

- (3) SEQ ID NO: 41 and SEQ ID NO: 57,
 (4) SEQ ID NO:115 and SEQ ID NO:131.

In some embodiments, the sequences of the heavy chain variable region and the light chain variable region of the anti-Claudin 18.2 antibody are SEQ ID NO: 41 and SEQ ID NO: 49, respectively.

In some embodiments, the heavy chain constant region of the anti-Claudin 18.2 antibody is selected from human IgG (e.g., IgG1, IgG2, IgG3, or IgG4), IgM, IgA, IgD, **IgE**, **IgA** constant regions, or mutants of the above constant regions, preferably human IgG1;

the light chain constant region of the anti-Claudin 18.2 antibody is selected from human lambda constant region, kappa constant region or a mutant of the above constant regions, preferably a human kappa constant region.

In some embodiments, the amino acid sequence of the heavy chain of the anti-Claudin 18.2 antibody comprises the sequence set forth in SEQ ID NO:65, or a sequence having greater than 70%, such as greater than 75%, 80%, 85%, 90%, 95%, 99% identity to SEQ ID NO: 65;

the amino acid sequence of the light chain of the anti-Claudin 18.2 antibody comprises a sequence as shown in SEQ ID NO: 66, or a sequence having greater than 70%, such as greater than 75%, 80%, 85%, 90%, 95%, 99% identity to SEQ ID NO: 66.

In some embodiments, p is 3.0-4.0.

In some embodiments, p is 3.0-3.8.

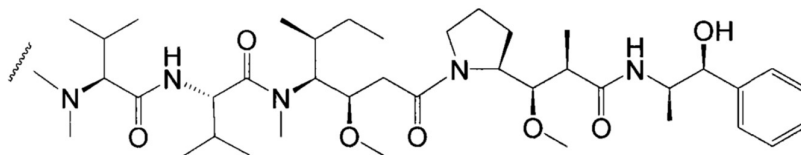
In some embodiments, p is 3.0, 3.4, 3.5, or 3.8.

In some embodiments, p is 3.8.

In some embodiments, the cytotoxic agent is selected from the group consisting of SN-38, Gemcitabine, Monomethyl auristatin E (MMAE), Monomethyl auristatin F (MMAF), maytansinoids (e.g., Maytansine DM1, Maytansine DM4), calicheamicin, MGBA (e.g., duocarmycin), doxorubicin, ricin, Diphtheria toxin and other toxins, I131, interleukins, tumor necrosis factor, chemokines and nanoparticles.

In some embodiments, the cytotoxic agent is MMAE.

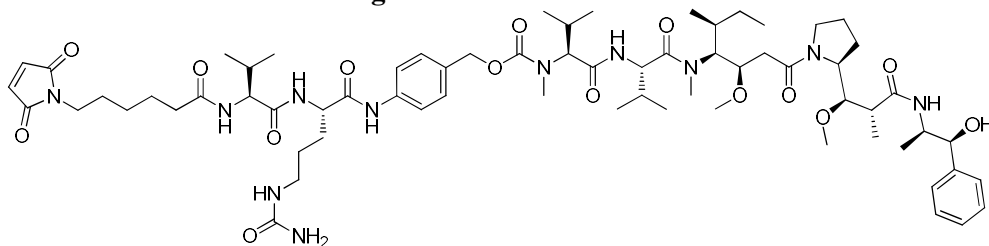
The structure of MMAE is:



In some embodiments, the linker is selected from the group consisting of 6-maleimidohexanoyl (MC), maleimidopropionyl (MP), N-succinimidyl 4-(2-pyridylthio) valerate (SPP), 4-(N-maleimidomethyl)-cyclohexan-1-formyl (MCC), N-succinimidyl(4-iodo-acetyl)aminobenzoate (SIAB), and 6-maleimidocaproyl-valine-citrulline-p-aminobenzyloxycarbonyl (MC-vc-PAB).

In some embodiments, the linker is 6-maleimidocaproyl-valine-citrulline-p-aminobenzyloxycarbonyl (MC-vc-PAB).

In some embodiments, L-D as described in Formula I is MC-vc-PAB-MMAE, and its structure is shown in the following formula:



5. The antibody drug conjugate of claim 1, its pharmaceutically acceptable salt, solvate or solvate of said salt, wherein:

the heavy chain variable region and the light chain variable region of the anti-Claudin 18.2 antibody are selected from the following sequence combinations:

- (1) SEQ ID NO: 17 and SEQ ID NO: 57,
- (2) SEQ ID NO: 41 and SEQ ID NO: 49,
- (3) SEQ ID NO: 41 and SEQ ID NO: 57,
- (4) SEQ ID NO: 115 and SEQ ID NO: 131;

preferably, the sequences of the heavy chain variable region and the light chain variable region of the anti-Claudin 18.2 antibody are SEQ ID NO: 41 and SEQ ID NO: 49, respectively.

6. The antibody drug conjugate of claim 1, its pharmaceutically acceptable salt, solvate or solvate of said salt, wherein:

the heavy chain constant region of the anti-Claudin 18.2 antibody is selected from human IgG (such as IgG1, IgG2, IgG3 or IgG4), IgM, IgA, IgD, ~~IgE~~~~IgA~~ constant region or a mutant of the above constant region, preferably human IgG1;

the light chain constant region of the anti-Claudin 18.2 antibody is selected from a human lambda constant region, a kappa constant region or a mutant of the above constant region, preferably a human kappa constant region.

7. The antibody drug conjugate of claim 1, its pharmaceutically acceptable salt, solvate or solvate of said salt, wherein:

the amino acid sequence of the heavy chain of the anti-Claudin 18.2 antibody comprises a sequence as shown in SEQ ID NO: 65, or a sequence having greater than 70%, such as greater than 75%, 80%, 85%, 90%, 95%, 99% identity to SEQ ID NO: 65;

the amino acid sequence of the light chain of the anti-Claudin 18.2 antibody comprises a sequence as shown in SEQ ID NO: 66, or a sequence having greater than 70%, such as greater than 75%, 80%, 85%, 90%, 95%, 99% identity to SEQ ID NO: 66.

8. The antibody drug conjugate of claim 1, its pharmaceutically acceptable salt, solvate or solvate of said salt, wherein p is 2.0-7.0, 2.0-6.0, 2.0-5.0, 2.0-4.0, 3.0-7.0, 3.0-6.0, 3.0-5.0 or 3.0-4.0, preferably p is 3.0-4.0, e.g. p is 3.0-3.8, preferably 3.0, 3.4, 3.5 or 3.8, more preferably 3.8.

9. The antibody drug conjugate of claim 1, its pharmaceutically acceptable salt, solvate or solvate of said salt, wherein the cytotoxic agent is selected from SN-38, Gemcitabine, Monomethyl auristatin E (MMAE), Monomethyl auristatin F (MMAF), maytansinoids (e.g. Maytansine DM1, Maytansine DM4), calicheamicin, MGBA (e.g. duocarmycin), doxorubicin, ricin, Diphtheria toxin and other toxins, I131, interleukins, tumor necrosis factor, chemokines and nanoparticles;

preferably, the cytotoxic agent is MMAE.

10. The antibody drug conjugate of claim 1, its pharmaceutically acceptable salt, solvate or solvate of said salt, wherein the linker is selected from 6-maleimidocaproyl (MC), maleimidopropionyl (MP), N-succinimidyl 4-(2-pyridylthio)valerate (SPP), 4-(N-maleimidomethyl)-cyclohexan-1-formyl (MCC), N-succinimidyl(4-iodo-acetyl)aminobenzoate (SIAB), and 6-maleimidocaproyl-valine-citrulline-p-aminobenzoyloxycarbonyl (MC-vc-PAB);

preferably, the linker is 6-maleimidocaproyl-valine-citrulline-p-aminobenzoyloxycarbonyl (MC-vc-PAB).

11. The antibody drug conjugate of claim 1, its pharmaceutically acceptable salt, solvate or solvate of said salt, wherein:

Ab includes:

(a) the heavy chain variable region CDR1, CDR2, CDR3 and the light chain variable region CDR1, CDR2, CDR3, wherein, the sequence of the heavy chain variable region CDR1 is shown in SEQ ID NO: 42, the sequence of the heavy chain variable region CDR2 is shown in SEQ ID NO: 43, the sequence of the heavy chain variable region CDR3 is shown in SEQ ID NO: 44, the sequence of the light chain variable region CDR1 is shown in SEQ ID NO: 50, the sequence of the light chain variable region CDR2 is shown in SEQ ID NO: 51, and the sequence of the light chain variable region CDR3 is shown in SEQ ID NO: 52;

(b) a heavy chain variable region and a light chain variable region, wherein the sequence of the heavy chain variable region is shown in SEQ ID NO: 41, and the sequence of the light chain variable region is shown in SEQ ID NO: 49; and /or

(c) heavy chain and light chain, wherein the sequence of the heavy chain is shown in SEQ ID NO: 65, and the sequence of the light chain is shown in SEQ ID NO: 66;

L is MC-vc-PAB; and

D is MMAE.

12. A composition comprising the antibody drug conjugate of any one of claims 1-11, its pharmaceutically acceptable salt, solvate or solvate of said salt; optionally, further comprising at least one of the chemotherapeutic drugs, immunotherapy drugs and immunosuppressants known for treating tumors; or optionally, at least one pharmaceutically acceptable carrier, diluent or excipient.

13. Use of the antibody drug conjugate of any one of claims 1-11, its pharmaceutically acceptable salt, solvate or solvate of said salt or the composition of claim 12 in the preparation of medicaments for preventing and/or treating a disease associated with Claudin 18.2;

preferably, the disease associated with Claudin 18.2 is gastric cancer, adenocarcinoma of the esophagogastric junction, and pancreatic cancer;

more preferably, the disease associated with Claudin 18.2 is gastric cancer.

~~14. A method for preventing and/or treating a disease associated with Claudin 18.2, comprising: administering to a subject in need a prophylactically and/or therapeutically effective amount of the antibody drug conjugate of any one of claims 1-11, its pharmaceutically acceptable salt, solvate or solvate of said salt, or the composition of claim 12;~~

~~preferably, the disease associated with Claudin 18.2 is gastric cancer, adenocarcinoma of the esophagogastric junction, and pancreatic cancer;~~

~~more preferably, the disease associated with Claudin 18.2 is gastric cancer.~~

~~15~~14. The antibody drug conjugate of any one of claims 1-11, its pharmaceutically acceptable salt, solvate or solvate of said salt, or the composition of claim 12, for use in preventing and/or treating a disease associated with Claudin 18.2;

preferably, the disease associated with Claudin 18.2 is gastric cancer, adenocarcinoma of the esophagogastric junction, and pancreatic cancer;

more preferably, the disease associated with Claudin 18.2 is gastric cancer.