

Claims

1. ~~Antibody drug conjugate, its pharmaceutically acceptable salt, solvate or solvate of said salt, the antibody drug conjugate has the structure shown in Formula I,~~



Formula I

wherein:

~~Ab is an anti-Claudin 18.2 antibody, the anti-Claudin 18.2 antibody comprises a heavy chain and a light chain, and the heavy chain variable region CDR1 comprises a sequence selected from a sequence as shown in SEQ ID NO: 2, 10, 18, 26, 34, 42, 68, 76, 84, 92, 100, 108 or 116 or a mutant thereof, the heavy chain variable region CDR2 comprises a sequence selected from a sequence as shown in SEQ ID NO: 3, 11, 19, 27, 35, 43, 69, 77, 85, 93, 101, 109 or 117 or a mutant thereof, the heavy chain variable region CDR3 comprises a sequence selected from a sequence as shown in SEQ ID NO: 4, 12, 20, 28, 36, 44, 70, 78, 86, 94, 102, 110 or 118 or a mutant thereof, the light chain variable region CDR1 comprises a sequence selected from a sequence as shown in SEQ ID NO: 50, 58, 124 or 132 or a mutant thereof, the light chain variable region CDR2 comprises a sequence selected from a sequence as shown in SEQ ID NO: 51, 59, 125 or 133 or a mutant thereof, and the light chain variable region CDR3 comprises a sequence selected from a sequence as shown in SEQ ID NO: 52, 60, 126 or 134 or a mutant thereof;~~

~~D is cytotoxic agent;~~

~~L is the linker for linking the anti-Claudin 18.2 antibody and the cytotoxic agent;~~

~~p is 2-8.~~

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

~~the heavy chain variable region CDR1 of the anti-Claudin 18.2 antibody comprises a sequence selected from a sequence as shown in SEQ ID NO: 2, 10, 18, 26, 34 or 42 or a mutant thereof, the heavy chain variable region CDR2 comprises a sequence selected from a sequence as shown in SEQ ID NO: 3, 11, 19, 27, 35 or 43 or a mutant thereof, the heavy chain variable region CDR3 comprises a sequence selected from a sequence as shown in SEQ ID NO: 4, 12, 20, 28, 36 or 44 or a mutant thereof, the light chain variable region CDR1 comprises a sequence selected from a sequence as shown in SEQ ID NO: 50 or 58 or a mutant thereof, the light chain variable region CDR2 comprises a sequence selected from a sequence as shown in SEQ ID NO: 51 or 59 or a mutant thereof, and the light chain variable region CDR3 comprises a sequence selected from a sequence as shown in SEQ ID NO: 52 or 60 or a mutant thereof; or~~

~~the heavy chain variable region CDR1 of the anti-Claudin 18.2 antibody comprises a sequence selected from a sequence as shown in SEQ ID NO: 68, 76, 84, 92, 100, 108 or 116 or a mutant thereof, the heavy chain variable region CDR2 comprises a sequence selected from a sequence as shown in SEQ ID NO: 69, 77, 85, 93, 101, 109 or 117 or a mutant thereof, the heavy chain variable region CDR3 comprises a sequence selected from a sequence as shown in SEQ ID NO: 70, 78, 86, 94, 102, 110 or 118 or a mutant thereof, the light chain variable region CDR1 comprises a sequence selected from a sequence as shown in SEQ ID NO: 124 or 132 or a mutant thereof, the light chain variable region CDR2 comprises a sequence selected from a sequence as shown in SEQ ID NO: 125 or 133 or a mutant thereof, and the light chain variable region CDR3 comprises a sequence selected from a sequence as shown in SEQ ID NO: 126 or 134 or a mutant thereof; or~~

~~the heavy chain variable region CDR1, CDR2 and CDR3 of the anti-Claudin 18.2 antibody are selected from the following sequence combinations:~~

~~(1) SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4,
(2) SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12,
(3) SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20,
(4) SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28,
(5) SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36,
(6) SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44,
(7) SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70,
(8) SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 78,
(9) SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 86,
(10) SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 94,
(11) SEQ ID NO: 100, SEQ ID NO: 101, SEQ ID NO: 102,
(12) SEQ ID NO: 108, SEQ ID NO: 109, SEQ ID NO: 110,
(13) SEQ ID NO: 116, SEQ ID NO: 117, SEQ ID NO: 118,
the light chain variable region CDR1, CDR2 and CDR3 of the anti-Claudin 18.2-
antibody are selected from the following sequence combinations:~~

~~(1) SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52,
(2) SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60,
(3) SEQ ID NO: 124, SEQ ID NO: 125, SEQ ID NO: 126,
(4) SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134;
preferably, the heavy chain variable region CDR1, CDR2 and CDR3 of the anti-
Claudin 18.2 antibody are selected from the following sequence combinations:~~

~~(1) SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4,
(2) SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12,
(3) SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20,
(4) SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28,
(5) SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36,
(6) SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44,
the light chain variable region CDR1, CDR2 and CDR3 of the anti-Claudin 18.2-
antibody are selected from the following sequence combinations:~~

~~(1) SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52,
(2) SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60; or
preferably, the heavy chain variable region CDR1, CDR2 and CDR3 of the anti-
Claudin 18.2 antibody are selected from the following sequence combinations:~~

~~(1) SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70,
(2) SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 78,
(3) SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 86,
(4) SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 94,
(5) SEQ ID NO: 100, SEQ ID NO: 101, SEQ ID NO: 102,
(6) SEQ ID NO: 108, SEQ ID NO: 109, SEQ ID NO: 110,
(7) SEQ ID NO: 116, SEQ ID NO: 117, SEQ ID NO: 118,
the light chain variable region CDR1, CDR2 and CDR3 of the anti-Claudin 18.2-
antibody are selected from the following sequence combinations:~~

~~(1) SEQ ID NO: 124, SEQ ID NO: 125, SEQ ID NO: 126,
(2) SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134.~~

~~3. The antibody drug conjugate of claim 1, its pharmaceutically acceptable salt, solvate or solvate of said salt, wherein:~~

~~the heavy chain variable region FR1 of the anti-Claudin 18.2 antibody comprises a sequence selected from a sequence as shown in SEQ ID NO: 5, 13, 21, 29, 37, 45, 71, 79, 87, 95, 103, 111 or 119 or a mutant thereof, the heavy chain variable region FR2 comprises a sequence selected from a sequence as shown in SEQ ID NO: 6, 14, 22, 30, 38, 46, 72, 80, 88,~~

~~96, 104, 112 or 120 or a mutant thereof, the heavy chain variable region FR3 comprises a sequence selected from a sequence as shown in SEQ ID NO: 7, 15, 23, 31, 39, 47, 73, 81, 89, 97, 105, 113 or 121 or a mutant thereof, the heavy chain variable region FR4 comprises a sequence selected from a sequence as shown in SEQ ID NO: 8, 16, 24, 32, 40, 48, 74, 82, 90, 98, 106, 114 or 122 or a mutant thereof, the light chain variable region FR1 comprises a sequence selected from a sequence as shown in SEQ ID NO: 53, 61, 127 or 135 or a mutant thereof, the light chain variable region FR2 comprises a sequence selected from a sequence as shown in SEQ ID NO: 54, 62, 128 or 136 or a mutant thereof, the light chain variable region FR3 comprises a sequence selected from a sequence as shown in SEQ ID NO: 55, 63, 129 or 137 or a mutant thereof, and the light chain variable region FR4 comprises a sequence selected from a sequence as shown in SEQ ID NO: 56, 64, 130 or 138 or a mutant thereof;~~

~~preferably, the heavy chain variable region FR1 of the anti-Claudin 18.2 antibody comprises a sequence selected from a sequence as shown in SEQ ID NO: 5, 13, 21, 29, 37 or 45 or a mutant thereof, the heavy chain variable region FR2 comprises a sequence selected from a sequence as shown in SEQ ID NO: 6, 14, 22, 30, 38 or 46 or a mutant thereof, the heavy chain variable region FR3 comprises a sequence selected from a sequence as shown in SEQ ID NO: 7, 15, 23, 31, 39 or 47 or a mutant thereof, the heavy chain variable region FR4 comprises a sequence selected from a sequence as shown in SEQ ID NO: 8, 16, 24, 32, 40 or 48 or a mutant thereof, the light chain variable region FR1 comprises a sequence selected from a sequence as shown in SEQ ID NO: 53 or 61, or a mutant thereof, the light chain variable region FR2 comprises a sequence selected from a sequence as shown in SEQ ID NO: 54 or 62 or a mutant thereof, the light chain variable region FR3 comprises a sequence selected from a sequence as shown in SEQ ID NO: 55 or 63 or a mutant thereof, and the light chain variable region FR4 comprises a sequence selected from a sequence as shown in SEQ ID NO: 56 or 64 or a mutant thereof; or~~

~~preferably, the heavy chain variable region FR1 of the anti-Claudin 18.2 antibody comprises a sequence selected from a sequence as shown in SEQ ID NO: 71, 79, 87, 95, 103, 111 or 119 or a mutant thereof, the heavy chain variable region FR2 comprises a sequence selected from a sequence as shown in SEQ ID NO: 72, 80, 88, 96, 104, 112 or 120 or a mutant thereof, the heavy chain variable region FR3 comprises a sequence selected from a sequence as shown in SEQ ID NO: 73, 81, 89, 97, 105, 113 or 121 or a mutant thereof, the heavy chain variable region FR4 comprises a sequence selected from a sequence as shown in SEQ ID NO: 74, 82, 90, 98, 106, 114 or 122 or a mutant thereof, the light chain variable region FR1 comprises a sequence selected from a sequence as shown in SEQ ID NO: 127 or 135 or a mutant thereof, the light chain variable region FR2 comprises a sequence selected from SEQ ID NO: 128 or 136 or a mutant thereof, the light chain variable region FR3 comprises a sequence selected from a sequence as shown in SEQ ID NO: 129 or 137 or a mutant thereof, and the light chain variable region FR4 comprises a sequence selected from a sequence as shown in SEQ ID NO: 130 or 138 or a mutant thereof; or~~

~~preferably, the heavy chain variable region FR1, FR2, FR3, FR4 of the anti-Claudin 18.2 antibody are selected from the following sequence combinations:~~

- ~~(1) SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8,~~
- ~~(2) SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16,~~
- ~~(3) SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24,~~
- ~~(4) SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32,~~
- ~~(5) SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40,~~
- ~~(6) SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48,~~
- ~~(7) SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74,~~
- ~~(8) SEQ ID NO: 79, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 82,~~
- ~~(9) SEQ ID NO: 87, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90,~~

~~(10) SEQ ID NO: 95, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 98,~~
~~(11) SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, SEQ ID NO: 106,~~
~~(12) SEQ ID NO: 111, SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 114,~~
~~(13) SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 122,~~
~~the light chain variable region FR1, FR2, FR3 and FR4 of the anti-Claudin 18.2-~~
~~antibody are selected from the following sequence combinations:~~
~~(1) SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56,~~
~~(2) SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64,~~
~~(3) SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130,~~
~~(4) SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137, SEQ ID NO: 138;~~
~~more preferably, the heavy chain variable region FR1, FR2, FR3 and FR4 of the anti-~~
~~Claudin 18.2 antibody are selected from the following sequence combinations:~~
~~(1) SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8,~~
~~(2) SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16,~~
~~(3) SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24,~~
~~(4) SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32,~~
~~(5) SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40,~~
~~(6) SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 48,~~
~~the light chain variable region FR1, FR2, FR3 and FR4 of the anti-Claudin 18.2-~~
~~antibody are selected from the following sequence combinations:~~
~~(1) SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56,~~
~~(2) SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64; or~~
~~more preferably, the heavy chain variable region FR1, FR2, FR3 and FR4 of the anti-~~
~~Claudin 18.2 antibody are selected from the following sequence combinations:~~
~~(1) SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74,~~
~~(2) SEQ ID NO: 79, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 82,~~
~~(3) SEQ ID NO: 87, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90,~~
~~(4) SEQ ID NO: 95, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 98,~~
~~(5) SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, SEQ ID NO: 106,~~
~~(6) SEQ ID NO: 111, SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 114,~~
~~(7) SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 122,~~
~~the light chain variable region FR1, FR2, FR3 and FR4 of the anti-Claudin 18.2-~~
~~antibody are selected from the following sequence combinations:~~
~~(1) SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130,~~
~~(2) SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137, SEQ ID NO: 138.~~

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

the heavy chain variable region of the anti-Claudin 18.2 antibody is selected from a sequence as shown in SEQ ID NO: 1, 9, 17, 25, 33, 41, 67, 75, 83, 91, 99, 107 or 115,

the light chain variable region of the anti-Claudin 18.2 antibody is selected from a sequence as shown in SEQ ID NO: 49, 57, 123 or 131;

preferably, the heavy chain variable region of the anti-Claudin 18.2 antibody is selected from a sequence as shown in SEQ ID NO: 1, 9, 17, 25, 33 or 41,

the light chain variable region of the anti-Claudin 18.2 antibody is selected from a sequence as shown in SEQ ID NO: 49 or 57; or

preferably, the heavy chain variable region of the anti-Claudin 18.2 antibody is selected from a sequence as shown in SEQ ID NO: 67, 75, 83, 91, 99, 107 or 115;

the light chain variable region of the anti-Claudin 18.2 antibody is selected from a sequence as shown in SEQ ID NO: 123 or 131.

~~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 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-iodoacetyl)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. 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.~~

Claims

1. Antibody drug conjugate, its pharmaceutically acceptable salt, solvate or solvate of said salt, the antibody drug conjugate has the structure shown in Formula I,



Formula I

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;

D is MMAE; and

p is 2.0-8.0.

2. The antibody drug conjugate according to 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.

3. The antibody drug conjugate according to claim 1, its pharmaceutically acceptable salt, solvate or solvate of said salt, wherein p is 3.0-4.0.

4. The antibody drug conjugate according to claim 1, its pharmaceutically acceptable salt, solvate or solvate of said salt, wherein p is 3.0-3.8.

5. The antibody drug conjugate according to claim 1, its pharmaceutically acceptable salt, solvate or solvate of said salt, wherein p is 3.0, 3.4, 3.5 or 3.8.

6. The antibody drug conjugate according to claim 1, its pharmaceutically acceptable salt, solvate or solvate of said salt, wherein p is 3.8.

7. A composition comprising the antibody drug conjugate according to any one of claims 1-6, 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.

8. Use of the antibody drug conjugate of any one of claims 1-6, its pharmaceutically acceptable salt, solvate or solvate of said salt or the composition of claim 7 in the preparation of medicaments for preventing and/or treating a disease associated with Claudin 18.2.

9. Use of the antibody drug conjugate, its pharmaceutically acceptable salt, solvate or solvate of said salt, or the composition of claim 8, wherein the disease associated with Claudin 18.2 is gastric cancer, adenocarcinoma of the esophagogastric junction, and pancreatic cancer.

10. Use of the antibody drug conjugate, its pharmaceutically acceptable salt, solvate or solvate of said salt, or the composition of claim 8, wherein the disease associated with Claudin 18.2 is gastric cancer.

11. The antibody drug conjugate of any one of claims 1-6, its pharmaceutically acceptable salt, solvate or solvate of said salt, or the composition of claim 7, for use in preventing and/or treating a disease associated with Claudin 18.2.

12. The antibody drug conjugate, its pharmaceutically acceptable salt, solvate or solvate of said salt, or the composition for use according to claim 11, wherein the disease associated with Claudin 18.2 is gastric cancer, adenocarcinoma of the esophagogastric junction, and pancreatic cancer.

13. The antibody drug conjugate, its pharmaceutically acceptable salt, solvate or solvate of said salt, or the composition for use according to claim 11, wherein the disease associated with Claudin 18.2 is gastric cancer.