

CLAIM(S):

1. An anti-PD-1 binding agent comprising an immunoglobulin heavy chain variable region and an immunoglobulin light chain variable region, wherein
- (a) the immunoglobulin heavy chain variable region comprises:
- a CDR1 comprising SEQ ID NO: 1;
 - a CDR2 comprising SEQ ID NO: 2; and
 - a CDR3 comprising SEQ ID NO: 3;
- and the immunoglobulin light chain variable region comprises
- a CDR1 comprising SEQ ID NO: 4;
 - a CDR2 comprising SEQ ID NO: 5; and
 - a CDR3 comprising SEQ ID NO: 6;
- (b) the immunoglobulin heavy chain variable region comprises at least 80% sequence identity to any one of SEQ ID NOs: 24-33, and/or comprises at least the CDR regions of any one of SEQ ID NOs: 24-33, and the immunoglobulin light chain variable region comprises at least 80% sequence identity to SEQ ID NO: 34 or 35, and/or comprises at least the CDR regions of any one of SEQ ID NO: 34 or 35;
- (c) the immunoglobulin heavy chain variable region comprises:
- a CDR1 comprising SEQ ID NO: 7;
 - a CDR2 comprising SEQ ID NO: 8; and
 - a CDR3 comprising SEQ ID NO: 9;
- and the immunoglobulin light chain variable region comprises
- a CDR1 comprising SEQ ID NO: 10;
 - a CDR2 comprising SEQ ID NO: 11; and
 - a CDR3 comprising SEQ ID NO: 12;
- or
- (d) the immunoglobulin heavy chain variable region comprises at least 80% sequence identity to any one of SEQ ID NOs: 43-47 or 61-63, and/or comprises at least the CDR regions of any one of SEQ ID NOs: 43-47 or 61-63, and the immunoglobulin light chain

variable region comprises at least 80% sequence identity to SEQ ID NOs: 48-50, and/or comprises at least the CDR regions of any one of SEQ ID NOs: 48-50.

2. The anti-PD-1 binding agent of claim 1, wherein the immunoglobulin heavy chain variable region comprises at least 90% sequence identity to any one of SEQ ID NOs: 24-33, and/or comprises at least the CDR regions of any one of SEQ ID NOs: 24-33.

3. The anti-PD-1 binding agent of claim 1, comprising the immunoglobulin heavy chain variable region of any one of SEQ ID NOs: 24-33.

4. The anti-PD-1 binding agent of any of claims 1-3, wherein the immunoglobulin light chain variable region comprises at least 90% sequence identity to SEQ ID NO: 34 or 35, and/or comprises at least the CDR regions of any one of SEQ ID NO: 34 or 35.

5. The anti-PD-1 binding agent of any of claims 1-3, comprising the immunoglobulin light chain variable region of SEQ ID NO: 34 or 35.

6. The anti-PD-1 binding agent of claim 1, wherein the immunoglobulin heavy chain variable region comprises:

- a CDR1 comprising SEQ ID NO: 1;
- a CDR2 comprising SEQ ID NO: 2; and
- a CDR3 comprising SEQ ID NO: 3;

and the immunoglobulin light chain variable region comprises

- a CDR1 comprising SEQ ID NO: 4;
- a CDR2 comprising SEQ ID NO: 5; and
- a CDR3 comprising SEQ ID NO: 6.

7. The anti-PD-1 binding agent of claim 6, wherein the immunoglobulin heavy chain variable region CDR1 comprises any one of SEQ ID NOs: 13-18.

8. The anti-PD-1 binding agent of claim 6 or 7, wherein the immunoglobulin heavy chain variable region CDR3 comprises any one of SEQ ID NOs: 19-21.

9. The anti-PD-1 binding agent of any one of claims 5-8, wherein the immunoglobulin light chain variable region CDR1 comprises SEQ ID NO: 22 or 23.

10. The anti-PD-1 binding agent of claim 4, wherein the immunoglobulin heavy chain variable region comprises:

- a CDR1 comprising SEQ ID NO: 15;
- a CDR2 comprising SEQ ID NO: 2; and
- a CDR3 comprising SEQ ID NO: 20;

and the immunoglobulin light chain variable region comprises

- a CDR1 comprising SEQ ID NO: 23;
- a CDR2 comprising SEQ ID NO: 5; and
- a CDR3 comprising SEQ ID NO: 6;

or

wherein the immunoglobulin heavy chain variable region comprises:

- a CDR1 comprising SEQ ID NO: 15;
- a CDR2 comprising SEQ ID NO: 2; and
- a CDR3 comprising SEQ ID NO: 21;

and the immunoglobulin light chain variable region comprises

- a CDR1 comprising SEQ ID NO: 23;
- a CDR2 comprising SEQ ID NO: 5; and
- a CDR3 comprising SEQ ID NO: 6;

or

wherein the immunoglobulin heavy chain variable region comprises:

- a CDR1 comprising SEQ ID NO: 13;
- a CDR2 comprising SEQ ID NO: 2; and
- a CDR3 comprising SEQ ID NO: 19;

and the immunoglobulin light chain variable region comprises

- a CDR1 comprising SEQ ID NO: 23;
- a CDR2 comprising SEQ ID NO: 5; and
- a CDR3 comprising SEQ ID NO: 6.

11. The anti-PD-1 binding agent of claim 1, wherein the immunoglobulin heavy chain variable region comprises at least 90% sequence identity to SEQ ID NO: 29, or comprises at least the CDR regions of SEQ ID NO: 29, and the immunoglobulin light chain variable region comprises at least 90% sequence identity to SEQ ID NO: 35, or comprises at least the CDR regions of SEQ ID NO: 35;

or wherein the immunoglobulin heavy chain variable region comprises at least 90% sequence identity to SEQ ID NO: 30, or comprises at least the CDR regions of SEQ ID NO: 30, and the immunoglobulin light chain variable region comprises at least 90% sequence identity to SEQ ID NO: 35, or comprises at least the CDR regions of SEQ ID NO: 35;

or wherein the immunoglobulin heavy chain variable region comprises at least 90% sequence identity to SEQ ID NO: 24, or comprises at least the CDR regions of SEQ ID NO: 24, and the immunoglobulin light chain variable region comprises at least 90% sequence identity to SEQ ID NO: 34, or comprises at least the CDR regions of SEQ ID NO: 34.

12. The anti-PD-1 binding agent of claim 11, wherein the immunoglobulin heavy chain variable region comprises SEQ ID NO: 29, and the immunoglobulin light chain variable region comprises SEQ ID NO: 35;

or wherein the immunoglobulin heavy chain variable region comprises SEQ ID NO: 30, and the immunoglobulin light chain variable region comprises SEQ ID NO: 35;

or wherein the immunoglobulin heavy chain variable region comprises SEQ ID NO: 24, and the immunoglobulin light chain variable region comprises SEQ ID NO: 34.

13. The anti-PD-1 binding agent of claim 1, wherein the immunoglobulin heavy chain variable region comprises at least 90% sequence identity to any one of SEQ ID NOs: 43-47 or 61-63, or comprises at least the CDR regions of any one of SEQ ID NOs: 43-47 or 61-63.

14. The anti-PD-1 binding agent of claim 1 or 13, wherein the immunoglobulin light chain variable region comprises at least 90% sequence identity to SEQ ID NOs: 48-50, or comprises at least the CDR regions of any one of SEQ ID NOs: 48-50.

15. The anti-PD-1 binding agent of claim 13 or 14, wherein the immunoglobulin heavy chain comprises any one of SEQ ID NOs: 43-47 or 61-63.

16. The anti-PD-1 binding agent of any of claims 13-15, comprising the immunoglobulin light chain variable region of any one of SEQ ID NOs: 48-50.

17. The anti-PD-1 binding agent of claim 1, wherein the immunoglobulin heavy chain variable region comprises:

a CDR1 comprising SEQ ID NO: 7;

a CDR2 comprising SEQ ID NO: 8; and

a CDR3 comprising SEQ ID NO: 9;

and the immunoglobulin light chain variable region comprises

a CDR1 comprising SEQ ID NO: 10;

a CDR2 comprising SEQ ID NO: 11; and

a CDR3 comprising SEQ ID NO: 12.

18. The anti-PD-1 binding agent of claim 17, wherein the immunoglobulin heavy chain variable region CDR1 comprises any one of SEQ ID NO: 57-60.

19. The anti-PD-1 binding agent of claim 17 or 18, wherein the immunoglobulin heavy chain variable region CDR2 comprises any one of SEQ ID NOs: 38-42.

20. The anti-PD-1 binding agent of claim 17, wherein the immunoglobulin heavy chain variable region comprises:

a CDR1 comprising SEQ ID NO: 57;

a CDR2 comprising SEQ ID NO: 42; and

a CDR3 comprising SEQ ID NO: 9;

and the immunoglobulin light chain variable region comprises

a CDR1 comprising SEQ ID NO: 10;

a CDR2 comprising SEQ ID NO: 11; and

a CDR3 comprising SEQ ID NO: 12;

or

wherein the immunoglobulin heavy chain variable region comprises:

a CDR1 comprising SEQ ID NO: 57;

a CDR2 comprising SEQ ID NO: 41; and
a CDR3 comprising SEQ ID NO: 9;
and the immunoglobulin light chain variable region comprises
a CDR1 comprising SEQ ID NO: 10;
a CDR2 comprising SEQ ID NO: 11; and
a CDR3 comprising SEQ ID NO: 12.

21. The anti-PD-1 binding agent of claim 1, wherein the immunoglobulin heavy chain variable region comprises at least 90% sequence identity to SEQ ID NO: 47, or comprises at least the CDR regions of SEQ ID NO: 47;

and the immunoglobulin light chain variable region comprises at least 90% sequence identity to SEQ ID NO: 49, or comprises at least the CDR regions of SEQ ID NO: 49;

or wherein the immunoglobulin heavy chain variable region comprises at least 90% sequence identity to SEQ ID NO: 46, or comprises at least the CDR regions of SEQ ID NO: 46;

and the immunoglobulin light chain variable region comprises at least 90% sequence identity to SEQ ID NO: 50, or comprises at least the CDR regions of SEQ ID NO: 50.

22. The anti-PD-1 binding agent of claim 21, comprising the immunoglobulin heavy chain variable region of SEQ ID NO: 47, and the immunoglobulin light chain variable region of SEQ ID NO: 49;

or comprising the immunoglobulin heavy chain variable region of SEQ ID NO: 46, and the immunoglobulin light chain variable region of SEQ ID NO: 50.

23. The anti-PD-1 binding agent of any one of claims 1-22, wherein the anti-PD-1 binding agent is an antibody, an antibody conjugate, or an antigen-binding fragment thereof.

24. The anti-PD-1 binding agent of any one of claims 1-23, wherein the anti-PD-1 binding agent is a F(ab')₂, Fab', Fab, Fv, scFv, dsFv, or a single chain binding polypeptide.

25. The anti-PD-1 binding agent of any one of claims 1-24, wherein the anti-PD-1 binding agent comprises an IgG Fc region that binds an Fc receptor on an antigen presenting cell.

26. The anti-PD-1 binding agent of any one of claims 1-25, wherein the anti-PD-1 binding agent comprises an Fc region of IgG1 or other Fc region that binds FcγR.

27. The anti-PD-1 binding agent of claim 1, comprising an immunoglobulin heavy chain comprising SEQ ID NO: 36 and an immunoglobulin light chain comprising SEQ ID NO: 37.

28. The anti-PD-1 binding agent of claim 1, comprising an immunoglobulin heavy chain comprising SEQ ID NO: 51 and an immunoglobulin light chain comprising SEQ ID NO: 52.

29. A pharmaceutical composition comprising (a) anti-PD-1 binding agent of any one of claims 1-28, and (b) a pharmaceutically acceptable carrier.

30. A method of inhibiting an immune response in a mammal, which method comprises administering the anti-PD-1 binding agent of any of claims 1-28 or pharmaceutical composition of claim 29 to the mammal.

31. A method of treating an inflammatory or autoimmune disorder in a mammal, which method comprises administering the anti-PD-1 binding agent of any of claims 1-28 or pharmaceutical composition of claim 29 to a mammal with an inflammatory or autoimmune disorder, whereupon the disorder is treated.

32. The method of claim 31, wherein the inflammatory or autoimmune disorder is Primary Biliary Cholangitis (PBC), Graft vs Host Disease (GvHD), Vitiligo, ANCA Vasculitis, Type 1 Diabetes, or Noninfectious Uveitis..

33. A nucleic acid encoding the immunoglobulin heavy chain and/or immunoglobulin light chain of the anti-PD-1 binding agent of any of claims 1-28, optionally in a vector.

34. A cell that expresses the anti-PD-1 binding agent of any of claims 1-28.

35. A method of preparing the anti-PD-1 binding agent of any one of claims 1-28, the method comprising expressing in a cell a nucleic acid sequence encoding the immunoglobulin heavy chain and a nucleic acid sequence encoding the immunoglobulin light chain of the anti-PD-1 binding agent of any of claims 1-28.

36. The anti-PD-1 binding agent of any of claims 1-28, or the pharmaceutical composition of claim 29, for inhibiting an immune response in a mammal.

37. The anti-PD-1 binding agent of any of claims 1-28, or the pharmaceutical composition of claim 29, for treating an inflammatory or autoimmune disorder in a mammal.

32. The anti-PD-1 binding agent or pharmaceutical composition of claim 37, wherein the inflammatory or autoimmune disorder is Primary Biliary Cholangitis (PBC), Graft vs Host Disease (GvHD), Vitiligo, ANCA Vasculitis, Type 1 Diabetes, or Noninfectious Uveitis.