

## CLAIMS

1. An antibody capable of specifically binding to PD-1 or a functional fragment thereof, wherein the antibody or the functional fragment thereof comprise a light chain and a heavy chain;

the light chain comprises a light chain CDR consisting of CDR-L1, CDR-L2 and CDR-L3; the heavy chain comprises a heavy chain CDR consisting of CDR-H1, CDR-H2 and CDR-H3;

the amino acid sequences of the CDR-L1, CDR-L2, and CDR-L3 are respectively set forth in SEQ ID NO: 1, 5 and 6, or respectively set forth in SEQ ID NO: 2, 5 and 6, or respectively set forth in SEQ ID NO: 3, 5 and 6, or respectively set forth in SEQ ID NO: 4, 5 and 6; the amino acid sequences of the CDR-H1, CDR-H2, and CDR-H3 are respectively set forth in SEQ ID NO: 7, 8 and 9.

2. The antibody or the functional fragment thereof according to claim 1, wherein the antibody or the functional fragment thereof is a PD-1 chimeric antibody or a functional fragment thereof, or a PD-1 humanized antibody or a functional fragment thereof.

3. The antibody or the functional fragment thereof according to claim 1, wherein the antibody comprises a constant region sequence of any one selected from the group consisting of human IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgE and IgD.

4. The antibody or the functional fragment thereof according to claim 1 or 2, wherein the functional fragment comprises one or more selected from the group consisting of F(ab')<sub>2</sub>, Fab', Fab, Fv, scFv, bispecific antibody and antibody minimal recognition unit.

5. The antibody or the functional fragment thereof according to any one of claims 2 to 4, wherein the amino acid sequences of light chain variable region and heavy chain

variable region of the PD-1 chimeric antibody or the functional fragment thereof are respectively set forth in SEQ ID NO: 10 and SEQ ID NO: 14.

6. The antibody or the functional fragment thereof according to claim 5, wherein the amino acid sequences of the light chain constant region and the heavy chain constant region of the PD-1 chimeric antibody or the functional fragment thereof are respectively set forth in SEQ ID NO: 15 and SEQ ID NO: 16.

7. The antibody or the functional fragment thereof according to any one of claims 2 to 4, wherein light chain framework region of the PD-1 humanized antibody or the functional fragment thereof comprises FR-L1, FR-L2, FR-L3 and FR-L4, and heavy chain framework region of the PD-1 humanized antibody or the functional fragment thereof comprises FR-H1, FR-H2, FR-H3 and FR-H4;

the FR-L1 is selected from the amino acid sequence set forth in SEQ ID NO: 17 and the amino sequence having the following substitution or a combination thereof:

the 1<sup>st</sup> amino acid D is replaced by E;

the 2<sup>nd</sup> amino acid V is replaced by I;

the 13<sup>th</sup> amino acid L is replaced by V;

the 19<sup>th</sup> amino acid A is replaced by V;

the FR-L2 is selected from the amino acid sequence set forth in SEQ ID NO: 18 and the amino sequence having the following substitution or a combination thereof:

the 6<sup>th</sup> amino acid P is replaced by S;

the 7<sup>th</sup> amino acid G is replaced by H;

the 9<sup>th</sup> amino acid A is replaced by S;

the FR-L3 is selected from the amino acid sequence set forth in SEQ ID NO: 19 and the amino sequence having the following substitution or a combination thereof:

the 22<sup>th</sup> amino acid L is replaced by V;

the 24<sup>th</sup> amino acid P is replaced by T;

the 28<sup>th</sup> amino acid A is replaced by G;

the 31<sup>th</sup> amino acid F is replaced by Y;

the FR-L4 is selected from the amino acid sequence set forth in SEQ ID NO: 20 and the amino sequence having the following substitution or a combination thereof:

the 7<sup>th</sup> amino acid V is replaced by L;

the FR-H1 is selected from the amino acid sequence set forth in SEQ ID NO: 21;

the FR-H2 is selected from the amino acid sequence set forth in SEQ ID NO: 22 and the amino sequence having the following substitution or a combination thereof:

the 5<sup>th</sup> amino acid A is replaced by T;

the 14<sup>th</sup> amino acid A is replaced by S;

the FR-H3 is selected from the amino acid sequence set forth in SEQ ID NO: 23 and the amino sequence having the following substitution or a combination thereof:

the 12<sup>th</sup> amino acid N is replaced by T;

the 14<sup>th</sup> amino acid Y is replaced by H;

the 18<sup>th</sup> amino acid N is replaced by S;

the FR-H4 is selected from the amino acid sequence set forth in SEQ ID NO: 24.

8. The antibody or the functional fragment thereof according to claim 7, wherein the light chain variable region sequence of the PD-1 humanized antibody or the functional fragment thereof is one selected from SEQ ID NO: 25 to 36.

9. The antibody or the functional fragment thereof according to claim 7, wherein the heavy chain variable region sequence of the PD-1 humanized antibody or the functional fragment thereof is one selected from SEQ ID NO: 37 to 42.

10. The antibody or the functional fragment thereof according to claim 7, wherein the light chain variable region sequence of the PD-1 humanized antibody or the functional fragment thereof is set forth in SEQ ID NO: 25; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 37;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 25; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 38;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 29; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 38;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 30; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 38;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 31; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 38;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 26; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 38;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 28; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 40;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 25; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 40;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 29; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 40;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 30; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 40;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 31; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 40;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 28; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 38;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 27; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 39;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 32; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 39;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 33; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 39;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 34; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 39;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 35; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 41;

alternatively, the light chain variable region sequence of the PD-1 humanized antibody and functional fragment thereof is set forth in SEQ ID NO: 36; the corresponding heavy chain variable region sequence is set forth in SEQ ID NO: 42.

11. The antibody or the functional fragment thereof according to claim 7, wherein the amino acid sequences of the light chain constant region sequence and the heavy chain constant region sequence of the PD-1 humanized antibody or the functional fragment thereof are set forth in SEQ ID NO: 15 and SEQ ID NO: 16, respectively.

12. An isolated nucleic acid molecule selected from:

- A) DNA or RNA, encoding the antibody or the functional fragment thereof according to any one of claims 1 to 11; and
- B) a nucleic acid complementary to the nucleic acid as defined in A).

13. A composition, comprising the antibody and/or the functional fragment thereof

according to any one of claims 1 to 11, or a compound of the antibody and other components, or a compound of the antibody functional fragment and other components, as an active ingredient.

14. The composition according to claim 13, wherein the antibody or the functional fragment thereof are coupled to at least one diagnostic agent and/or therapeutic agent to form an immunoconjugate.

15. The composition according to claim 13, wherein the diagnostic agent is one or more selected from the group consisting of a radionuclide, a radioactive contrast agent, a paramagnetic ion, a metal, a fluorescent label, a chemiluminescent label, an ultrasound contrast agent, and a photosensitizer.

16. The composition according to claim 15, wherein the radionuclide is one or more selected from the group consisting of  $^{110}\text{In}$ ,  $^{111}\text{In}$ ,  $^{177}\text{Lu}$ ,  $^{18}\text{F}$ ,  $^{52}\text{Fe}$ ,  $^{62}\text{Cu}$ ,  $^{64}\text{Cu}$ ,  $^{67}\text{Cu}$ ,  $^{67}\text{Ga}$ ,  $^{68}\text{Ga}$ ,  $^{86}\text{Y}$ ,  $^{90}\text{Y}$ ,  $^{89}\text{Zr}$ ,  $^{94}\text{mTc}$ ,  $^{94}\text{Tc}$ ,  $^{99}\text{mTc}$ ,  $^{120}\text{I}$ ,  $^{123}\text{I}$ ,  $^{124}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{154-158}\text{Gd}$ ,  $^{32}\text{P}$ ,  $^{11}\text{C}$ ,  $^{13}\text{N}$ ,  $^{15}\text{O}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{51}\text{Mn}$ ,  $^{52}\text{mMn}$ ,  $^{55}\text{Co}$ ,  $^{72}\text{As}$ ,  $^{75}\text{Br}$ ,  $^{76}\text{Br}$ ,  $^{82}\text{mRb}$  and  $^{83}\text{Sr}$ .

17. The composition according to claim 15, wherein the paramagnetic ion is one or more selected from the group consisting of chromium (III), manganese (II), iron (III), iron (II), cobalt (II), nickel (II), copper (II), neodymium (III), samarium (III), ytterbium (III), gadolinium (III), vanadium (II), terbium (III), dysprosium (III), holmium (III) and erbium (III).

18. The composition according to claim 15, wherein the fluorescent label is one or more selected from the group consisting of Alexa 350, Alexa 405, Alexa 430, Alexa 488, Alexa 555, Alexa 647, AMCA, aminoacridine, BODIPY 630/650, BODIPY 650/665, BODIPY-FL, BODIPY-R6G, BODIPY-TMR, BODIPY-TRX, 5-carboxy-4',5'-dichloro-2',7'-dimethoxyfluorescence, 5-carboxy-2',4',5',7'-tetrachlorofluorescein, 5-carboxyfluorescein,

5-carboxyrhodamine, 6-carboxyrhodamine, 6-carboxytetramethylrhodamine, Cascade Blue, Cy2, Cy3, Cy5, Cy7, 6-FAM, dansyl chloride, fluorescein, HEX, 6-JOE, NBD (7-nitrobenzo-2-oxa-1,3-diazole), Oregon Green 488, Oregon Green 500, Oregon Green 514, Pacific Blue, phthalic acid, terephthalic acid, isophthalic acid, cresyl fast violet, cresyl violet, brilliant cresyl blue, 4-aminobenzoic acid, erythrosine, phthalocyanine, azomethine, cyanine, xanthine, succinyl fluorescein, rare earth metal cryptate, tri-bipyridyldiamine europium, europium cryptate compound or chelate, diamine, dicyanine, La Jolla blue dye, allophycocyanin, allococyanin B, phycocyanin C, phycocyanin R, thiamine, R-phycoerythrin, C-Phycocyanin, phycoerythrin R, REG, rhodamine green, rhodamine isothiocyanate, rhodamine red, ROX, TAMRA, TET, TRIT (tetramethylrhodamine isothiol), tetramethylrhodamine and Texas Red.

19. The composition according to claim 14, wherein the therapeutic agent is one or more selected from the group consisting of a naked antibody, a cytotoxic agent, a drug, a radionuclide, a boron atom, an immunomodulator, an anti-apoptotic agent, a photosensitizing therapeutic, an immunoconjugate and an oligonucleotide.

20. The composition according to claim 19, wherein the drug is one or more selected from the group consisting of methotrexate, fluorouracil, mercaptopurine, hydroxyurea, cytarabine, nitrogen mustard, cyclophosphamide, thiotepa, cisplatin, mitomycin, bleomycin, camptothecin, podophyllotoxin, actinomycin D, doxorubicin, daunorubicin, vinblastine, paclitaxel, cephalotaxus alkaloids and L-asparaginase.

21. The composition according to claim 19, wherein the oligonucleotide is one or more selected from the group consisting of shRNA, miRNA and siRNA.

22. The composition according to claim 19, wherein the immunomodulator is one or more selected from the group consisting of a cytokine, a chemokine, a stem cell growth factor, a lymphotoxin, a hematopoietic factor, a colony stimulating factor (CSF), an interferon, an erythropoietin, a thrombopoietin, a tumor necrosis factor

(TNF), an interleukin (IL), granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (GM-CSF) and stem cell growth factor.

23. The composition according to claim 19, wherein the radionuclide is one or more selected from the group consisting of  $^{111}\text{In}$ ,  $^{111}\text{At}$ ,  $^{177}\text{Lu}$ ,  $^{211}\text{Bi}$ ,  $^{212}\text{Bi}$ ,  $^{213}\text{Bi}$ ,  $^{211}\text{At}$ ,  $^{62}\text{Cu}$ ,  $^{67}\text{Cu}$ ,  $^{90}\text{Y}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{133}\text{I}$ ,  $^{32}\text{P}$ ,  $^{33}\text{P}$ ,  $^{47}\text{Sc}$ ,  $^{111}\text{Ag}$ ,  $^{67}\text{Ga}$ ,  $^{153}\text{Sm}$ ,  $^{161}\text{Tb}$ ,  $^{152}\text{Dy}$ ,  $^{166}\text{Dy}$ ,  $^{161}\text{Ho}$ ,  $^{166}\text{Ho}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{189}\text{Re}$ ,  $^{211}\text{Pb}$ ,  $^{212}\text{Pb}$ ,  $^{223}\text{Ra}$ ,  $^{225}\text{Ac}$ ,  $^{77}\text{As}$ ,  $^{89}\text{Sr}$ ,  $^{99}\text{Mo}$ ,  $^{105}\text{Rh}$ ,  $^{149}\text{Pm}$ ,  $^{169}\text{Er}$ ,  $^{194}\text{Ir}$ ,  $^{58}\text{Co}$ ,  $^{80}\text{mBr}$ ,  $^{99}\text{mTc}$ ,  $^{103}\text{mRh}$ ,  $^{109}\text{Pt}$ ,  $^{119}\text{Sb}$ ,  $^{189}\text{mOs}$ ,  $^{192}\text{Ir}$ ,  $^{219}\text{Rn}$ ,  $^{215}\text{Po}$ ,  $^{221}\text{Fr}$ ,  $^{255}\text{Fm}$ ,  $^{11}\text{C}$ ,  $^{13}\text{N}$ ,  $^{15}\text{O}$ ,  $^{75}\text{Br}$ ,  $^{198}\text{Au}$ ,  $^{199}\text{Au}$ ,  $^{224}\text{Ac}$ ,  $^{77}\text{Br}$ ,  $^{113}\text{mIn}$ ,  $^{95}\text{Ru}$ ,  $^{97}\text{Ru}$ ,  $^{103}\text{Ru}$ ,  $^{105}\text{Ru}$ ,  $^{107}\text{Hg}$ ,  $^{203}\text{Hg}$ ,  $^{121}\text{mTe}$ ,  $^{122}\text{mTe}$ ,  $^{125}\text{mTe}$ ,  $^{165}\text{Tm}$ ,  $^{167}\text{Tm}$ ,  $^{168}\text{Tm}$ ,  $^{197}\text{Pt}$ ,  $^{109}\text{Pd}$ ,  $^{142}\text{Pr}$ ,  $^{143}\text{Pr}$ ,  $^{161}\text{Tb}$ ,  $^{57}\text{Co}$ ,  $^{58}\text{Co}$ ,  $^{51}\text{Cr}$ ,  $^{59}\text{Fe}$ ,  $^{75}\text{Se}$ ,  $^{201}\text{Tl}$ ,  $^{76}\text{Br}$  and  $^{169}\text{Yb}$ .

24. Use of the composition according to any one of claims 13 to 23 for the manufacture of a medicament in prevention and/or treatment of a tumor,

wherein the tumor is one or more selected from the group consisting of leukemia, lymphoma, myeloma, brain tumor, head and neck squamous cell carcinoma, non-small cell lung cancer, nasopharyngeal carcinoma, esophageal cancer, gastric cancer, pancreatic cancer, gallbladder cancer, liver cancer, colorectal cancer, breast cancer, ovarian cancer, cervical cancer, endometrial cancer, uterine sarcoma, prostate cancer, bladder cancer, renal cell carcinoma, and melanoma.

25. Use of the antibody or the functional fragment thereof according to any one of claims 1 to 11 for the manufacture of a medicament in prevention and/or treatment of a tumor,

wherein the tumor is one or more selected from the group consisting of leukemia, lymphoma, myeloma, brain tumor, head and neck squamous cell carcinoma, non-small cell lung cancer, nasopharyngeal carcinoma, esophageal cancer, gastric

cancer, pancreatic cancer, gallbladder cancer, liver cancer, colorectal cancer, breast cancer, ovarian cancer, cervical cancer, endometrial cancer, uterine sarcoma, prostate cancer, bladder cancer, renal cell carcinoma, and melanoma.

26. A drug for prevention and/or treatment of a tumor, comprising the antibody capable of specifically binding to PD-1 or the functional fragment capable of specifically binding to PD-1 thereof according to any one of claims 1 to 11, and a pharmaceutically acceptable carrier; or

the composition according to any one of claims 13 to 23 and a pharmaceutically acceptable carrier.