

CLAIMS

1. An antibody that is capable of binding Lymphocyte Activation Gene-3 (LAG-3), wherein said antibody comprises

a heavy chain variable region having at least 90% identity to SEQ ID NO:1 and comprising:

a CDR-H1 comprising an amino acid sequence of SEQ ID NO: 5;

a CDR-H2 comprising an amino acid sequence of SEQ ID NO: 6;

a CDR-H3 comprising an amino acid sequence of SEQ ID NO: 7;

and

a light chain variable region having at least 90% identity to SEQ ID NO:2 and comprising:

a CDR-L1 defined by an amino acid sequence of SEQ ID NO: 8;

a CDR-L2 defined by an amino acid sequence of SEQ ID NO: 9; and

a CDR-L3 defined by an amino acid sequence of SEQ ID NO: 10;

and wherein the antibody binds to LAG-3 with a KD between about 1 picomolar (pM) and about 1 micromolar (μ M).

2. An antibody that is capable of binding Lymphocyte Activation Gene-3 (LAG-3), comprising:

a heavy chain antibody sequence according to SEQ ID NO: 1;

and

a light chain antibody sequence according to SEQ ID NO:2;

and wherein the antibody binds to LAG-3 with a KD between about 1 picomolar (pM) and about 1 micromolar (μ M).

3. A composition comprising the antibody of claim 1 and a pharmaceutically acceptable carrier.

4. Use of a pharmaceutically effective amount of the composition of claim 3 in the manufacture of a medicament for the treatment of a cancer characterized by overexpression of LAG-3, wherein the pharmaceutically effective amount of the composition is to be administered to a human in need thereof.

5. The use of claim 4, wherein the cancer is:

- i) a cancer associated with a high tumor mutation burden (TMB);
- ii) a cancer that is microsatellite stable (MSS),
- iii) a cancer that is characterized by microsatellite instability,
- iv) a cancer that has a high microsatellite instability status (MSI-H),
- v) a cancer that has a low microsatellite instability status (MSI-L),
- vi) a cancer associated with high TMB and MSI-H,
- vii) a cancer associated with high TMB and MSI-L or MSS,
- viii) a cancer that has a defective DNA mismatch repair system,
- ix) a cancer that has a defect in a DNA mismatch repair gene,
- x) a hypermutated cancer,
- xi) a cancer comprising a mutation in polymerase delta (POLD)
- xii) a cancer comprising a mutation in polymerase epsilon (POLE),
- xiii) a cancer that has homologous recombination repair deficiency/homologous repair deficiency (“HRD”) or is characterized by a homologous recombination repair (HRR) gene mutation or deletion;
- xiv) adenocarcinoma, endometrial cancer, breast cancer, ovarian cancer, cervical cancer, fallopian tube cancer, testicular cancer, primary peritoneal cancer, colon cancer, colorectal cancer, small intestine cancer, squamous cell carcinoma of the anus, squamous cell carcinoma of the penis, squamous cell carcinoma of the cervix, squamous cell carcinoma of the vagina, squamous cell carcinoma of the vulva, soft tissue sarcoma, melanoma, renal cell carcinoma, lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, squamous cell carcinoma of the lung, stomach cancer, bladder cancer, gall bladder cancer, liver cancer, thyroid cancer, laryngeal cancer, salivary gland cancer, esophageal cancer, head and neck cancer, squamous cell carcinoma of the head and neck, prostate cancer, pancreatic cancer, mesothelioma, Merkel cell carcinoma, sarcoma, glioblastoma, a hematological cancer, multiple myeloma, B-cell lymphoma, T-cell lymphoma, Hodgkin’s lymphoma/primary mediastinal B-cell lymphoma, chronic myelogenous leukemia, acute myeloid leukemia, acute lymphoblastic leukemia, non-Hodgkin’s lymphoma, neuroblastoma, a CNS tumor, diffuse intrinsic pontine glioma (DIPG), Ewing’s sarcoma, embryonal rhabdomyosarcoma, osteosarcoma, or Wilms tumor; or
- xv) a cancer of xiv), wherein the cancer is MSS or MSI-L, is characterized by microsatellite instability, is MSI-H, has high TMB, has high TMB and is MSS or MSI-L, has high TMB and is MSI-H, has a defective DNA mismatch repair system, has a defect in a

DNA mismatch repair gene, is a hypermutated cancer, is an HRD or HRR cancer, comprises a mutation in polymerase delta (POLD), or comprises a mutation in polymerase epsilon (POLE).

6. The use of claim 5, wherein the use further comprises another therapeutic agent or treatment to be administered.

7. The use of claim 6, wherein the use further comprises one or more of surgery, a radiotherapy, a chemotherapy, an immunotherapy, an anti-angiogenic agent, or an anti-inflammatory to be administered.

8. The use of claim 5, wherein the human has been further administered or will be administered an immune checkpoint inhibitor.

9. The use of claim 8, wherein an immune checkpoint inhibitor is an inhibitor of PD-1, TIM-3, CTLA-4, TIGIT, CEACAM, VISTA, BTLA, LAIR1, CD160, 2B4, CD80, CD86, B7-H3 (CD276), B7-H4 (VTCN1), HVEM, KIR, A2aR, MHC class I, MHC class II, GALS, adenosine, TGFR, B7-H1, B7-H4 (VTCN1), OX-40, CD137, CD40, IDO, or CSF1R.

10. The use of claim 5, wherein the antibody that is capable of binding LAG-3 is to be administered at a dose of about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, about 1000 mg, about 1100 mg, about 1200 mg, about 1300 mg, about 1400 mg, about 1500 mg, or about 2000 mg.

11. The use of claim 5, wherein the antibody that is capable of binding LAG-3 is to be administered every week, every two weeks, every three weeks, every four weeks, every five weeks, every six weeks, every seven weeks, or every eight weeks.

12. The use of claim 5, wherein the antibody that is capable of binding LAG-3 is to be administered at a dose of about 20 mg, about 80 mg, about 240 mg, about 500 mg, about 720 mg, about 900 mg, about 1000 mg, or about 1500 mg every two weeks, or about 240-720 mg or about 240-1500 mg every two weeks.

13. The use of claim 5, wherein the antibody that is capable of binding LAG-3 is to be administered parenterally, intravenously, or subcutaneously.

14. Use of an anti-LAG-3 antibody in the manufacture of a medicament for the treatment of cancer in a human, wherein the cancer is characterized by overexpression of LAG-3, wherein the anti-LAG-3 antibody comprising a heavy chain at least 90% identical to SEQ ID NO: 1 and a light chain at least 90% identical to SEQ ID NO: 2, and wherein the anti-LAG-3 antibody is to be administered intravenously.

15. The use of claim 14, wherein the cancer is non-small cell lung cancer.

16. Use of an anti-LAG-3 antibody in the manufacture of a medicament for the treatment of cancer in a human, wherein the cancer is characterized by overexpression of LAG-3, wherein the anti-LAG-3 antibody comprises:

(i) a heavy chain variable region comprising:

a CDR-H1 comprising an amino acid sequence at least 80% identical to SEQ ID NO: 5;

a CDR-H2 comprising an amino acid sequence at least 90% identical to SEQ ID NO: 6; and

a CDR-H3 comprising an amino acid sequence at least 80% identical to SEQ ID NO: 7; and

(ii) a light chain variable region comprising:

a CDR-L1 comprising an amino acid sequence at least 90% identical to SEQ ID NO: 8;

a CDR-L2 comprising an amino acid sequence at least 90% identical to SEQ ID NO: 9; and

a CDR-L3 comprising an amino acid sequence at least 85% identical to SEQ ID NO: 10;

wherein the antibody binds to LAG-3 with a KD between about 1 pM and about 1 μ M,

and wherein the anti-LAG-3 antibody is to be administered intravenously.

17. The use of claim 16, wherein the cancer is non-small cell lung cancer.

18. The use of claim 16, wherein the use further comprises one or more checkpoint inhibitors to be administered.