In one aspect, the present disclosure provides a use of an antibody-drug conjugate comprising an antibody having the ability of binding to CLDN18.2 covalently attached to at least one toxin drug moiety, in the manufacture of a medicament for treating or preventing a CLDN18.2-expressing cancer in a cancer patient,

wherein the antibody is selected from the group consisting of:

(a) an antibody binding to CLDN18.2, said antibody comprising an antibody heavy chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 32 and an antibody light chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 39; and
(b) an antibody binding to CLDN18.2, said antibody comprising an antibody heavy chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 30 and an antibody light chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 35,
wherein the antibody is covalently attached to the toxin drug moiety by a linker which is cleavable under intracellular conditions.

In another aspect, the present disclosure provides an antibody-drug conjugate comprising an antibody having the ability of binding to CLDN18.2 covalently attached to at least one toxin drug moiety, wherein the antibody is selected from the group consisting of:

(a) an antibody binding to CLDN18.2, said antibody comprising an antibody heavy chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 32 and an antibody light chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 39; and
(b) an antibody binding to CLDN18.2, said antibody comprising an antibody heavy chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 30 and an antibody light chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 35,
wherein the antibody is covalently attached to the toxin drug moiety by a linker which is cleavable under intracellular conditions.

In another aspect, the present disclosure provides a use of the antibody drug conjugate as described herein, the pharmaceutical composition as described herein or the medical

preparation as described herein in the manufacture of a medicament for treating or preventing a CLDN18.2-expressing cancer.

CLAIMS

1. Use of an antibody-drug conjugate comprising an antibody having the ability of binding to CLDN18.2 covalently attached to at least one toxin drug moiety, in the manufacture of a medicament for treating or preventing a CLDN18.2-expressing cancer in a cancer patient,
wherein the antibody is selected from the group consisting of:
(a) an antibody binding to CLDN18.2, said antibody comprising an antibody heavy chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 32 and an antibody light chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 39; and
(b) an antibody binding to CLDN18.2, said antibody comprising an antibody heavy chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 30 and an antibody light chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 35,
wherein the antibody is covalently attached to the toxin drug moiety by a linker which is cleavable under intracellular conditions.

2. The use of claim 1, wherein the antibody-drug conjugate is to be internalized into cells.

3. The use of claim 1 or 2, wherein the antibody having the ability of binding to CLDN18.2 specifically binds to CLDN18.2.

4. The use of any one of claims 1 to 3, wherein the antibody-drug conjugate specifically binds to CLDN18.2.

5. The use of any one of claims 1 to 4, wherein the antibody having the ability of binding to CLDN18.2 is a monoclonal antibody or an antigen-binding fragment thereof, a bispecific antibody, a humanized or chimeric antibody.

6. The use of any one of claims 1 to 5, wherein the antibody having the ability of binding to CLDN18.2 binds to an extracellular domain of CLDN18.2.

7. The use of any one of claims 1 to 6, wherein the antibody having the ability of binding to CLDN18.2 binds to the first extracellular loop of CLDN18.2.

8. The use of any one of claims 1 to 6, wherein the toxin drug moiety is cell membrane-permeable.

9. The use of any one of claims 1 to 8, wherein the toxin drug moiety is a cytotoxic or cytostatic agent.

10. The use of any one of claims 1 to 9, wherein the toxin drug moiety is a maytansinoid or an auristatin.

11. The use of claim 10, wherein the maytansinoid is selected from the group consisting of DM1 and DM4.

12. The use of claim 10, wherein the auristatin is selected from the group consisting of monomethyl auristatin E (MMAE) and monomethyl auristatin F (MMAF).

13. The use of any one of claims 1 to 12, wherein the linker is hydrolyzable at a pH of less than 5.5.

14. The use of any one of claims 1 to 13, wherein the linker is cleavable by an intracellular protease.

15. The use of any one of claims 1 to 14, wherein the linker is a cathepsin-cleavable linker.

16. The use of any one of claims 1 to 15, wherein the linker comprises a dipeptide.

17. The use of claim 16, wherein the dipeptide is valine-citrulline or phenylalanine-lysine.

18. The use of any one of claims 1 to 17, wherein the antibody-drug conjugate is to be administered in an amount effective for the treatment or prevention of the CLDN18.2-expressing cancer.

19. The use of any one of claims 1 to 18, wherein the antibody-drug conjugate is to be administered at a dose of between 3 to 30 mg/kg body weight.

20. The use of any one of claims 1 to 19, wherein the antibody-drug conjugate is to be administered at a dose of between 9 to 90 mg/m^2 body surface of a human patient.

21. The use of any one of claims 1 to 20, wherein a single dose of the antibody-drug conjugate or two or more doses of the antibody-drug conjugate are to be administered.

22. The use of any one of claims 1 to 21, wherein the antibody-drug conjugate is to be administered by intravenous injection.

23. The use of any one of claims 1 to 22, wherein the medicament is formulated to be administered in combination with surgery, chemotherapy and/or radiation therapy.

24. The use of any one of claims 1 to 23, wherein the cancer is an adenocarcinoma, in particular an advanced adenocarcinoma.

25. The use of any one of claims 1 to 24, wherein the cancer is selected from the group consisting of gastric cancer, esophageal cancer, pancreatic cancer, lung cancer such as non small cell lung cancer (NSCLC), breast cancer, ovarian cancer, colon cancer, hepatic cancer, head-neck cancer, cancer of the gallbladder and the metastasis thereof, a Krukenberg tumor, peritoneal metastasis and/or lymph node metastasis.

26. The use of any one of claims 1 to 25, wherein the cancer is selected from the group consisting of cancer of the stomach, cancer of the esophagus, in particular the lower esophagus, cancer of the eso-gastric junction and gastroesophageal cancer.

27. The use of any one of claims 1 to 26, wherein the patient is a HER2/neu negative patient or a patient with HER2/neu positive status but not eligible to trastuzumab therapy.

28. The use of any one of claims 1 to 27, wherein CLDN18.2 has the amino acid sequence according to SEQ ID NO: 1.

29. An antibody-drug conjugate comprising an antibody having the ability of binding to CLDN18.2 covalently attached to at least one toxin drug moiety, wherein the antibody is selected from the group consisting of:
(a) an antibody binding to CLDN18.2, said antibody comprising an antibody heavy chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 32 and an antibody light chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 39; and
(b) an antibody binding to CLDN18.2, said antibody comprising an antibody heavy chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 30 and an antibody light chain sequence comprising CDR1, CDR2 and CDR3 of the amino acid sequence represented by SEQ ID NO: 35,
wherein the antibody is covalently attached to the toxin drug moiety by a linker which is cleavable under intracellular conditions.

30. The antibody-drug conjugate of claim 29, wherein the antibody having the ability of binding to CLDN18.2 specifically binds to CLDN18.2.

31. The antibody-drug conjugate of claim 29 or 30, wherein the antibody-drug conjugate specifically binds to CLDN18.2.

32. The antibody-drug conjugate of any one of claims 29 to 31, wherein the antibody having the ability of binding to CLDN18.2 is a monoclonal antibody or an antigen-binding fragment thereof, a bispecific antibody, a humanized or chimeric antibody.

33. The antibody-drug conjugate of any one of claims 29 to 32, wherein the antibody having the ability of binding to CLDN18.2 binds to an extracellular domain of CLDN18.2.

34. The antibody-drug conjugate of any one of claims 29 to 33, wherein the antibody having the ability of binding to CLDN18.2 binds to the first extracellular loop of CLDN18.2.

35. The antibody-drug conjugate of any one of claims 29 to 34, wherein the toxin drug moiety is cell membrane-permeable.

36. The antibody-drug conjugate of any one of claims 29 to 35, wherein toxin drug moiety is a cytotoxic or cytostatic agent.

37. The antibody-drug conjugate of any one of claims 29 to 36, wherein the toxin drug moiety is a maytansinoid or an auristatin.

38. The antibody-drug conjugate of claim 34, wherein the maytansinoid is selected from the group consisting of DM1 and DM4.

39. The antibody-drug conjugate of claim 38, wherein the auristatin is selected from the group consisting of monomethyl auristatin E (MMAE) and monomethyl auristatin F (MMAF).

40. The antibody-drug conjugate of any one of claims 29 to 39, wherein the linker is hydrolyzable at a pH of less than 5.5.

41. The antibody-drug conjugate of any one of claims 29 to 40, wherein the linker is cleavable by an intracellular protease.

42. The antibody-drug conjugate of any one of claims 29 to 41, wherein the linker is a cathepsin-cleavable linker.

43. The antibody-drug conjugate of any one of claims 29 to 42, wherein the linker comprises a dipeptide.

44. The antibody-drug conjugate of claim 43, wherein the dipeptide is valine-citrulline or phenylalanine-lysine.

45. A pharmaceutical formulation comprising the antibody-drug conjugate of any one of claims 29 to 44, and a pharmaceutically acceptable diluent, carrier or excipient.

46. A medical preparation comprising the antibody-drug conjugate of any one of claims 29 to 44.

47. The medical preparation of claim 46 which is present in the form of a kit comprising a container including the antibody-drug conjugate.

48. Use of the antibody-drug conjugate of any one of claims 29 to 44, the pharmaceutical composition of claim 45 or the medical preparation of claim 46 or 47 in the manufacture of a medicament for treating or preventing a CLDN18.2-expressing cancer.

49. The use of claim 48, wherein the medical preparation further including printed instructions for use of the preparation in treating or preventing a CLDN18.2-expressing cancer.

50. The use of claim 48 or 49, wherein the medical preparation is formulated for treating or preventing cancer.