CLAIMS

1. Use of an anti-CLDN4/anti-CD137 bispecific antibody in the manufacture of a pharmaceutical composition for treating cancer, wherein the pharmaceutical composition is to be used in combination with a PD-1 signal inhibitor, wherein the bispecific antibody comprises a heavy chain variable region and a light chain variable region of an anti-CLDN4 antibody, and a heavy chain variable region and a light chain variable region of an anti-CD137 antibody, and

wherein the heavy chain variable region of the anti-CLDN4 antibody comprises a CDR1 consisting of an amino acid sequence at amino acid positions 31-35 of SEQ ID NO: 2, a CDR2 consisting of an amino acid sequence at amino acid positions 50-66 of SEQ ID NO: 2, and a CDR3 consisting of an amino acid sequence at amino acid positions 99-112 of SEQ ID NO: 2, and the light chain variable region of the anti-CLDN4 antibody comprises a CDR1 consisting of an amino acid sequence at amino acid positions 24-35 of SEQ ID NO: 4, a CDR2 consisting of an amino acid sequence at amino acid positions 51-57 of SEQ ID NO: 4, and a CDR3 consisting of an amino acid sequence at amino acid positions 90-98 of SEQ ID NO: 4.

2. The use according to claim 1, wherein the heavy chain variable region of the anti-CLDN4 antibody consists of an amino acid sequence at amino acid positions 1-123 of SEQ ID NO: 2, and the light chain variable region of the anti-CLDN4 antibody consists of an amino acid sequence at amino acid positions 1-109 of SEQ ID NO: 4.

3. The use according to claim 1 or 2, wherein the anti-CLDN4/anti-CD137 bispecific antibody comprises an IgG antibody (anti-CLDN4 IgG antibody) consisting of a heavy chain comprising the heavy chain variable region of the anti-CLDN4 antibody and a light chain comprising the light chain variable region of the anti-CLDN4 antibody.

4. The use according to claim 3, comprising either LALA mutation (L234A and L235A) or P331G mutation (wherein a position of the mutation is an amino acid position in

human Igγ1 constant region according to EU index) or both in a Fc region of the anti-CLDN4 IgG antibody.

5. The use according to claim 1, wherein the heavy chain variable region of the anti-CD137 antibody comprises a CDR1 consisting of an amino acid sequence at amino acid positions 625-629 of SEQ ID NO: 2, a CDR2 consisting of an amino acid sequence at amino acid positions 644-659 of SEQ ID NO: 2, and a CDR3 consisting of an amino acid sequence at amino acid positions 692-701 of SEQ ID NO: 2, and the light chain variable region of the anti-CD137 antibody comprises a CDR1 consisting of an amino acid sequence at amino acid positions 486-498 of SEQ ID NO: 2, a CDR2 consisting of an amino acid sequence at amino acid positions 514-520 of SEQ ID NO: 2, and a CDR3 consisting of an amino acid sequence at amino acid positions 553-563 of SEQ ID NO: 2.

6. The use according to claim 1, wherein the heavy chain variable region of the anti-CD137 antibody consists of an amino acid sequence at amino acid positions 595-712 of SEQ ID NO: 2, and the light chain variable region of the anti-CD137 antibody consists of an amino acid sequence at amino acid positions 464-573 of SEQ ID NO: 2.

7. The use according to claim 5 or 6, wherein the anti-CLDN4/anti-CD137 bispecific antibody comprises an anti-CD137 single chain variable fragment (anti-CD137 scFv) comprising the heavy chain variable region and the light chain variable region of the anti-CD137 antibody.

8. The use according to claim 7, wherein the anti-CD137 scFv consists of an amino acid sequence at amino acid positions 464-712 of SEQ ID NO: 2.

9. The use according to claim 8, wherein the anti-CLDN4/anti-CD137 bispecific antibody comprises an anti-CLDN4 IgG antibody and the anti-CD137 scFv, and an amino terminal of the anti-CD137 scFv is linked to a heavy chain carboxy terminal of the anti-CLDN4 IgG antibody via a linker.

10. Use of an anti-CLDN4/anti-CD137 bispecific antibody in the manufacture of a pharmaceutical composition for treating cancer, wherein the pharmaceutical composition is

to be used in combination with a PD-1 signal inhibitor, wherein the bispecific antibody comprises a heavy chain of an anti-CLDN4 antibody comprising a heavy chain variable region consisting of an amino acid sequence at amino acid positions 1-123 of SEQ ID NO: 2 and a light chain of an anti-CLDN4 antibody comprising a light chain variable region consisting of an amino acid sequence at amino acid positions 1-109 of SEQ ID NO: 4, and an anti-CD137 scFv comprising a light chain variable region of an anti-CD137 antibody consisting of an amino acid sequence at amino acid positions 464-573 of SEQ ID NO: 2 and a heavy chain variable region of an anti-CD137 antibody consisting of an amino acid sequence at amino acid positions 595-712 of SEQ ID NO: 2, wherein an amino terminal of the anti-CD137 scFv is linked to a heavy chain carboxy terminal of the anti-CLDN4 antibody via a linker.

11. Use of an anti-CLDN4/anti-CD137 bispecific antibody in the manufacture of a pharmaceutical composition for treating cancer, wherein the pharmaceutical composition is to be used in combination with a PD-1 signal inhibitor, wherein the bispecific antibody comprises a heavy chain of an anti-CLDN4 antibody consisting of an amino acid sequence at amino acid positions 1-453 of SEQ ID NO: 2 and a light chain of an anti-CLDN4 antibody consisting of an amino acid sequence at amino acid positions 1-215 of SEQ ID NO: 4, and an anti-CD137 scFv consisting of an amino acid sequence at amino acid positions 464-712 of SEQ ID NO: 2, wherein an amino terminal of the anti-CD137 scFv is linked to a heavy chain carboxy terminal of the anti-CLDN4 antibody via a linker.

12. The use according to claim 10 or 11, wherein the linker is a GS linker.

13. Use of an anti-CLDN4/anti-CD137 bispecific antibody in the manufacture of a pharmaceutical composition for treating cancer, wherein the pharmaceutical composition is to be used in combination with a PD-1 signal inhibitor, wherein the bispecific antibody comprises a polypeptide comprising a heavy chain of an anti-CLDN4 antibody and an anti-CD137 scFv, consisting of an amino acid sequence of SEQ ID NO: 2, and a light chain of an anti-CLDN4 antibody consisting of an amino acid sequence of SEQ ID NO: 4.

14. The use according to claim 13, wherein the anti-CLDN4/anti-CD137 bispecific antibody is post-translationally modified.

15. The use according to claim 14, wherein the pharmaceutical composition is to be used in combination with the PD-1 signal inhibitor simultaneously, continuously, or sequentially.

16. The use according to claim 15, wherein the anti-CLDN4/anti-CD137 bispecific antibody and the PD-1 signal inhibitor are (i) comprised in the same pharmaceutical composition and are to be administered simultaneously or (ii) comprised in separate pharmaceutical compositions and to be used in combination simultaneously, continuously, or sequentially.

17. The use according to claim 16, wherein the cancer is selected from the group consisting of colorectal cancer, bladder cancer, and lung cancer.

18. The use according to any one of claims 1-2, 5-6, 10-11 and 13-17, wherein the PD-1 signal inhibitor is an antibody binding to one or more proteins selected from the group consisting of PD-1, PD-L1, and PD-L2, or an antigen binding fragment thereof.

19. The use according to claim 18, wherein the PD-1 signal inhibitor is an anti-PD-1 antibody selected from the group consisting of nivolumab, pembrolizumab, pidilizumab, spartalizumab, and cemiplimab.

20. The use according to claim 18, wherein the PD-1 signal inhibitor is an anti-PD-L1 antibody selected from the group consisting of atezolizumab, durvalumab, and avelumab.