

What is claimed is:

1. An isolated antibody or antigen-binding fragment thereof that binds specifically to human lymphocyte activation gene 3 (LAG3) protein, wherein the antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) contained within a heavy chain variable region (HCVR) amino acid sequence of SEQ ID NO: 418 and three light chain CDRs (LCDR1, LCDR2 and LCDR3) contained within a light chain variable region (LCVR) amino acid sequence of SEQ ID NO: 426.
2. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof interacts with one or more amino acids contained within the extracellular domain of LAG3 (amino acids 28-71 of SEQ ID NO: 588), as determined by hydrogen/deuterium exchange.
3. The isolated antibody or antigen-binding fragment of claim 2 wherein the antibody or antigen-binding fragment thereof interacts with one or more amino acids contained within SEQ ID NO: 589, as determined by hydrogen/deuterium exchange.
4. The isolated antibody or antigen-binding fragment of claim 2, wherein the antibody or antigen-binding fragment thereof interacts with an amino acid sequence selected from the group consisting of (a) amino acids 28 to 69 of SEQ ID NO: 588; (b) amino acids 28 to 71 of SEQ ID NO: 588; (c) amino acids 31 to 52 of SEQ ID NO: 588; and (d) amino acids 32 to 69 of SEQ ID NO: 588.

5. The isolated antibody or antigen-binding fragment thereof of claim 3 wherein the antibody or antigen-binding fragment thereof interacts with at least ten amino acids contained within SEQ ID NO: 589.
6. The isolated antibody or antigen-binding fragment thereof of claim 3, wherein the antibody or antigen-binding fragment thereof interacts with at least twenty amino acids contained within SEQ ID NO: 589.
7. The isolated antibody or antigen-binding fragment thereof of claim 2, wherein the antibody or antigen-binding fragment thereof interacts with the amino acid sequence of SEQ ID NO: 589.
8. The isolated antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof has one or more properties selected from the group consisting of:
 - (a) binds monomeric human LAG3 with a binding dissociation equilibrium constant (K_D) of less than about 1.5 nM as measured in a surface plasmon resonance assay at 25° C.;
 - (b) binds monomeric human LAG3 with a K_D less than about 2 nM as measured in a surface plasmon resonance assay at 37° C.;
 - (c) binds dimeric human LAG3 with a K_D less than about 20 pM as measured in a surface plasmon resonance assay at 25° C.;
 - (d) binds dimeric human LAGS with a K_D less than about 90 pM as measured in a surface plasmon resonance assay at 37° C.;

- (e) binds to a hLAG3-expressing cell with an EC_{50} less than about 2 nM as measured in a flow cytometry assay;
- (f) binds to a mLAG3-expressing cell with a EC_{50} less than about 2.3 nM as measured in a flow cytometry assay;
- (g) blocks binding of hLAG3 to human MHC class II with IC_{50} less than about 20 nM as determined by a cell adherence assay;
- (h) blocks binding of hLAG3 to mouse MHC class II with IC_{50} less than about 15 nM as determined by a cell adherence assay;
- (i) blocks binding of hLAG3 to MHC class II by more than 90% as determined by a cell adherence assay;
- (j) rescues LAG3-mediated inhibition of T cell activity with EC_{50} less than about 2.5 nM as determined in a luciferase reporter assay; and
- (k) binds to activated CD4⁺ and CD8⁺ T cells with EC_{50} less than about 1.2 nM, as determined in a fluorescence assay.

9. The isolated antibody or antigen-binding fragment thereof of claim 1 comprising a HCVR having the amino acid sequence of SEQ ID NO: 418.

10. The isolated antibody or antigen-binding fragment thereof of claim 1 comprising a LCVR having the amino acid sequence of SEQ ID NO: 426.

11. The isolated antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment comprises HCDR1-HCDR2-HCDR3-LCDR1-LCDR2-LCDR3 comprising amino acid sequences of SEQ ID NOs: 420-422-424-428-430-432.

12. The isolated antibody or antigen-binding fragment of claim 11, wherein the antibody or antigen-binding fragment thereof comprises a HCVR/LCVR amino acid sequence pair of SEQ ID NOs: 418/426.
13. The isolated antibody of claim 12 comprising a heavy chain and a light chain, wherein the heavy chain comprises an amino acid sequence of SEQ ID NO: 577.
14. The isolated antibody of claim 12 comprising a heavy chain and a light chain, wherein the light chain comprises an amino acid sequence of SEQ ID NO: 578.
15. The isolated antibody or antigen-binding fragment of claim 12 comprising a heavy chain/light chain amino acid sequence pair of SEQ ID NOs: 577/578.
16. A pharmaceutical composition comprising an isolated antibody or antigen-binding fragment thereof of claim 1 and a pharmaceutically acceptable carrier or diluent.
17. An isolated antibody or antigen-binding fragment thereof that binds specifically to human LAG3 protein, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain/light chain amino acid sequence pair of SEQ ID NOs: 577/578.
18. A pharmaceutical composition comprising an isolated antibody or antigen-binding fragment thereof of claim 17 and a pharmaceutically acceptable carrier or diluent.