

WHAT IS CLAIMED IS:

1. An isolated antibody or an antigen binding fragment thereof, comprising a heavy chain variable region and a light chain variable region,
 - a) wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:53, and the light chain variable region comprises the amino acid sequence of SEQ ID NO:55; or
 - b) wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 53, and the light chain variable region comprises the amino acid sequence of SEQ ID NO:67.
2. The antibody or an antigen binding fragment thereof of claim 1, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 53, and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 55.
3. The antibody or an antigen binding fragment thereof of claim 1, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 53; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 67.
4. The antibody or an antigen binding fragment thereof of any one of claims 1 to 3 which,
 - i) is capable of specifically binding to human PD-1 at an K_d value no more than 10^{-8} M as measured by plasmon resonance binding assay; and/or
 - ii) binds to monkey PD-1 at an EC_{50} of no more than 100nM, or no more than 10nM, and/or does not bind to mouse PD-1; and/or iii) is capable of inhibiting binding of human or monkey PD-1 to its ligand at an IC_{50} of no more than 100 nM; and/or
 - iv) does not substantially bind to CD28 or CTLA4; and/or
 - v) does not mediate ADCC or CDC or both.
5. The antibody or an antigen binding fragment thereof of any one of claims 1 to 4, which is
 - i) a fully human monoclonal antibody or ii) a fully human monoclonal antibody produced by a transgenic rat.
6. The antibody or antigen-binding fragment thereof of any one of claims 1 to 4, which is a diabody, a scFv, an scFv dimer, a BsFv, a dsFv, a (dsFv)₂, a dsFv-dsFv', an Fv fragment, a Fab, a Fab', a F(ab')₂, or a ds diabody.
7. The antibody or an antigen binding fragment thereof of any one of claims 1 to 6, capable of blocking binding of human PD-1 to its ligand and thereby providing at least one of the following activities:
 - a) inducing production of IL-2 in CD4⁺T cells;

- b) inducing production of IFN γ in CD4⁺T cells;
 - c) inducing proliferation of CD4⁺T cells; and
 - d) reversing T reg's suppressive function.
8. The antibody or antigen-binding fragment thereof of any one of claims 1 to 7, further comprising an immunoglobulin constant region, and/or further comprising a conjugate.
 9. An isolated polynucleotide or polynucleotides encoding the antibody or an antigen binding fragment thereof of any one of claims 1 to 8.
 10. A vector or vectors comprising the isolated polynucleotide or polynucleotides of claim 9.
 11. A host cell comprising the vector or vectors of claim 10.
 12. A method of expressing the antibody or antigen-binding fragment thereof, comprising culturing the host cell of claim 11 under the condition at which the polynucleotide or polynucleotides encoding the antibody or an antigen binding fragment thereof is or are expressed.
 13. An antigen or an antigen binding fragment thereof when expressed by the method of claim 12.
 14. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1 to 8 or 13, and one or more pharmaceutically acceptable carriers.
 15. A kit comprising the antibody or antigen-binding fragment thereof of any one of claims 1 to 8 or 13, or the pharmaceutical composition of claim 14.
 16. Use of the antibody or antigen-binding fragment thereof of any one of claims 1 to 8 or 13 in the manufacture of a medicament for treating cancer or chronic viral infection associated with PD-1 in an subject, wherein the subject has been identified as having cancer or chronic viral infection likely to respond to a PD-1 antagonist, and/or wherein the subject has been identified as positive for the presence or upregulated level of the PD-L1 in a test biological sample from the subject.
 17. The use of the antibody or antigen-binding fragment thereof of any one of claims 1 to 8 or 13 in the manufacture of a medicament for treating cancer or chronic viral infection in a subject.