of at least 1000 mg/m$^2$. Furthermore, the data presented herein demonstrate that the antibody is fully functional in these patients to execute anti-tumor cell effects and evidence for antitumoral activity was obtained.

## SUMMARY

In one aspect, the present disclosure refers to an *in vitro* method of determining the responsiveness of a cancer patient to treatment of a cancer disease with an antibody binding to an epitope of CLDN18.2, said method comprising the step of determining the blood level of one or more markers, wherein the one or more markers are selected from the group consisting of CA 125, CA 15-3, CA 19-9, CEA, IL-2, IL-15, IL-6, IFNγ, and TNFα, wherein the antibody comprises either an antibody heavy chain comprising the amino acid sequence shown in SEQ ID NO: 32 and an antibody light chain comprising the amino acid sequence shown in SEQ ID NO: 39, or wherein the antibody is a functional variant of said antibody which binds to the same epitope of CLDN18.2.

In another aspect, the present disclosure refers to an *in vitro* method of determining whether a cancer patient is amenable to treatment of a cancer disease, said method comprising the step of determining the percentage of CLDN18.2 positive cancer cells, wherein the antibody either comprises an antibody heavy chain comprising the amino acid sequence shown in SEQ ID NO: 32 and an antibody light chain comprising the amino acid sequence shown in SEQ ID NO: 39, or wherein the antibody is a functional variant of said antibody which binds to the same epitope of CLDN18.2.

In yet another aspect, the present disclosure refers to a use of an antibody having the ability of binding to CLDN18.2 and inducing killing of cells expressing CLDN18.2 in the manufacture of a medicament for treating or preventing a cancer disease of a patient, wherein the treatment comprises that an antibody to provide a serum level of at least 50 µg/ml is to be administered to the patient, wherein the antibody comprises either an antibody heavy chain comprising the amino acid sequence shown in SEQ ID NO: 32 and an antibody light chain comprising the amino acid sequence shown in SEQ ID NO: 39, or wherein the antibody is a functional variant of said antibody which binds to the same epitope of CLDN18.2.

In yet another aspect, the present disclosure refers to a use of an antibody having the ability of binding to CLDN18.2 and inducing killing of cells expressing CLDN18.2 in the manufacture of

a medicament for treating or preventing a cancer disease of a patient, wherein the treatment comprises that an antibody to provide a serum level of at least 50 µg/ml is to be administered to the patient, wherein at least 50% of the cancer cells of the patient are CLDN18.2 positive and/or at least 40% of the cancer cells of the patient are positive for surface expression of CLDN18.2, wherein the antibody either comprises an antibody heavy chain comprising the amino acid sequence shown in SEQ ID NO: 32 and an antibody light chain comprising the amino acid sequence shown in SEQ ID NO: 39, or wherein the antibody is a functional variant of said antibody which binds to the same epitope of CLDN18.2.

In yet another aspect, the present disclosure refers to a use of an antibody having the ability of binding to CLDN18.2 and inducing killing of cells expressing CLDN18.2 in the manufacture of a medicament for treating or preventing a cancer disease of a patient, wherein the treatment comprises a combination therapy of the antibody with one or more selected from the group consisting of antiemetics, antispasmodics, parasympatholytics and agents which protect gastric mucosa, wherein the antibody is to be administered to provide a serum level at 50 µg/ml and wherein the antibody comprises either an antibody heavy chain comprising the amino acid sequence shown in SEQ ID NO: 32 and an antibody light chain comprising the amino acid sequence shown in SEQ ID NO: 39, or wherein the antibody is a functional variant of said antibody which binds to the same epitope of CLDN18.2.

In a first example, the present disclosure refers to the use of an antibody having the ability of binding to CLDN18.2 in the manufacture of a medicament for treating or preventing a cancer disease in a patient, wherein the antibody is to be administered so as to provide a serum level of at least 40 µg/ml. In another example, the present disclosure refers to the use of an antibody having the ability of binding to CLDN18.2 in the manufacture of a medicament for treating or preventing a cancer disease in a patient, wherein the antibody is to be administered at a dose of at least 300 mg/m$^2$. In still another example, the present disclosure refers to the use of an antibody having the ability of binding to CLDN18.2 in the manufacture of a medicament for treating or preventing a cancer disease in a patient, wherein at least 50% of the cancer cells of the patient are CLDN18.2 positive and/or at least 40% of the cancer cells of the patient are positive for surface expression of CLDN18.2. In still another example, the present disclosure refers to the use of an antibody having the ability of binding to CLDN18.2 in the manufacture of a medicament for achieving stable disease in a cancer patient. In a further example, the present disclosure refers to the use of an antibody having the ability of binding to CLDN18.2 in the manufacture of a

medicament for treating or preventing a cancer disease in a patient, wherein the antibody is to be administered in multiple doses. In a further example, the present disclosure refers to the use of an antibody having the ability of binding to CLDN18.2 in the manufacture of a medicament for treating or preventing a cancer disease in a patient wherein the antibody is to be administered with one or more selected from the group consisting of antiemetics, antispasmodics, parasympatholytics and agents which protect gastric mucosa. In a further example, the present disclosure refers to an *in vitro* method of determining the responsiveness of a cancer patient to treatment or prevention of a cancer disease comprising determining the blood level of one or more markers in a sample obtained from the patient, wherein the one or more markers are selected from the group consisting of CA 125, CA 15-3, CA 19-9, CEA, IL-2, IL-15, IL-6, IFNγ, and TNFα, and wherein said treatment or prevention of a cancer disease comprises the administration of an antibody having the ability of binding to CLDN18.2. In a further example, the present disclosure refers to an *in vitro* method of determining whether a cancer patient is amenable to treatment or prevention of a cancer disease comprising determining the percentage of CLDN18.2 positive cancer cells in a sample obtained from the cancer patient, and wherein said treatment or prevention of a cancer disease comprises the administration of an antibody having the ability of binding to CLDN18.2.

The present disclosure generally provides a therapy for effectively treating and/or preventing diseases associated with cells expressing CLDN18.2, including cancer diseases such as gastric cancer, esophageal cancer, pancreatic cancer, lung cancer such as non small cell lung cancer (NSCLC), ovarian cancer, colon cancer, hepatic cancer, head-neck cancer, and cancer of the gallbladder and metastases thereof, in particular gastric cancer metastasis such as Krukenberg tumors, peritoneal metastasis and lymph node metastasis. Particularly preferred cancer diseases are adenocarcinomas of the stomach, the esophagus, the pancreatic duct, the bile ducts, the lung and the ovary.

In a first example, the present disclosure provides a method of treating or preventing a cancer disease comprising administering to a patient an antibody having the ability of binding to CLDN18.2, wherein the antibody is administered so as to provide a serum level of at least 40 µg/ml. In different further examples, the antibody is administered so as to provide a serum level of at least 50 µg/ml, at least 150 µg/ml, at least 300 µg/ml, at least 400 µg/ml or at least 500 µg/ml. In different further examples, the antibody is administered so as to provide a serum level of not more than 800 µg/ml, 700 µg/ml, 600 µg/ml, 550 µg/ml or 500 µg/ml. In one example, the

serum level provided is between 40 µg/ml and 700 µg/ml, preferably 40 µg/ml and 600 µg/ml, preferably 50 µg/ml and 500 µg/ml such as between 150 µg/ml and 500 µg/ml or 300 µg/ml and 500 µg/ml. By the term "serum level", as used in the present specification, it is meant a concentration of the substance in question in the blood serum. In one example, the serum level is provided for at least 7 days or at least 14 days. In one example, the method comprises administering a dose/doses of the antibody of at least 300 mg/m$^2$ such as at least 600 mg/m$^2$ and preferably up to 1500 mg/m$^2$, up to 1200 mg/m$^2$ or up to 1000 mg/m$^2$.

In a second example, the present disclosure provides a method of treating or preventing a cancer disease comprising administering to a patient an antibody having the ability of binding to CLDN18.2, wherein the antibody is administered at a dose of at least 300 mg/m$^2$ such as at least 600 mg/m$^2$ and preferably up to 1500 mg/m$^2$, up to 1200 mg/m$^2$ or up to 1000 mg/m$^2$.

In a third example, the present disclosure provides a method of treating or preventing a cancer disease comprising administering to a patient an antibody having the ability of binding to CLDN18.2, wherein at least 50%, preferably 60%, 70%, 80% or 90% of the cancer cells of the patient are CLDN18.2 positive and/or at least 40%, preferably 50% or 60% of the cancer cells of the patient are positive for surface expression of CLDN18.2. In this example, the present disclosure also provides a method of treating or preventing a cancer disease, said method comprising: a. identifying a patient exhibiting at least 50%, preferably 60%, 70%, 80% or 90% CLDN18.2 positive cancer cells and/or at least 40%, preferably 50% or 60% cancer cells which are positive for surface expression of CLDN18.2; and b. administering to said patient an antibody having the ability of binding to CLDN18.2. In one example, at least 95% or at least 98% of the cancer cells of the patient are CLDN18.2 positive. In one example, at least 70%, at least 80% or at least 90% of the cancer cells of the patient are positive for surface expression of CLDN18.2.

In one instance of the method of any of the first to eighth examples disclosed herein, treatment of the cancer disease results in achieving stable disease. In one example, stable disease is achieved for at least 2 months, at least 3 months or at least 6 months.

In a fourth example, the present disclosure provides a method of achieving stable disease in a cancer patient comprising administering to the patient an antibody having the ability of binding to CLDN18.2. In one example, stable disease is achieved for at least 2 months, at least 3 months or at least 6 months.

In one example of the method of any of the first to eighth examples described herein, the antibody is administered in a single dose or in multiple doses.

In a fifth example, the present disclosure provides a method of treating or preventing a cancer disease comprising administering to a patient an antibody having the ability of binding to CLDN18.2, wherein the antibody is administered in multiple doses.

If acccording to the disclosure the antibody is administered in multiple doses, the antibody is preferably administered in at least 3 doses, at least 4 doses, at least 5 doses, at least 6 doses, at least 7 doses, at least 8 doses, at least 9 doses or at least 10 doses and preferably up to 30, 25, 20, 15 or 10 doses. The doses of the antibody are preferably administered in time intervals of at least 7 days, at least 10 days, at least 14 days, or at least 20 days. The doses of the antibody are preferably administered in time intervals of between 7 and 30 days, 10 and 20 days and preferably about 14 days.

In one instance of the method of the third, fourth or fifth example, the antibody is administered so as to provide a serum level of at least 40 µg/ml. In different examples, the antibody is administered so as to provide a serum level of at least 50 µg/ml, at least 150 µg/ml, at least 300 µg/ml, at least 400 µg/ml or at least 500 µg/ml. In different examples, the antibody is administered so as to provide a serum level of not more than 800 µg/ml, 700 µg/ml, 600 µg/ml, 550 µg/ml or 500 µg/ml. In one example, the serum level provided is between 40 µg/ml and 700 µg/ml, preferably 40 µg/ml and 600 µg/ml, preferably 50 µg/ml and 500 µg/ml such as between 150 µg/ml and 500 µg/ml or 300 µg/ml and 500 µg/ml. In one example, the serum level is provided for at least 7 days or at least 14 days. In one example, the method comprises administering a dose/doses of the antibody of at least 300 mg/m$^2$ such as at least 600 mg/m$^2$ and preferably up to 1500 mg/m$^2$, up to 1200 mg/m$^2$ or up to 1000 mg/m$^2$.

In one example of the method of any of the above aspects, the method further comprises administering one or more selected from the group consisting of antiemetics, antispasmodics, parasympatholytics and agents which protect gastric mucosa.

In a sixth example, the present disclosure provides a method of treating or preventing a cancer disease comprising administering to a patient an antibody having the ability of binding to CLDN18.2 and one or more selected from the group consisting of antiemetics, antispasmodics, parasympatholytics and agents which protect gastric mucosa.

If the method of the disclosure comprises administering one or more selected from the group consisting of antiemetics, antispasmodics, parasympatholytics and agents which protect gastric

mucosa, the method in different embodiments comprises administering: (i) an antiemetic and an antispasmodic, (ii) an antispasmodic and an agent which protects gastric mucosa, (iii) an antiemetic and an agent which protects gastric mucosa or (iv) an antiemetic, an antispasmodic and an agent which protects gastric mucosa.

In one example, an antiemetic is administered as antiemetic prophylaxis prior to administration of the antibody. In one example, an antiemetic is administered as antiemetic intervention simultaneously with and/or following administration of the antibody. In one example, the antiemetic comprises a 5-HT3 receptor antagonist and/or a neurokinin 1 (NK1) receptor antagonist. Preferably, the NK1 receptor antagonist comprises Aprepitant (e.g. Emend) and the 5-HT3 receptor antagonist comprises Ondansetron (e.g. Zofran), Granisetron (e.g. Kytril, Sancuso) or Palonosetron (e.g. Aloxi), or a combination of two or more thereof.

In one example, the antispasmodic comprises butylscopolamine (Buscopan).

In one example, the agent which protects gastric mucosa comprises an agent which reduces production of gastric acid. In one embodiment, the agent which protects gastric mucosa comprises an agent selected from the group consisting of proton pump inhibitors, Misoprostol and Omeprazole. In one example, the agent which protects gastric mucosa comprises a combination of a proton pump inhibitor and Misoprostol. In one embodiment, the proton pump inhibitor comprises Pantoprazole (e.g. Pantozol).

In one example, the method of the disclosure comprises administering to the patient a NK1 receptor antagonist such as Aprepitant (e.g. Emend), a 5-HT3 receptor antagonist such as Ondansetron (e.g. Zofran), Granisetron (e.g. Kytril, Sancuso) or Palonosetron (e.g. Aloxi), or a combination of two or more thereof, an antispasmodic such as butylscopolamine (e.g. Buscopan) and a proton pump inhibitor such as Pantoprazole (e.g. Pantozol).

In one example of the method of any of the above first to sixth examples, the antibody is administered by i.v. infusion. In one example, the i.v. infusion is over a time period of between 1 and 4 hours, preferably about 2 hours.

In a seventh example, the present disclosure provides a method of determining the responsiveness of a cancer patient to treatment or prevention of a cancer disease comprising administering an antibody having the ability of binding to CLDN18.2, said method comprising the step of determining the blood level of one or more markers in the patient, wherein the one or more markers are selected from the group consisting of CA 125, CA 15-3, CA 19-9, CEA, IL-2, IL-15, IL-6, IFNγ, and TNFα. In this example, prior to and following administration of an antibody having the ability of binding to CLDN18.2, such as

following administration of a single dose of the antibody, biological samples such as blood may be taken from the patient to establish the level of the one or more markers. Multiple samples may be taken from the same tissue to determine average levels and to account for possible fluctuations in those levels. The level of the one or more markers following administration of the antibody is compared with the level determined prior to administration. The effect of the antibody on the patient can therefore be identified by a desired change in the level of marker following administering an antibody having the ability of binding to CLDN18.2. If the patient shows a desired change in the level of marker following administering an antibody having the ability of binding to CLDN18.2 treatment with the antibody having the ability of binding to CLDN18.2 may be commenced.

In one example, the level is determined in blood, plasma or serum.

In one example, the one or more markers are selected from the group consisting of CA 125, CA 15-3, CA 19-9, CEA, IL-2, IL-15, IFNγ, and TNFα and a decrease in the level of at least one of the markers following administration of the antibody indicates that the patient is responsive to treatment or prevention of a cancer disease.

In one example, the marker is IL-6 and an increase in the level of the marker following administration of the antibody indicates that the patient is responsive to treatment or prevention of a cancer disease.

In an eighth example, the present disclosure provides a method of determining whether a cancer patient is amenable to treatment or prevention of a cancer disease comprising administering an antibody having the ability of binding to CLDN18.2, said method comprising the step of determining the percentage of CLDN18.2 positive cancer cells.

In this example, prior to administration of an antibody having the ability of binding to CLDN18.2, a biological sample such as a tumor sample (e.g. a tumor biopsy) may be taken from the patient to establish the level of CLDN18.2 positive cancer cells. Multiple samples may be taken to determine an average level and to account for possible fluctuations in those levels. If a patient has the desired level of CLDN18.2 positive cancer cells an antibody having the ability of binding to CLDN18.2 may be administered.

In one example, a level of at least 50%, prefeferably 60%, 70%, 80% or 90%, at least 95% or at least 98% CLDN18.2 positive cancer cells indicates that the patient is amenable to treatment or prevention of a cancer disease. In one example, a level of at least 40%, preferably at least 50%, at least 60%, at least 70%, at least 80% or at least 90% cancer cells which are positive for surface expression of CLDN18.2 indicates that the patient is amenable to treatment or prevention of a cancer disease.

The antibody having the ability of binding to CLDN18.2 may bind to native epitopes of CLDN18.2 present on the surface of living cells. In one example, the antibody having the ability of binding to CLDN18.2 binds to the first extracellular loop of CLDN18.2. In one example, the antibody having the ability of binding to CLDN18.2 mediates cell killing by one or more of complement dependent cytotoxicity (CDC) mediated lysis, antibody dependent cellular cytotoxicity (ADCC) mediated lysis, induction of apoptosis and inhibition of proliferation. In one example, the antibody having the ability of binding to CLDN18.2 is a monoclonal, chimeric or humanized antibody, or a fragment of an antibody. In one example, the antibody having the ability of binding to CLDN18.2 is an antibody selected from the group consisting of (i) an antibody produced by and/or obtainable from a clone deposited under the accession no. DSM ACC2737, DSM ACC2738, DSM ACC2739, DSM ACC2740, DSM ACC2741, DSM ACC2742, DSM ACC2743, DSM ACC2745, DSM ACC2746, DSM ACC2747, DSM ACC2748, DSM ACC2808, DSM ACC2809, or DSM ACC2810, (ii) an antibody which is a chimerized or humanized form of the antibody under (i), (iii) an antibody having the specificity of the antibody under (i), and (iv) an antibody comprising the antigen binding portion or antigen binding site, in particular the variable region, of the antibody under (i) and preferably having the specificity of the antibody under (i). In one embodiment, the antibody is coupled to a therapeutic agent such as a toxin, a radioisotope, a drug or a cytotoxic agent.

In one example, the cancer is CLDN18.2 positive. In one example, cells of the cancer express CLDN18.2. In one example, expression of CLDN18.2 is at the surface of the cells. In one example, at least 50%, prefeferably 60%, 70%, 80% or 90% of the cancer cells are CLDN18.2 positive and/or at least 40%, preferably at least 50% of the cancer cells are positive for surface expression of CLDN18.2. In one example, at least 95% or at least 98% of the cancer cells are CLDN18.2 positive. In one examplet, at least 60%, at least 70%, at least 80% or at least 90% of the cancer cells are positive for surface expression of CLDN18.2.

In one example, the cancer disease is selected from the group consisting of gastric cancer, esophageal cancer, pancreatic cancer, lung cancer, ovarian cancer, colon cancer, hepatic cancer, head-neck cancer, cancer of the gallbladder and the metastasis thereof. The cancer disease may be a Krukenberg tumor, peritoneal metastasis and/or lymph node metastasis. In one example, the cancer is an adenocarcinoma, in particular an advanced adenocarcinoma. In one example, 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. In a particularly preferred embodiment, the cancer is gastroesophageal cancer such as metastatic, refractory or recurrent advanced gastroesophageal cancer. The patient may be a HER2/neu negative patient or a patient with HER2/neu positive status but not eligible to trastuzumab therapy. In one example, the patient had prior therapy with at least one drug selected from the group consisting of pyrimidine analogs (e.g. fluorouracil and/or capecitabine), platinum compounds (e.g. cisplatin and/or oxaliplatin), epirubicine, docetaxel and detoxifying agents for antineoplastic treatment (e.g. calcium folinate and/or folinic acid). In one example, the patient has an ECOG performance status of between 0 and 1 and/or a Karnofsky Index of between 70 and 100%. In a particularly preferred example, the patient is a human patient

According to the disclosure, CLDN18.2 preferably has the amino acid sequence according to SEQ ID NO: 1.

The present disclosure also provides the agents described herein such as the antibody having the ability of binding to CLDN18.2 for use in the methods described herein.

Other features and advantages of the instant disclosure will be apparent from the following detailed description and claims.

## BRIEF DESCRIPTION OF THE DRAWINGS

**Figure 1. Mean blood concentration of IMAB362 during the study.**

**Figure 2. ADCC activity of patient PBMCs.** (**A**) PBMCs were purified from 6 patient blood samples 7 days (open square) or 14 days (black squares) after IMAB362 administration. Specific

**Claims**

1. An *in vitro* method of determining the responsiveness of a cancer patient to treatment of a cancer disease with an antibody binding to an epitope of CLDN18.2, said method comprising the step of determining the blood level of one or more markers, wherein the one or more markers are selected from the group consisting of CA 125, CA 15-3, CA 19-9, CEA, IL-2, IL-15, IL-6, IFNγ, and TNFα, wherein the antibody comprises either an antibody heavy chain comprising the amino acid sequence shown in SEQ ID NO: 32 and an antibody light chain comprising the amino acid sequence shown in SEQ ID NO: 39, or wherein the antibody is a functional variant of said antibody which binds to the same epitope of CLDN18.2.

2. The method of claim 1 wherein the level is determined in blood, plasma or serum.

3. The method of claim 1 or 2 wherein the marker is IL-6 and an increase in the level of the marker following administration of the antibody indicates that the patient is responsive to treatment of the cancer disease.

4. An *in vitro* method of determining whether a cancer patient is amenable to treatment of a cancer disease, said method comprising the step of determining the percentage of CLDN18.2 positive cancer cells, wherein the antibody either comprises an antibody heavy chain comprising the amino acid sequence shown in SEQ ID NO: 32 and an antibody light chain comprising the amino acid sequence shown in SEQ ID NO: 39, or wherein the antibody is a functional variant of said antibody which binds to the same epitope of CLDN18.2.

5. The method of claim 4 wherein a level of at least 50% CLDN18.2 positive cancer cells indicates that the patient is amenable to treatment of the cancer disease.

6. The method of claim 4 or 5 wherein a level of at least 50% cancer cells which are positive for surface expression of CLDN18.2 indicates that the patient is amenable to treatment of a cancer disease.

7. The method of any one of claims 1 to 6, wherein the antibody mediates cell killing by one or more of complement dependent cytotoxicity (CDC) mediated lysis, antibody

dependent cellular cytotoxicity (ADCC) mediated lysis, induction of apoptosis and inhibition of proliferation.

8. The method of any one of claims 1 to 7 wherein the cancer is gastroesophageal cancer.

9. The method of any one of claims 1 to 8 wherein the cancer is metastatic, refractory or recurrent advanced gastroesophageal cancer.

10. The method of any one of claims 1 to 9 wherein the patient had prior therapy with at least one drug selected from the group consisting of pyrimidine analogs, platinum compounds, epirubicine, docetaxel and detoxifying agents for antineoplastic treatment.

11. The method of any one of claims 1 to 9 wherein the patient is to be treated in a combination therapy with an agent stabilizing or increasing expression of CLDN18.2, which agent is selected from the group consisting of (i) oxaliplatin and 5-fluorouracil, (ii) epirubicin, oxaliplatin and 5-fluorouracil, (iii) 5-fluorouracil, folinic acid and oxaliplatin, (iv) irinotecan, (v) docetaxel and (vi) cisplatin, and prodrugs thereof.

12. The method of any one of claims 1 to 11 wherein CLDN18.2 has the amino acid sequence according to SEQ ID NO: 1.

13. Use of an antibody having the ability of binding to CLDN18.2 and inducing killing of cells expressing CLDN18.2 in the manufacture of a medicament for treating or preventing a cancer disease of a patient, wherein the treatment comprises that an antibody to provide a serum level of at least 50 µg/ml is to be administered to the patient, wherein the antibody comprises either an antibody heavy chain comprising the amino acid sequence shown in SEQ ID NO: 32 and an antibody light chain comprising the amino acid sequence shown in SEQ ID NO: 39, or wherein the antibody is a functional variant of said antibody which binds to the same epitope of CLDN18.2.

14. The use of claim 13 wherein the antibody is to be administered to provide a serum level of between 50 µg/ml and 700 µg/ml.

15. The use of claim 13 or 14 wherein the serum level is provided for at least 7 days.

16. The use of any one of claims 13 to 15 wherein the treatment comprises that a dose of the antibody of 300 mg/m$^2$ is to be administered.

17. Use of an antibody having the ability of binding to CLDN18.2 and inducing killing of cells expressing CLDN18.2 in the manufacture of a medicament for treating or preventing a cancer disease of a patient, wherein the treatment comprises that an antibody to provide a serum level of at least 50 µg/ml is to be administered to the patient, wherein at least 50% of the cancer cells of the patient are CLDN18.2 positive and/or at least 40% of the cancer cells of the patient are positive for surface expression of CLDN18.2, wherein the antibody either comprises an antibody heavy chain comprising the amino acid sequence shown in SEQ ID NO: 32 and an antibody light chain comprising the amino acid sequence shown in SEQ ID NO: 39, or wherein the antibody is a functional variant of said antibody which binds to the same epitope of CLDN18.2.

18. The use of any one of claims 13 to 17 wherein treatment of the cancer disease results in achieving stable disease for at least 2 months.

19. The use of any one of claims 13 to 18 wherein the antibody is to be administered in a single dose or in multiple doses.

20. The use of claim 19 wherein the antibody is to be administered in at least 3 doses.

21. The use of claims 19 or 20 wherein the doses of the antibody are to be administered in time intervals of at least 7 days.

22. Use of an antibody having the ability of binding to CLDN18.2 and inducing killing of cells expressing CLDN18.2 in the manufacture of a medicament for treating or preventing a cancer disease of a patient, wherein the treatment comprises a combination therapy of the antibody with one or more selected from the group consisting of antiemetics, antispasmodics, parasympatholytics and agents which protect gastric mucosa, wherein the antibody is to be administered to provide a serum level at 50 µg/ml and wherein the antibody comprises either an antibody heavy chain comprising the amino acid sequence shown in SEQ ID NO: 32 and

an antibody light chain comprising the amino acid sequence shown in SEQ ID NO: 39, or wherein the antibody is a functional variant of said antibody which binds to the same epitope of CLDN18.2.

23. The use of any one of claims 13 to 22 wherein the antibody is to be administered by i.v. infusion over a time period of between 1 and 4 hours.

24. The use of any one of claims 17 to 23, wherein the antibody is to be administered to provide a serum level of between 50 µg/ml and 700 µg/ml.

25. The use of any one of claims 17 to 24, wherein the treatment comprises that a dose of the antibody of 300 $mg/m^2$ is to be administered.