(e.g., a bispecific antibody).

In one embodiment of the present invention, the antibody that specifically binds to CD47 binds to human CD47 protein with a ~~KD~~K_D less than about 10^{-5} M, e.g., less than about 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M or 10^{-10} M or less. Preferably, the ~~KD~~K_D is measured by a Fortebio system.

In one embodiment of the present invention, the antibody that specifically binds to CD47 binds to human CD47 protein with an EC_{50} less than about 100 nM, e.g., less than about 10 nM, 1 nM, 0.9 nM, 0.8 nM, 0.7 nM, 0.6 nM, 0.5 nM, 0.4 nM, 0.3 nM, 0.2 nM or 0.1 nM or less. Specifically, the EC_{50} is measured by indirect ELISA.

In one embodiment of the present invention, the antibody that specifically binds to CD47 comprises constant regions, and the constant regions are derived from species other than murine, e.g., from a human antibody, preferably from a human IgG, more preferably from IgG1 or IgG4.

In one embodiment of the present invention, the constant regions of the antibody that specifically binds to CD47 are humanized, e.g., the heavy chain constant region is Ig gamma-1 chain C region, more preferably Ig gamma-1 chain C region under GenBank ACCESSION No. P01857 (SEQ ID NO: 58), or is Ig gamma-4 chain C region, more preferably Ig gamma-4 chain C region under GenBank ACCESSION No. P01861.1 (SEQ ID NO: 56); the light chain constant region is Ig kappa chain C region, more preferably Ig kappa chain C region under GenBank ACCESSION No. P01834 (SEQ ID NO: 57). The antibodies disclosed herein use the following constant regions on the basis of the variable regions of 6F7 H1L1, 6F7 H2L2 and 6F7 H3L3: the heavy chain constant region is Ig gamma-1 chain C region under ACCESSION No. P01857 (SEQ ID NO: 58) or the heavy chain constant region is Ig gamma-4 chain C region under ACCESSION No. P01861.1 (SEQ ID NO: 56), and on this basis, S228P mutation is introduced to improve the stability; the light chain constant region is Ig kappa chain C region, ACCESSION No. P01834 (SEQ ID NO: 57).

Another aspect of the present invention relates to an isolated polynucleotide encoding a polypeptide comprising sequences set forth in SEQ ID NOs: 5, 6 and 7, wherein the polypeptide, as part of an anti-human CD47 antibody,

(5) a heavy chain set forth in SEQ ID NO: 67 and a light chain set forth in SEQ ID NO: 68; and

(6) a heavy chain set forth in SEQ ID NO: 69 and a light chain set forth in SEQ ID NO: 70;

the anti-PD-1/anti-CTLA4 antibody comprises or consists of a heavy chain and a light chain selected from the group consisting of the following:

a heavy chain set forth in SEQ ID NO: 78 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 77) and a light chain set forth in SEQ ID NO: 80 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 79);

the anti-PD-1/anti-VEGFA antibody comprises or consists of a heavy chain and a light chain selected from the group consisting of the following:

a heavy chain set forth in SEQ ID NO: 141 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 142) and a light chain set forth in SEQ ID NO: 143 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 144);

the anti-PD-1 monoclonal antibody comprises or consists of a heavy chain and a light chain selected from the group consisting of the following: a heavy chain set forth in SEQ ID NO: 82 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 81) and a light chain set forth in SEQ ID NO: 84 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 83).

7. The pharmaceutical composition according to any one of items 1–6, wherein the antigen-binding fragment is selected from Fab, Fab', $F(ab')_2$, Fd, Fv, dAb, Fab/c, complementarity determining region (CDR) fragment, single-chain antibody (e.g., scFv), bivalent antibody and domain antibody.

8. The pharmaceutical composition according to any one of items 1–7, wherein the antibody that specifically binds to CD47 is a humanized antibody, a chimeric antibody or a multispecific antibody (e.g., a bispecific antibody).

9. The pharmaceutical composition according to any one of items 1–8, wherein the antibody that specifically binds to CD47 binds to human CD47 protein with a ~~KD~~K_D less than about 10^{-5} M, e.g., less than about 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M, or 10^{-10} M or less, or the antibody that specifically binds to CD47 binds to human CD47

the component A or the component B is administered at a unit dose of 0.1–100 mg, preferably 1–10 mg per kg body weight of the subject; or the component A or the component B is administered at a unit dose of 10–1000 mg, preferably 50–500 mg, 100–400 mg, 150–300 mg, 150–250 mg or 200 mg in each subject;

preferably, the component B2 is in a unit dose of 0.1–100 mg, 0.5–50 mg, 1–20 mg, 2–15 mg, 4–12 mg or 8–12 mg;

preferably, the dose is administered from twice daily to about once every other day, or once every 3 days, 4 days, 5 days, 6 days, 10 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks or 6 weeks;

preferably, the route of administration is intravenous drip infusion, subcutaneous injection, intradermal injection, intravenous injection, intramuscular injection or intralesional injection.

17. The pharmaceutical composition according to any one of items 1–13, the kit according to item 14 or 15, or the method according to item 16, wherein the tumor is preferably a tumor expressing CD47, and preferably a cancer; the cancer includes a solid tumor, a hematological tumor, lymphoma, blastoma, sarcoma, leukemia or lymphoid malignancy, and more preferably includes squamous cell carcinoma, myeloma, lung cancer, small cell lung cancer, non-small cell lung cancer, head and neck squamous cell carcinoma, glioma (e.g., neuroglioma and recurrent glioma), acute myelocytic leukemia, Hodgkin's lymphoma, non-Hodgkin's lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, acute lymphocytic leukemia, acute myeloblastic leukemia, chronic lymphocytic leukemia, chronic myeloblastic leukemia, primary mediastinal large B-cell lymphoma~~, mantle cell lymphoma~~, small lymphocytic lymphoma, T cell/histiocyte-rich large B-cell lymphoma, multiple myeloma, myeloid leukemia-1 protein, relapsed and refractory peripheral T-cell lymphoma, myelodysplastic syndrome, anaplastic large cell lymphoma, mantle cell lymphoma, marginal zone lymphoma, myelofibrosis, polycythemia vera, bone marrow cancer, myeloproliferative disease, aggressive systemic mastocytosis, eosinophilia, dermatofibrosarcoma protuberans, chronic eosinophilic leukemia, gastrointestinal cancer, gastric adenocarcinoma or gastroesophageal junction

A "derivative" of a polypeptide is a polypeptide (e.g., an antigen-binding protein or an antibody) that is chemically modified in other manners than insertion, deletion or substitution, e.g., by conjugation with another chemical moiety, e.g., a PEG-conjugated polypeptide.

In the present invention, letters before the position number represent amino acids before mutation, and letters after the position number represent amino acids after mutation, unless otherwise specified.

In some embodiments of the present invention, a disulfide bond is present between the VH and VL of the single-chain antibody. Methods for introducing a disulfide bond between the VH and VL of an antibody are well known in the art, see, for example, US 5,747,654; Rajagopal et al., *Prot. Engin*. 10(1997)1453-1459; Reiter et al., *Nat. Biotechnol*. 14(1996)1239-1245; Reiter et al., *Protein Engineering* 8(1995)1323-1331; Webber et al., *Molecular Immunology* 32(1995)249-258; Reiter et al., *Immunity* 2(1995)281-287; Reiter et al., *JBC* 269(1994)18327-18331; Reiter et al., *Inter. J. of Cancer* 58(1994)142-149; or Reiter et al., *Cancer Res*. 54(1994)2714-2718, which are incorporated herein by reference.

As used herein, the term "specifically bind" refers to a non-random binding reaction between two molecules, such as a reaction between an antibody and an antigen it targets. In some embodiments, an antibody that specifically binds to an antigen (or an antibody that is specific for an antigen) means that the antibody binds to the antigen with an affinity (K_D) less than about 10^{-5} M, such as less than about 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M or 10^{-10} M or less.

As used herein, the term "K_D" refers to a dissociation equilibrium constant for a specific antibody-antigen interaction, which is used to describe the binding affinity between the antibody and the antigen. Among several parameters measured by molecular binding kinetics, the K_D value is the dissociation equilibrium constant. In antibody drug research, it is the parameter characterizing the intensity of the affinity between an antibody of interest and the target antigen molecule, and is calculated by the formula: ~~KD~~$\underline{K_D}$ = k_{dis}/k_{on}. A smaller equilibrium dissociation constant indicates a more intensive antibody-antigen binding and a higher affinity between the antibody

activity was evaluated. The ADCP activity of each group, represented by P%, was calculated according to the following formula:

$$P\% = \frac{\textit{Number of macrophages involved in phagocytosis}}{\textit{Total number of macrophages}} \times 100\%$$

Results: In this study, the phagocytic activity (ADCP) mediated by 6F7H1L1(hG4) in combination with rituximab was determined using HPMMs as the effector cells and Raji cells as the target cells. The results, as shown in **Figure 1**~~**Error! Citation source not found.**~~, demonstrated that the phagocytic indexes of rituximab and 6F7H1L1(hG4) were significantly higher than those of the blank control and the isotype control (human IgG4), indicating that rituximab and 6F7H1L1(hG4) have ADCP activity. The phagocytic indexes of 6F7H1L1(hG4) in combination with rituximab were significantly higher than those of 6F7H1L1(hG4), indicating that the ADCP activity of 6F7H1L1(hG4) in combination with rituximab is stronger than that of the monotherapy.

2. Phagocytosis of tumor cells by macrophages promoted by 6F7H1L1(hG4) in combination with azacitidine

Objective: In this study, the effects of 6F7H1L1(hG4) in combination with azacitidine and 6F7H1L1(hG4) alone on the antibody-dependent cellular phagocytosis (ADCP) mediated by acute myelocytic leukemia (AML) HL-60 cells were compared at the cytological level *in vitro*. In the assay system, HPMMs were used as the effector cells, and AML HL-60 cells treated with different concentrations of azacitidine were used as the target cells.

Procedures: HL-60 cells were conventionally collected and plated in a 6-well plate at 4×10^5 cells/2 mL of 1640 complete medium per well. Different concentrations of azacitidine (at working concentrations of 3 μM or 1 μM) were added. A blank HL-60 group was set. The cells were incubated in an incubator for 24 h. The next day, the treated and blank HL-60 cells were collected, centrifuged at 170× g for 5 min, resuspended and counted. Then the cells were analyzed for viability and washed once with PBS. CFSE was diluted to 2.5 μM with PBS. HL-60 cells were

resuspended in the diluted CFSE at a staining density of 1×10^7 cells/mL and incubated in an incubator for 20 min. 6 mL of 1640 complete medium (containing 10% FBS) was added to stop staining. The cells were centrifuged at 170× g for 5 min, and the supernatant was discarded. Then 1 mL of 1640 complete medium was added for resuspension, and the cells were incubated in an incubator for 10 min. The antibodies were diluted with 1640 complete medium to 20 μg/mL and 2 μg/mL (the working concentrations were 10 μg/mL and 1 μg/mL), and an isotype control antibody (an anti-HEL antibody, human IgG4) group was set. The antibodies and the target cells were added into V-bottom plates containing HPMMs (the final volume was 100 μL, the effector-to-target ratio was 5×10^4:1.5×10^5), and the mixtures were well mixed for resuspension and incubated in an incubator at 37 °C for 2 h. 150 μL of 1% PBSA (PBS containing 1% of BSA) at room temperature was added to each well, and the system was centrifuged at 1000× g for 5 min, and the supernatant was discarded. The cells were washed once with 200 μL of 1% PBSA. APC anti-human CD11c antibody (diluted 400-fold with 1% PBSA) was added to the corresponding samples at 100 μL/sample for labeling, and the samples were incubated on ice for 40 min. 150 μL of 1% PBSA was added to each well. The mixture was centrifuged at 1000× g for 5 min and the supernatant was discarded. The cells were washed once with 200 μL of 1% PBSA. 200 μL of 1% PBSA was added to each well for resuspension, and the cells were detected on an FACS Calibur flow cytometer. Macrophages in the system were APC-CD11b$^+$ positive, and macrophages involved in phagocytosis were APC-CD11b$^+$ and CFSE$^+$ dual positive. The phagocytic index was determined as the ratio of the number of dual positive cells to the number of APC positive cells, and the antibody-mediated ADCP activity was evaluated. The ADCP activity of each group, represented by P%, was calculated according to the formula shown in (1) of this example.

Results: In this study, the ADCP activity assay of 6F7H1L1(hG4) in combination with azacitidine was conducted by using Hu5F9-G4 targeting CD47 as the positive control, HPMMs as the effector cells and HL-60 cells as the target cells. The results, as shown in Figure 2~~**Error! Citation source not found.**~~, demonstrated that the phagocytic

6F7H1L1(hG4) and cetuximab (prepared by Akeso Biopharma, Inc., Lot No: 20200917) were diluted to the desired concentrations with 1640 complete medium, and an isotype control antibody group was set. Human macrophages were collected and centrifuged at ~~7~~170x~~×~~ g for 5 min, and the supernatant was discarded. The cells were counted, transferred to 1.5 mL EP tubes and centrifuged at 1200× g for 5 min, and the supernatant was discarded. The tumor cells + antibody suspension (50 μL each) were added into the 1.5 mL EP tubes containing macrophages, and the mixtures were well mixed for resuspension and incubated in an incubator at 37 °C for 2 h. 800 μL of 1% PBSA at room temperature was added to each tube. The tubes were centrifuged at 1200× g for 5 min, and the supernatant was discarded. The cells were washed once with 800 μL of PBSA. APC anti-mouse/human CD11b antibody (Biolegend, Cat. No: 101212, concentration: 0.2 mg/mL; diluted 500-fold with PBSA) was added to the corresponding samples at 100 μL/sample, and the mixtures were well mixed and incubated on ice for 40 min. 800 μL of 1% PBSA was added to each tube. The tubes were centrifuged at 1200× g for 5 min, and the supernatant was discarded. The cells in each tube were washed once with 800 μL of PBSA. 200 μL of 1% PBSA was added to each tube for resuspension, and the cells were transferred to a flow cytometry tube and detected.

Results: In this study, the phagocytic activity (ADCP) mediated by 6F7H1L1(hG4) in combination with cetuximab was determined using HPMMs as the effector cells and HT29 cells as the target cells. The results, as shown in FIG. 7, demonstrated that the phagocytic indexes of cetuximab and 6F7H1L1(hG4) were significantly higher than those of the blank control and the isotype control (human IgG4), indicating that cetuximab and 6F7H1L1(hG4) have ADCP activity. The phagocytic indexes of 6F7H1L1(hG4) in combination with cetuximab were significantly higher than those of 6F7H1L1(hG4), indicating that the ADCP activity of 6F7H1L1(hG4) in combination with cetuximab is stronger than that of the monotherapy.

Example 8: Phagocytosis of tumor cells by macrophages promoted by 6F7H1L1(hG4) in combination with obinutuzumab

SEQ ID NO: 7 HCDR3 of 6F7CDR

ARLYRWYFDV

SEQ ID NO: 8 LCDR1 of 6F7CDR

EIVGTY

SEQ ID NO: 9 LCDR2 of 6F7CDR

GAS

SEQ ID NO: 10 LCDR3 of 6F7CDR

GQSYNFPYT

SEQ ID NO: 11 nucleotide sequence of heavy chain variable region of 6F7H1

CAGGTGCAGCTGGTGCAGAGCGGAGCAGAGGTGGTGAAGCCAGGAGCCTCTGTGAAG
CTGAGCTGTAAGGCCTCCGGCTACACCTTCACAAGCTATTGGATGAACTGGGTGCGGCA
GAGACCAGGACAGGGACTGGAGTGGATCGGAATGATCGACCCTTCCGATTCTGAGACC
CACAATGCCCAGAAGTTTCAGGGCAAGGCCACCCTGACAGTGGACAAGAGCACCTCC
ACAGCCTACATGCACCTGAGCTCCCTGCGGTCCGAGGACACAGCCGTGTACTATTGCGC
CAGGCTGTACCGCTGGTATTTTGACGTGTGGGGAGCAGGAACCACAGTGACCGTGTCT
AGC

SEQ ID NO: 12 amino acid sequence of heavy chain variable region of 6F7H1

QVQLVQSGAEVVKPGASVKLSCKASGYTFTSYWMNWVRQRPGQGLEWIGMIDPSDSETH
NAQKFQGKATLTVDKSTSTAYMHLSSLRSEDTAVYYCARLYRWYFDVWGAGTTVTVSS

SEQ ID NO: 13 nucleotide sequence of light chain variable region of 6F7L1

AACATCGTGATGACCCAGTCCCCAGCCACAATGTCTATGAGCCCAGGAGAGAGGGTGA
CCCTGTCCTGTAGAGCCTCTGAGATCGTGGGCACATACGTGTCTTGGTTTCAGCAGAAG
CCAGGACAGGCACCTAGGCTGCTGATCTACGGAGCAAGCAACAGGTATACCGGAGTGC
CAGCACGCTTCTCCGGCTCTGGCAGCGGCACAGACTTTACCCTGACAATCAGCTCCGT
GCAGCCTGAGGACCTGGCCGATTATCACTGCGGCCAGTCTTACAATTTCCCATATACCTT
TGGCGGCGGCACAAAGCTGGAGATCAAG

SGSGSGTDFTLTISSLQPEDLADYYCGQSYNFPYTFGGGTKLEIKRTVAAPSVFIFPPSDEQ
LKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSK
ADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 63 amino acid sequence of heavy chain of 6F7H3L3(G1M)
QVQLVQSGAEVVKPGASVKVSCKASGYTFTSYWMNWVRQAPGQGLEWIGIIDPSDSETS
YAQKFQGRVTLTVDKSTSTAYMELSSLRSEDTAVYYCARLYRWYFDVWGAGTTVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS
VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS
TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL
TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: ~~6F7~~64 amino acid sequence of light chain of 6F7H3L3(G1M)
NIVMTQSPATLSLSPGERVTLSCRASEIVGTYLSWYQQKPGQAPRLLIYGASTRATGIPARF
SGSGSGTDFTLTISSLQPEDFAVYYCGQSYNFPYTFGGGTKLEIKRTVAAPSVFIFPPSDEQL
KSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA
DYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 65 amino acid sequence of heavy chain of 6F7H1L1(hG4)
QVQLVQSGAEVVKPGASVKLSCKASGYTFTSYWMNWVRQRPGQGLEWIGMIDPSDSET
HNAQKFQGKATLTVDKSTSTAYMHLSSLRSEDTAVYYCARLYRWYFDVWGAGTTVTVS
SASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS
GLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPSCPAPEFLGGPSVF
LFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTK
NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEG
NVFSCSVMHEALHNHYTQKSLSLSLGK

SEQ ID NO: 66 amino acid sequence of light chain of 6F7H1L1(hG4)

CLAIMS

1. A pharmaceutical composition, preferably for treating a tumor, comprising a component A and a component B, wherein the component A is an antibody that specifically binds to CD47 or an antigen-binding fragment thereof;

the component B is selected from one or more of the following: a component B1, a component B2 and a component B3, wherein the component B1 is a bispecific antibody or an antigen-binding fragment thereof, the component B2 is an anti-tumor chemotherapeutic, and the component B3 is an anti-PD-1 monoclonal antibody or an antigen-binding fragment thereof;

preferably, the composition further comprises a component C, wherein the component C is an anti-tumor therapeutic agent, and the component C is different from component B;

for example, according to the Kabat, IMGT, Chothia or AbM numbering system,

the antibody that specifically binds to CD47 comprises CDR sequences selected from those comprised in the following heavy chain variable regions and light chain variable regions:

(1) an HCDR1, an HCDR2 and an HCDR3 comprised in a heavy chain variable region set forth in SEQ ID NO: 2, and

an LCDR1, an LCDR2 and an LCDR3 comprised in a light chain variable region set forth in SEQ ID NO: 4; or

(2) an HCDR1, an HCDR2 and an HCDR3 comprised in a heavy chain variable region set forth in SEQ ID NO: 12, and

an LCDR1, an LCDR2 and an LCDR3 comprised in a light chain variable region set forth in SEQ ID NO: 14; or

(3) an HCDR1, an HCDR2 and an HCDR3 comprised in a heavy chain variable region set forth in SEQ ID NO: 16, and

an LCDR1, an LCDR2 and an LCDR3 comprised in a light chain variable region set forth in SEQ ID NO: 18; or

(4) an HCDR1, an HCDR2 and an HCDR3 comprised in a heavy chain variable

region set forth in SEQ ID NO: 20, and

an LCDR1, an LCDR2 and an LCDR3 comprised in a light chain variable region set forth in SEQ ID NO: 22

(preferably, according to the IMGT numbering system, the antibody comprises:

an HCDR1 comprising or consisting of a sequence set forth in SEQ ID NO: 5 or a variant thereof,

an HCDR2 comprising or consisting of a sequence set forth in SEQ ID NO: 6 or a variant thereof, and

an HCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 7 or a variant thereof; and the antibody further comprises:

an LCDR1 comprising or consisting of amino acids set forth in SEQ ID NO: 8 or a variant thereof,

an LCDR2 comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 9 or a variant thereof, and

an LCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 10 or a variant thereof);

the bispecific antibody is an anti-PD-1/anti-CTLA4 antibody or an anti-PD-1/anti-VEGFA antibody or a combination of the two; the bispecific antibody comprises a first protein functional region and a second protein functional region, wherein the first protein functional region targets PD-1, and the second protein functional region targets CTLA4 or VEGFA; the first protein functional region is an immunoglobulin, and the second protein functional region is a single-chain antibody; or the first protein functional region is a single-chain antibody, and the second protein functional region is an immunoglobulin;

preferably, two single-chain antibody molecules (preferably, two identical single-chain antibody molecules) are linked to one immunoglobulin molecule; preferably, the immunoglobulin is of IgG1 subtype (preferably, human IgG1 subtype); preferably, the single-chain antibody is linked to the N terminus or C terminus of the heavy chain of the immunoglobulin, wherein the numbers of the first protein functional region and the second protein functional region are each

independently 1, 2 or more; preferably, the first protein functional region is linked to the second protein functional region either directly or via a first linker fragment; and/or the heavy chain variable region of the single-chain antibody is linked to the light chain variable region of the single-chain antibody either directly or via a second linker fragment; the first linker fragment and the second linker fragment are identical or different; preferably, the linker fragment is (GGGGS)n, wherein n is a positive integer, or more preferably, n is 1, 2, 3, 4, 5 or 6; preferably, the first linker fragment and the second linker fragment comprise amino acid sequences independently selected from SEQ ID NO: 119 and SEQ ID NO: 120; more preferably, the first linker fragment and the second linker fragment comprise an amino acid sequence set forth in SEQ ID NO: 120;

when the bispecific antibody is an anti-PD-1/anti-CTLA4 antibody,

the first protein functional region comprises HCDR1–HCDR3 comprised in a heavy chain variable region set forth in SEQ ID NO: 87, and LCDR1–LCDR3 comprised in a light chain variable region set forth in SEQ ID NO: 88 (preferably, according to the IMGT numbering system, the first protein functional region comprises an HCDR1 comprising or consisting of a sequence set forth in SEQ ID NO: 89 or a variant thereof,

an HCDR2 comprising or consisting of a sequence set forth in SEQ ID NO: 90 or a variant thereof,

an HCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 91 or a variant thereof,

an LCDR1 comprising or consisting of amino acids set forth in SEQ ID NO: 92 or a variant thereof,

an LCDR2 comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 93 or a variant thereof, and

an LCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 94 or a variant thereof);

the second protein functional region comprises HCDR1–HCDR3 in a heavy chain variable region set forth in SEQ ID NO: 95, and LCDR1–LCDR3 in a light chain

variable region set forth in SEQ ID NO: 96 (preferably, according to the IMGT numbering system, the second protein functional region comprises an HCDR1 comprising or consisting of a sequence set forth in SEQ ID NO: 97 or a variant thereof,

an HCDR2 comprising or consisting of a sequence set forth in SEQ ID NO: 98 or a variant thereof,

an HCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 99 or a variant thereof,

an LCDR1 comprising or consisting of amino acids set forth in SEQ ID NO: 100 or a variant thereof,

an LCDR2 comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 101 or a variant thereof, and

an LCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 102 or a variant thereof);

or

when the bispecific antibody is an anti-PD-1/anti-VEGFA antibody,

the first protein functional region comprises HCDR1–HCDR3 comprised in a heavy chain variable region set forth in SEQ ID NO: 103, and LCDR1–LCDR3 comprised in a light chain variable region set forth in SEQ ID NO: 104 (preferably, according to the IMGT numbering system, the first protein functional region comprises an HCDR1 comprising or consisting of a sequence set forth in SEQ ID NO: 105 or a variant thereof,

an HCDR2 comprising or consisting of a sequence set forth in SEQ ID NO: 106 or a variant thereof,

an HCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 107 or a variant thereof,

an LCDR1 comprising or consisting of amino acids set forth in SEQ ID NO: 108 or a variant thereof,

an LCDR2 comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 109 or a variant thereof, and

an LCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 110 or a variant thereof);

the second protein functional region comprises HCDR1–HCDR3 in a heavy chain variable region set forth in SEQ ID NO: 111, and LCDR1–LCDR3 in a light chain variable region set forth in SEQ ID NO: 112 (preferably, according to the IMGT numbering system, the second protein functional region comprises an HCDR1 comprising or consisting of a sequence set forth in SEQ ID NO: 113 or a variant thereof,

an HCDR2 comprising or consisting of a sequence set forth in SEQ ID NO: 114 or a variant thereof,

an HCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 115 or a variant thereof,

an LCDR1 comprising or consisting of amino acids set forth in SEQ ID NO: 116 or a variant thereof,

an LCDR2 comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 117 or a variant thereof, and

an LCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 118 or a variant thereof);

wherein,

the anti-PD1 monoclonal antibody comprises HCDR1–HCDR3 comprised in a heavy chain variable region set forth in SEQ ID NO: 121, and LCDR1–LCDR3 comprised in a light chain variable region set forth in SEQ ID NO: 122 (preferably, according to the IMGT numbering system, the anti-PD1 monoclonal antibody comprises an HCDR1 comprising or consisting of a sequence set forth in SEQ ID NO: 123 or a variant thereof,

an HCDR2 comprising or consisting of a sequence set forth in SEQ ID NO: 124 or a variant thereof,

an HCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 125 or a variant thereof,

an LCDR1 comprising or consisting of amino acids set forth in SEQ ID NO: 126 or

a variant thereof,

an LCDR2 comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 127 or a variant thereof, and

an LCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 128 or a variant thereof);

wherein the variant comprises a sequence having at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% homology to the corresponding sequence, or the variant comprises a sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the corresponding sequence.

2. The pharmaceutical composition according to claim 1, wherein the antibody that specifically binds to CD47 further comprises framework regions (FRs) in the heavy chain variable region and framework regions (FRs) in the light chain variable region selected from the group consisting of the following:

(1) the framework regions (FRs) in the heavy chain variable region including an FR-H1, an FR-H2, an FR-H3 and an FR-H4, wherein the FR-H1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 23 or a variant thereof; the FR-H2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 24 or a variant thereof; the FR-H3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 25 or a variant thereof; the FR-H4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 26 or a variant thereof;

the framework regions (FRs) in the light chain variable region including an FR-L1, an FR-L2, an FR-L3 and an FR-L4, wherein the FR-L1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 27 or a variant thereof; the FR-L2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 28 or a variant thereof; the FR-L3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 29 or a variant thereof; the FR-L4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 30 or a variant thereof;

(2) the framework regions (FRs) in the heavy chain variable region including an

FR-H1, an FR-H2, an FR-H3 and an FR-H4, wherein the FR-H1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 31 or a variant thereof; the FR-H2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 32 or a variant thereof; the FR-H3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 33 or a variant thereof; the FR-H4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 34 or a variant thereof;
the framework regions (FRs) in the light chain variable region including an FR-L1, an FR-L2, an FR-L3 and an FR-L4, wherein the FR-L1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 35 or a variant thereof; the FR-L2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 36 or a variant thereof; the FR-L3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 37 or a variant thereof; the FR-L4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 38 or a variant thereof;
(3) the framework regions (FRs) in the heavy chain variable region including an FR-H1, an FR-H2, an FR-H3 and an FR-H4, wherein the FR-H1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 39 or a variant thereof; the FR-H2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 40 or a variant thereof; the FR-H3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 41 or a variant thereof; the FR-H4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 42 or a variant thereof;
the framework regions (FRs) in the light chain variable region including an FR-L1, an FR-L2, an FR-L3 and an FR-L4, wherein the FR-L1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 43 or a variant thereof; the FR-L2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 44 or a variant thereof; the FR-L3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 45 or a variant thereof; the FR-L4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 46 or a variant thereof;
(4) the framework regions (FRs) in the heavy chain variable region including an FR-H1, an FR-H2, an FR-H3 and an FR-H4, wherein the FR-H1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 47 or a variant thereof;

the FR-H2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 48 or a variant thereof; the FR-H3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 49 or a variant thereof; the FR-H4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 50 or a variant thereof;
the framework regions (FRs) in the light chain variable region including an FR-L1, an FR-L2, an FR-L3 and an FR-L4, wherein the FR-L1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 51 or a variant thereof; the FR-L2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 52 or a variant thereof; the FR-L3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 53 or a variant thereof; the FR-L4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 54 or a variant thereof,
wherein the variant comprises a sequence having at least 80%, preferably at least 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% homology to the corresponding sequence or having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the corresponding sequence.
3. The pharmaceutical composition according to claim 1 or 2, wherein the antibody that specifically binds to CD47 comprises:
(1) a heavy chain variable region comprising or consisting of:
an amino acid sequence set forth in SEQ ID NO: 2 or a variant thereof, and
a light chain variable region comprising or consisting of:
an amino acid sequence set forth in SEQ ID NO: 4 or a variant thereof;
(2) a heavy chain variable region comprising or consisting of:
an amino acid sequence set forth in SEQ ID NO: 12 or a variant thereof, and
a light chain variable region comprising or consisting of:
an amino acid sequence set forth in SEQ ID NO: 14 or a variant thereof;
(3) a heavy chain variable region comprising or consisting of:
an amino acid sequence set forth in SEQ ID NO: 16 or a variant thereof, and
a light chain variable region comprising or consisting of:

an amino acid sequence set forth in SEQ ID NO: 18 or a variant thereof; and

(4) a heavy chain variable region comprising or consisting of:

an amino acid sequence set forth in SEQ ID NO: 20 or a variant thereof, and

a light chain variable region comprising or consisting of:

an amino acid sequence set forth in SEQ ID NO: 22 or a variant thereof,

the first protein functional region of the anti-PD-1/anti-CTLA4 antibody comprises:

(1) a heavy chain variable region comprising or consisting of:

a sequence set forth in SEQ ID NO: 87 or a variant thereof, and

a light chain variable region comprising or consisting of:

a sequence set forth in SEQ ID NO: 88 or a variant thereof; and

(2) a heavy chain variable region comprising or consisting of:

a sequence set forth in SEQ ID NO: 129 or a variant thereof, and

a light chain variable region comprising or consisting of:

a sequence set forth in SEQ ID NO: 130 or a variant thereof;

the second protein functional region of the anti-PD-1/anti-CTLA4 antibody comprises:

(1) a heavy chain variable region comprising or consisting of:

a sequence set forth in SEQ ID NO: 95 or a variant thereof, and

a light chain variable region comprising or consisting of:

a sequence set forth in SEQ ID NO: 96 or a variant thereof;

(2) a heavy chain variable region comprising or consisting of:

a sequence set forth in SEQ ID NO: 133 or a variant thereof, and

a light chain variable region comprising or consisting of:

a sequence set forth in SEQ ID NO: 134 or a variant thereof;

(3) a heavy chain variable region comprising or consisting of:

a sequence set forth in SEQ ID NO: 135 or a variant thereof, and

a light chain variable region comprising or consisting of:

a sequence set forth in SEQ ID NO: 136 or a variant thereof;

(4) a heavy chain variable region comprising or consisting of:

a sequence set forth in SEQ ID NO: 137 or a variant thereof, and

a light chain variable region comprising or consisting of:
a sequence set forth in SEQ ID NO: 138 or a variant thereof; and
(5) a heavy chain variable region comprising or consisting of:
a sequence set forth in SEQ ID NO: 131 or a variant thereof, and
a light chain variable region comprising or consisting of:
a sequence set forth in SEQ ID NO: 132 or a variant thereof;
preferably, the immunoglobulin of the anti-PD-1/anti-CTLA4 antibody comprises a heavy chain having an amino acid sequence set forth in SEQ ID NO: 139, and targets PD-1;
the first protein functional region of the anti-PD-1/anti-VEGFA antibody comprises:
(1) a heavy chain variable region comprising or consisting of:
a sequence set forth in SEQ ID NO: 103 or a variant thereof, and
a light chain variable region comprising or consisting of:
a sequence set forth in SEQ ID NO: 104 or a variant thereof;
the second protein functional region of the anti-PD-1/anti-VEGFA antibody comprises:
(1) a heavy chain variable region comprising or consisting of:
a sequence set forth in SEQ ID NO: 111 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 145) or a variant thereof, and
a light chain variable region comprising or consisting of:
a sequence set forth in SEQ ID NO: 112 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 146) or a variant thereof;
preferably, the immunoglobulin of the anti-PD-1/anti-VEGFA antibody comprises a heavy chain having an amino acid sequence set forth in SEQ ID NO: 140, and targets VEGFA;
the anti-PD-1 monoclonal antibody comprises or consists of a heavy chain variable region set forth in SEQ ID NO: 121 and a light chain variable region set forth in SEQ ID NO: 122;
wherein the variant has at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or higher sequence identity to the

corresponding sequence, or comprises an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the corresponding sequence.

4. The pharmaceutical composition according to any one of claims 1–3, wherein the antibody that specifically binds to CD47 further comprises a heavy chain constant region and a light chain constant region, and the constant regions are derived from species other than murine, e.g., from a human antibody, preferably from a human IgG or IgM, and more preferably from IgG1; preferably, the heavy chain constant region is Ig gamma-1 chain C region, ACCESSION No. P01857 (SEQ ID NO: 58) or Ig gamma-4 chain C region, ACCESSION No. P01861.1 (SEQ ID NO: 56); the light chain constant region is Ig kappa chain C region, ACCESSION No. P01834 (SEQ ID NO: 57); preferably, the antibody that specifically binds to CD47 is secreted by a hybridoma cell line LT012 under CCTCC NO. 2018135.

5. The pharmaceutical composition according to any one of claims 1–4, wherein, according to the EU numbering system, the antibody that specifically binds to CD47 and the immunoglobulin comprise a heavy chain constant region having mutations at any 1, 2 or 3 of positions 234, 235 and 237, and the affinity constant of the bispecific antibody for FcγRIIIa and/or C1q is reduced after the mutation as compared to that before the mutation; preferably, the affinity constant is measured by a Fortebio Octet system;

preferably, the antibody that specifically binds to CD47 comprises an L234A and/or L235A mutation according to the EU numbering system;

more preferably, the heavy chain constant region of the immunoglobulin has one of the following combinations of mutations:

L234A and L235A; or

L234A and G237A; or

L235A and G237A; or

L234A, L235A and G237A;

still more preferably,

according to the EU numbering system, the heavy chain constant region of the immunoglobulin further has one of the combinations of the following mutations: N297A, D265A, D270A, P238D, L328E, E233D, H268D, P271G, A330R, C226S, C229S, E233P, P331S, S267E, L328F, A330L, M252Y, S254T, T256E, N297Q, P238S, P238A, A327Q, A327G, P329A, K322A, T394D, G236R, G236A, L328R, A330S, P331S, H268A, E318A and K320A.

6. The pharmaceutical composition according to any one of claims 1–5, wherein the antibody that specifically binds to CD47 comprises or consists of a heavy chain and a light chain selected from the group consisting of the following:

(1) a heavy chain set forth in SEQ ID NO: 59 and a light chain set forth in SEQ ID NO: 60;

(2) a heavy chain set forth in SEQ ID NO: 61 and a light chain set forth in SEQ ID NO: 62;

(3) a heavy chain set forth in SEQ ID NO: 63 and a light chain set forth in SEQ ID NO: 64;

(4) a heavy chain set forth in SEQ ID NO: 65 and a light chain set forth in SEQ ID NO: 66;

(5) a heavy chain set forth in SEQ ID NO: 67 and a light chain set forth in SEQ ID NO: 68; and

(6) a heavy chain set forth in SEQ ID NO: 69 and a light chain set forth in SEQ ID NO: 70;

the anti-PD-1/anti-CTLA4 antibody comprises or consists of a heavy chain and a light chain selected from the group consisting of the following:

a heavy chain set forth in SEQ ID NO: 78 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 77) and a light chain set forth in SEQ ID NO: 80 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 79);

the anti-PD-1/anti-VEGFA antibody comprises or consists of a heavy chain and a light chain selected from the group consisting of the following:

a heavy chain set forth in SEQ ID NO: 141 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 142) and a light chain set forth in SEQ ID NO:

143 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 144);

the anti-PD-1 monoclonal antibody comprises or consists of a heavy chain and a light chain selected from the group consisting of the following: a heavy chain set forth in SEQ ID NO: 82 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 81) and a light chain set forth in SEQ ID NO: 84 (preferably encoded by a nucleotide sequence set forth in SEQ ID NO: 83).

7. The pharmaceutical composition according to any one of claims 1–6, wherein the antigen-binding fragment is selected from Fab, Fab', $F(ab')_2$, Fd, Fv, dAb, Fab/c, complementarity determining region (CDR) fragment, single-chain antibody (e.g., scFv), bivalent antibody and domain antibody.

8. The pharmaceutical composition according to any one of claims 1–7, wherein the antibody that specifically binds to CD47 is a humanized antibody, a chimeric antibody or a multispecific antibody (e.g., a bispecific antibody).

9. The pharmaceutical composition according to any one of claims 1–8, wherein the antibody that specifically binds to CD47 binds to human CD47 protein with a KD less than about 10^{-5} M, e.g., less than about 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M, or 10^{-10} M or less, or the antibody that specifically binds to CD47 binds to human CD47 protein with an EC_{50} less than about 100 nM, e.g., less than about 10 nM, 1 nM, 0.9 nM, 0.8 nM, 0.7 nM, 0.6 nM, 0.5 nM, 0.4 nM, 0.3 nM, 0.2 nM, 0.1 nM or less.

10. The pharmaceutical composition according to any one of claims 1–9, wherein the antibody that specifically binds to CD47 is in the form of an antibody conjugate comprising the antibody that specifically binds to CD47 or the antigen-binding fragment thereof according to any one of claims 1–9 and a conjugated moiety conjugated thereto, wherein the conjugated moiety is a purification tag (e.g., a His tag), a cytotoxic agent or a detectable label; preferably, the conjugated moiety is a radioisotope, a luminescent substance, a colored substance, an enzyme or polyethylene glycol; or

the antibody that specifically binds to CD47 is in the form of a multispecific antibody, preferably a bispecific antibody, comprising the antibody that specifically binds to CD47 or the antigen-binding fragment thereof according to any one of

claims 1–9, and an antibody against another antigen and/or another antigenic epitope or an antigen-binding fragment thereof; or the antibody that specifically binds to CD47 is in the form of a fusion protein comprising the antibody that specifically binds to CD47 or the antigen-binding fragment thereof according to any one of claims 1–9.

11. The pharmaceutical composition according to any one of claims 1–10, wherein the anti-tumor therapeutic agent is selected from one or more of the following: a tyrosine kinase inhibitor, a DNA polymerase inhibitor, an anti-human CD20 antibody, an anti-human PDL-1 antibody, an anti-human PD-1 antibody, an anti-human CTLA-4 antibody, a BCL-2 inhibitor, an anti-human EGFR antibody, an anti-human HER2 antibody, an anti-human HER3 antibody, acalabrutinib, a cyclin-dependent kinase inhibitor, an anti-human VEGFR2 antibody, an anti-human VEGF antibody, a proteasome inhibitor, an angiogenesis inhibitor, a rapidly accelerated fibrosarcoma (RAF) inhibitor, a bispecific antibody and a fusion protein drug; preferably, the therapeutic agent is cetuximab, obinutuzumab or rituximab;

preferably, the anti-tumor chemotherapeutic is selected from one or more of the following: an alkylating agent, an anthracycline, an antimetabolite, an antibiotic, a plant-based and/or hormonal drug, a platinum-based drug (e.g., cisplatin, carboplatin and oxaliplatin), adriamycin, cyclophosphamide, a taxane (e.g., albumin-bound paclitaxel, liposome paclitaxel and docetaxel), etoposide, gemcitabine, pemetrexed, capecitabine, olaparib, rucaparib, niraparib, talazoparib, fluzoparib, vinca alkaloid, tamoxifen, megestrol, goserelin, asparaginase, a fluorouracil antineoplastic drug (e.g., 5-fluorouracil), azacitidine, cytarabine and cyclocytidine.

12. The pharmaceutical composition according to any one of claims 1–11, wherein the pharmaceutical composition further comprises a pharmaceutically acceptable carrier and/or excipient.

13. The pharmaceutical composition according to any one of claims 1–12, wherein, based on the mass of the antibody, the component A and the component B1 are in a mass ratio of (1:5)–(5:1), e.g., 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1 or 5:1;

the component A and the component B3 are in a mass ratio of (1:5)–(5:1), e.g., 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1 or 5:1;

or

the component B2 and the component A are in a mass ratio of 1:(1–1000), preferably 1:(5–500), and more preferably 1:(10–100);

preferably, the component A and the component B in the pharmaceutical composition are in a form suitable for administration by intravenous drip infusion, subcutaneous injection, intradermal injection, intravenous injection, intramuscular injection or intralesional injection.

14. A kit, preferably for treating a tumor, comprising a product A and a product B, wherein the product A comprises the antibody that specifically binds to CD47 or the antigen-binding fragment thereof as defined in any one of claims 1–13;

the product B is selected from one or more of the following: a product B1, a product B2 and a product B3, wherein the product B1 is the bispecific antibody or the antigen-binding fragment thereof as defined in any one of claims 1–13 (preferably, when the bispecific antibody is a combination of an anti-PD-1/anti-CTLA4 antibody and an anti-PD-1/anti-VEGFA antibody, the anti-PD-1/anti-CTLA4 antibody and the anti-PD-1/anti-VEGFA antibody are packaged either separately or together), the product B2 is the anti-tumor chemotherapeutic as defined in any one of claims 1–13, and the product B3 is the anti-PD-1 monoclonal antibody or the antigen-binding fragment thereof as defined in any one of claims 1–13, wherein the product B1, the product B2 and the product B3 are packaged either separately or together;

preferably, the kit further comprises a product C, wherein the product C is the anti-tumor therapeutic agent as defined in any one of claims 1–13, and the product C is different from the product B;

preferably, the kit further comprises a package insert.

15. The kit according to claim 14, wherein, based on the mass of the antibody, the product A and the product B1 are in a mass ratio of (1:5)–(5:1), e.g., 1:5, 1:4, 1:3, 1:2, 1:1, 2:1, 3:1, 4:1 or 5:1;

the product A and the product B3 are in a mass ratio of (1:5)–(5:1), e.g., 1:5, 1:4,

1:3, 1:2, 1:1, 2:1, 3:1, 4:1 or 5:1;

or

the anti-tumor chemotherapeutic is in a unit dose of 0.1–100 mg, 0.5–50 mg, 1–20 mg, 2–15 mg, 4–12 mg or 8–12 mg;

preferably, the product A, the product B or the product C in the kit is in a form suitable for administration by intravenous drip infusion, subcutaneous injection, intradermal injection, intravenous injection, intramuscular injection or intralesional injection.

16. A method for treating or preventing a tumor, comprising administering to a subject in need an effective amount of the component A and the component B as defined in any one of claims 1–13, wherein preferably, the method further comprises administering to the subject in need an effective amount of the component C as defined in any one of claims 1–13;

preferably, the component A, the component B and the component C are administered simultaneously or sequentially; more preferably, the component A, the component B and the component C are administered before or after a surgical treatment and/or before or after a radiotherapy;

preferably, when the component B is the component B1 and/or the component B3, the component A or the component B is administered at a unit dose of 0.1–100 mg, preferably 1–10 mg per kg body weight of the subject; or the component A or the component B is administered at a unit dose of 10–1000 mg, preferably 50–500 mg, 100–400 mg, 150–300 mg, 150–250 mg or 200 mg in each subject;

preferably, the component B2 is in a unit dose of 0.1–100 mg, 0.5–50 mg, 1–20 mg, 2–15 mg, 4–12 mg or 8–12 mg;

preferably, the dose is administered from twice daily to about once every other day, or once every 3 days, 4 days, 5 days, 6 days, 10 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks or 6 weeks;

preferably, the route of administration is intravenous drip infusion, subcutaneous injection, intradermal injection, intravenous injection, intramuscular injection or intralesional injection.

17. The pharmaceutical composition according to any one of claims 1–13, the kit according to claim 14 or 15, or the method according to claim 16, wherein the tumor is preferably a tumor expressing CD47, and preferably a cancer; the cancer includes a solid tumor, a hematological tumor, lymphoma, blastoma, sarcoma, leukemia or lymphoid malignancy, and more preferably includes squamous cell carcinoma, myeloma, lung cancer, small cell lung cancer, non-small cell lung cancer, head and neck squamous cell carcinoma, glioma (e.g., neuroglioma and recurrent glioma), acute myelocytic leukemia, Hodgkin's lymphoma, non-Hodgkin's lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, acute lymphocytic leukemia, acute myeloblastic leukemia, chronic lymphocytic leukemia, chronic myeloblastic leukemia, primary mediastinal large B-cell lymphoma~~, mantle cell lymphoma~~, small lymphocytic lymphoma, T cell/histiocyte-rich large B-cell lymphoma, multiple myeloma, myeloid leukemia-1 protein, relapsed and refractory peripheral T-cell lymphoma, myelodysplastic syndrome, anaplastic large cell lymphoma, mantle cell lymphoma, marginal zone lymphoma, myelofibrosis, polycythemia vera, bone marrow cancer, myeloproliferative disease, aggressive systemic mastocytosis, eosinophilia, dermatofibrosarcoma protuberans, chronic eosinophilic leukemia, gastrointestinal cancer, gastric adenocarcinoma or gastroesophageal junction adenocarcinoma, ovarian cancer, liver cancer, lymphocytic leukemia, large intestine cancer, endometrial cancer, prostate cancer, thyroid cancer, melanoma, chondrosarcoma, neuroblastoma, adenocarcinoma, pancreatic cancer, pancreatic ductal adenocarcinoma, glioblastoma multiforme, bone cancer, Ewing's sarcoma, cervical cancer, nasopharyngeal cancer, brain cancer, bladder cancer, breast cancer, triple negative breast cancer, intestinal cancer, rectal cancer, colorectal cancer, colon cancer, hepatocellular carcinoma, renal cell carcinoma, clear cell renal cell carcinoma, head and neck cancer, throat cancer, hepatobiliary cancer, central nervous system cancer, esophageal carcinoma, esophageal squamous cell carcinoma, malignant pleural mesothelioma, systemic light chain amyloidosis, lymphocytic lymphoma, myeloproliferative neoplasm, neuroendocrine tumor, Merkel cell carcinoma, testicular cancer and skin cancer, peritoneal cancer, fallopian

tube cancer, urothelial cancer, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) cancer and mesothelioma.

18. A unit formulation, preferably for treating a tumor, comprising 1–10000 mg (preferably 10–1000 mg, and preferably 50–500 mg, 100–400 mg, 150–300 mg, 150–250 mg or 200 mg) of the component A and the component B as defined in any one of claims 1–13,

wherein, when the component B is the component B1 and/or the component B3, the unit formulation comprises 1–10000 mg (preferably 1–1000 mg, and preferably 50–500 mg, 100–400 mg, 150–300 mg, 150–250 mg, 200 mg or 100 mg) of the component B as defined in any one of claims 1–13;

when the component B is the component B2, the unit formulation comprises 0.1–100 mg, 0.5–50 mg, 1–20 mg, 2–15 mg, 4–12 mg, or 8–12 mg of the component B;

preferably, the unit formulation further comprises one or more of the components C as defined in any one of claims 1–13;

wherein the component A, the component B and the component C are packaged separately.

19. A single dose unit, preferably for treating a tumor, comprising 0.1–10000 mg (preferably 1–1000 mg, and preferably 50–500 mg, 100–400 mg, 150–300 mg, 150–250 mg, 200 mg or 100 mg) of the component A and the component B as defined in any one of claims 1–13,

wherein, when the component B is the component B1 and/or the component B3, the single dose unit comprises 0.1–10000 mg (preferably 1–1000 mg, and preferably 50–500 mg, 100–400 mg, 150–300 mg, 150–250 mg, 200 mg or 100 mg) of the component B as defined in any one of claims 1–13;

when the component B is the component B2, the single dose unit comprises 0.1–100 mg, 0.5–50 mg, 1–20 mg, 2–15 mg, 4–12 mg, or 8–12 mg of the component B.