CLAIMS

1. An immunoconjugate, comprising

(i) an anti-PD-1 antibody or antigen-binding fragment thereof and

(ii) an IL-2 mutant protein, wherein the IL-2 mutant protein comprises, relative to SEQ ID NO:3:

(a) a mutation at positions 35,42, 88, 127 and/or 130; and

(b) a shortened B'C' loop region having a sequence positioned between amino acid residues (aa) 72 and (aa) 84, wherein the shortened B'C' loop region is less than 10 amino acids in length, and comprises a sequence of GDASIH or AQSKNFH.

2. The immunoconjugate according to claim 1, wherein the shortened B'C' loop region consists of the amino acid sequence AGDASIH, SGDASIH, or AQSKNFH.

3. The immunoconjugate according to claim 1 or 2, wherein the IL-2 mutant protein further comprises, relative to SEQ ID NO:3, a substitution mutation at position 3, preferably the substitution mutation at position 3 is T3A.

4. The immunoconjugate of claim 1, wherein the IL-2 mutant protein comprises, relative to SEQ ID NO: 3, a substitution mutation at position 88, preferably the substitution mutation at position 88 is N88R or N88D.

5. The immunoconjugate of claim 4, wherein the shortened B'C' loop region consists of the amino acid sequence of AGDASIH and the substitution mutation at position 88 is N88R.

6. The immunoconjugate of claim 1, wherein the IL-2 mutant protein comprises one or more substitution mutations selected from the group consisting of F42A, K35E, S127E, and S130R, preferably the one or more substitution mutations is an S130R substitution mutation.

7. The immunoconjugate of claim 1, wherein the PD-1 antibody or the antigen-binding fragment thereof comprises a heavy chain comprising a heavy chain variable region, wherein the heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 set forth in amino acid sequences of SEQ ID NOs: 9, 10 and 11, respectively, and a light chain comprising a light chain variable region, wherein the light chain variable region comprises LCDR1, LCDR2 and LCDR3 set forth in amino acid sequences of SEQ ID NOs: 16, 17 and 18, respectively.

8. The immunoconjugate of claim 7, wherein the anti-PD-1 antibody or the antigen-binding fragment thereof comprises a heavy chain variable region comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 8; and a light chain variable region comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 15.

9. The immunoconjugate of claim 1, wherein the IL-2 mutant protein is fused directly or via a linker to an Fc fragment; and/or the anti-PD-1 antibody is fused directly or via a linker to an Fc fragment.

10. The immunoconjugate of claim 9, wherein the linker comprises the amino acid sequence of GGGGSGGGGS (SEQ ID NO: 5).

11. The immunoconjugate of claim 9, wherein the Fc fragment comprises: one or more mutations forming a Knob, preferably the one or more mutations are selected from T366W, S354C, and combinations thereof; or one or more mutations forming a Hole, preferably the one or more mutations are selected from Y349C, T366S, L368A, Y407V, and combinations thereof.

12. The immunoconjugate of claim 9, wherein the Fc fragment comprises an amino acid sequence as set forth in SEQ ID NO: 6, 12 or 42.

13. The immunoconjugate of claim 1, wherein the IL-2 mutant protein comprises, relative to SEQ ID NO: 3:

(a) a shortened B'C' loop region comprising the amino acid sequence of AGDASIH; an N88D substitution mutation; and a T3A substitution mutation; or

(b) a shortened B'C' loop region comprising the amino acid sequence of AQSKNFH; an N88R substitution mutation; an F42A substitution mutation; an S127E substitution mutation; and a T3A substitution mutation; or

(c) a shortened B'C' loop region comprising the amino acid sequence of AGDASIH; an N88R substitution mutation; an F42A substitution mutation; an S127E substitution mutation; and a T3A substitution mutation; or

(d) a shortened B'C' loop region comprising the amino acid sequence of AQSKNFH; an N88R substitution mutation; a K35E substitution mutation; an S127E substitution mutation; and a T3A substitution mutation.

14. The immunoconjugate of claim 1, wherein the IL-2 mutant protein comprises the amino acid sequence set forth in any one of SEQ ID NOs: 4, 23, 25, 27, 29 or 31.

15. The immunoconjugate of claim 1, wherein the immunoconjugate comprises (i) a first monomer comprising the anti-PD-1 antibody or antigen-binding fragment thereof and an Fc fragment, and (ii) a second monomer comprising the IL-2 mutant protein fused directly or via a linker to an Fc fragment, wherein:

the anti-PD-1 antibody or antigen-binding fragment thereof comprises a heavy chain comprising a heavy chain variable region, wherein the heavy chain variable region comprises HCDR1, HCDR2, and HCDR3 set forth in amino acid sequences of SEQ ID NOs: 9, 10, and 11, respectively, and a light chain

comprising a light chain variable region, wherein the light chain variable region comprises LCDR1, LCDR2 and LCDR3 set forth in amino acid sequences of SEQ ID NOs: 16, 17, and 18, respectively; and

the IL-2 mutant protein comprises the amino acid sequence set forth in SEQ ID NO: 25;

wherein (a) the Fc fragment of the first monomer comprises a Knob and the Fc fragment of the second monomer comprises a Hole, or (b) the Fc fragment of the first monomer comprises a Hole and the Fc fragment of the second monomer comprises a Knob.

16. The immunoconjugate of claim 1, wherein the immunoconjugate comprises: (i) a first monomer comprising the anti-PD-1 antibody or antigen-binding fragment thereof, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO: 14, and a light chain comprising the amino acid sequence set forth in SEQ ID NO: 20; and (ii) a second monomer comprising the IL-2 mutant protein, a linker, and an Fc fragment, wherein the second monomer comprises the amino acid sequence set forth in SEQ ID NO: 26.

17. The immunoconjugate of claim 1, wherein the mutation at positions 88 and 130 weakens the binding to an IL-2Rβγ, at a binding interface of IL-2 to IL-2Rβγ.

18. A pharmaceutical composition, comprising the immunoconjugate according to any one of claims 1-17, and optionally a pharmaceutical supplementary material.

19. Use of the immunoconjugate according to any one of claims 1-17 or the pharmaceutical composition according to claim 18 in the manufacture of a medicament for preventing and/or treating cancer.

20. The use according to claim 19, wherein the pharmaceutical composition further comprises a second therapeutic agent.

21. The use of claim 19, wherein the cancer is a solid tumor or a hematological tumor.

22. The use according to claim 21, wherein the solid tumor or a hematological tumor, is a PD-1 antibody treatment-resistant cancer.

23. A pharmaceutical composition comprising an immunoconjugate, wherein the immunoconjugate comprises (i) a first monomer comprising an anti-PD-1 antibody or antigen-binding fragment thereof, and (ii) a second monomer comprising an IL-2 mutant protein fused directly or via a linker to an Fc fragment, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises a heavy chain comprising a heavy chain variable region, wherein the heavy chain variable region comprises HCDR1, HCDR2 and HCDR3 set forth in amino acid sequences of SEQ ID NOs: 9, 10 and 11, respectively, and a light chain comprising a light chain variable region, wherein the light chain variable region comprises LCDR1, LCDR2

and LCDR3 set forth in amino acid sequences of SEQ ID NOs: 16, 17 and 18, respectively; and
the IL-2 mutant protein comprises the amino acid sequence set forth in SEQ ID NO: 25; wherein
(a) the Fc fragment of the first monomer comprises a Knob and the Fc fragment of the second monomer comprises a Hole, or
(b) the Fc fragment of the first monomer comprises a Hole and the Fc fragment of the second monomer comprises a Knob.

24. A pharmaceutical composition comprising an immunoconjugate, wherein the immunoconjugate comprises

(i) a first monomer comprising an anti-PD-1 antibody comprising a heavy chain comprising the amino acid sequence set forth in SEQ ID NO: 14, and a light chain comprising the amino acid sequence set forth in SEQ ID NO: 20; and

(ii) a second monomer comprising an IL-2 mutant protein, a linker, and an Fc fragment, wherein the second monomer comprises the amino acid sequence set forth in SEQ ID NO: 26.