

The present disclosure also provides an antibody or antigen-binding fragment thereof that specifically binds LAG3 (e.g., human or cynomolgous monkey) comprising (1) a light chain variable domain comprising CDR-L1 that comprises the amino acid sequence:

5 In one aspect, the disclosure provides an antibody or antigen-binding fragment that specifically binds human LAG3 comprising:

(1)

a light chain variable domain comprising:

CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSDMN (SEQ ID NO: 38);

10 CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and

CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and

a heavy chain variable domain comprising:

CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33);

CDR-H2 that comprises the amino acid sequence: DINPNNGGTIYAQKFQE (SEQ ID NO:

15 458); and

CDR-H3 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35); or

(2)

a light chain variable domain comprising:

CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSDMN (SEQ ID NO: 38);

20 CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and

CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and

a heavy chain variable domain comprising:

CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33);

CDR-H2 that comprises the amino acid sequence: DINPNSGGTIYAQKFQE (SEQ ID NO:

25 456); and

CDR-H3 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35); or

(3)

a light chain variable domain comprising:

CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSDMN (SEQ ID NO: 38);

30 CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and

CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and

a heavy chain variable domain comprising:

CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33);

CDR-H2 that comprises the amino acid sequence: DINPNDGGTIYAQKFQE (SEQ ID NO:

35 457); and

CDR-H3 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35); or

(4)

a light chain variable domain comprising:

CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSDMN (SEQ ID NO: 38);

5 CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and
CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and
a heavy chain variable domain comprising:
CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33);
CDR-H2 that comprises the amino acid sequence: DINPNQGGTIYAQKFQE (SEQ ID NO:
10 455); and
CDR-H3 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35); or
(5)
a light chain variable domain comprising:
CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSMDN (SEQ ID NO: 38);
15 CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and
CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and
a heavy chain variable domain comprising:
CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33);
CDR-H2 that comprises the amino acid sequence: DINPNQGGTIYAQKFQE (SEQ ID NO:
20 454); and
CDR-H3 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35).

In another aspect, the disclosure provides an antibody or antigen-binding fragment that
specifically binds to human LAG3 comprising:

(1)
25 a light chain immunoglobulin comprising CDR-L1, CDR-L2 and CDR-L3 of the
immunoglobulin comprising the amino acid sequence of amino acids 21-131 of SEQ ID NO: 126
thereof, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in
amino acids 21-131 of SEQ ID NO: 126, and
a heavy chain immunoglobulin comprising CDR-H1, CDR-H2 and CDR-H3 of the
30 immunoglobulin comprising the amino acid sequence of amino acids 1-119 of SEQ ID NO: 106, and
having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids
1-119 of SEQ ID NO: 106; or
(2)
a light chain immunoglobulin comprising CDR-L1, CDR-L2 and CDR-L3 of the
35 immunoglobulin comprising the amino acid sequence of amino acids 21-131 of SEQ ID NO: 126,
and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino
acids 21-131 of SEQ ID NO: 126, and
a heavy chain immunoglobulin comprising CDR-H1, CDR-H2 and CDR-H3 of the
immunoglobulin comprising the amino acid sequence of amino acids 1-119 of SEQ ID NO: 108, and

5 having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 108; or

(3)

10 a light chain immunoglobulin comprising CDR-L1, CDR-L2 and CDR-L3 of the immunoglobulin comprising the amino acid sequence of amino acids 21-131 of SEQ ID NO: 126, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

15 a heavy chain immunoglobulin comprising CDR-H1, CDR-H2 and CDR-H3 of the immunoglobulin comprising the amino acid sequence of amino acids 1-119 of SEQ ID NO: 110, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 110; or

(4)

20 a light chain immunoglobulin comprising CDR-L1, CDR-L2 and CDR-L3 of the immunoglobulin comprising the amino acid sequence of amino acids 21-131 of SEQ ID NO: 126, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising CDR-H1, CDR-H2 and CDR-H3 of the immunoglobulin comprising the amino acid sequence of amino acids 1-119 of SEQ ID NO: 112, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 112; or

25 (5)

a light chain immunoglobulin comprising CDR-L1, CDR-L2 and CDR-L3 of the immunoglobulin comprising the amino acid sequence of amino acids 21-131 of SEQ ID NO: 126, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

30 a heavy chain immunoglobulin comprising CDR-H1, CDR-H2 and CDR-H3 of the immunoglobulin comprising the amino acid sequence of amino acids 1-119 of SEQ ID NO: 122, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 122.

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the various mature light and/or mature heavy chain immunoglobulin variable regions and having at least 90% overall amino acid sequence identity to the unprocessed immunoglobulin variable region (including the signal sequence), *i.e.*, variability occurs outside the mature immunoglobulin chain sequences.

10

5 The present disclosure provides an antibody or antigen-binding fragment thereof that specifically binds LAG3 (*e.g.*, human or cynomolgous monkey LAG3) that comprises a mature or unprocessed V_L domain or light chain immunoglobulin of SEQ ID NO: 7, 17, 27, 37, 57, 59, 61, 63, 65, 101, 126, 130, 132, 136, 138, 208, 210, 224, 226, 228, 230, 232, 241, 257, 259, 261, 263, 351, 369, 371, 373, 375, 401, 403, 405, 426, 427, 451-453 or 459-461; and/or a mature or
10 unprocessed V_H domain or heavy chain immunoglobulin of SEQ ID NO: 2, 12, 22, 32, 45, 47, 49, 51, 53, 55, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 103, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 128, 134, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 212, 214, 216, 218, 220, 222, 234, 235, 237, 239, 243, 245, 247,
15 249, 251, 253, 255, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 353, 355, 357, 359, 361, 363, 365, 367, 377, 379, 381, 383, 385, 387, 389, 391, 393, 395, 397, 399, 406-419, 434-442, 448, 449, 462, 463 or 464. In an embodiment of the disclosure, the antibody or antigen-binding fragment thereof comprises:
20 (1) a light chain variable domain comprising: CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSMDN (SEQ ID NO: 38); CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and/or a heavy chain variable domain comprising: CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33); CDR-H2 that comprises the amino acid sequence:
25 DINPNNGGTIYAQKFQE (SEQ ID NO: 458); and CDR-H3 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35); or (2) a light chain variable domain comprising: CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSMDN (SEQ ID NO: 38); CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and/or a heavy chain variable domain
30 comprising: CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33); CDR-H2 that comprises the amino acid sequence: DINPNNGGTIYAQKFQE (SEQ ID NO: 456); and CDR-H3

- 5 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35); or (3) a light chain variable domain comprising: CDR-L1 that comprises the amino acid sequence:

5 and/or by protecting hydrogens on the amide backbone of such residues from exchange with a
deuterium. The present disclosure also provides any such antibody or fragment in a
pharmaceutically acceptable carrier or diluent. In an embodiment of the disclosure, the anti-
LAG3 antibody or fragment is immobilized to a solid substrate. In an embodiment of the
disclosure the anti-LAG3 antibody or antigen-binding fragment thereof is Ab1, Ab2, Ab3, Ab4,
10 Ab5, Ab6, Ab7, Ab8 or Ab9 (as set forth herein).

In another aspect, the disclosure provides an antibody or antigen-binding fragment thereof
that comprises a light chain variable domain comprising the amino acids 21-131 of SEQ ID NO:
126 and a heavy chain variable domain comprising amino acids 1-119 of SEQ ID NO: 116.

15 In another aspect, the disclosure provides an antibody which consists of two heavy chain
immunoglobulins and two light chain immunoglobulins, wherein each light chain
immunoglobulin consists of the amino acid sequence set forth in amino acids 21-238 of SEQ ID
NO: 126 and each heavy chain immunoglobulin consists of the amino acid sequence set forth in
amino acids 1-119 of SEQ ID NO: 116 and a human IgG4 constant region with a S228P
20 mutation according to the EU system.

In another aspect, the disclosure provides an antibody which consists of two heavy chain
immunoglobulins and two light chain immunoglobulins, wherein each light chain
immunoglobulin consists of the amino acid sequence set forth in amino acids 21-238 of SEQ ID

5 NO: 126 and each heavy chain immunoglobulin consists of the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 116 and a human IgG4 constant region.

In another aspect, the disclosure provides an antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin comprises the amino acid sequence set forth in amino acids 21-238 of SEQ ID
10 NO: 126 and each heavy chain immunoglobulin comprises the amino acid sequence set forth in SEQ ID NO: 116.

In another aspect, the disclosure provides an antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin consists of the amino acid sequence set forth in amino acids 21-238 of SEQ ID
15 NO: 126 and each heavy chain immunoglobulin consists of the amino acid sequence set forth in SEQ ID NO: 116.

In another aspect, the disclosure provides an antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin consists of the amino acid sequence set forth in amino acids 21-238 of SEQ ID
20 NO: 126 and each heavy chain immunoglobulin comprises the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 116.

The present disclosure also provides a complex comprising an anti-LAG3 antibody or fragment discussed herein (*e.g.*, 4A10, 19E8, 11C9 and/or 22D2; *e.g.*, Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8 and/or Ab9) complexed with LAG3 (*e.g.*, human or cynomolgous monkey)
25 or a fragment thereof or with a secondary antibody (*e.g.*, detectably labeled secondary antibody) that binds specifically to the anti-LAG3 antibody or fragment. In an embodiment of the disclosure, the antibody or fragment is *in vitro* (*e.g.*, is immobilized to a solid substrate) or is in the body of a subject. In an embodiment of the disclosure, the LAG3 is *in vitro* (*e.g.*, is immobilized to a solid substrate) or is on the surface of a cell or is in the body of a subject.

30 The present disclosure further provides a composition comprising a plurality of anti-LAG3 antibodies or antigen-binding fragments of the present disclosure which are isolated, monoclonal antibodies or antigen-binding fragments thereof, *e.g.*, which are humanized, *e.g.*, humanized antagonistic antibodies and antigen-binding fragments thereof.

In another aspect, the disclosure provides a composition comprising the antibody or antigen-
35 binding fragment as discussed herein and an anti-PD-1 antibody.

In another aspect, the disclosure provides a composition comprising an antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin consists of the amino acid sequence set forth in amino acids

5 21-238 of SEQ ID NO: 126 and each heavy chain immunoglobulin consists of the amino acid sequence set forth in SEQ ID NO: 116, and pembrolizumab.

In another aspect, the disclosure provides a composition comprising an antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin consists of the amino acid sequence set forth in amino acids
10 21-238 of SEQ ID NO: 126 and each heavy chain immunoglobulin comprises the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 116, and pembrolizumab.

In another aspect, the disclosure provides a composition comprising an antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin consists of the amino acid sequence set forth in amino acids
15 21-238 of SEQ ID NO: 126 and each heavy chain immunoglobulin consists of the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 116 and a human IgG4 constant region with a S228P mutation according to the EU system, and pembrolizumab.

In another aspect, the disclosure provides composition comprising the antibody or antigen-binding fragment as discussed herein and a pharmaceutically acceptable carrier or diluent.

20 In another aspect, the disclosure provides an injection device comprising the antibody or antigen-binding fragment as discussed herein or a composition as discussed herein.

The present disclosure also provides a composition comprising anti-LAG3 antibodies or antigen-binding fragments thereof as discussed herein in association with a further therapeutic agent (*e.g.*, a monoclonal antibody or antigen-binding fragment thereof or an organic small
25 molecule) such as an inhibitor of an immunomodulatory receptor, an anti-emetic, an mTOR (mammalian target of rapamycin) inhibitor, a cytotoxic agent, a platinum agent, an EGFR (epidermal growth factor receptor) inhibitor, a VEGF (vascular epidermal growth factor) inhibitor, a microtubule stabilizer, a taxane, a CD20 inhibitor, a CD52 inhibitor, a CD30 inhibitor, a RANK (Receptor activator of nuclear factor kappa-B) inhibitor, a RANKL (Receptor
30 activator of nuclear factor kappa-B ligand) inhibitor, an ERK inhibitor, a MAP Kinase inhibitor, an AKT inhibitor, a MEK inhibitor, a PI3K inhibitor, a HER1 inhibitor, a HER2 inhibitor, a HER3 inhibitor, a HER4 inhibitor, a Bcl2 inhibitor, a CD22 inhibitor, a CD79b inhibitor, an ErbB2 inhibitor, and/or a farnesyl protein transferase inhibitor. In an embodiment of the disclosure, the further therapeutic agent is an anti-PD1 antibody or an antigen-binding fragment
35 thereof, pembrolizumab, nivolumab, CT-011, anti-CTLA4 antibody or an antigen-binding fragment thereof, anti-TIM3

- 5 antibody or an antigen-binding fragment thereof, anti-CS1 antibody or an antigen-binding fragment thereof, elotuzumab, anti-KIR2DL1/2/3 antibody or an antigen-

5 darbepoetin alfa. In an embodiment of the disclosure, the anti-LAG3 antibody or antigen-binding fragment thereof is in association with pembrolizumab. In an embodiment of the disclosure, the anti-LAG3 antibody or antigen-binding fragment thereof is in association with novolumab. In an embodiment of the disclosure, the anti-LAG3 antibody or antigen-binding fragment thereof is in association with CT-011. In an embodiment of the disclosure, the anti-
10 LAG3 antibody or antigen-binding fragment thereof is in association with BMS-936559.

 In another aspect, the disclosure provides a polynucleotide encoding: any one of the light or heavy chain of the antibodies or antigen binding fragments as discussed herein. The present disclosure also provides a polynucleotide encoding any of such polypeptides, *e.g.*, comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1, 6, 11, 16, 21, 26, 31,
15 36, 46, 48, 50, 52, 54, 56, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 236, 238, 240, 242, 244, 246,
20 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354,

5 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392,
394, 396, 398, 400, 402 and 404; or a mature fragment thereof. In another aspect, the disclosure
provides a vector comprising the polynucleotide as discussed herein. Also included in the present
disclosure is a vector (*e.g.*, a plasmid) comprising the polynucleotide. In another aspect, the
disclosure provides a host cell comprising the antibody, antigen-binding fragment,
10 polynucleotide or vector as discussed herein. A host cell (*e.g.*,

5 mammalian, bacterial, Chinese hamster ovary (CHO), lower eukaryotic, fungal, yeast, *Pichia*,
Pichia pastoris) is also part of the present disclosure wherein the host cell comprises an
antibody, fragment, polypeptide, polynucleotide and/or vector set forth herein.

10 The present disclosure also provides vaccines comprising an antibody or fragment set forth
herein, an antigen (*e.g.*, viral peptide antigen, virus-like particle, tumor peptide antigen) and a
pharmaceutically acceptable carrier.

The present disclosure also provides a vessel (*e.g.*, plastic or glass vial) or an injection
device (*e.g.*, a syringe such as a pre-filled syringe or an autoinjector) comprising any antibody,
fragment, polypeptide, polynucleotide, vector, composition or vaccine discussed herein.

15 The present disclosure also provides a method of treating a cancer (*e.g.*, osteosarcoma,
rhabdomyosarcoma, neuroblastoma, kidney cancer, leukemia, renal transitional cell cancer,
bladder cancer, Wilm's cancer, ovarian cancer, pancreatic cancer, breast cancer, prostate cancer,
bone cancer, lung cancer, gastric cancer, colorectal cancer, cervical cancer, synovial sarcoma,
head and neck cancer, squamous cell carcinoma, multiple myeloma, renal cell cancer,
20 retinoblastoma, hepatoblastoma, hepatocellular carcinoma, melanoma, rhabdoid tumor of the
kidney, Ewing's sarcoma, chondrosarcoma, brain cancer, glioblastoma, meningioma, pituitary
adenoma, vestibular schwannoma, a primitive neuroectodermal tumor, medulloblastoma,
astrocytoma, anaplastic astrocytoma, oligodendroglioma, ependymoma, choroid plexus
papilloma, polycythemia vera, thrombocythemia, idiopathic myelofibrosis, soft tissue sarcoma,
25 thyroid cancer, endometrial cancer, carcinoid cancer or liver cancer, breast cancer or gastric
cancer) in a subject, comprising administering to the subject a effective amount of an anti-LAG3
antibody or antigen-binding fragment or vaccine discussed herein optionally, in association with
a further therapeutic agent or a therapeutic procedure (*e.g.*, surgical tumorectomy or anti-cancer
radiation therapy).

The present disclosure also provides a method of administering an anti-LAG3 antibody, fragment, composition, polypeptide, vaccine or polynucleotide discussed herein, or a pharmaceutical composition thereof, to a subject comprising injecting the antibody, fragment, polypeptide, vaccine or polynucleotide into the body of the subject using an injection device;

10 and, optionally, also administering a further therapeutic agent to the subject.

The present disclosure also provides a method of producing an anti-LAG3 antibody or antigen-binding fragment thereof or polypeptide discussed herein comprising: a. culturing a host cell comprising a polynucleotide encoding the polypeptide or an immunoglobulin chain of the antibody or fragment in culture medium under conditions favorable to expression of the

15 polynucleotide; and b. optionally, recovering the antibody, fragment or polypeptide from the host

5 cell and/or culture medium. In another aspect, the disclosure provides a method of producing an antibody or antigen-binding fragment thereof as discussed herein comprising: a. culturing a host cell comprising a polynucleotide encoding a light and/or heavy chain of the antibody or antigen-binding fragment in a culture medium under conditions favorable to expression of the polynucleotide; and b. optionally, recovering the antibody or antigen-binding fragment from the
10 host cell and/or culture medium.

In an embodiment of the disclosure, the method comprises the step of introducing the polynucleotide into the host cell, *e.g.*, by transformation or transfection.

The present disclosure provides a method for detecting the presence of a LAG3 peptide or a fragment thereof in a sample comprising contacting the sample with an anti-LAG3 antibody or
15 fragment discussed herein and detecting the presence of a complex between the antibody or fragment and the peptide; wherein detection of the complex indicates the presence of the LAG3 peptide.

In another aspect, the disclosure provides an antibody or antigen-binding fragment or composition as discussed herein for use in the treatment of cancer. In another aspect, the
20 disclosure provides a composition as discussed herein for use in the treatment of cancer.

In another aspect, the disclosure provides use of the antibody or antigen-binding fragment or composition as discussed herein in the preparation of a medicament for the treatment of cancer. In another aspect, the disclosure provides use of the composition as discussed herein in the preparation of a medicament for the treatment of cancer.

25

BRIEF DESCRIPTION OF THE FIGURES

Figure 1. Binding of anti-human LAG3 clones to human and cynomolgus monkey LAG3 expressing CHO-K1 cells.

Figure 2. Binding of LAG3 clones to cynomolgous monkey and human primary T-cells.

30 **Figure 3.** Three-dimensional structure of human LAG3. The location of the antibody 22D2, 11C9 and 4A10 epitopes are indicated.

Figure 4 (a-c). Heat map indicating regions in human LAG3 which are strongly or weakly protected from deuteration by antibody binding. (a) human LAG3 / 22D2 Difference heatmap; (b) human LAG3 / 11C9 Difference heatmap; (c) human LAG3 / 4A10 Difference heatmap.

Figure 5 (a-b). Combined heatmaps indicating (a) regions on human LAG3 which are protected from deuteration by 22D2, 11C9 and 4A10 binding and (b) the location in human LAG3 mediating MHC2 binding.

Figure 6. Predominant N-linked glycans for monoclonal antibodies produced in Chinese hamster ovary cells (CHO N-linked glycans) and in engineered yeast cells (engineered yeast N-linked glycans): squares: N-acetylglucosamine (GlcNAc); circles: mannose (Man); diamonds: galactose (Gal); triangles: fucose (Fuc).

Figure 7. Effect of anti-human LAG-3 antibody treatment +/- anti-PD-1 treatment on IL-2 production in SEB stimulated human PBMCs. PBMC were activated by SEB for 3 days and IL-2 concentration in culture supernatants was determined by MSD. Donor 090 : SEB 60 ng/mL, Donor 089 : SEB 30 ng/mL. Anti-PD1 was used at 10 µg/mL.

Figure 8. Effect of hu22D2 treatment +/- anti-PD-1 treatment on IFN-γ and TNFα production in MLR stimulated human PBMCs. PBMC were activated with allogeneic monocyte-derived DC for 7 days and IFN-γ and TNF-α concentration in culture supernatants was determined by MSD. Anti-PD-1 was used at 3 µg/mL. Isotype was used at 200nM.

WE CLAIM:

1. An antibody or antigen-binding fragment that specifically binds human LAG3 comprising:

(1)

a light chain variable domain comprising:

CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSDMN (SEQ ID NO: 38);

CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and

CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and

a heavy chain variable domain comprising:

CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33);

CDR-H2 that comprises the amino acid sequence: DINPNNGGTIYAQKFQE (SEQ ID NO: 458); and

CDR-H3 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35); or

(2)

a light chain variable domain comprising:

CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSDMN (SEQ ID NO: 38);

CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and
 CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and
 a heavy chain variable domain comprising:
 CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33);
 CDR-H2 that comprises the amino acid sequence: DINPNSGGTIYAQKFQE (SEQ ID NO: 456); and
 CDR-H3 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35); or
 (3)
 a light chain variable domain comprising:
 CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSDMN (SEQ ID NO: 38);
 CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and
 CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and
 a heavy chain variable domain comprising:
 CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33);
 CDR-H2 that comprises the amino acid sequence: DINPNDGGTIYAQKFQE (SEQ ID NO: 457); and
 CDR-H3 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35); or
 (4)
 a light chain variable domain comprising:
 CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSDMN (SEQ ID NO: 38);
 CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and
 CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and
 a heavy chain variable domain comprising:
 CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33);
 CDR-H2 that comprises the amino acid sequence: DINPNQGGTIYAQKFQE (SEQ ID NO: 455); and
 CDR-H3 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35); or
 (5)
 a light chain variable domain comprising:
 CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSDMN (SEQ ID NO: 38);
 CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and
 CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and
 a heavy chain variable domain comprising:
 CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33);

CDR-H2 that comprises the amino acid sequence: DINPNGGGTTIYAQKFQE (SEQ ID NO: 454); and
CDR-H3 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35).

2. The antibody or antigen-binding fragment thereof of claim 1 comprising:

a light chain variable domain comprising:

CDR-L1 that comprises the amino acid sequence: KASQSLDYEGDSDMN (SEQ ID NO: 38);

CDR-L2 that comprises the amino acid sequence: GASNLES (SEQ ID NO: 39); and

CDR-L3 that comprises the amino acid sequence: QQSTEDPRT (SEQ ID NO: 40); and

a heavy chain variable domain comprising:

CDR-H1 that comprises the amino acid sequence: DYNVD (SEQ ID NO: 33);

CDR-H2 that comprises the amino acid sequence: DINPNDGGTTIYAQKFQE (SEQ ID NO: 457); and

CDR-H3 that comprises the amino acid sequence: NYRWFGAMDH (SEQ ID NO: 35).

3. The antibody or antigen-binding fragment of claim 2, wherein the light chain variable domain comprises the CDR-L1, CDR-L2 and CDR-L3, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and the heavy chain variable domain comprises the CDR-H1, CDR-H2 and CDR-H3, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 106.

4. The antibody or antigen-binding fragment of claim 1 comprising:

(1)

a light chain variable domain comprising the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

a heavy chain variable domain comprising the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 106; or

(2)

a light chain variable domain comprising the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

a heavy chain variable domain comprising the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 108; or

(3)

a light chain variable domain comprising the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

a heavy chain variable domain comprising the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 110; or

(4)

a light chain variable domain comprising the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

a heavy chain variable domain comprising the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 112; or

(5)

a light chain variable domain comprising the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

a heavy chain variable domain comprising the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 122.

5. The antibody or antigen-binding fragment of claim 1 comprising:

(1)

a light chain immunoglobulin comprising the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 106; or

(2)

a light chain immunoglobulin comprising the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 108; or

(3)

a light chain immunoglobulin comprising the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 110; or

(4)

a light chain immunoglobulin comprising the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 112; or

(5)

a light chain immunoglobulin comprising the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 114; or

(6)

a light chain immunoglobulin comprising the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 116; or

(7)

a light chain immunoglobulin comprising the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 118; or

(8)

a light chain immunoglobulin comprising the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 120; or

(9)

a light chain immunoglobulin comprising the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 122.

6. An antibody or antigen-binding fragment that specifically binds to human LAG3 comprising:

(1)

a light chain immunoglobulin comprising CDR-L1, CDR-L2 and CDR-L3 of the immunoglobulin comprising the amino acid sequence of amino acids 21-131 of SEQ ID NO: 126 thereof, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising CDR-H1, CDR-H2 and CDR-H3 of the immunoglobulin comprising the amino acid sequence of amino acids 1-119 of SEQ ID NO: 106, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 106; or

(2)

a light chain immunoglobulin comprising CDR-L1, CDR-L2 and CDR-L3 of the immunoglobulin comprising the amino acid sequence of amino acids 21-131 of SEQ ID NO: 126, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising CDR-H1, CDR-H2 and CDR-H3 of the immunoglobulin comprising the amino acid sequence of amino acids 1-119 of SEQ ID NO: 108, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 108; or

(3)

a light chain immunoglobulin comprising CDR-L1, CDR-L2 and CDR-L3 of the immunoglobulin comprising the amino acid sequence of amino acids 21-131 of SEQ ID NO: 126, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising CDR-H1, CDR-H2 and CDR-H3 of the immunoglobulin comprising the amino acid sequence of amino acids 1-119 of SEQ ID NO: 110, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 110; or

(4)

a light chain immunoglobulin comprising CDR-L1, CDR-L2 and CDR-L3 of the immunoglobulin comprising the amino acid sequence of amino acids 21-131 of SEQ ID NO: 126, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising CDR-H1, CDR-H2 and CDR-H3 of the immunoglobulin comprising the amino acid sequence of amino acids 1-119 of SEQ ID NO: 112, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 112; or

(5)

a light chain immunoglobulin comprising CDR-L1, CDR-L2 and CDR-L3 of the immunoglobulin comprising the amino acid sequence of amino acids 21-131 of SEQ ID NO: 126, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 21-131 of SEQ ID NO: 126, and

a heavy chain immunoglobulin comprising CDR-H1, CDR-H2 and CDR-H3 of the immunoglobulin comprising the amino acid sequence of amino acids 1-119 of SEQ ID NO: 122, and having at least 90% amino acid sequence identity to the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 122.

7. The antibody or antigen-binding fragment of claim 3 or 6, wherein said sequence identity is at least 95%.

8. The antibody or antigen-binding fragment of any one of claims 1-7 which is an antibody.

9. The antibody or antigen binding fragment of any one of claims 1-8 that is humanized.

10. An antibody or antigen-binding fragment thereof that comprises a light chain variable domain comprising the amino acids 21-131 of SEQ ID NO: 126 and a heavy chain variable domain comprising amino acids 1-119 of SEQ ID NO: 116.

11. The antibody or antigen-binding fragment of claim 10 that comprises a light chain immunoglobulin comprising the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126 and a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 116.

12. An antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin consists of the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126 and each heavy chain immunoglobulin consists of the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 116 and a human IgG4 constant region with a S228P mutation according to the EU system.

13. An antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin consists of the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126 and each heavy chain immunoglobulin consists of the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 116 and a human IgG4 constant region.

14. An antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin comprises the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126 and each heavy chain immunoglobulin comprises the amino acid sequence set forth in SEQ ID NO: 116.

15. An antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin consists of the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126 and each heavy chain immunoglobulin consists of the amino acid sequence set forth in SEQ ID NO: 116.

16. An antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin consists of the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126 and each heavy chain

immunoglobulin comprises the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 116.

17. The antibody or antigen-binding fragment of any one of claims 1-16 that is expressed from a Chinese hamster ovary cell.

18. The antibody or antigen-binding fragment of any one of claims 1-17 which is glycosylated with one or more of CHO N-linked glycans selected from the group consisting of G0-F, G1-F, G2-F, G0, G1, G2 and Man5.

19. A composition comprising the antibody or antigen-binding fragment of any one of claims 1-18 and an anti-PD-1 antibody.
20. A composition comprising an antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin consists of the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126 and each heavy chain immunoglobulin consists of the amino acid sequence set forth in SEQ ID NO: 116, and pembrolizumab.
21. A composition comprising an antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin consists of the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126 and each heavy chain immunoglobulin comprises the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 116, and pembrolizumab.
22. A composition comprising an antibody which consists of two heavy chain immunoglobulins and two light chain immunoglobulins, wherein each light chain immunoglobulin consists of the amino acid sequence set forth in amino acids 21-238 of SEQ ID NO: 126 and each heavy chain immunoglobulin consists of the amino acid sequence set forth in amino acids 1-119 of SEQ ID NO: 116 and a human IgG4 constant region with a S228P mutation according to the EU system, and pembrolizumab.
23. A composition comprising the antibody or antigen-binding fragment of any one of claims 1 to 18 and a pharmaceutically acceptable carrier or diluent.
24. An injection device comprising the antibody or antigen-binding fragment of any one of claims 1-18 or a composition of any one of claims 19-23.

25. A polynucleotide encoding: any one of the light or heavy chain of the antibodies or antigen binding fragments of claims 1-18.
26. A vector comprising the polynucleotide of claim 25.
27. A host cell comprising the antibody, antigen-binding fragment, polynucleotide or vector of any of claims 1-18 and 25-26.

28. A method of producing an antibody or antigen-binding fragment thereof of any one of claims 1-18 comprising:
- a. culturing a host cell comprising a polynucleotide encoding a light and/or heavy chain of the antibody or antigen-binding fragment in a culture medium under conditions favorable to expression of the polynucleotide; and
 - b. optionally, recovering the antibody or antigen-binding fragment from the host cell and/or culture medium.
29. The method of claim 28 wherein the host cell is a Chinese hamster ovary cell.
30. Use of an antibody or antigen-binding fragment or composition according to any one of claims 1-18 and 23, in the preparation of a medicament for the treatment of cancer.
31. The use of claim 30, wherein the treatment is in combination with pembrolizumab.
32. An antibody or antigen-binding fragment or composition according to any one of claims 1-18 and 23 for use in the treatment of cancer.
33. The antibody or antigen-binding fragment or composition according to claim 32, wherein the antibody or antigen-binding fragment or composition is to be co-administered with pembrolizumab.
34. Use of a composition according to any one of claims 20-22 in the preparation of a medicament for the treatment of cancer.
35. A composition according to any one of claims 20-22 for use in the treatment of cancer.