

CLAIMS

What is claimed is:

1. An antibody-drug conjugate, comprising a drug moiety covalently attached to an antibody or fragment thereof having binding specificity to a wild-type human claudin 18.2 (CLDN18.2) protein,
 wherein the antibody or the antigen-binding fragment thereof comprises a light chain variable region comprising light chain complementarity determining regions CDRL1, CDRL2, and CDRL3 and a heavy chain variable region comprising heavy chain complementarity determining regions CDRH1, CDRH2, and CDRH3, wherein
 - (a) the CDRL1 has the amino acid sequence of SEQ ID NO:304,
 the CDRL2 has the amino acid sequence of SEQ ID NO:229;
 the CDRL3 has the amino acid sequence of SEQ ID NO:8
 the CDRH1 has the amino acid sequence of SEQ ID NO:242;
 the CDRH2 has the amino acid sequence of SEQ ID NO:263; and
 the CDRH3 has the amino acid sequence of SEQ ID NO: 289;
 or
 - (b) the CDRL1 has the amino acid sequence of SEQ ID NO:309,
 the CDRL2 has the amino acid sequence of SEQ ID NO:227,
 the CDRL3 has the amino acid sequence of SEQ ID NO:13,
 the CDRH1 has the amino acid sequence of SEQ ID NO:246,
 the CDRH2 has the amino acid sequence of SEQ ID NO:311, and
 the CDRH3 has the amino acid sequence of SEQ ID NO:294.

2. The antibody-drug conjugate of claim 1, wherein:
 - the CDRL1 has the amino acid sequence of SEQ ID NO:304,
 - the CDRL2 has the amino acid sequence of SEQ ID NO:229,
 - the CDRL3 has the amino acid sequence of SEQ ID NO:8,
 - the CDRH1 has the amino acid sequence of SEQ ID NO:242,

the CDRH2 has the amino acid sequence of SEQ ID NO:263, and
the CDRH3 has the amino acid sequence of SEQ ID NO:289.

3. The antibody-drug conjugate of claim 2, wherein the antibody or the antigen-binding fragment thereof comprises a light chain variable region comprising an amino acid sequence of SEQ ID NO:203 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:181.

4. The antibody-drug conjugate of claim 1, wherein:
the CDRL1 comprises the amino acid sequence of SEQ ID NO:309,
the CDRL2 comprises the amino acid sequence of SEQ ID NO:227,
the CDRL3 comprises the amino acid sequence of SEQ ID NO:13,
the CDRH1 comprises the amino acid sequence of SEQ ID NO:246,
the CDRH2 comprises the amino acid sequence of SEQ ID NO:311, and
the CDRH3 comprises the amino acid sequence of SEQ ID NO:294.

5. The antibody-drug conjugate of claim 4, wherein the antibody or the fragment thereof comprises a light chain variable region comprising an amino acid sequence of SEQ ID NO:202 and a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:197.

6. The antibody-drug conjugate of any preceding claim, wherein the drug moiety is a cytotoxic or cytostatic agent.

7. The antibody-drug conjugate of claim 6, wherein the drug moiety is a maytansinoid or an auristatin.

8. The antibody-drug conjugate of claim 7, wherein the drug moiety comprises DM1 or DM4.
9. The antibody-drug conjugate of claim 7, wherein the drug moiety comprises monomethyl auristatin E (MMAE) or monomethyl auristatin F (MMAF).
10. The antibody-drug conjugate of any preceding claim, wherein the drug moiety is attached to the antibody or fragment thereof through a linker.
11. The antibody-drug conjugate of claim 10, wherein the linker is hydrolyzable under acidic conditions.
12. Use of the antibody-drug conjugate of any one of claims 1-11 for the manufacture of a medicament for the treatment of cancer.
13. The use of claim 12, wherein the cancer is selected from the group consisting of bladder cancer, liver cancer, colon cancer, rectal cancer, endometrial cancer, leukemia, lymphoma, pancreatic cancer, small cell lung cancer, non-small cell lung cancer, breast cancer, urethral cancer, head and neck cancer, gastrointestinal cancer, stomach cancer, oesophageal cancer, ovarian cancer, renal cancer, melanoma, prostate cancer and thyroid cancer.
14. The use of claim 12, wherein the cancer is gastric cancer.
15. The use of claim 12, wherein the patient has a M149L mutant of the CLDN18.2 protein.