CLAIMS

1. An antibody capable of specifically binding to PD-1 or an antigen-binding fragment thereof, comprising:

(a) a VH CDR1 or a variant thereof, a VH CDR2 or a variant thereof, and a VH CDR3 or a variant thereof comprised in a heavy chain variable region (VH) set forth in SEQ ID NO: 31 or 39; and/or a VL CDR1 or a variant thereof, a VL CDR2 or a variant thereof, and a VL CDR3 or a variant thereof comprised in a light chain variable region (VL) set forth in SEQ ID NO: 32 or 40; or

(b) a VH CDR1 or a variant thereof, a VH CDR2 or a variant thereof, and a VH CDR3 or a variant thereof comprised in a heavy chain variable region (VH) set forth in SEQ ID NO: 7 or 15; and/or a VL CDR1 or a variant thereof, a VL CDR2 or a variant thereof, and a VL CDR3 or a variant thereof comprised in a light chain variable region (VL) set forth in SEQ ID NO: 8 or 16;

wherein the variant has one or several amino acid substitutions, deletions or additions (e.g., 1, 2 or 3 amino acid substitutions, deletions or additions, such as conservative substitutions) compared to the sequence from which the variant is derived; preferably, the substitutions are conservative substitutions;

preferably, the antibody or the antigen-binding fragment thereof comprises:

(a) three CDRs comprised in a heavy chain variable region (VH) set forth in SEQ ID NO: 31 or 39; and/or three CDRs comprised in a light chain variable region (VL) set forth in SEQ ID NO: 32 or 40; or

(b) three CDRs comprised in a heavy chain variable region (VH) set forth in SEQ ID NO: 7 or 15; and/or three CDRs comprised in a light chain variable region (VL) set forth in SEQ ID NO: 8 or 16.

2. The antibody or the antigen-binding fragment thereof according to claim 1, comprising:

(a) a heavy chain variable region (VH) comprising the following three complementary determining regions (CDRs): a VH CDR1 set forth in SEQ ID NO: 1, a VH CDR2 set forth in SEQ ID NO: 2, and a VH CDR3 set forth in SEQ ID NO: 3; and/or a light chain variable region (VL) comprising the following three complementary determining regions (CDRs): a VL CDR1 set forth in SEQ ID NO: 4, a VL CDR2 set forth in SEQ ID NO: 5, and a VL CDR3 set forth in SEQ ID NO: 6; or,

(b) a heavy chain variable region (VH) comprising the following three complementary

determining regions (CDRs): a VH CDR1 set forth in SEQ ID NO: 25, a VH CDR2 set forth in SEQ ID NO: 26, and a VH CDR3 set forth in SEQ ID NO: 27; and/or a light chain variable region (VL) comprising the following three complementary determining regions (CDRs): a VL CDR1 set forth in SEQ ID NO: 28, a VL CDR2 set forth in SEQ ID NO: 29, and a VL CDR3 set forth in SEQ ID NO: 30;

wherein the CDR is defined by the Kabat numbering system.

3. The antibody or the antigen-binding fragment thereof according to claim 1 or 2, comprising:

(a) a heavy chain variable region (VH) comprising a sequence as set forth in SEQ ID NO: 7 or a variant thereof; and/or a light chain variable region (VL) comprising a sequence as set forth in SEQ ID NO: 8 or a variant thereof; or,

(b) a heavy chain variable region (VH) comprising a sequence as set forth in SEQ ID NO: 31 or a variant thereof; and/or a light chain variable region (VL) comprising a sequence as set forth in SEQ ID NO: 32 or a variant thereof;

wherein the variant has one or several amino acid substitutions, deletions or additions (e.g., 1, 2, 3, 4, or 5 amino acid substitutions, deletions or additions), or a sequence with at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity compared to the sequence from which the variant is derived; preferably, the substitutions are conservative substitutions;

preferably, the antibody or the antigen-binding fragment thereof comprises: a VH comprising a sequence as set forth in SEQ ID NO: 7 and a VL comprising a sequence as set forth in SEQ ID NO: 8;

preferably, the antibody or the antigen-binding fragment thereof comprises: a VH comprising a sequence as set forth in SEQ ID NO: 31 and a VL comprising a sequence as set forth in SEQ ID NO: 32.

4. The antibody or the antigen-binding fragment thereof according to claim 1 or 2, wherein the antibody or the antigen-binding fragment thereof comprises a framework region sequence derived from a human immunoglobulin;

preferably, the antibody or the antigen-binding fragment thereof comprises: a heavy chain framework region of a human heavy chain germline sequence, and/or a light chain framework region of a human light chain germline sequence.

5. The antibody or the antigen-binding fragment thereof according to claim 4, wherein the antibody or the antigen-binding fragment thereof comprises:

(a) a heavy chain variable region (VH) comprising a sequence as set forth in SEQ ID NO: 15 or a variant thereof; and/or a light chain variable region (VL) comprising a sequence as set forth in SEQ ID NO: 16 or a variant thereof; or,

(b) a heavy chain variable region (VH) comprising a sequence as set forth in SEQ ID NO: 39 or a variant thereof; and/or a light chain variable region (VL) comprising a sequence as set forth in SEQ ID NO: 40 or a variant thereof;

wherein the variant has one or several amino acid substitutions, deletions or additions (e.g., 1, 2, 3, 4, or 5 amino acid substitutions, deletions or additions), or has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity compared to the sequence from which the variant is derived;

preferably, the substitutions are conservative substitutions;

preferably, the antibody or the antigen-binding fragment thereof comprises:

(a) a heavy chain variable region (VH) comprising a sequence as set forth in SEQ ID NO: 15; and/or a light chain variable region (VL) comprising a sequence as set forth in SEQ ID NO: 16; or,

(b) a heavy chain variable region (VH) comprising a sequence as set forth in SEQ ID NO: 39; and/or a light chain variable region (VL) comprising a sequence as set forth in SEQ ID NO: 40.

6. The antibody or the antigen-binding fragment thereof according to any one of claims 1-5, wherein the antibody or the antigen-binding fragment thereof further comprises a constant region derived from a mammal (e.g., human or mouse) immunoglobulin;

preferably, a heavy chain of the antibody or the antigen-binding fragment thereof comprises a heavy chain constant region derived from a human immunoglobulin (such as IgG, e.g., IgG1, IgG2, IgG3, or IgG4), and/or a light chain of the antibody or the antigen-binding fragment thereof comprises a light chain constant region derived from a human immunoglobulin (e.g., κ or λ).

7. The antibody or the antigen-binding fragment thereof according to claim 6, wherein the antibody or the antigen-binding fragment thereof comprises a variant of the human immunoglobulin heavy chain constant region, which has enhanced binding activity to Fc receptors (e.g., CD32A, CD32B and/or CD16A) compared with the wild-type human immunoglobulin heavy

chain constant region;

preferably, the antibody or the antigen-binding fragment thereof comprises a human IgG1 or IgG4 heavy chain constant region variant, the heavy chain constant region variant comprises a substitution at one or more of the following positions numbered according to EU: 239, 268; preferably, the substitution is selected from S239D/H268D or S239D/Q268D.

8. The antibody or the antigen-binding fragment thereof according to claim 6 or 7, wherein the antibody or the antigen-binding fragment thereof comprises:

(1) a heavy chain comprising a sequence as set forth in SEQ ID NO: 11 and a light chain comprising a sequence as set forth in SEQ ID NO: 12;

(2) a heavy chain comprising a sequence as set forth in SEQ ID NO: 19 and a light chain comprising a sequence as set forth in SEQ ID NO: 20;

(3) a heavy chain comprising a sequence as set forth in SEQ ID NO: 23 and a light chain comprising a sequence as set forth in SEQ ID NO: 20;

(4) a heavy chain comprising a sequence as set forth in SEQ ID NO: 35 and a light chain comprising a sequence as set forth in SEQ ID NO: 36;

(5) a heavy chain comprising a sequence as set forth in SEQ ID NO: 43 and a light chain comprising a sequence as set forth in SEQ ID NO: 44; or,

(6) a heavy chain comprising a sequence as set forth in SEQ ID NO: 47 and a light chain comprising a sequence as set forth in SEQ ID NO: 44.

9. The antibody or the antigen-binding fragment thereof according to any one of claims 1-8, wherein the antigen-binding fragment is selected from Fab, Fab', $F(ab')_2$, Fd, Fv, disulfide-linked Fv, scFv, di-scFv, $(scFv)_2$, a diabody, and a single domain antibody (sdAb); and/or the antibody is a murine antibody, a humanized antibody, a chimeric antibody, a bispecific antibody, or a multispecific antibody.

10. An isolated nucleic acid molecule encoding the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, or the heavy chain variable region and/or the light chain variable region thereof, or the heavy chain and/or the light chain thereof.

11. A vector, comprising the isolated nucleic acid molecule according to claim 10; preferably, the vector is a cloning vector or an expression vector.

12. A host cell, comprising the isolated nucleic acid molecule according to claim 10 or the

vector according to claim 11.

13. A method for preparing the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, comprising: culturing the host cell of claim 12 under conditions allowing the expression of the antibody or the antigen-binding fragment thereof, and recovering the antibody or the antigen-binding fragment thereof from the cultured host cell culture.

14. A bispecific or multispecific molecule, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-9;

preferably, the bispecific or multispecific molecule specifically binds to PD-1, and additionally specifically binds to one or more other targets;

preferably, the bispecific or multispecific molecule further comprises at least one molecule (e.g., a second antibody) with a second binding specificity for a second target.

15. An immunoconjugate, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-9 and a therapeutic agent linked to the antibody or the antigen-binding fragment thereof;

preferably, the therapeutic agent is a cytotoxic agent.

16. A pharmaceutical composition, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, the isolated nucleic acid molecule according to claim 10, the vector according to claim 11, the host cell according to claim 12, the bispecific or multispecific molecule according to claim 14 or the immunoconjugate according to claim 15, and a pharmaceutically acceptable carrier and/or excipient;

preferably, the pharmaceutical composition further comprises an additional pharmaceutically active agent;

preferably, the additional pharmaceutically active agent is an immunosuppressant;

preferably, the additional pharmaceutically active agent is a drug for treating autoimmune diseases, allergic diseases, graft-versus-host disease, transplant rejection, or lymphoma.

17. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, the isolated nucleic acid molecule according to claim 10, the vector according to claim 11, the host cell according to claim 12, the bispecific or multispecific molecule according to claim 14, the immunoconjugate according to claim 15 or the pharmaceutical composition according to claim 16 in the preparation of PD-1 signaling pathway activators.

18. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, the isolated nucleic acid molecule according to claim 10, the vector according to claim 11, the host cell according to claim 12, the bispecific or multispecific molecule according to claim 14, the immunoconjugate according to claim 15 or the pharmaceutical composition according to claim 16 in the preparation of immunosuppressants (such as T-cell activity inhibitors).

19. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-9, the isolated nucleic acid molecule according to claim 10, the vector according to claim 11, the host cell according to claim 12, the bispecific or multispecific molecule according to claim 14, the immunoconjugate according to claim 15 or the pharmaceutical composition according to claim 16 in the preparation of a drug, wherein the drug is used for preventing and/or treating autoimmune diseases, allergic diseases, graft-versus-host disease, transplant rejection, or lymphoma in a subject;

preferably, the autoimmune disease is selected from arthritis, rheumatoid arthritis, psoriatic arthritis, lupus, lupus nephritis, systemic lupus erythematosus, psoriasis, vitiligo, alopecia areata, inflammatory bowel disease, ulcerative colitis, Crohn's disease, type I diabetes, multiple sclerosis, autoimmune hepatitis, primary biliary cirrhosis, celiac disease, scleroderma, Graves' disease, Hashimoto's thyroiditis, ankylosing spondylitis, myasthenia gravis, Sjögren's syndrome, IgA nephropathy, IgG4-related disease, vasculitis, ANCA-associated vasculitis, uveitis, pemphigus, pemphigoid, or autoimmune hemolytic anemia;

preferably, the allergic disease is selected from idiopathic thrombocytopenic purpura, atopic dermatitis, asthma, allergic rhinitis, drug allergy, food allergy, anaphylaxis, allergic conjunctivitis, urticaria, eosinophilic sinusitis, eosinophilic gastrointestinal disease, or allergic bronchopulmonary aspergillosis;

preferably, the lymphoma is T-cell lymphoma;

preferably, the subject is a mammal, such as a human or a non-human primate (e.g., cynomolgus monkey);

preferably, the antibody or the antigen-binding fragment thereof is used alone or in combination with an additional pharmaceutically active agent; preferably, the additional pharmaceutically active agent is an immunosuppressant; preferably, the additional pharmaceutically active agent is a drug for treating autoimmune diseases, allergic diseases, graft-versus-host disease, transplant rejection, or lymphoma.

20. A conjugate, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-9 and a detectable label linked to the antibody or the antigen-binding fragment thereof;

preferably, the detectable label is selected from an enzyme (e.g., horseradish peroxidase or alkaline phosphatase), a chemiluminescent reagent (e.g., acridinium ester compounds, luminol and derivatives thereof, or ruthenium derivatives), a fluorescent dye (e.g., fluorescein or fluorescent protein), a radionuclide, or a biotin.

21. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-9 or the conjugate according to claim 20 in the preparation of a detection reagent, wherein the detection reagent is used for detecting the presence or level of PD-1 in a sample and/or diagnosing a PD-1-related disease;

preferably, the PD-1-related disease includes autoimmune disorders, allergic diseases, graft-versus-host disease, transplant rejection, lymphoma, or any combination thereof;

preferably, the PD-1-related disease is selected from tumors.