CLAIMS

1. An isolated monoclonal antibody or antigen-binding fragment thereof comprising a heavy chain complementarity determining region 1 (HCDR1), HCDR2, HCDR3, a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the polypeptide sequences of:

(a) SEQ ID NOs: 21, 22, 23, 51, 52, and 53, respectively; or

(b) SEQ ID NOs: 36, 37, 38, 66, 67, and 68, respectively; wherein the antibody or antigen-binding fragment thereof specifically binds claudin 18.2 (CLDN18.2).

2. The isolated monoclonal antibody or antigen-binding fragment thereof of claim 1, comprising a heavy chain variable region having a polypeptide sequence at least 95% identical to SEQ ID NO: 1 or 11, or a light chain variable region having a polypeptide sequence at least 95% identical to SEQ ID NO: 2 or 12.

3. The isolated monoclonal antibody or antigen-binding fragment thereof of claim 1, comprising

(a) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:1, and a light chain variable region having the polypeptide sequence of SEQ ID NO:2; or

(b) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:11, and a light chain variable region having the polypeptide sequence of SEQ ID NO:12.

4. The isolated monoclonal antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof is chimeric or human or humanized.

5. The isolated monoclonal antibody or antigen-binding fragment thereof of claim 4, wherein the isolated humanized antibody or antigen-binding fragment thereof comprises:

(a) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:142, and a light chain variable region having the polypeptide sequence of SEQ ID NO:144;

(b) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:142, and a light chain variable region having the polypeptide sequence of SEQ ID NO:145;

(c) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:143, and a light chain variable region having the polypeptide sequence of SEQ ID NO:144;

(d) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:143, and a light chain variable region having the polypeptide sequence of SEQ ID NO:145;

(e) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:151, and a light chain variable region having the polypeptide sequence of SEQ ID NO:153; or

(f) a heavy chain variable region having the polypeptide sequence of SEQ ID NO:152, and a light chain variable region having the polypeptide sequence of SEQ ID NO:153.

6. An isolated nucleic acid encoding the monoclonal antibody or antigen-binding fragment thereof of claim 1.

7. A vector comprising the isolated nucleic acid of claim 6.

8. A host cell comprising the vector of claim 7.

9. A pharmaceutical composition, comprising the isolated monoclonal antibody or antigen-binding fragment thereof of claim 1 and a pharmaceutically acceptable carrier.

10. The pharmaceutical composition of claim 9 for use in therapy.

11. Use of the pharmaceutical composition of claim 9 in the manufacture of a medicament for the treatment of a claudin 18.2 (CLDN18.2) positive cancer in a subject in need thereof, wherein the pharmaceutical composition is to be administered to the subject.

12. The use of claim 11, wherein the cancer is selected from the group consisting of a gastric cancer, an esophageal cancer, a colon cancer, a pancreatic cancer, a bile duct cancer, and a cholangiocarcinoma.

13. A method of producing the monoclonal antibody or antigen-binding fragment thereof of claim 1, comprising culturing a cell comprising a nucleic acid encoding the monoclonal antibody or antigen-binding fragment thereof under conditions to produce the monoclonal antibody or antigen-binding fragment thereof and recovering the antibody or antigen-binding fragment thereof from the cell or culture.

14. A method of producing a pharmaceutical composition comprising the monoclonal antibody or antigen-binding fragment of claim 1, comprising combining the monoclonal antibody or antigen-binding fragment thereof with a pharmaceutically acceptable carrier to obtain the pharmaceutical composition.

15. An *in vitro* method of determining a level of CLDN18.2 in a sample that is to be obtained from a subject, wherein the sample is to be contacted with the isolated monoclonal antibody or antigen-binding fragment thereof of claim 1; and the level of CLDN18.2 in the sample is to be determined.

16. The method of claim 15, wherein the sample is a tissue sample or a blood sample.

17. The method of claim 16, wherein the tissue sample is a cancer tissue sample.