the C_H2 domain of the antibody and the primary amine comprised in the side chain of the lysine residue comprised in the linker.

~~64~~22. The antibody-drug conjugate according to claim ~~63~~21, wherein the drug moiety

B is linked to the N- or C-terminus of the amino acid sequence comprised in the linker via a self-immolative moiety, in particular -

~~65. The antibody drug conjugate according to claim 64,~~ wherein the self-immolative moiety comprises a p-aminobenzyl carbamoyl (PABC) moiety; and/or-

~~66. The antibody drug conjugate according to any one of claims 63 to 65,~~ wherein the IgG antibody is a glycosylated IgG antibody, in particular wherein the IgG antibody is glycosylated at residue N297 (EU numbering) of the C_H2 domain; and/or-

~~67. The antibody drug conjugate according to any one of claims 63 to 66,~~ wherein the IgG antibody is an IgG1 antibody; and/or-

~~68. The antibody drug conjugate according to any one of claims 63 to 67,~~ wherein the IgG antibody is Polatuzumab or an antibody comprising a heavy chain as set forth in SEQ ID NO:5 and a light chain as set forth in SEQ ID NO:6, or-

~~69. The antibody drug conjugate according to any one of claims 63 to 67,~~ wherein the IgG antibody is Trastuzumab or an antibody comprising a heavy chain as set forth in SEQ ID NO:7 and a light chain as set forth in SEQ ID NO:8, or-

~~70. The antibody drug conjugate according to any one of claims 63 to 67,~~ wherein the IgG antibody is Enfortumab or an antibody comprising a heavy chain as set forth in SEQ ID NO:9 and a light chain as set forth in SEQ ID NO:10 or 11; and/or-

~~71. The antibody drug conjugate according to any one of claims 63 to 70,~~ wherein the drug is a toxin selected from the group consisting of:

- a pyrrolobenzodiazepine (e.g., PBD);
- an auristatin (e.g., MMAE, MMAF);
- a maytansinoid (e.g., maytansine, DM1, DM4, DM21);
- a duocarmycin;
- a nicotinamide phosphoribosyltransferase (NAMPT) inhibitor;
- a tubulysin;
- an enediyne (e.g. calicheamicin);
- an anthracycline derivative (PNU) (e.g., doxorubicin);
- a pyrrole-based kinesin spindle protein (KSP) inhibitor;
- a cryptophycin;

- a drug efflux pump inhibitor;
- a sandramycin;
- an amanitin (e.g., α -amanitin); and
- a camptothecin (e.g., exatecans, deruxtecans).

~~72~~23. The antibody-drug conjugate according to ~~any one of claims 21 or 22~~63 to 71, wherein the linker has the structure RKAA-PABC-B, in particular wherein B is an auristatin or a maytansinoid, in particular wherein the auristatin is MMAE and wherein the maytansinoid is DM1 or maytansine, ~~or~~.

~~73.~~ ~~The antibody drug conjugate according to any one of claims 63 to 71,~~ wherein the linker has the structure RKA-PABC-B, in particular wherein B is an auristatin or a maytansinoid, in particular wherein the auristatin is MMAE and wherein the maytansinoid is DM1 or maytansine, ~~or~~.

~~74.~~ ~~The antibody drug conjugate according to any one of claims 63 to 71,~~ wherein the linker has the structure ARK-PABC-B, in particular wherein B is an auristatin or a maytansinoid, in particular wherein the auristatin is MMAE and wherein the maytansinoid is DM1 or maytansine, ~~or~~.

~~75.~~ ~~The antibody drug conjugate according to any one of claims 63 to 71,~~ wherein the linker has the structure RKR-PABC-B, in particular wherein B is an auristatin or a maytansinoid, in particular wherein the auristatin is MMAE and wherein the maytansinoid is DM1 or maytansine, ~~or~~.

~~76.~~ ~~The antibody drug conjugate according to any one of claims 63 to 71,~~ wherein the linker has the structure RK-Val-Cit-PABC-B, in particular wherein B is an auristatin or a maytansinoid, in particular wherein the auristatin is MMAE and wherein the maytansinoid is DM1 or maytansine.

~~77~~24. A linker construct comprising the structure:

(Sp₁)-RK-(Sp₂)-B-(Sp₃) or

(Sp₁)-B-(Sp₂)-RK-(Sp₃); wherein

- (Sp₁) is a chemical spacer or is absent;
- (Sp₂) is a chemical spacer or is absent;

- (Sp₃) is a chemical spacer or is absent;
- R is arginine or an arginine derivative or an arginine mimetic;
- K is lysine or a lysine derivative or a lysine mimetic;
- B is a linking moiety or a payload.

~~78~~25. The linker construct according to claim ~~77~~24, wherein the chemical spacers (Sp₁), (Sp₂) and (Sp₃) each independently comprise between 0 and 12 amino acid residues; ~~and/or~~-

~~79~~—The linker construct according to claim ~~77 or 78~~, wherein the linker comprises not more than 25, 20, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4 amino acid residues; ~~and/or~~-

~~80~~—The linker construct according to any one of claims ~~77 to 79~~, wherein the net charge of the linker is neutral or positive; ~~and/or~~-

~~81~~—The linker construct according to any one of claims ~~77 to 80~~, wherein the linker comprises no negatively-charged amino acid residues.

~~82~~26. The linker construct according to ~~any one of claims 77 to 81~~24 or 25, wherein the linker comprises the amino acid sequence RCAA (SEQ ID NO:1), RKA (SEQ ID NO:2), ARK (SEQ ID NO:3), RKR (SEQ ID NO:4) or RK-Val-Cit (SEQ ID NO:54).

~~83~~27. The linker construct according to any one of claims ~~77 to 82~~24 to 26, wherein B is a linking moiety, ~~in particular~~-

~~84~~—The linker construct according to claim ~~83~~, wherein the linking moiety B comprises

- a bioorthogonal marker group, or
- a non-bio-orthogonal entity for crosslinking, ~~in particular~~-

~~85~~—The linker construct according to claim ~~84~~, wherein the bioorthogonal marker group or the non-bio-orthogonal entity for crosslinking consists of or comprises at least one molecule or moiety selected from the group consisting of:

- -N-N≡N, or -N₃;
- Lys(N₃);
- a tetrazine;
- an alkyne;

- a strained cyclooctyne;
- BCN;
- a strained alkene;
- a photoreactive group;
- an aldehyde;
- an acyltrifluoroborate;
- a protein degradation agent ('PROTAC');
- a cyclopentadiene/spirolocyclopentadiene;
- a thio-selective electrophile;
- -SH; and
- cysteine.

~~86~~28. The linker construct according to any one of claims ~~77 to 85~~24 to 27, wherein the linker construct consists of or comprises the structure R_{KAA}-B, in particular wherein B is Lys(N₃) or cysteine, ~~or~~.

~~87.~~ ~~The linker construct according to any one of claims 77 to 85,~~ wherein the linker construct consists of or comprises the structure R_{KA}-B, in particular wherein B is Lys(N₃) or cysteine, ~~or~~.

~~88.~~ ~~The linker construct according to any one of claims 77 to 85,~~ wherein the linker construct consists of or comprises the structure AR_K-B, in particular wherein B is Lys(N₃) or cysteine, ~~or~~.

~~89.~~ ~~The linker construct according to any one of claims 77 to 85,~~ wherein the linker construct consists of or comprises the structure B-R_{KR}, in particular wherein B is Lys(N₃) or cysteine.

~~90~~29. The linker construct according to any one of claims ~~77 to 82~~24 to 26, wherein B is a payload, ~~in particular~~.

~~91.~~ ~~The linker construct according to claim 90,~~ wherein the payload comprises at least one of:

- a toxin;
- a cytokine;
- a growth factor;
- a radionuclide;

- a hormone;
- an anti-viral agent;
- an anti-bacterial agent;
- a fluorescent dye;
- an immunoregulatory/immunostimulatory agent;
- a half-life increasing moiety;
- a solubility increasing moiety;
- a polymer-toxin conjugate;
- a nucleic acid;
- a biotin or streptavidin moiety;
- a vitamin;
- a protein degradation agent ('PROTAC');
- a target binding moiety; and/or
- an anti-inflammatory agent, in particular:-

~~92. The linker construct according to claim 91,~~ wherein the toxin is at least one selected from the group consisting of

- a pyrrolobenzodiazepine (e.g., PBD);
- an auristatin (e.g., MMAE, MMAF);
- a maytansinoid (e.g., maytansine, DM1, DM4, DM21);
- a duocarmycin;
- a nicotinamide phosphoribosyltransferase (NAMPT) inhibitor;
- a tubulysin;
- an enediyne (e.g. calicheamicin);
- an anthracycline derivative (PNU) (e.g., doxorubicin);
- a pyrrole-based kinesin spindle protein (KSP) inhibitor;
- a cryptophycin;
- a drug efflux pump inhibitor;
- a sandramycin;
- an amanitin (e.g., α -amanitin); and
- a camptothecin (e.g., exatecans, deruxtecans).

~~93~~30. The linker construct according to ~~any one of claims 90 to 92~~29, wherein the chemical spacer (Sp₂) comprises a self-immolative moiety, in particular:-

~~94. The linker construct according to claim 93,~~ wherein the self-immolative moiety is directly attached to the payload B, and/or:-

~~95.— The linker construct according to claim 93 or 94,~~ wherein the self-immolative moiety comprises a p-aminobenzyl carbamoyl (PABC) moiety.

~~96~~31. The linker construct according to ~~any one of claims 90 to 95~~29 or 30, wherein the linker construct consists of or comprises the structure R_KAA-PABC-B, in particular wherein B is an auristatin or a maytansinoid, in particular wherein the auristatin is MMAE and wherein the maytansinoid is DM1 or maytansine, or.

~~97.— The linker construct according to any one of claims 90 to 95,~~ wherein the linker construct consists of or comprises the structure R_KA-PABC-B, in particular wherein B is an auristatin or a maytansinoid, in particular wherein the auristatin is MMAE and wherein the maytansinoid is DM1 or maytansine, or.

~~98.— The linker construct according to any one of claims 90 to 95,~~ wherein the linker construct consists of or comprises the structure ARK-PABC-B, in particular wherein B is an auristatin or a maytansinoid, in particular wherein the auristatin is MMAE and wherein the maytansinoid is DM1 or maytansine, or.

~~99.— The linker construct according to any one of claims 90 to 95,~~ wherein the linker construct consists of or comprises the structure B-PABC-RKR, in particular wherein B is an auristatin or a maytansinoid, in particular wherein the auristatin is MMAE and wherein the maytansinoid is DM1 or maytansine, or.

~~100.— The linker construct according to any one of claims 90 to 95,~~ wherein the linker construct consists of or comprises the structure R_K-Val-Cit-PABC-B, in particular wherein B is an auristatin or a maytansinoid, in particular wherein the auristatin is MMAE and wherein the maytansinoid is DM1 or maytansine.

~~101~~32. Use of a linker construct according to any one of claims ~~77 to 100~~24 to 31 in the production of an antibody-linker conjugate by means of a microbial transglutaminase, in particular.

~~102.— The use according to claim 99,~~ wherein the antibody is an IgG antibody, in particular an IgG1 antibody, and/or.

~~103.— The use according to claim 101 or 102,~~ wherein the antibody is Polatuzumab or Trastuzumab or Enfortumab.

~~104~~33. A pharmaceutical composition comprising

a) the antibody-linker conjugate according to any one of claims ~~34~~12 to ~~63~~20, in particular wherein the antibody-linker conjugate comprises at least one payload;

or

b) the antibody drug-conjugate according to any one of claims ~~64~~to 76~~21 to 23~~; and the pharmaceutical composition comprising at least one pharmaceutically acceptable ingredient.

~~105~~34. The pharmaceutical composition according to claim ~~104~~33 comprising at least one additional therapeutically active agent.

~~106~~35. The antibody-linker conjugate according to any one of claims ~~34~~12 to ~~63~~20, in particular wherein the antibody-linker conjugate comprises at least one payload, the antibody-drug conjugate according to any one of claims ~~64~~to 76~~21 to 23~~, or the pharmaceutical composition according to claim ~~104~~or 105~~33 or 34~~ for use in therapy and/or diagnostics.

~~107. The antibody-linker conjugate according to any one of claims 34 to 63, in particular wherein the antibody-linker conjugate comprises at least one payload, the antibody-drug conjugate according to any one of claims 64 to 76, or the pharmaceutical composition according to claim 104 or 105 for use in the treatment of a patient~~

- ~~• suffering from,~~
- ~~• being at risk of developing, and/or~~
- ~~• being diagnosed for~~

~~a neoplastic disease, a neurological disease, an autoimmune disease, an inflammatory disease or an infectious disease.~~

36. Use of the antibody-linker conjugate according to any one of claims 12 to 20, in particular wherein the antibody-linker conjugate comprises at least one payload, the antibody-drug conjugate according to any one of claims 21 to 23, or the pharmaceutical composition according to claim 33 or 34 for the manufacture of a medicament for the treatment of a patient

- suffering from,
- being at risk of developing, and/or
- being diagnosed for

a neoplastic disease, neurological disease, an autoimmune disease, an inflammatory disease or an infectious disease.

~~10837.~~ The ~~antibody-linker conjugate, the antibody-drug conjugate or the pharmaceutical composition for use according to claim 10736,~~ wherein the antibody-linker conjugate or the antibody-drug conjugate comprised in the pharmaceutical composition comprises Polatuzumab and wherein the neoplastic disease is a B-cell associated cancer, in particular-

~~109. — The antibody-linker conjugate, the antibody-drug conjugate or the pharmaceutical composition for use according to claim 108,~~ wherein the B-cell associated cancer is non-Hodgkin lymphoma, in particular wherein the B-cell associated cancer is diffuse large B-cell lymphoma, and/or-

~~110. — The antibody-linker conjugate, the antibody-drug conjugate or the pharmaceutical composition for use according to claim 108 or 109,~~ wherein the antibody-linker conjugate, the antibody-drug conjugate or the pharmaceutical composition is to be administered in combination with bendamustine and/or rituximab, or-

~~111. — The antibody-linker conjugate, the antibody-drug conjugate or the pharmaceutical composition for use according to claim 107,~~ wherein the antibody-linker conjugate or the antibody-drug conjugate comprised in the pharmaceutical composition comprises Trastuzumab and wherein the neoplastic disease is a HER2-positive cancer, in particular HER2-positive breast, gastric, ovarian or lung cancer, in particular -

~~112. — The antibody-linker conjugate, the antibody-drug conjugate or the pharmaceutical composition for use according to claim 111,~~ wherein the antibody-linker conjugate, the antibody-drug conjugate or the pharmaceutical composition is to be administered in combination with lapatinib, capecitabine and/or a taxane, or-

~~113. — The antibody-linker conjugate, the antibody-drug conjugate or the pharmaceutical composition for use according to claim 107,~~ wherein the antibody-linker conjugate or the antibody-drug conjugate comprised in the pharmaceutical composition comprises Enfortumab or an Enfortumab variant and wherein the neoplastic disease is a Nectin-4 positive cancer, in particular Nectin-4 positive pancreatic cancer, lung cancer, bladder cancer or breast cancer, in particular-

~~114. The antibody-linker conjugate, the antibody-drug conjugate or the pharmaceutical composition for use according to claim 113,~~ wherein the antibody-linker conjugate, the antibody-drug conjugate or the pharmaceutical composition is to be administered in combination with a cisplatin-based chemotherapeutic agent and/or Pembrolizumab.

~~115. Use of the antibody-linker conjugate according to any one of claims 34 to 63, in particular wherein the antibody-linker conjugate comprises at least one payload, the antibody-drug conjugate according to any one of claims 64 to 76, or the pharmaceutical composition according to claim 104 or 105 for the manufacture of a medicament for the treatment of a patient~~

- ~~• suffering from,~~
- ~~• being at risk of developing, and/or~~
- ~~• being diagnosed for~~

~~a neoplastic disease, neurological disease, an autoimmune disease, an inflammatory disease or an infectious disease.~~

~~116. A method of treating or preventing a neoplastic disease, said method comprising administering to a patient in need thereof the antibody-linker conjugate according to any one of claims 34 to 63, in particular wherein the antibody-linker conjugate comprises at least one payload, the antibody-drug conjugate according to any one of claims 64 to 76, or the pharmaceutical composition according to claim 104 or 105.~~