

WHAT IS CLAIMED IS:

1. A pharmaceutical formulation comprising an antibody or antigen-binding fragment thereof that
 - (a) binds to an epitope of human PD-1 recognized by an antibody comprising a light chain variable region having an amino acid sequence of SEQ ID NO:8 and a heavy chain variable region having an amino acid sequence of SEQ ID NO:13; or
 - (b) competes for the binding to human PD-1 with an antibody comprising a light chain variable region having an amino acid sequence of SEQ ID NO:8 and a heavy chain variable region having an amino acid sequence of SEQ ID NO:13.
2. A pharmaceutical formulation comprising an antibody or antigen-binding fragment thereof that binds to PD-1, wherein the antibody or antigen-binding fragment thereof comprises:
 - (a) a light chain variable region (VL) comprising VL complementarity determining region 1 (CDR1), VL CDR2, and VL CDR3 of any one of antibodies PD1AB-1, PD1AB-2, PD1AB-3, PD1AB-4, PD1AB-5, or PD1AB-6 as set forth in Table 1; and/or
 - (b) a heavy chain variable region (VH) comprising VH complementarity determining region 1 (CDR1), VH CDR2, and VH CDR3 of any one of antibodies PD1AB-1, PD1AB-2, PD1AB-3, PD1AB-4, PD1AB-5, or PD1AB-6 as set forth in Table 2.
3. The pharmaceutical formulation of claim 2, wherein the antibody or antigen-binding fragment thereof comprises:
 - (a) a VL further comprising VL framework 1 (FR1), VL FR2, VL FR3, and VL FR4 of any one of antibodies PD1AB-1, PD1AB-2, PD1AB-3, PD1AB-4, PD1AB-5, or PD1AB-6 as set forth in Table 3; and/or

- (b) a VH further comprising VH framework 1 (FR1), VH FR2, VH FR3, and VH FR4 of any one of antibodies PD1AB-1, PD1AB-2, PD1AB-3, PD1AB-4, PD1AB-5, or PD1AB-6 as set forth in Table 4.
- 4. The pharmaceutical formulation of claim 2, wherein
 - (a) the VL CDR1, VL CDR2, and VL CDR3 comprise amino acid sequences of SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, respectively, and the VH CDR1, VH CDR2, and VH CDR3 comprise amino acid sequences of SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6, respectively; or
 - (b) the VL CDR1, VL CDR2, and VL CDR3 comprise amino acid sequences of SEQ ID NO:7, SEQ ID NO:2, and SEQ ID NO:3, respectively, and the VH CDR1, VH CDR2, and VH CDR3 comprise amino acid sequences of SEQ ID NO:4, SEQ ID NO:5, and SEQ ID NO:6, respectively.
- 5. The pharmaceutical formulation of claim 2, wherein the antibody or antigen-binding fragment thereof comprises (i) a VL comprising an amino acid sequence of SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10; or (ii) a VH comprising an amino acid sequence of SEQ ID NO:11 or SEQ ID NO:12, or SEQ ID NO:13.
- 6. The pharmaceutical formulation of claim 2, wherein the antibody or antigen-binding fragment thereof comprises:
 - (a) a VL comprising an amino acid sequence of SEQ ID NO:8; and a VH comprising an amino acid sequence of SEQ ID NO:11;
 - (b) a VL comprising an amino acid sequence of SEQ ID NO:9; and a VH comprising an amino acid sequence of SEQ ID NO:11;
 - (c) a VL comprising an amino acid sequence of SEQ ID NO:10; and a VH comprising an amino acid sequence of SEQ ID NO:11;
 - (d) a VL comprising an amino acid sequence of SEQ ID NO:8; and a VH comprising an amino acid sequence of SEQ ID NO:12;

- (e) a VL comprising an amino acid sequence of SEQ ID NO:9; and a VH comprising an amino acid sequence of SEQ ID NO:12;
 - (f) a VL comprising an amino acid sequence of SEQ ID NO:10; and a VH comprising an amino acid sequence of SEQ ID NO:12;
 - (g) a VL comprising an amino acid sequence of SEQ ID NO:8; and a VH comprising an amino acid sequence of SEQ ID NO:13;
 - (h) a VL comprising an amino acid sequence of SEQ ID NO:9; and a VH comprising an amino acid sequence of SEQ ID NO:13; or
 - (i) a VL comprising an amino acid sequence of SEQ ID NO:10; and a VH comprising an amino acid sequence of SEQ ID NO:13.
7. The pharmaceutical formulation of any one of claims 1 to 6, wherein the antibody or antigen-binding fragment thereof comprises a human IgG1 Fc region, a human IgG4 Fc region, a human IgG4P Fc region, a human IgG4PE Fc region, or a mutant thereof.
 8. The pharmaceutical formulation of any one of claims 1 to 6, wherein the antibody or antigen-binding fragment thereof comprises a human IgG1-K322A Fc region.
 9. The pharmaceutical formulation of any one of claims 1 to 6, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain Fc region comprising an amino acid sequence selected from the group consisting of SEQ ID NOS:36-40.
 10. The pharmaceutical formulation of claim 9, wherein the antibody or antigen-binding fragment thereof further comprises a light chain constant region comprising an amino acid sequence of SEQ ID NO:41.
 11. The pharmaceutical formulation of any one of claims 1 to 10, wherein the antibody or antigen-binding fragment thereof comprises a light chain comprising an amino acid sequence of SEQ ID NO:31.

12. The pharmaceutical formulation of any one of claims 1 to 10, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain comprising an amino acid sequence of SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34 or SEQ ID NO:35.
13. The pharmaceutical formulation of any one of claims 1 to 10, wherein the antibody or antigen-binding fragment thereof comprises:
 - (a) a light chain comprising an amino acid sequence of SEQ ID NO:31; and a heavy chain comprising an amino acid sequence of SEQ ID NO:32;
 - (b) a light chain comprising an amino acid sequence of SEQ ID NO:31; and a heavy chain comprising an amino acid sequence of SEQ ID NO:33;
 - (c) a light chain comprising an amino acid sequence of SEQ ID NO:31; and a heavy chain comprising an amino acid sequence of SEQ ID NO:34; or
 - (d) a light chain comprising an amino acid sequence of SEQ ID NO:31; and a heavy chain comprising an amino acid sequence of SEQ ID NO:35.
14. The pharmaceutical formulation of any one of claims 1 to 13, wherein, when bound to PD-1, the antibody or antigen-binding fragment binds to at least one of residues 100-109 within an amino acid sequence of SEQ ID NO:42; wherein optionally the antibody or antigen-binding fragment binds to at least one of residues 100-105 within an amino acid sequence of SEQ ID NO:42.
15. The pharmaceutical formulation of any one of claims 1 to 13, wherein, when bound to PD-1, the antibody or antigen-binding fragment binds to at least one residue selected from the group consisting of N33, T51, S57, L100, N102, G103, R104, D105, H107, and S109 within an amino acid sequence of SEQ ID NO:42; wherein optionally the antibody or antigen-binding fragment binds to G103 and R104.
16. The pharmaceutical formulation of any one of claims 1 to 15, wherein the antibody or antigen-binding fragment thereof:
 - (a) (i) attenuates T cell activity;

wherein optionally the attenuation of T cell activity occurs in human PBMC or whole blood samples; and/or the attenuation of T cell activity is measured by inhibition of cytokine production; wherein optionally the cytokine comprises IL-1, IL-2, IL-6, IL-12, IL-17, IL-22, IL-23, GM-CSF, TNF- α , and/or IFN- γ ;

wherein optionally the maximal percent attenuation of T cell activity is at least about 10%, 20%, 30%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%;

wherein optionally the EC₅₀ for attenuating T cell activity is from about 1 pM to about 10 pM, from about 10 pM to about 100 pM, from about 100 pM to about 1 nM, from about 1 nM to about 10 nM, or from about 10 nM to about 100 nM; and/or

(ii) downregulates PD-1 expression on the surface of T cells

wherein optionally the downregulation of PD-1 expression on the surface of T cells occurs as early as 4 hours after the treatment with the antibody or antigen-binding fragment thereof; and/or is concurrent with or precedes cytokine inhibition;

wherein optionally the maximal percent downregulation of PD-1 expression is at least about 10%, 20%, 30%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%;

(b) specifically binds to human PD-1 and/or monkey PD-1, but not rodent PD-1;

wherein optionally the K_D for binding to purified human PD-1 is from about 100 pM to about 10 nM, and the K_D for binding to human PD-1 expressed on cell surface and monkey PD-1 expressed on cell surface is from about 100 pM to about 10 nM; and/or

(c) has attenuated ADCC activity and/or attenuated CDC activity.

17. The pharmaceutical formulation of any one of claims 1 to 16, wherein
- (a) the antibody is a monoclonal antibody;
 - (b) the antibody is a humanized, human, or chimeric antibody; wherein optionally the humanized antibody is a deimmunized antibody or a composite human antibody;
 - (c) the antibody or antigen-binding fragment thereof is a Fab, a Fab', a F(ab')₂, a Fv, a scFv, a dsFv, a diabody, a triabody, a tetrabody, or a multispecific antibody formed from antibody fragments; and/or
 - (d) the antibody or antigen-binding fragment thereof is conjugated to an agent, wherein optionally the agent selected from the group consisting of a radioisotope, a metal chelator, an enzyme, a fluorescent compound, a bioluminescent compound, and a chemiluminescent compound.
18. The pharmaceutical formulation of any one of claims 1 to 17, further comprising a buffer system; wherein optionally the buffer system is selected from the group consisting of acetate buffer, succinate buffer, histidine buffer, and citrate buffer.
19. The pharmaceutical formulation of claim 18, wherein the concentration of the buffer system is within the range of 0.1 mM to 1 M; wherein optionally the concentration of the buffer system is within the range of 1 mM to 100 mM; wherein optionally the concentration of the buffer system is 10 mM.
20. The pharmaceutical formulation of claim 18 or 19, wherein the pH of the buffer system is within the range of pH 4-6.5; wherein optionally the pH of the buffer system is within the range of pH 4.7-5.7; wherein optionally the pH of the buffer system is pH 5.2.
21. The pharmaceutical formulation of any one of claims 1 to 20, further comprising a polyol; wherein optionally the polyol is selected from the group consisting of sugar, sugar alcohol, and sugar acid; and wherein optionally the sugar is sucrose; wherein optionally the concentration of the sucrose is within the range of 5-10% (w/v); and wherein optionally the concentration of the sucrose is 8.5% (w/v).

22. The pharmaceutical formulation of any one of claims 1 to 21, further comprising a surfactant; wherein optionally the surfactant is polysorbate-20 or polysorbate-80; wherein optionally the concentration of the polysorbate-80 is within the range of 0.001-0.1% (w/v); and wherein optionally the concentration of the polysorbate-80 is 0.005% (w/v).
23. A pharmaceutical formulation comprising an antibody or antigen-binding fragment thereof that binds to PD-1, 10 mM sodium acetate buffer (pH 5.2), 8.5% (w/v) sucrose, and 0.005% (w/v) polysorbate-80; wherein optionally the antibody or antigen-binding fragment thereof comprises:
- (a) a light chain variable region (VL) comprising VL complementarity determining region 1 (CDR1), VL CDR2, and VL CDR3 of any one of antibodies PD1AB-1, PD1AB-2, PD1AB-3, PD1AB-4, PD1AB-5, or PD1AB-6 as set forth in Table 1; and/or
 - (b) a heavy chain variable region (VH) comprising VH complementarity determining region 1 (CDR1), VH CDR2, and VH CDR3 of any one of antibodies PD1AB-1, PD1AB-2, PD1AB-3, PD1AB-4, PD1AB-5, or PD1AB-6 as set forth in Table 2.
24. The pharmaceutical formulation of any one of claims 1 to 23, wherein the pharmaceutical formulation is stable for at least 12 months when stored at $-70\text{ }^{\circ}\text{C} \pm 10\text{ }^{\circ}\text{C}$ or stable for at least 6 months when stored at $5\text{ }^{\circ}\text{C} \pm 3\text{ }^{\circ}\text{C}$.
25. A method of making the pharmaceutical formulation of any one of claims 1 to 24, comprising:
- (a) culturing a cell in a medium, wherein the cell comprises one or more polynucleotides comprising nucleotide sequences encoding a heavy chain, a light chain, or both a heavy chain and a light chain of the antibody or antigen-binding fragment thereof;
 - (b) harvesting the medium;
 - (c) subjecting the medium to a series of purification steps; wherein optionally the purification steps comprise:

- (i) an affinity chromatography; wherein optionally the affinity chromatography is a protein A affinity chromatography;
- (ii) a viral inactivation;
- (i) an ion exchange chromatography; wherein optionally the ion exchange chromatography is an anion exchange chromatography
- (iv) a viral filtration; wherein optionally the viral inactivation step is a low-pH viral inactivation step; and
- (v) an ultrafiltration/diafiltration; and

wherein optionally the method further comprises a formulation step.