SUMMARY

The disclosure provides anti-CDH17 antibodies and antibody-drug conjugates and methods of using the same. The anti-cancer efficacy of antibody-drug conjugates is thought to rely on their uptake by cancer cells expressing the surface antigen, so the insufficient internalization of CDH17-targeting monoclonal antibody is an urgent problem to be solved. In general ADC development needs to take into account all these key components, including the selection of target antigen, antibody, toxin drug, as well as linker.

The technical problem to be solved by the present disclosure is to develop the advanced anti-CDH17 antibody-drug conjugate which show very strong antitumor effects in cancers. The antitumor effects may be due to higher DAR and robust endocytosis.

Specifically, the present disclosure encompasses the following:

The present disclosure relates to an antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof and pharmaceutical use thereof, wherein the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof comprises an anti-CDH17 antibody or an antigen-binding fragment thereof conjugated to a toxin drug optionally by a linker.

The present disclosure relates to an antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof and pharmaceutical use thereof, wherein the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof comprises an anti-CDH17 antibody or an antigen-binding fragment thereof conjugated to a toxin drug optionally by a linker, wherein the anti-CDH17 antibody or the antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region of the antibody, wherein: a) a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 01, SEQ ID NO: 11 and SEQ ID NO: 22, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 32, SEQ ID NO: 43 and SEQ ID NO: 48, respectively; or b) a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 02, SEQ ID NO: 12 and SEQ ID NO:23, respectively; and a light chain variable region sequence comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 33, SEQ ID NO: 44 and SEQ ID NO: 49, respectively; or c) a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 03, SEQ ID NO: 13 and SEQ ID NO: 24, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 34, SEQ ID NO: 43 and SEQ ID NO: 50, respectively; or d) a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 04, SEQ ID NO: 14 and SEQ ID NO: 25, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 35, SEQ ID NO: 43 and SEQ ID NO: 49, respectively; or e) a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 05, SEQ ID NO: 15 and SEQ ID NO: 26, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 36, SEQ ID NO: 43 and SEQ ID NO: 51, respectively; or f) a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 06, SEQ ID NO: 16 and SEQ ID NO: 27, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 37, SEQ ID NO: 43 and SEQ ID NO: 52,

respectively; or g) a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 07, SEQ ID NO:17 and SEQ ID NO: 28, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 38, SEQ ID NO: 45 and SEQ ID NO: 53, respectively; or h) a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 01, SEQ ID NO: 18 and SEQ ID NO: 22, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 39, SEQ ID NO: 43 and SEQ ID NO: 48, respectively; or i) a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 08, SEQ ID NO:19 and SEQ ID NO:29, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 40, SEQ ID NO: 46 and SEQ ID NO: 51, respectively; or j) a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 09, SEQ ID NO:20 and SEQ ID NO: 30, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 41, SEQ ID NO: 43 and SEQ ID NO: 52, respectively; or k) a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 10, SEQ ID NO:21 and SEQ ID NO: 31, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 42, SEQ ID NO: 47 and SEQ ID NO: 54, respectively.

Where mentioned above, the anti-CDH17 antibody or antigen-binding fragment thereof in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof is a monoclonal antibody or antigen-binding fragment thereof, a polyclonal antibody or antigen-binding fragment thereof, a multi-specific antibody or antigen-binding fragment thereof, a murine antibody or antigen-binding fragment thereof, a chimeric antibody or antigen-binding fragment thereof, a humanized antibody or antigen-binding fragment thereof, a recombinant antibody or antigen-binding fragment thereof, a human antibody or antigen-binding fragment thereof; preferably, the multi-specific antibody is a bispecific antibody, a tri-specific antibody or a tetra-specific antibody.

Where mentioned above, the anti-CDH17 antibody or the antigen-binding fragment thereof in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof comprises a heavy chain variable region comprising an amino acid sequence selected from: SEQ ID NOs: 55-65, or sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or a light chain variable region comprising an amino acid sequence selected from: SEQ ID NOs: 66-76, or sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith.

Where mentioned above, the anti-CDH17 antibody or the antigen-binding fragment thereof in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof comprises a heavy chain variable region comprising an amino acid sequence selected from: SEQ ID NOs: 65, 61, 59, or sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or a light chain variable region comprising an amino acid sequence selected from: SEQ ID NOs: 76, 72, 70, or sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith.

Where mentioned above, the anti-CDH17 antibody or the antigen-binding fragment thereof in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof comprises: a) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 55, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 66, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or b) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 56, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 67, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or c) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 57, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 68, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or d) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 58, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 69, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or e) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 59, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 70, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or f) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 60, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 71, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or g) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 61, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 72, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or h) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 62, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 73, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or i) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 63, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 74, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or j) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 64, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 75, or having the amino acid sequence of at least

80%, 85%, 90%, 95% or 99% sequence identity therewith; or k) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 65, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 76, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith.

Where mentioned above, the anti-CDH17 antibody or the antigen-binding fragment thereof in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof comprise: a) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 55; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 66; or b) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 56; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 67; or c) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 57; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 68; or d) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 58; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 69; or e) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 59; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 70; or f) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 60; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 71; or g) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 61; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 72; or h) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 62; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 73; or i) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 63; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 74; or j) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 64; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 75; or k) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 65; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 76.

Where mentioned above, the anti-CDH17 antibody or the antigen-binding fragment thereof in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof comprises: a) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 55; and the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 66; or b) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 56; and the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 67; or c) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 57; and the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 68; or d) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 58; and the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 69; or e) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 59; and the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 70; or f) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 60; and the light

chain variable region having the amino acid sequence as shown in SEQ ID NO: 71; or g) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 61; and the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 72; or h) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 62; and the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 73; or i) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 63; and the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 74; or j) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 64; and the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 75; or k) the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 65; and the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 76.

Where mentioned above, the anti-CDH17 antibody or the antigen-binding fragment thereof in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof comprises human antibody constant regions; preferably, the heavy chain constant region of the human antibody constant regions is selected from constant regions of human IgG1, IgG2, IgG3 and IgG4 and conventional variants thereof, and the light chain constant region of the human antibody constant regions is selected from κ and λ chain constant regions of human antibody and conventional variants thereof; more preferably, the full-length antibody comprises a human antibody heavy chain constant region of SEQ ID NO: 99 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith, a human light chain constant region of SEQ ID NO: 100 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; further preferably the full-length antibody comprises a human antibody heavy chain constant region of SEQ ID NO: 99 and a human light chain constant region of SEQ ID NO: 100.

Where mentioned above, the anti-CDH17 antibody or the antigen-binding fragment thereof in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof comprises a heavy chain having the amino acid sequence as shown in SEQ ID NO: 97 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith, and a light chain having the amino acid sequence as shown in SEQ ID NO: 98 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or

a heavy chain having the amino acid sequence as shown in SEQ ID NO: 89 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith, and a light chain having the amino acid sequence as shown in SEQ ID NO: 90 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or

a heavy chain having the amino acid sequence as shown in SEQ ID NO: 85 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith, and a light chain having the amino acid sequence as shown in SEQ ID NO: 86 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith.

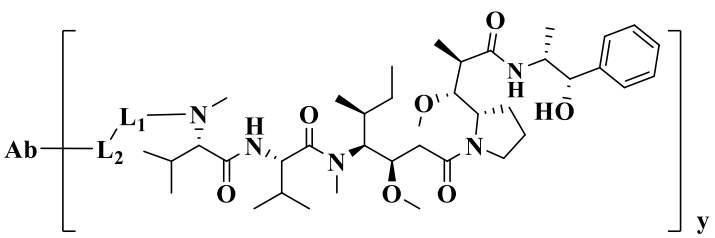
Where mentioned above, the anti-CDH17 antibody or the antigen-binding fragment thereof in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof comprises: a) a heavy chain having the amino acid sequence as shown in SEQ ID NO:77 and a light chain having the amino acid sequence as shown in SEQ ID NO:78; or b) a heavy chain having the amino acid sequence as shown

in SEQ ID NO:79 and a light chain having the amino acid sequence as shown in SEQ ID NO:80; or c) a heavy chain having the amino acid sequence as shown in SEQ ID NO:81 and a light chain having the amino acid sequence as shown in SEQ ID NO:82; or d) a heavy chain having the amino acid sequence as shown in SEQ ID NO:83 and a light chain having the amino acid sequence as shown in SEQ ID NO:84; or e) a heavy chain having the amino acid sequence as shown in SEQ ID NO:85 and a light chain having the amino acid sequence as shown in SEQ ID NO:86; or f) a heavy chain having the amino acid sequence as shown in SEQ ID NO:87 and a light chain having the amino acid sequence as shown in SEQ ID NO:88; or g) a heavy chain having the amino acid sequence as shown in SEQ ID NO:89 and a light chain having the amino acid sequence as shown in SEQ ID NO:90; or h) a heavy chain having the amino acid sequence as shown in SEQ ID NO:91 and a light chain having the amino acid sequence as shown in SEQ ID NO:92; or i) a heavy chain having the amino acid sequence as shown in SEQ ID NO:93 and a light chain having the amino acid sequence as shown in SEQ ID NO:94; or j) a heavy chain having the amino acid sequence as shown in SEQ ID NO:95 and a light chain having the amino acid sequence as shown in SEQ ID NO:96; or k) a heavy chain having the amino acid sequence as shown in SEQ ID NO:97 and a light chain having the amino acid sequence as shown in SEQ ID NO:98.

In some examples of the present disclosure, the anti-CDH17 antibody or the antigen-binding fragment in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof, the anti-CDH17 antigen-binding fragment is selected from the group consisting of Fab, Fab', F(ab')2, variable fragment (Fv), single chain variable fragment (scFv), dimerized domain V (diabody), disulfide stabilized Fv (dsFv) and CDR-containing peptides.

Where mentioned above, the toxin drug in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof is selected from the group consisting of tubulin inhibitors, topoisomerase inhibitors, DNA intercalators, and RNA polymerase inhibitors or pharmaceutically acceptable salt, ester or analog thereof; preferably the toxin drug is selected from the group consisting of auristatin analogues, camptothecin derivatives, maytansine analogues; more preferably the toxin drug is selected from the group consisting of MMAE, MMAF, Exatecan, MMAD, DM1, DM4, eribulin, pyrrolobenzodiazepine(PBD), DGN-549-C, SN-38, irinotecan, topotecan, belotecan, rubitecan, doxorubicin, PNU-159682, duocarmycin, daunorubicin, mitoxantrone, podophyllotoxin, etoposide, α-amanitin, or a pharmaceutically acceptable salt, ester or analog thereof.

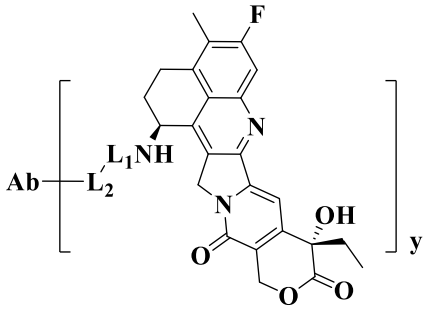
Where mentioned above, the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof is an antibody drug conjugate of general formula (A):



(A)

wherein: L_1 and L_2 are linking units; y is a number selected from 1 to 10, preferably a number selected from 2 to 8, and most preferably 2, 4, 5, 6, 7, 8; Ab is the anti-CDH17 antibody or antigen-binding fragment thereof mention above.

Where mentioned above, the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof is an antibody drug conjugate of general formula (I):

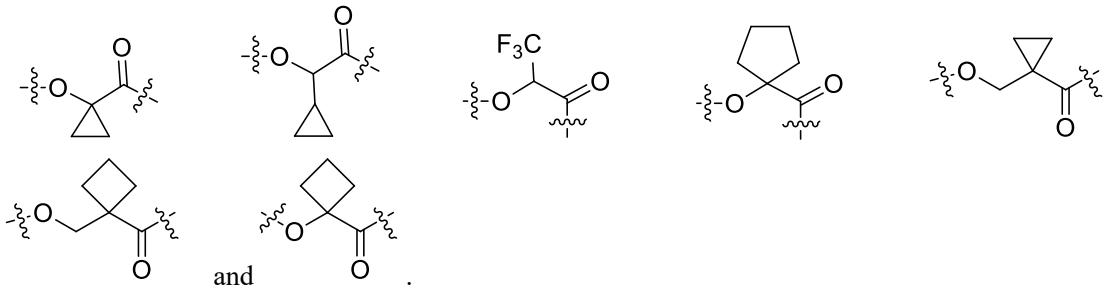


(I)

,

wherein: L_1 and L_2 are linking units; y is a number selected from 1 to 10, preferably a number selected from 2 to 8, and most preferably 2, 4, 6, 8; Ab is the anti-CDH17 antibody or antigen-binding fragment thereof mentioned above.

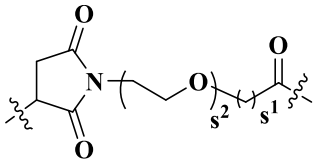
Where mentioned above, in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof L_1 is selected from the group consisting of:



and .

In some examples of the present disclosure, in the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof according to any one of the aforementioned examples wherein L_2 is $-L^a-L^b-L^c-L^d-$, wherein

the L^a is as shown in general formula (II-a):



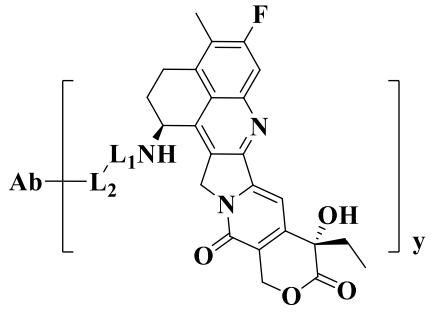
(II-a)

,

wherein: s^1 and s^2 are each independently an integer selected from 0-8, Preferably, s^1 and s^2 are independently selected from 1, 2, 3, 4, 5 or 6; Or, s^1 is an integer from 1-8, s^2 is 0, Preferably, s^1 is selected from 4, 5, 6, 7 or 8, and s^2 is 0; Or, s^2 is selected from an integer from 2 to 8, s^1 is 2, Preferably, s^2 is selected from 2, 3, 4, 5 or 6, and s^1 is 2; the L^b is a chemical bond; the L^c is a tetrapeptide residue; preferably, L^c is a tetrapeptide residue of glycine-glycine-phenylalanine-

glycine (GGFG); the L^d is $–NR_1(CR_2R_3)s^3$-, wherein R_1, R_2 and R_3 are identical or different and are each independently hydrogen or alkyl, and s^3 is 1 or 2; wherein the L^a terminus is connected to Ab, and the L^d terminus is connected to L_1.

In the present disclosure, the antibody-drug conjugate of general formula (I), or a pharmaceutically acceptable salt or solvate thereof,

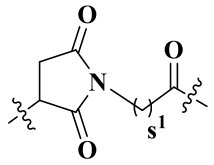


(I) ;

wherein:

L_1 and L_2 are linking units; wherein the L_2 is -La-Lb-Lc-Ld-,

the La is as shown in general formula (II-b):



(II) , s1 is selected from 4, 5, 6, 7 or 8;

the Lb is a chemical bond;

the Lc is a tetrapeptide residue; preferably, Lc is a tetrapeptide residue of glycine-glycine-phenylalanine-glycine (GGFG);

the Ld is –NR1(CR2R3)s3-, wherein R1, R2 and R3 are identical or different and are each independently hydrogen or alkyl, and s3 is 1 or 2; wherein the La terminus is connected to Ab, and the Ld terminus is connected to L1;

y is a number selected from 1 to 10, preferably a number selected from 2 to 8, and most preferably 2, 4, 6, 8;

Ab is the anti-CDH17 antibody or antigen-binding fragment thereof, wherein the anti-CDH17 antibody or the antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region of the antibody, wherein:

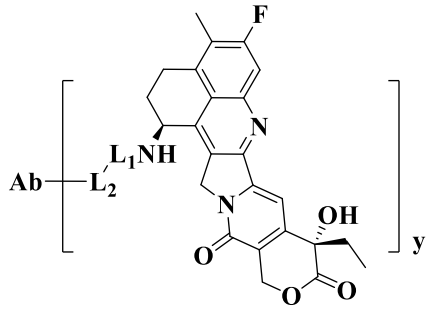
a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 10, SEQ ID NO:21 and SEQ ID NO: 31, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 42, SEQ ID NO: 47 and SEQ ID NO: 54, respectively; or

a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 07, SEQ ID NO:17 and SEQ ID NO: 28, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 38, SEQ ID NO: 45 and SEQ ID NO: 53, respectively; or

a heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 having the amino acid

sequences as shown in SEQ ID NO: 05, SEQ ID NO: 15 and SEQ ID NO: 26, respectively; and a light chain variable region comprises LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 36, SEQ ID NO: 43 and SEQ ID NO: 51, respectively.

In one aspect, the present disclosure provides an antibody-drug conjugate of general formula (I), or a pharmaceutically acceptable salt or solvate thereof,

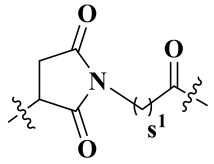


(I) ;

wherein:

L_1 and L_2 are linking units; wherein L_2 is -La-Lb-Lc-Ld-, and

La is as shown in general formula (II-b):



(II-b) , where s^1 is selected from 4, 5, 6, 7 or 8;

Lb is a chemical bond;

Lc is a tetrapeptide residue; preferably, a tetrapeptide residue of glycine-glycine-phenylalanine-glycine (GGFG) (SEQ ID NO: 101);

Ld is –NR1(CR2R3)s3-, wherein R1, R2 and R3 are identical or different and are each independently hydrogen or alkyl, and s3 is 1 or 2; wherein the La terminus is connected to Ab, and the Ld terminus is connected to L1;

y is a number selected from 1 to 10, preferably a number selected from 2 to 8, and most preferably 2, 4, 6, or 8;

Ab is an anti-CDH17 antibody or antigen-binding fragment thereof, wherein the anti-CDH17 antibody or the antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region, and wherein:

the heavy chain variable region comprises an HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 10, SEQ ID NO:21 and SEQ ID NO: 31, respectively; and the light chain variable region comprises an LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 42, SEQ ID NO: 47 and SEQ ID NO: 54, respectively; or

the heavy chain variable region comprises an HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 07, SEQ ID NO:17 and SEQ ID NO: 28, respectively; and the light chain variable region comprises an LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 38, SEQ ID NO: 45 and SEQ ID NO: 53, respectively; or

the heavy chain variable region comprises an HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 05, SEQ ID NO: 15 and SEQ ID NO: 26, respectively; and the light chain variable region comprises an LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 36, SEQ ID NO: 43 and SEQ ID NO: 51, respectively.

In some examples of the present disclosure, the anti-CDH17 antibody or antigen-binding fragment thereof is a monoclonal antibody or antigen-binding fragment thereof, a polyclonal antibody or antigen-binding fragment thereof, a multi-specific antibody or antigen-binding fragment thereof, a murine antibody or antigen-binding fragment thereof, a chimeric antibody or antigen-binding fragment thereof, a humanized antibody or antigen-binding fragment thereof, a recombinant antibody or antigen-binding fragment thereof, a human antibody or antigen-binding fragment thereof; preferably, the multi-specific antibody is a bispecific antibody, a tri-specific antibody or a tetra-specific antibody.

In some examples of the present disclosure, the anti-CDH17 antibody or antigen-binding fragment thereof comprises: a heavy chain variable region comprising an amino acid sequence selected from: SEQ ID NOs: 65, 61, 59, or sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or a light chain variable region comprising an amino acid sequence selected from: SEQ ID NOs: 76, 72, 70, or sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith.

In some examples of the present disclosure, the anti-CDH17 antibody or antigen-binding fragment thereof comprising:the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 65, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 76, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 61, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 72, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 59, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 70, or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith;

In some examples of the present disclosure, the anti-CDH17 antibody or antigen-binding fragment thereof comprising: the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 65; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 76; or the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 61; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 72; or the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 59; and/or the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 70.

In some examples of the present disclosure, the anti-CDH17 antibody or antigen-binding fragment thereof comprising: the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 65 and the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 76; or the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 61 and the light chain variable region having the amino acid sequence as

shown in SEQ ID NO: 72; or the heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 59 and the light chain variable region having the amino acid sequence as shown in SEQ ID NO: 70.

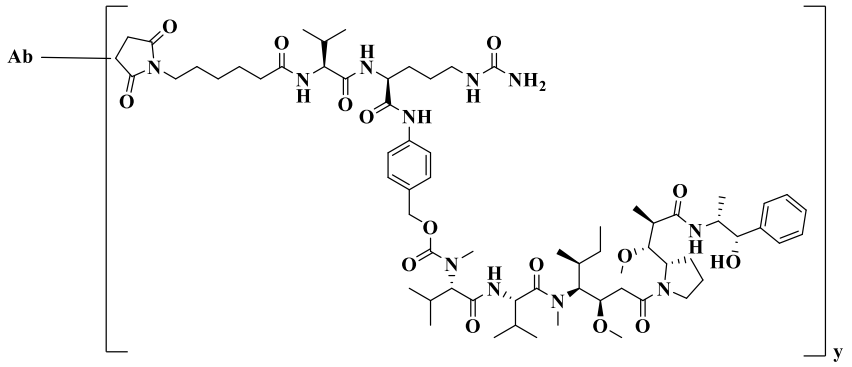
In some examples of the present disclosure, the anti-CDH17 antibody or antigen-binding fragment thereof further comprising human antibody constant regions; preferably, the heavy chain constant region of the human antibody constant regions is selected from constant regions of human IgG1, IgG2, IgG3 and IgG4 and conventional variants thereof, and the light chain constant region of the human antibody constant regions is selected from κ and λ chain constant regions of human antibody and conventional variants thereof; more preferably, the full-length antibody comprises a human antibody heavy chain constant region of SEQ ID NO: 99 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith, a human light chain constant region of SEQ ID NO: 100 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; further preferably, the full-length antibody comprises a human antibody heavy chain constant region of SEQ ID NO: 99 and a human light chain constant region of SEQ ID NO: 100.

In some examples of the present disclosure, the anti-CDH17 antibody or antigen-binding fragment thereof comprising: a heavy chain having the amino acid sequence as shown in SEQ ID NO: 97 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith, and a light chain having the amino acid sequence as shown in SEQ ID NO: 98 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or a heavy chain having the amino acid sequence as shown in SEQ ID NO: 89 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith, and a light chain having the amino acid sequence as shown in SEQ ID NO: 90 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or a heavy chain having the amino acid sequence as shown in SEQ ID NO: 85 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith, and a light chain having the amino acid sequence as shown in SEQ ID NO: 86 or having the amino acid sequence of at least 80%, 85%, 90%, 95% or 99% sequence identity therewith.

In some examples of the present disclosure, the anti-CDH17 antibody or antigen-binding fragment thereof comprising: a heavy chain having the amino acid sequence as shown in SEQ ID NO: 97 and a light chain having the amino acid sequence as shown in SEQ ID NO: 98; or a heavy chain having the amino acid sequence as shown in SEQ ID NO: 89 and a light chain having the amino acid sequence as shown in SEQ ID NO: 90; or a heavy chain having the amino acid sequence as shown in SEQ ID NO: 85 and a light chain having the amino acid sequence as shown in SEQ ID NO: 86.

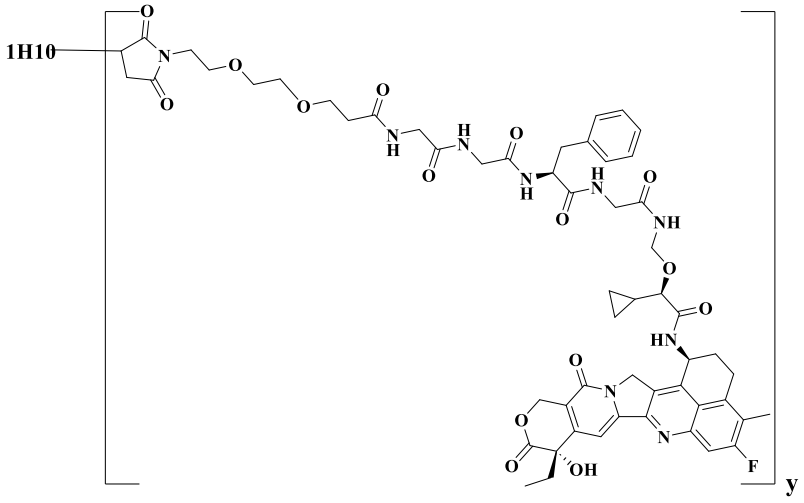
In some examples of the present disclosure, the anti-CDH17 antigen-binding fragment is selected from the group consisting of Fab, Fab', F(ab')2, variable fragment (Fv), single chain variable fragment (scFv), dimerized domain V (diabody), disulfide stabilized Fv (dsFv) and CDR-containing peptides.

Where mentioned above, the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof is as the following structure:



y is a number selected from 1 to 10, preferably a number selected from 2 to 8, and most preferably 2, 4, 5, 6, 7, 8; Ab is the anti-CDH17 antibody or antigen-binding fragment thereof mention above.

Where mentioned above, the antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof is selected from the group consisting of the following compounds:



The present disclosure provides a pharmaceutical composition comprising the antibody-drug conjugate as described herein and one or more pharmaceutically acceptable excipients, diluents or carriers.

In another aspect, the present disclosure provides a pharmaceutical composition comprising the antibody-drug conjugate as described herein, or the pharmaceutically acceptable salt or solvate thereof, and one or more pharmaceutically acceptable carriers.

The present disclosure provides use of the antibody-drug conjugate as described herein or a pharmaceutical composition comprising the

same as a medicament.

The present disclosure provides use of the antibody-drug conjugate as described herein or a pharmaceutical composition comprising the same in preparing a medicament for the treatment and/or prevention of a CDH17-mediated disease or condition.

In some examples of the present disclosure, the CDH17-mediated disease or condition is a tumor or cancer. The tumor or cancer is associated with high CDH17 expression. Or, the tumor or cancer is associated with moderate CDH17 expression.

The present disclosure provides use of the antibody-drug conjugate as described herein or a pharmaceutical composition comprising the same in preparing a medicament for the treatment or prevention of a tumor or cancer; preferably the tumor or cancer is gastrointestinal cancer, pancreatic cancer, gallbladder cancer, cholangiocarcinoma, stomach cancer, intestinal cancer, ovarian cancer, colorectal cancer, lung cancer, breast cancer, anal cancer, prostate cancer, kidney cancer, bladder cancer, pharynx cancer, cancer of the nose, skin cancer, oral cancer, cancer of the tongue, esophageal cancer, vaginal cancer, cervical cancer, cancer of the spleen, testicular cancer, or glioblastoma.

In another aspect, the present disclosure provides the antibody-drug conjugate or pharmaceutically acceptable salt or solvate thereof as described herein, or the pharmaceutical composition as described herein for use in therapy.

In another aspect, the present disclosure provides use of the antibody-drug conjugate or pharmaceutically acceptable salt or solvate thereof as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for the treatment and/or prevention of a CDH17-mediated disease or condition, wherein:

(i) the CDH17-mediated disease or condition is a tumor or cancer; or

(ii) the CDH17-mediated disease or condition is a tumor or cancer associated with moderate or high CDH17 expression.

In another aspect, the present disclosure provides use of the antibody drug conjugate or pharmaceutically acceptable salt or solvate thereof as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for the treatment and/or prevention of a tumor or cancer; optionally wherein the tumor or cancer is gastrointestinal cancer, pancreatic cancer, gallbladder cancer, cholangiocarcinoma, stomach cancer, intestinal cancer, ovarian cancer, colorectal cancer, lung cancer, breast cancer, anal cancer, prostate cancer, kidney cancer, bladder cancer, pharynx cancer, cancer of the nose, skin cancer, oral cancer, cancer of the tongue, esophageal cancer, vaginal cancer, cervical cancer, cancer of the spleen, testicular cancer, or glioblastoma.

The present disclosure further relates to a method for treating and/or preventing a tumor or cancer, wherein the method comprises administering to a patient in need thereof a therapeutically effective dose of the antibody-drug conjugate as described herein or a pharmaceutical composition comprising the same; preferably the tumor or cancer is associated with high CDH17 expression, or the tumor or cancer is associated with moderate CDH17 expression.

The present disclosure further relates to a method for treating or preventing a tumor or cancer, wherein the method comprises administering to a patient in need thereof a therapeutically effective dose of the antibody-drug conjugate as described herein or a pharmaceutical composition comprising the same; preferably the tumor or cancer is gastrointestinal cancer, pancreatic cancer, gallbladder cancer, cholangiocarcinoma, stomach cancer, intestinal cancer, ovarian cancer, colorectal cancer, lung cancer, breast cancer, anal cancer, prostate cancer, kidney cancer, bladder cancer, pharynx cancer, cancer of the nose, skin cancer, oral cancer, cancer of the tongue, esophageal cancer, vaginal cancer, cervical cancer, cancer of the spleen, testicular cancer, or glioblastoma.

The active compound (e.g., a ligand-drug conjugate according to the present disclosure, or the pharmaceutically acceptable salt or solvate thereof) may be formulated in a form suitable for administration by any suitable route, preferably in a form of a unit dose, or in a form of a single dose that can be self-administered by a subject. The unit dose of the present disclosure may be in a tablet, a capsule, a cachet, a vial, a powder, a granule, a lozenge, a suppository, a regenerating powder or a liquid formulation.

The administration dose of the active compound or composition used in the treatment method of the present disclosure will generally vary with the severity of the disease, the weight of the subject, and the efficacy of the active compound. However, as a general guide, a suitable unit dose may be 0.01 to 1000 mg.

The pharmaceutical composition of the present disclosure may comprise, in addition to the active compound, one or more excipients selected from the group consisting of: a filler, a diluent, a binder, a wetting agent, a disintegrating agent, an excipient and the like. Depending on the method

of administration, the composition may comprise 0.01 to 99.9 wt.% of active compound.

Advantageous Effects of the Disclosure:

The CDH17 antibody and the antibody-drug conjugate provided by the present disclosure have good affinity for cell surface antigens, good endocytosis efficiency and high tumor inhibition efficiency as well as wider drug application windows, and are suitable for clinical drug application.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1. *In vitro* binding characterization of hybridoma clones to AsPC1 (A), GP2d (B), SW480 (C) cells by flow cytometric analysis.

Figure 2. Cell internalization activity of selected hybridoma clones were characterized using indirect killing assay.

Figure 3. *In vitro* binding characterization of anti-CDH17 recombinant antibodies to AsPC1 (A) cells and SW480 (B) cells was determined by flow cytometric analysis, with HBMAB81 served as positive control and B12 as isotype control antibody (C).

Figure 4. Dose-response curves of anti-CDH17 recombinant antibody internalization by indirect-killing assay.

Figure 5. Binding competition: (A) 20B4; (B) HBMAB81.

Figure 6. Dose-response curves of ADCs *in vitro* cytotoxicity activities on tumor cells.

Figure 7. Comparison of the *in vitro* cytotoxicity of anti-CDH17 ADCs with different DAR values in GP2d cell line

Figure 8. Comparison of the *in vitro* cytotoxicity of anti-CDH17 ADCs with different DAR values in AsPC1 cell line

Figure 9. Comparison of the *in vitro* cytotoxicity of anti-CDH17 ADCs with different DAR values in SK-CO-1 cell line

Figure 10. Comparison of the *in vitro* cytotoxicity of anti-CDH17 ADCs with different DAR values in AsPC1 cell line

Figure 11. Anti-CDH17 ADCs inhibit tumor growth in AsPC1 tumor-bearing mice

Figure 12. Anti-CDH17 ADCs inhibit tumor growth in GP2d tumor-bearing mice.

Figure 13. Anti-CDH17 ADCs inhibit tumor growth in SNU16 tumor-bearing mice.

Figure 14. Pharmacokinetic test of anti-CDH17 ADCs. Serum concentration levels of total antibody (A) and ADC (B)

Figure 15. Pharmacokinetic test of anti-CDH17 ADCs. Serum concentration levels of total antibody and ADC

DETAILED DESCRIPTION

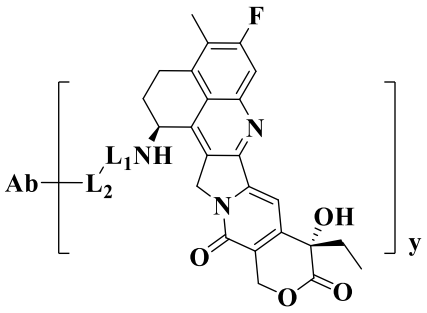
DEFINITIONS OF TERMS

The present invention is based on the development of an antibody which can specifically bind to CDH17. Antibodies of the present invention may optionally be conjugated to a growth inhibitory agent or cytotoxic agent such as a toxin, including, for example, a topoisomerase inhibitor or auristatin.

The titles used in the present section are for convenience of specification only, and do not limit the present invention. Unless otherwise defined herein, the scientific and technical terms used herein have the same meaning as commonly understood by those skilled in the art. Further, unless the

What claimed is:

1. An antibody-drug conjugate of general formula (I), or a pharmaceutically acceptable salt or solvate thereof,

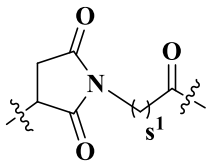


(I) ;

wherein:

L_1 and L_2 are linking units; wherein L_2 is -La-Lb-Lc-Ld-, and

La is as shown in general formula (II-b):



(II-b) , where s^1 is selected from 4, 5, 6, 7 or 8;

Lb is a chemical bond;

Lc is a tetrapeptide residue; preferably, a tetrapeptide residue of glycine-glycine-phenylalanine-glycine (GGFG) (SEQ ID NO: 101);

Ld is –NR1(CR2R3)s3-, wherein R1, R2 and R3 are identical or different and are each independently hydrogen or alkyl, and s3 is 1 or 2; wherein the La terminus is connected to Ab, and the Ld terminus is connected to L1;

y is a number selected from 1 to 10, preferably a number selected from 2 to 8, and most preferably 2, 4, 6, or 8;

Ab is an anti-CDH17 antibody or antigen-binding fragment thereof, wherein the anti-CDH17 antibody or the antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region, and wherein:

the heavy chain variable region comprises an HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 10, SEQ ID NO:21 and SEQ ID NO: 31, respectively; and the light chain variable region comprises an LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 42, SEQ ID NO: 47 and SEQ ID NO: 54, respectively; or

the heavy chain variable region comprises an HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 07, SEQ ID NO:17 and SEQ ID NO: 28, respectively; and the light chain variable region comprises an LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 38, SEQ ID NO: 45 and SEQ ID NO: 53, respectively; or

the heavy chain variable region comprises an HCDR1, HCDR2 and HCDR3 having the amino acid sequences as shown in SEQ ID NO: 05, SEQ ID NO: 15 and SEQ ID NO: 26, respectively;

and the light chain variable region comprises an LCDR1, LCDR2 and LCDR3 having the amino acid sequences as shown in SEQ ID NO: 36, SEQ ID NO: 43 and SEQ ID NO: 51, respectively.

2. The antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof according to claim 1, wherein the anti-CDH17 antibody or antigen-binding fragment thereof is a monoclonal antibody or antigen-binding fragment thereof, a polyclonal antibody or antigen-binding fragment thereof, a multi-specific antibody or antigen-binding fragment thereof, a murine antibody or antigen-binding fragment thereof, a chimeric antibody or antigen-binding fragment thereof, a humanized antibody or antigen-binding fragment thereof, a recombinant antibody or antigen-binding fragment thereof, a human antibody or antigen-binding fragment thereof; preferably, the multi-specific antibody is a bispecific antibody, a tri-specific antibody or a tetra-specific antibody.

3. The antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof according to claim 1 or 2 , wherein the anti-CDH17 antibody or antigen-binding fragment thereof comprises: a heavy chain variable region comprising an amino acid sequence selected from: SEQ ID NOs: 65, 61, 59, or sequences having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or a light chain variable region comprising an amino acid sequence selected from: SEQ ID NOs: 76, 72, 70, or sequences having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith.

4. The antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof according to anyone of claims 1 to 3, wherein the anti-CDH17 antibody or antigen-binding fragment thereof comprises:

a heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 65, or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or a light chain variable region having the amino acid sequence as shown in SEQ ID NO: 76, or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith;

or

a heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 61, or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or a light chain variable region having the amino acid sequence as shown in SEQ ID NO: 72, or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith;

or

a heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 59, or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and/or a light chain variable region having the amino acid sequence as shown in SEQ ID NO: 70, or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith.

5. The antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof according to anyone of claims 1 to 4, wherein the anti-CDH17 antibody or antigen-binding fragment thereof comprises:

(i) a heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 65; and/or a light chain variable region having the amino acid sequence as shown in SEQ ID NO: 76;

or

(ii) a heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 61; and/or a light chain variable region having the amino acid sequence as shown in SEQ ID NO: 72;

or

(iii) a heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 59; and/or a light chain variable region having the amino acid sequence as shown in SEQ ID NO: 70; or

(iv) a heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 65 and a light chain variable region having the amino acid sequence as shown in SEQ ID NO: 76;

or

(v) a heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 61 and a light chain variable region having the amino acid sequence as shown in SEQ ID NO: 72;

or

(vi) a heavy chain variable region having the amino acid sequence as shown in SEQ ID NO: 59 and a light chain variable region having the amino acid sequence as shown in SEQ ID NO: 70.

6. The antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof according to anyone of claims 1 to 5, wherein the anti-CDH17 antibody or antigen-binding fragment thereof further comprises human antibody constant regions; optionally wherein:

(i) the heavy chain constant region of the human antibody constant regions is selected from constant regions of human IgG1, IgG2, IgG3 and IgG4 and conventional variants thereof, and the light chain constant region of the human antibody constant regions is selected from κ and λ chain constant regions of human antibody and conventional variants thereof;

(ii) the full-length antibody comprises a human antibody heavy chain constant region of SEQ ID NO: 99 or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith, and a human light chain constant region of SEQ ID NO: 100 or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; and / or

(iii) the full-length antibody comprises a human antibody heavy chain constant region of SEQ ID NO: 99 and a human light chain constant region of SEQ ID NO: 100.

7. The antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof according to any one of claims 1 to 6, wherein the anti-CDH17 antibody or antigen-binding fragment thereof comprises:

(i) a heavy chain having the amino acid sequence as shown in SEQ ID NO: 97 or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith, and a light chain having the amino acid sequence as shown in SEQ ID NO: 98 or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or

(ii) a heavy chain having the amino acid sequence as shown in SEQ ID NO: 89 or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith, and a light chain having the amino acid sequence as shown in SEQ ID NO: 90 or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or

(iii) a heavy chain having the amino acid sequence as shown in SEQ ID NO: 85 or an amino acid sequence having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith, and a light chain having the amino acid sequence as shown in SEQ ID NO: 86 or an amino acid sequence

having at least 80%, 85%, 90%, 95% or 99% sequence identity therewith; or

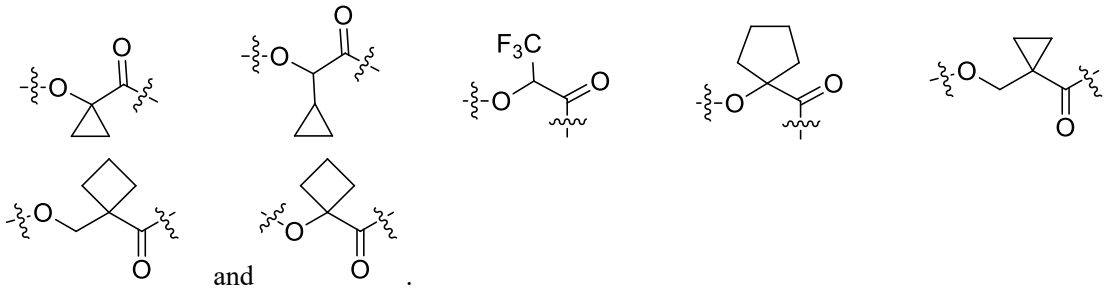
(iv) a heavy chain having the amino acid sequence as shown in SEQ ID NO: 97 and a light chain having the amino acid sequence as shown in SEQ ID NO: 98; or

(v) a heavy chain having the amino acid sequence as shown in SEQ ID NO: 89 and a light chain having the amino acid sequence as shown in SEQ ID NO: 90; or

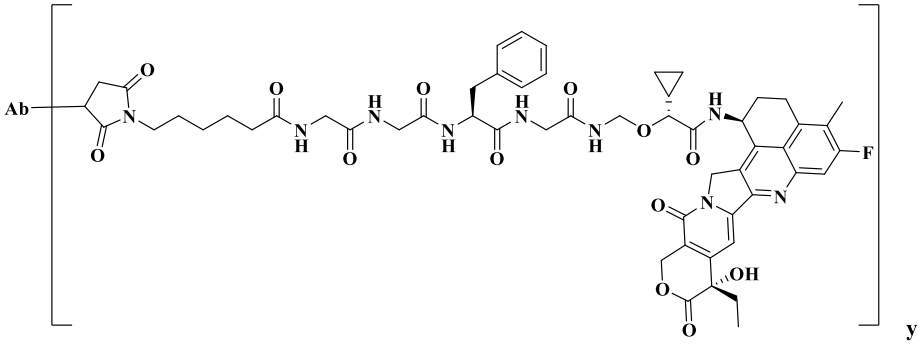
(vi) a heavy chain having the amino acid sequence as shown in SEQ ID NO: 85 and a light chain having the amino acid sequence as shown in SEQ ID NO: 86.

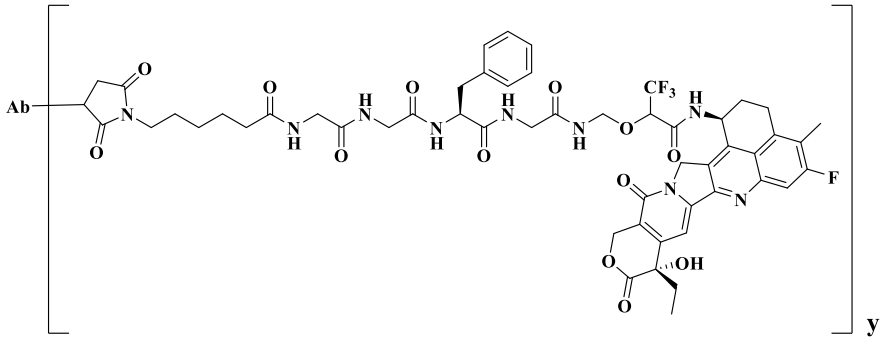
8. The antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof according to any one of claims 1 to 7, wherein the anti-CDH17 antigen-binding fragment is selected from the group consisting of: a Fab, Fab', F(ab')2, variable fragment (Fv), single chain variable fragment (scFv), dimerized domain V (diabody), disulfide stabilized Fv (dsFv), and a CDR-containing peptide.

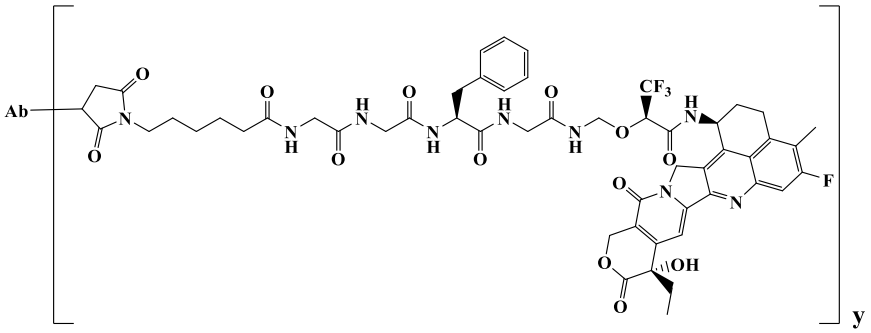
9. The antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof according to any one of claims 1 to 8, wherein L_1 is selected from the group consisting of:

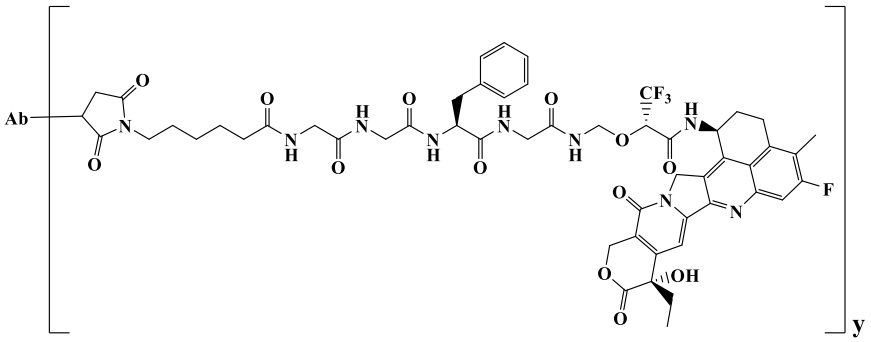


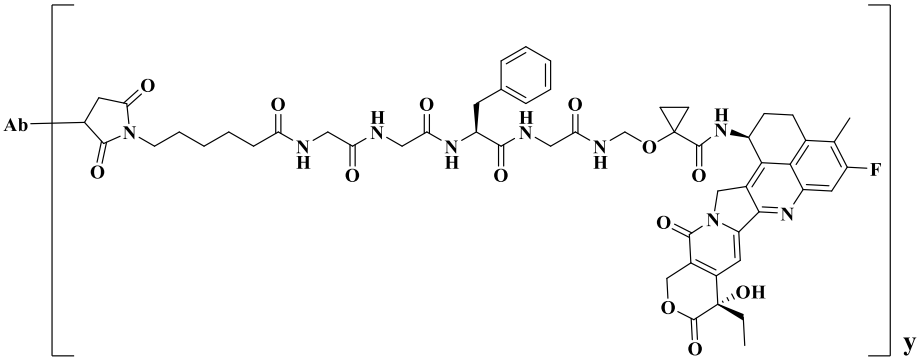
10. The antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof according to any one of claims 1 to 9, wherein the antibody-drug conjugate has the following structure:

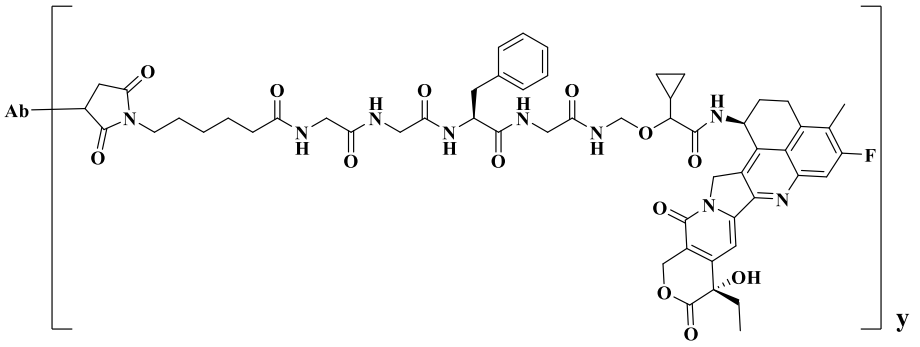


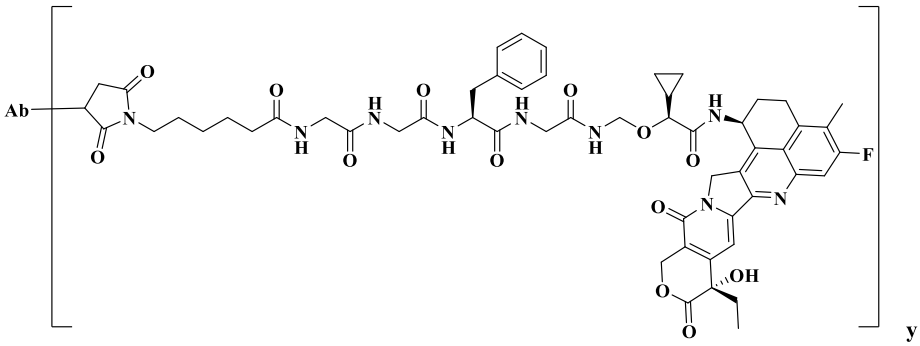


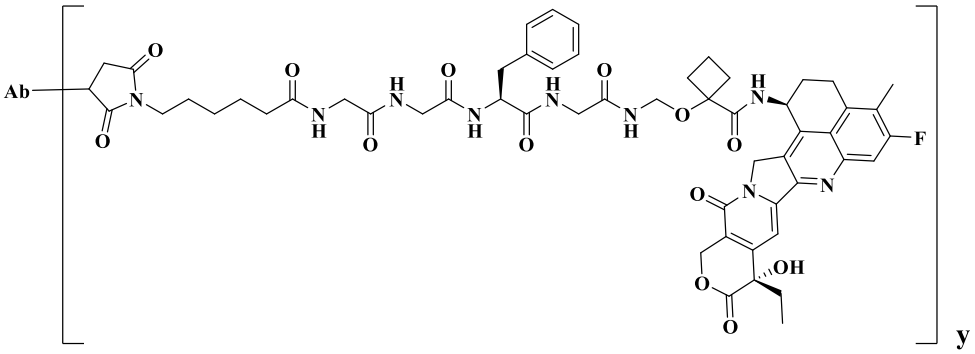


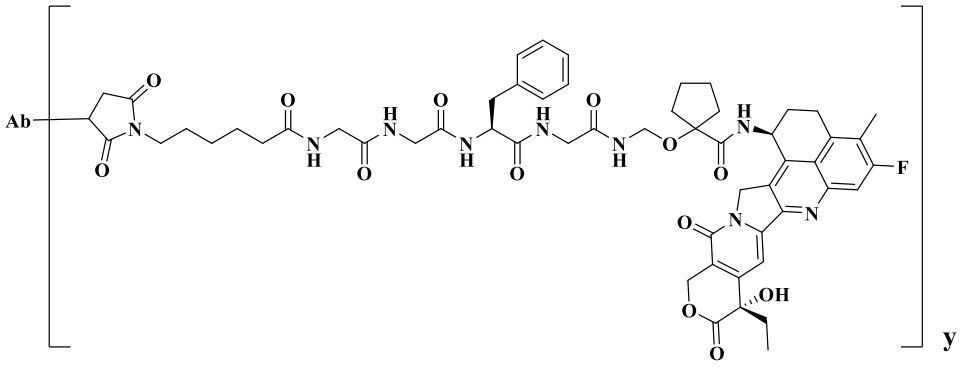


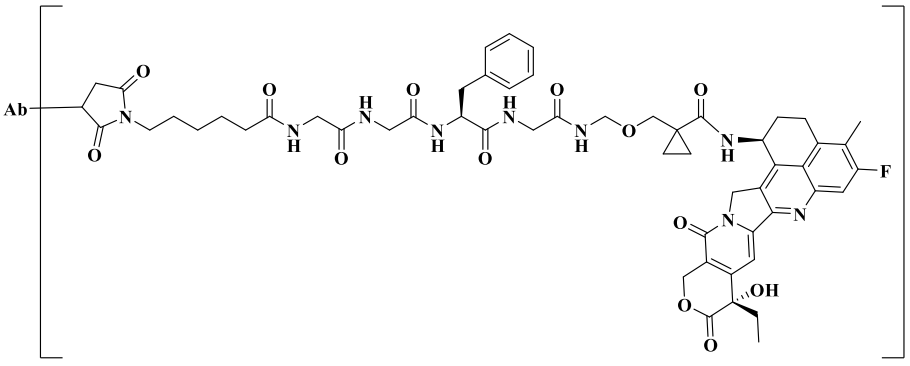




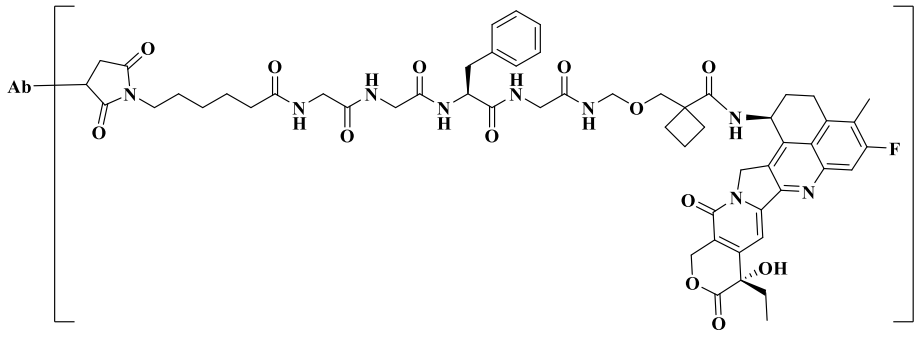








or

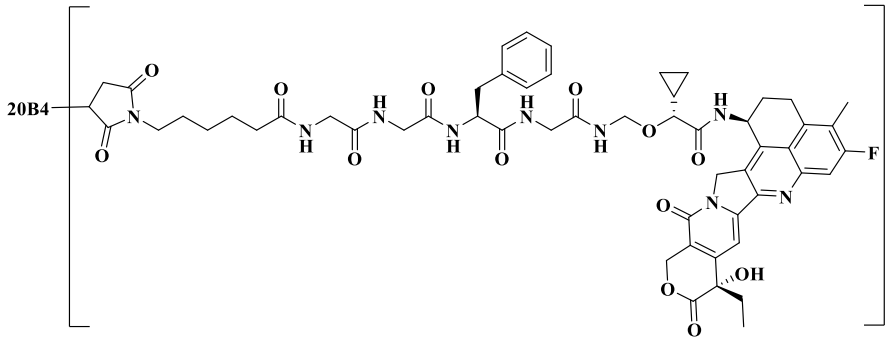


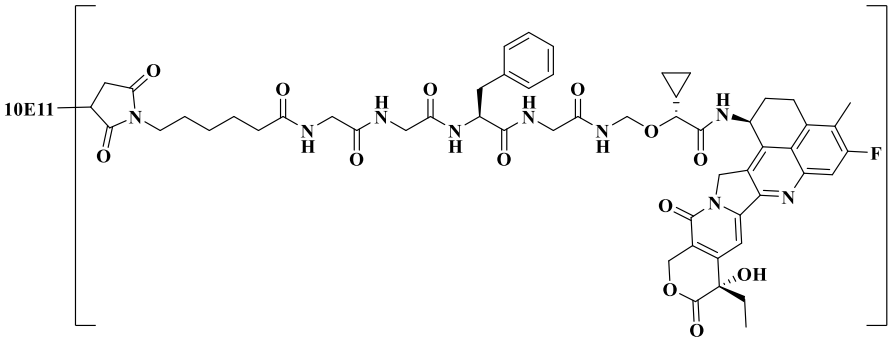
;

wherein y is a number selected from 1 to 10, preferably a number selected from 2 to 8, and most preferably 2, 4, 5, 6, 7, or 8; and

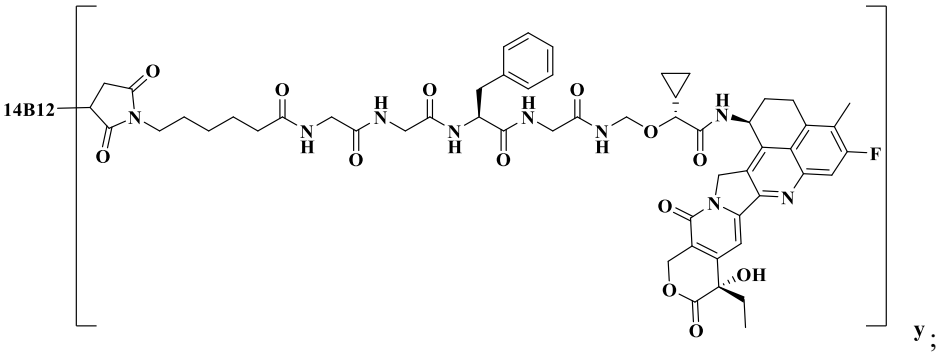
Ab is an anti-CDH17 antibody or antigen-binding fragment thereof as defined in any one of claims 1 to 8.

11. The antibody-drug conjugate or the pharmaceutically acceptable salt or solvate thereof according to any one of claims 1 to 10, wherein the antibody-drug conjugate is selected from the group consisting of the following compounds:





and



wherein:

y is a number selected from 1 to 10, preferably a number selected from 2 to 8, more preferably a number selected from 4 to 8, further preferably a number selected from 4 to 6 or 6 to 8, and most preferably 4, 5, 6, 7 or 8.

12. A pharmaceutical composition comprising the antibody-drug conjugate according to any one of claims 1 to 11, or the pharmaceutically acceptable salt or solvate thereof, and one or more pharmaceutically acceptable carriers.

13. The antibody-drug conjugate or pharmaceutically acceptable salt or solvate thereof according to any one of claims 1 to 11, or the pharmaceutical composition according to claim 12 for use in therapy.

14. Use of the antibody-drug conjugate or pharmaceutically acceptable salt or solvate thereof according to any one of claims 1 to 11, or the pharmaceutical composition according to claim 12 in the manufacture of a medicament for the treatment and/or prevention of a CDH17-mediated disease or condition, wherein:

(i) the CDH17-mediated disease or condition is a tumor or cancer; or

(ii) the CDH17-mediated disease or condition is a tumor or cancer associated with moderate or high CDH17 expression.

15. Use of the antibody drug conjugate or pharmaceutically acceptable salt or solvate thereof according to any one of claims 1 to 11, or the pharmaceutical composition according to claim 12 in the manufacture of a medicament for the treatment and/or prevention of a tumor or cancer; optionally wherein the tumor or cancer is gastrointestinal cancer, pancreatic cancer, gallbladder cancer, cholangiocarcinoma, stomach cancer, intestinal cancer, ovarian cancer, colorectal cancer, lung cancer, breast cancer, anal cancer, prostate cancer, kidney cancer, bladder cancer, pharynx cancer, cancer of the nose, skin cancer, oral cancer, cancer of the tongue, esophageal cancer, vaginal cancer, cervical cancer, cancer of the spleen, testicular cancer, or glioblastoma.