

Claims

1. A multispecific antibody that comprises an antigen binding site that binds an extracellular part of CD137 and an antigen binding site that binds an extracellular part of a second membrane protein for use in a method of treatment of cancer in a subject in need thereof, wherein the multispecific antibody is administered in a dose of between 25-300 mg, preferably between 25-150 mg or 25-100 mg, more preferably between 50-100 mg.

2. A method of treating cancer in a subject in need thereof, the method comprising administering between 25-300 mg, preferably between 25-150 mg or 25-100 mg, more preferably between 50-100 mg, of a multispecific antibody that comprises an antigen binding site that binds an extracellular part of CD137 and an antigen binding site that binds an extracellular part of a second membrane protein to the subject in need thereof.

3. The multispecific antibody for use according to claim 1 or method according to claim 2, wherein the cancer is selected from:

any solid tumor harboring MSI-high alterations;
cervical cancer, in particular PD-L1 positive cervical cancer, more in particular cervical cancer with high expression of PD-L1;
endometrial cancer, in particular MSI-high endometrial cancer;
lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular PD-L1 positive NSCLC, more in particular NSCLC with high expression of PD-L1;
brain cancer, in particular glioblastoma; and
breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC).

4. The multispecific antibody for use according to claim 1 or method according to claim 2, wherein the cancer is selected from:

any solid tumor harboring MSI-high alterations;
endometrial cancer, in particular MSI-high endometrial cancer;
lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular NSCLC with high expression of PD-L1; and

breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC).

5 5. A multispecific antibody that comprises an antigen binding site that binds an extracellular part of CD137 and an antigen binding site that binds an extracellular part of a second membrane protein for use in a method of treatment of cancer in a subject in need thereof, wherein the cancer is selected from:

any solid tumor harboring Microsatellite Instability-High (MSI-high) alterations; cervical cancer, in particular PD-L1 positive cervical cancer, more in particular cervical cancer with high expression of PD-L1;

10 endometrial cancer, in particular MSI-high endometrial cancer; lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular PD-L1 positive NSCLC, more in particular NSCLC with high expression of PD-L1;

brain cancer, in particular glioblastoma; and

15 breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC), and

wherein the multispecific antibody is administered in a dose of between 10-1200 mg, preferably between 25-600 or mg 25-300 mg, more preferably between 25-150 mg or 25-100 mg or 25-75 mg, most preferably between 25-50 mg or 50-100 mg.

20 6. The multispecific antibody for use according to claim 5, wherein the cancer is selected from:

any solid tumor harboring Microsatellite Instability-High (MSI-high) alterations; endometrial cancer, in particular MSI-high endometrial cancer;

25 lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular NSCLC with high expression of PD-L1; and

breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC), and

30 wherein the multispecific antibody is administered in a dose of between 10-1200 mg, preferably between 25-600 or mg 25-300 mg, more preferably between 25-150 mg or 25-100 mg, most preferably between 50-100 mg.

7. A method of treating cancer in a subject in need thereof, the method comprising administering between 10-1200 mg, preferably between 25-600 or mg 25-300 mg, more preferably between 25-150 mg or 25-100 mg or 25-75 mg, most preferably between 25-50 mg or 50-100 mg, of a multispecific antibody that comprises an antigen binding site that binds an extracellular part of CD137 and an antigen binding site that binds an extracellular part of a second membrane protein to a subject having cancer, wherein the cancer is selected from:

any solid tumor harboring Microsatellite Instability-High (MSI-high) alterations; cervical cancer, in particular PD-L1 positive cervical cancer, more in particular cervical cancer with high expression of PD-L1; endometrial cancer, in particular MSI-high endometrial cancer; lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular PD-L1 positive NSCLC, more in particular NSCLC with high expression of PD-L1; brain cancer, in particular glioblastoma; and breast cancer, in particular metastatic breast cancer or triple negative breast cancer (TNBC).

8. The method according to claim 7, the method comprising administering between 10-1200 mg, preferably between 25-600 or mg 25-300 mg, more preferably between 25-150 mg or 25-100 mg, most preferably between 50-100 mg, of a multispecific antibody that comprises an antigen binding site that binds an extracellular part of CD137 and an antigen binding site that binds an extracellular part of a second membrane protein to a subject having cancer, wherein the cancer is selected from:

any solid tumor harboring Microsatellite Instability-High (MSI-high) alterations; endometrial cancer, in particular MSI-high endometrial cancer; lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular NSCLC with high expression of PD-L1; and breast cancer, in particular metastatic breast cancer or triple negative breast cancer (TNBC).

9. The multispecific antibody for use or method according to any one of claims 1-8, wherein the multispecific antibody is administered intravenously.

10. The multispecific antibody for use or method according to any one of claims 1-9, wherein the multispecific antibody is administered once every two weeks.

11. The multispecific antibody for use or method according to any one of claims 1-10, wherein said second membrane protein is not a member of the TNF receptor superfamily.

12. The multispecific antibody for use or method according to any one of claims 1-11, wherein said second membrane protein is a member of the B7 family.

13. The multispecific antibody for use or method according to any one of claims 1-12 wherein the second membrane protein is PD-L1 or PD-L2, preferably PD-L1.

14. The multispecific antibody for use or method according to any one of claims 1-13, wherein the multispecific antibody comprises one antigen binding site that binds the PD-1 binding domain of PD-L1.

15. The multispecific antibody for use or method according to any one of claims 1-14, wherein the multispecific antibody comprises one antigen binding site that binds the CD137L binding domain of CD137.

16. The multispecific antibody for use or method according to any one of claims 1-15, wherein the multispecific antibody comprises one antigen binding site that blocks the binding of a ligand to CD137 or binds an extracellular ligand-blocking binding site of CD137, preferably a CD137L blocking binding site.

17. The multispecific antibody for use or method according to any one of claims 1-16, wherein the variable domain that binds an extracellular part of CD137 is defined as a variable domain that, when in a bivalent monospecific antibody format that comprises two of said variable domains that bind CD137, does not stimulate activity of CD137 on a cell or does so at a reduced level in comparison to one of said variable domain as part of a bispecific antibody having a second variable domain binding a tumor associated antigen, preferably a member of the B7 family, more preferably PD-L1.

18. The multispecific antibody for use or method according to any one of claims 1-17, wherein the variable domain that binds an extracellular part of CD137 is capable of stimulating activity of CD137 on a cell when combined in a multispecific antibody with a second variable domain which binds to PD-L1, when the multispecific antibody is in the presence of a first cell expressing CD137 and a second cell expressing PD-L1.

19. The multispecific antibody for use or method according to any one of claims 1-18, wherein the multispecific antibody is capable of binding CD137 and PD-L1, preferably simultaneously.

20. The multispecific antibody for use or method according to any one of claims 1-19, wherein the multispecific antibody only induces or activates CD137 signaling in the presence of PD-L1 expressing cells.

21. The multispecific antibody for use or method according to any one of claims 1-20, wherein the antigen binding sites of said multispecific antibody consist of one immunoglobulin variable domain that binds CD137 and one immunoglobulin variable domain that binds the extracellular part of a second membrane protein.

22. The multispecific antibody for use or method according to any one of claims 1-21, wherein said multispecific antibody is a full length antibody.

23. The multispecific antibody for use or method according to any one of claims 1-22, wherein said multispecific antibody is an IgG1 molecule without Fc effector function.

24. The multispecific antibody for use or method according to any one of claims 1-23, wherein the second membrane protein is not to a significant extent expressed by a T-cell.

25. The multispecific antibody for use or method according to any one of claims 1-24, wherein said second membrane protein is present on the cell membrane as a part of a multimeric membrane protein comprising two or more of said second membrane proteins.

26. The multispecific antibody for use or method according to any one of claims 1-25, wherein said second membrane protein is present on the cell membrane as a part of a homodimer or a homotrimer.

27. The multispecific antibody for use or method according to any one of claims 1-26, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of CD137 comprising a CDR3 region having an amino acid sequence as set forth in SEQ ID NO: 23; SEQ ID NO: 27; SEQ ID NO: 34 or SEQ ID NO: 52, or variants thereof.

28. The multispecific antibody for use or method according to any one of claims 1-27, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of CD137 comprising a CDR2 region having an amino acid sequence as set forth in SEQ ID NO: 22; SEQ ID NO: 26; SEQ ID NO: 33; or SEQ ID NO: 51, or variants thereof.

29. The multispecific antibody for use or method according to any one of claims 1-27, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of CD137 comprising a CDR1 region having an amino acid sequence as set forth in SEQ ID NO: 21; SEQ ID NO: 25; SEQ ID NO: 32; or SEQ ID NO: 50, or variants thereof.

30. The multispecific antibody for use or method according to any one of claims 1-29, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of CD137 having an amino acid sequence as set forth in SEQ ID NO: 1; SEQ ID NO: 5; SEQ ID NO: 9; SEQ ID NO: 13; SEQ ID NO: 17; SEQ ID NO: 20; SEQ ID NO: 24; SEQ ID NO: 28; SEQ ID NO: 31; SEQ ID NO: 35; SEQ ID NO: 39; SEQ ID NO: 43; SEQ ID NO: 46; or SEQ ID NO: 49, preferably SEQ ID NO: 20; SEQ ID NO: 24; SEQ ID NO: 31; or SEQ ID NO: 49, or variants thereof.

31. The multispecific antibody for use or method according to any one of claims 1-30, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of PD-L1 comprising a CDR3 region having an amino acid sequence as set forth in SEQ ID NO: 56; SEQ ID NO: 58; SEQ ID NO: 61; SEQ ID NO: 84; SEQ ID NO: 88; SEQ ID NO:

91; SEQ ID NO: 95; SEQ ID NO: 102; or SEQ ID NO: 106, preferably SEQ ID NO: 56; SEQ ID NO: 91; SEQ ID NO: 95; or SEQ ID NO: 102, or variants thereof.

32. The multispecific antibody for use or method according to any one of claims 1-31, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of PD-L1 comprising a CDR2 region having an amino acid sequence as set forth in SEQ ID NO: 3; SEQ ID NO: 55; SEQ ID NO: 63; SEQ ID NO: 66; SEQ ID NO: 79; SEQ ID NO: 83; SEQ ID NO: 87; SEQ ID NO: 94; SEQ ID NO: 101; or SEQ ID NO: 105, or variants thereof.

33. The multispecific antibody for use or method according to any one of claims 1-32, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of PD-L1 comprising a CDR1 region having an amino acid sequence as set forth in SEQ ID NO: 54; SEQ ID NO: 60; SEQ ID NO: 65; SEQ ID NO: 68; SEQ ID NO: 74; SEQ ID NO: 82; SEQ ID NO: 86; SEQ ID NO: 90; or SEQ ID NO: 93, or variants thereof.

34. The multispecific antibody for use or method according to any one of claims 1-33, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of PD-L1 having an amino acid sequence as set forth in SEQ ID NO: 53; SEQ ID NO: 57; SEQ ID NO: 59; SEQ ID NO: 62; SEQ ID NO: 64; SEQ ID NO: 67; SEQ ID NO: 69; SEQ ID NO: 73; SEQ ID NO: 77; SEQ ID NO: 81; SEQ ID NO: 85; SEQ ID NO: 89; SEQ ID NO: 92; SEQ ID NO: 96; SEQ ID NO: 97; SEQ ID NO: 100; SEQ ID NO: 103; SEQ ID NO: 104; SEQ ID NO: 107, preferably SEQ ID NO: 67, SEQ ID NO: 89, SEQ ID NO: 92, or SEQ ID NO: 100, or variants thereof.

35. The multispecific antibody for use or method according to any one of claims 1-34, wherein the multispecific antibody comprises CDR 1, 2 and 3 of MF6797 and CDRs 1, 2 and 3 of MF7702, or variants thereof.

36. The multispecific antibody for use or method according to any one of claims 1-34, wherein the multispecific antibody comprises SEQ ID NO. 49 and SEQ ID NO. 67, or variants thereof.

37. A multispecific antibody for use in a method of treatment of cancer in a subject in need thereof, wherein the antibody comprises a binding domain that binds CD137 comprising:

5 a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 50, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 51 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 52; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 40, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 41
10 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 42; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 21, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 22 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 23; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth
15 in SEQ ID NO: 32, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 33 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 34; and/or

wherein the antibody comprises a binding domain that binds PD-L1, comprising:

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 68, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 55
20 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 56; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 93, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 94 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 95; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth
25 in SEQ ID NO: 93, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 101 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 102; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 90, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 79 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 91,

30 each of the individual SEQ ID NOs having 0, 1, 2, 3, 4 or 5 amino acid insertions, deletions, or substitutions, or a combination thereof,

wherein the multispecific antibody is administered in a dose of between 25-300 mg, preferably between 25-150 or mg 25-100 mg or 25-75 mg, more preferably between 25-50 mg or 50-100 mg.

5 38. The multispecific antibody for use according to claim 37, wherein the multispecific antibody is administered in a dose of between 25-300 mg, preferably between 25-150 or mg 25-100 mg, more preferably between 50-100 mg.

10 39. A method of treating cancer in a subject in need thereof, the method comprising administering between 25-300 mg, preferably between 25-150 or mg 25-100 mg or 25-75 mg, more preferably between 25-50 mg or 50-100 mg, of a multispecific antibody that comprises a binding domain that binds CD137, comprising:

15 a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 50, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 51 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 52; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 40, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 41 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 42; or

20 a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 21, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 22 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 23; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 32, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 33 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 34; and/or

25 wherein the antibody comprises a binding domain that binds PD-L1, comprising: a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 68, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 55 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 56; or

30 a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 93, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 94 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 95; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 93, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 101 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 102; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 90, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 79 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 91,

each of the individual SEQ ID NOs having 0, 1, 2, 3, 4 or 5 amino acid insertions, deletions, or substitutions, or a combination thereof.

40. The method according to claim 39, wherein the multispecific antibody is administered in a dose of between 25-300 mg, preferably between 25-150 or mg 25-100 mg, more preferably between 50-100 mg.

41. The multispecific antibody for use or method according to any one of claims 37-40, wherein the cancer is selected from:

any solid tumor harboring MSI-high alterations;
cervical cancer, in particular PD-L1 positive cervical cancer, more in particular cervical cancer with high expression of PD-L1;
endometrial cancer, in particular MSI-high endometrial cancer;
lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular PD-L1 positive NSCLC, more in particular NSCLC with high expression of PD-L1;
brain cancer, in particular glioblastoma; and
breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC).

42. The multispecific antibody for use or method according to any one of claims 37-40, wherein the cancer is selected from:

any solid tumor harboring MSI-high alterations;
endometrial cancer, in particular MSI-high endometrial cancer;
lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular NSCLC with high expression of PD-L1; and

breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC).

43. A multispecific antibody for use in a method of treatment of cancer in a subject in need thereof, wherein the antibody comprises a binding domain that binds CD137 comprising:

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 50, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 51 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 52; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 40, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 41 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 42; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 21, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 22 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 23; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 32, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 33 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 34; and/or

wherein the antibody comprises a binding domain that binds PD-L1, comprising:

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 68, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 55 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 56; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 93, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 94 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 95; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 93, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 101 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 102; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 90, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 79 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 91,

each of the individual SEQ ID NOs having 0, 1, 2, 3, 4 or 5 amino acid insertions, deletions, or substitutions, or a combination thereof,

wherein the cancer is selected from:

any solid tumor harboring MSI-high alterations;

5 cervical cancer, in particular PD-L1 positive cervical cancer, more in particular cervical cancer with high expression of PD-L1;

endometrial cancer, in particular MSI-high endometrial cancer;

lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular PD-L1 positive NSCLC, more in particular NSCLC with high expression of PD-L1;

10 brain cancer, in particular glioblastoma; and

breast cancer, in particular metastatic breast cancer or triple negative breast cancer (TNBC), and

wherein the multispecific antibody is administered in a dose of between 10-1200 mg, preferably between 25-600 or mg 25-300 mg, more preferably between 25-150 mg or 25-100
15 mg or 25-75 mg, most preferably between 25-50 mg or 50-100 mg.

44. The multispecific antibody for use according to claim 43, wherein the cancer is selected from:

any solid tumor harboring MSI-high alterations;

20 endometrial cancer, in particular MSI-high endometrial cancer;

lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular NSCLC with high expression of PD-L1; and

breast cancer, in particular metastatic breast cancer or triple negative breast cancer (TNBC), and

25 wherein the multispecific antibody is administered in a dose of between 10-1200 mg, preferably between 25-600 or mg 25-300 mg, more preferably between 25-150 mg or 25-100 mg, most preferably between 50-100 mg.

45. A method of treating cancer in a subject in need thereof, wherein the cancer is
30 selected from:

any solid tumor harboring MSI-high alterations;

cervical cancer, in particular PD-L1 positive cervical cancer, more in particular cervical cancer with high expression of PD-L1;

endometrial cancer, in particular MSI-high endometrial cancer;

lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular

5 PD-L1 positive NSCLC, more in particular NSCLC with high expression of PD-L1;

brain cancer, in particular glioblastoma; and

breast cancer, in particular metastatic breast cancer or triple negative breast cancer (TNBC),

10 the method comprising administering between 10-1200 mg, preferably between 25-600 or mg 25-300 mg, more preferably between 25-150 mg or 25-100 mg or 25-75 mg, most preferably between 25-50 mg or 50-100 mg, of a multispecific antibody that comprises a binding domain that binds CD137, comprising:

15 a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 50, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 51 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 52; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 40, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 41 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 42; or

20 a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 21, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 22 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 23; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 32, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 33 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 34; and/or

25 wherein the antibody comprises a binding domain that binds PD-L1, comprising:

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 68, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 55 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 56; or

30 a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 93, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 94 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 95; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 93, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 101 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 102; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 90, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 79 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 91,

each of the individual SEQ ID NOs having 0, 1, 2, 3, 4 or 5 amino acid insertions, deletions, or substitutions, or a combination thereof.

46. The method according to claim 45, wherein the cancer is selected from:
any solid tumor harboring MSI-high alterations;
endometrial cancer, in particular MSI-high endometrial cancer;
lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular NSCLC with high expression of PD-L1; and

breast cancer, in particular metastatic breast cancer or triple negative breast cancer (TNBC), and

wherein the multispecific antibody is administered in a dose of between 10-1200 mg, preferably between 25-600 mg or 25-300 mg, more preferably between 25-150 mg or 25-100 mg, most preferably between 50-100 mg.

47. The multispecific antibody for use or method according to any one of claims 37-46, wherein the multispecific antibody is administered intravenously.

48. The multispecific antibody for use or method according to any one of claims 37-47, wherein the multispecific antibody is administered once every two weeks.

49. The multispecific antibody for use or method according to any one of claims 37-48, wherein the multispecific antibody comprises CDR 1, 2 and 3 of MF6797 and CDRs 1, 2 and 3 of MF7702, or variants thereof.

50. The multispecific antibody for use or method according to claim 49, wherein the multispecific antibody comprises SEQ ID NO. 49 and SEQ ID NO. 67, or variants thereof.

51. The multispecific antibody for use or method according to any one of claims 37-48, wherein the multispecific antibody comprises CDR 1, 2 and 3 of MF6783 and CDRs 1, 2 and 3 of MF5542, or variants thereof.

5 52. The multispecific antibody for use or method according to claim 51, wherein the multispecific antibody comprises SEQ ID NO. 1 and SEQ ID NO. 92, or variants thereof.

53. The multispecific antibody for use or method according to any one of claims 37-48, wherein the multispecific antibody comprises CDR 1, 2 and 3 of MF6754 and CDRs 1, 2 and 3 of MF5561, or variants thereof.

54. The multispecific antibody for use or method according to claim 53, wherein the multispecific antibody comprises SEQ ID NO. 20 and SEQ ID NO. 100, or variants thereof.

15 55. The multispecific antibody for use or method according to any one of claims 37-48, wherein the multispecific antibody comprises CDR 1, 2 and 3 of MF6785 and CDRs 1, 2 and 3 of MF5439, or variants thereof.

20 56. The multispecific antibody for use or method according to claim 55, wherein the multispecific antibody comprises SEQ ID NO. 31 and SEQ ID NO. 89, or variants thereof.

25 57. The multispecific antibody for use or method according to any one of claims 37-48, wherein the multispecific antibody comprises CDR 1, 2 and 3 of MF6795 and CDRs 1, 2 and 3 of MF5442, or variants thereof.

58. The multispecific antibody for use or method according to claim 57, wherein the multispecific antibody comprises SEQ ID NO. 9 and SEQ ID NO. 92, or variants thereof.

30 59. The multispecific antibody for use or method according to any one of claims 1-58, wherein the antibody comprises a common light chain variable domain having an amino acid sequence as set forth in SEQ ID NO: 110, or a common light chain having an amino acid sequence as set forth in SEQ ID NO: 109, or variants thereof.

60. The multispecific antibody for use or method according to any one of claims 1-59, wherein the antibody comprises a heavy chain constant domain 1 (CH1) having an amino acid sequence as set forth in SEQ ID NO: 112, a heavy chain constant domain 2 (CH2) having an amino acid sequence as set forth in SEQ ID NO: 114, a heavy chain constant domain 3 (CH3) having an amino acid sequence as set forth in SEQ ID NO: 115, and a heavy chain constant domain 3 (CH3) having an amino acid sequence as set forth in SEQ ID NO: 116, or variants thereof.

61. A kit of parts comprising a multispecific antibody as defined in any one of the preceding claims and instructions for use of the multispecific antibody at a dose, or flat dose, of between 25-75 mg or between 25-50 mg or between 25-40 mg or between 25-30 mg, or at 25 mg or 30 mg or 40 mg or 50 mg or 60 mg or 70 mg or 75 mg.

62. The kit of parts according to claim 61, wherein the kit comprises instructions for use of the multispecific antibody in any one the indications selected from the group consisting of:

- any solid tumor harboring MSI-high alterations;
- cervical cancer, in particular PD-L1 positive cervical cancer, more in particular cervical cancer with high expression of PD-L1;
- endometrial cancer, in particular MSI-high endometrial cancer;
- lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular PD-L1 positive NSCLC, more in particular NSCLC with high expression of PD-L1;
- brain cancer, in particular glioblastoma; and
- breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC).

Claims

1. Use of a multispecific antibody that comprises an antigen binding site that binds an extracellular part of CD137 and an antigen binding site that binds an extracellular part of a second membrane protein in the manufacture of a medicament for the treatment of cancer in a subject in need thereof, wherein the multispecific antibody is formulated for administration in a dose of between 25-300 mg, preferably between 25-150 mg or 25-100 mg, more preferably between 50-100 mg.

2. The use according to claim 1, wherein the cancer is selected from:
any solid tumor harboring MSI-high alterations;
cervical cancer, in particular PD-L1 positive cervical cancer, more in particular cervical cancer with high expression of PD-L1;
endometrial cancer, in particular MSI-high endometrial cancer;
lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular PD-L1 positive NSCLC, more in particular NSCLC with high expression of PD-L1;
brain cancer, in particular glioblastoma; and
breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC).

3. The use according to claim 1, wherein the cancer is selected from:
any solid tumor harboring MSI-high alterations;
endometrial cancer, in particular MSI-high endometrial cancer;
lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular NSCLC with high expression of PD-L1; and
breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC).

4. Use of a multispecific antibody that comprises an antigen binding site that binds an extracellular part of CD137 and an antigen binding site that binds an extracellular part of a second membrane protein in the manufacture of a medicament for the treatment of cancer in a subject in need thereof, wherein the cancer is selected from:
any solid tumor harboring Microsatellite Instability-High (MSI-high) alterations;

cervical cancer, in particular PD-L1 positive cervical cancer, more in particular cervical cancer with high expression of PD-L1;

endometrial cancer, in particular MSI-high endometrial cancer;

lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular

5 PD-L1 positive NSCLC, more in particular NSCLC with high expression of PD-L1;

brain cancer, in particular glioblastoma; and

breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC), and

10 wherein the multispecific antibody is formulated for administration in a dose of between 10-1200 mg, preferably between 25-600 or mg 25-300 mg, more preferably between 25-150 mg or 25-100 mg or 25-75 mg, most preferably between 25-50 mg or 50-100 mg.

5. The use according to claim 4, wherein the cancer is selected from:

any solid tumor harboring Microsatellite Instability-High (MSI-high) alterations;

15 endometrial cancer, in particular MSI-high endometrial cancer;

lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular NSCLC with high expression of PD-L1; and

breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC), and

20 wherein the multispecific antibody is formulated for administration in a dose of between 10-1200 mg, preferably between 25-600 or mg 25-300 mg, more preferably between 25-150 mg or 25-100 mg, most preferably between 50-100 mg.

25 6. The use according to any one of claims 1-5, wherein the multispecific antibody is formulated for administration intravenously.

7. The use according to any one of claims 1-6, wherein the multispecific antibody is formulated for administration once every two weeks.

30 8. The use according to any one of claims 1-7, wherein said second membrane protein is not a member of the TNF receptor superfamily.

9. The use according to any one of claims 1-8, wherein said second membrane protein is a member of the B7 family.

5 10. The use according to any one of claims 1-9 wherein the second membrane protein is PD-L1 or PD-L2, preferably PD-L1.

11. The use according to any one of claims 1-10, wherein the multispecific antibody comprises one antigen binding site that binds the PD-1 binding domain of PD-L1.

10 12. The use according to any one of claims 1-11, wherein the multispecific antibody comprises one antigen binding site that binds the CD137L binding domain of CD137.

15 13. The use according to any one of claims 1-12, wherein the multispecific antibody comprises one antigen binding site that blocks the binding of a ligand to CD137 or binds an extracellular ligand-blocking binding site of CD137, preferably a CD137L blocking binding site.

20 14. The use according to any one of claims 1-13, wherein the variable domain that binds an extracellular part of CD137 is defined as a variable domain that, when in a bivalent monospecific antibody format that comprises two of said variable domains that bind CD137, does not stimulate activity of CD137 on a cell or does so at a reduced level in comparison to one of said variable domain as part of a bispecific antibody having a second variable domain binding a tumor associated antigen, preferably a member of the B7 family, more preferably PD-L1.

25 15. The use according to any one of claims 1-14, wherein the variable domain that binds an extracellular part of CD137 is capable of stimulating activity of CD137 on a cell when combined in a multispecific antibody with a second variable domain which binds to PD-L1, when the multispecific antibody is in the presence of a first cell expressing CD137 and a second cell expressing PD-L1.

30 16. The use according to any one of claims 1-15, wherein the multispecific antibody is capable of binding CD137 and PD-L1, preferably simultaneously.

17. The use according to any one of claims 1-16, wherein the multispecific antibody only induces or activates CD137 signaling in the presence of PD-L1 expressing cells.

5 18. The use according to any one of claims 1-17, wherein the antigen binding sites of said multispecific antibody consist of one immunoglobulin variable domain that binds CD137 and one immunoglobulin variable domain that binds the extracellular part of a second membrane protein.

10 19. The use according to any one of claims 1-18, wherein said multispecific antibody is a full length antibody.

20. The use according to any one of claims 1-19, wherein said multispecific antibody is an IgG1 molecule without Fc effector function.

15 21. The use according to any one of claims 1-20, wherein the second membrane protein is not to a significant extent expressed by a T-cell.

20 22. The use according to any one of claims 1-21, wherein said second membrane protein is present on the cell membrane as a part of a multimeric membrane protein comprising two or more of said second membrane proteins.

23. The use according to any one of claims 1-22, wherein said second membrane protein is present on the cell membrane as a part of a homodimer or a homotrimer.

25 24. The use according to any one of claims 1-23, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of CD137 comprising a CDR3 region having an amino acid sequence as set forth in SEQ ID NO: 23; SEQ ID NO: 27; SEQ ID NO: 34 or SEQ ID NO: 52, or variants thereof.

30 25. The use according to any one of claims 1-24, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of CD137 comprising a CDR2

region having an amino acid sequence as set forth in SEQ ID NO: 22; SEQ ID NO: 26; SEQ ID NO: 33; or SEQ ID NO: 51, or variants thereof.

26. The use according to any one of claims 1-24, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of CD137 comprising a CDR1 region having an amino acid sequence as set forth in SEQ ID NO: 21; SEQ ID NO: 25; SEQ ID NO: 32; or SEQ ID NO: 50, or variants thereof.

27. The use according to any one of claims 1-26, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of CD137 having an amino acid sequence as set forth in SEQ ID NO: 1; SEQ ID NO: 5; SEQ ID NO: 9; SEQ ID NO: 13; SEQ ID NO: 17; SEQ ID NO: 20; SEQ ID NO: 24; SEQ ID NO: 28; SEQ ID NO: 31; SEQ ID NO: 35; SEQ ID NO: 39; SEQ ID NO: 43; SEQ ID NO: 46; or SEQ ID NO: 49, preferably SEQ ID NO: 20; SEQ ID NO: 24; SEQ ID NO: 31; or SEQ ID NO: 49, or variants thereof.

28. The use according to any one of claims 1-27, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of PD-L1 comprising a CDR3 region having an amino acid sequence as set forth in SEQ ID NO: 56; SEQ ID NO: 58; SEQ ID NO: 61; SEQ ID NO: 84; SEQ ID NO: 88; SEQ ID NO: 91; SEQ ID NO: 95; SEQ ID NO: 102; or SEQ ID NO: 106, preferably SEQ ID NO: 56; SEQ ID NO: 91; SEQ ID NO: 95; or SEQ ID NO: 102, or variants thereof.

29. The use according to any one of claims 1-28, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of PD-L1 comprising a CDR2 region having an amino acid sequence as set forth in SEQ ID NO: 3; SEQ ID NO: 55; SEQ ID NO: 63; SEQ ID NO: 66; SEQ ID NO: 79; SEQ ID NO: 83; SEQ ID NO: 87; SEQ ID NO: 94; SEQ ID NO: 101; or SEQ ID NO: 105, or variants thereof.

30. The use according to any one of claims 1-29, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of PD-L1 comprising a CDR1 region having an amino acid sequence as set forth in SEQ ID NO: 54; SEQ ID NO: 60; SEQ ID NO: 65; SEQ ID NO: 68; SEQ ID NO: 74; SEQ ID NO: 82; SEQ ID NO: 86; SEQ ID NO: 90; or SEQ ID NO: 93, or variants thereof.

31. The use according to any one of claims 1-30, wherein the antibody comprises a heavy chain variable region that binds an extracellular part of PD-L1 having an amino acid sequence as set forth in SEQ ID NO: 53; SEQ ID NO: 57; SEQ ID NO: 59; SEQ ID NO: 62; SEQ ID NO: 64; SEQ ID NO: 67; SEQ ID NO: 69; SEQ ID NO: 73; SEQ ID NO: 77; SEQ ID NO: 81; SEQ ID NO: 85; SEQ ID NO: 89; SEQ ID NO: 92; SEQ ID NO: 96; SEQ ID NO: 97; SEQ ID NO: 100; SEQ ID NO: 103; SEQ ID NO: 104; SEQ ID NO: 107, preferably SEQ ID NO: 67, SEQ ID NO: 89, SEQ ID NO: 92, or SEQ ID NO: 100, or variants thereof.

32. The use according to any one of claims 1-31, wherein the multispecific antibody comprises CDR 1, 2 and 3 of MF6797 and CDRs 1, 2 and 3 of MF7702, or variants thereof.

33. The use according to any one of claims 1-31, wherein the multispecific antibody comprises SEQ ID NO. 49 and SEQ ID NO. 67, or variants thereof.

34. Use of a multispecific antibody in the manufacture of a medicament for the treatment of cancer in a subject in need thereof, wherein the antibody comprises a binding domain that binds CD137 comprising:

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 50, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 51 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 52; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 40, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 41 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 42; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 21, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 22 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 23; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 32, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 33 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 34; and/or

wherein the antibody comprises a binding domain that binds PD-L1, comprising:

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 68, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 55 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 56; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 93, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 94 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 95; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 93, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 101 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 102; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 90, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 79 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 91,

each of the individual SEQ ID NOs having 0, 1, 2, 3, 4 or 5 amino acid insertions, deletions, or substitutions, or a combination thereof,

wherein the multispecific antibody is administered in a dose of between 25-300 mg, preferably between 25-150 or mg 25-100 mg or 25-75 mg, more preferably between 25-50 mg or 50-100 mg.

35. The use according to claim 34, wherein the multispecific antibody is formulated for administration in a dose of between 25-300 mg, preferably between 25-150 or mg 25-100 mg, more preferably between 50-100 mg.

36. The use according to claim 34 or claim 35, wherein the cancer is selected from: any solid tumor harboring MSI-high alterations;

cervical cancer, in particular PD-L1 positive cervical cancer, more in particular cervical cancer with high expression of PD-L1;

endometrial cancer, in particular MSI-high endometrial cancer;

lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular PD-L1 positive NSCLC, more in particular NSCLC with high expression of PD-L1;

brain cancer, in particular glioblastoma; and

breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC).

37. The use according to claim 34 or claim 35, wherein the cancer is selected from:
any solid tumor harboring MSI-high alterations;
endometrial cancer, in particular MSI-high endometrial cancer;
lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular

5 NSCLC with high expression of PD-L1; and

breast cancer, in particular metastatic breast cancer and triple negative breast
cancer (TNBC).

10 38. Use of a multispecific antibody in the manufacture of a medicament for the
treatment of cancer in a subject in need thereof, wherein the antibody comprises a binding
domain that binds CD137 comprising:

a variable domain that comprises a CDR1 having an amino acid sequence as set forth
in SEQ ID NO: 50, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 51
and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 52; or

15 a variable domain that comprises a CDR1 having an amino acid sequence as set forth
in SEQ ID NO: 40, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 41
and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 42; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth
in SEQ ID NO: 21, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 22
20 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 23; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth
in SEQ ID NO: 32, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 33
and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 34; and/or

wherein the antibody comprises a binding domain that binds PD-L1, comprising:

25 a variable domain that comprises a CDR1 having an amino acid sequence as set forth
in SEQ ID NO: 68, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 55
and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 56; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth
in SEQ ID NO: 93, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 94
30 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 95; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth
in SEQ ID NO: 93, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 101
and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 102; or

a variable domain that comprises a CDR1 having an amino acid sequence as set forth in SEQ ID NO: 90, a CDR2 having an amino acid sequence as set forth in SEQ ID NO: 79 and a CDR3 having an amino acid sequence as set forth in SEQ ID NO: 91.

each of the individual SEQ ID NOs having 0, 1, 2, 3, 4 or 5 amino acid insertions, deletions, or substitutions, or a combination thereof,

wherein the cancer is selected from:

any solid tumor harboring MSI-high alterations;

cervical cancer, in particular PD-L1 positive cervical cancer, more in particular cervical cancer with high expression of PD-L1;

endometrial cancer, in particular MSI-high endometrial cancer;

lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular PD-L1 positive NSCLC, more in particular NSCLC with high expression of PD-L1;

brain cancer, in particular glioblastoma; and

breast cancer, in particular metastatic breast cancer or triple negative breast cancer (TNBC), and

wherein the multispecific antibody is formulated for administration in a dose of between 10-1200 mg, preferably between 25-600 or mg 25-300 mg, more preferably between 25-150 mg or 25-100 mg or 25-75 mg, most preferably between 25-50 mg or 50-100 mg.

39. The use according to claim 38, wherein the cancer is selected from:

any solid tumor harboring MSI-high alterations;

endometrial cancer, in particular MSI-high endometrial cancer;

lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular NSCLC with high expression of PD-L1; and

breast cancer, in particular metastatic breast cancer or triple negative breast cancer (TNBC), and

wherein the multispecific antibody is formulated for administration in a dose of between 10-1200 mg, preferably between 25-600 or mg 25-300 mg, more preferably between 25-150 mg or 25-100 mg, most preferably between 50-100 mg.

40. The use according to claim 34-39, wherein the multispecific antibody is formulated for administration intravenously.

41. The use according to any one of claims 34-40, wherein the multispecific antibody is formulated for administration once every two weeks.

42. The use according to any one of claims 37-41, wherein the multispecific antibody comprises CDR 1, 2 and 3 of MF6797 and CDRs 1, 2 and 3 of MF7702, or variants thereof.

43. The use according to claim 42, wherein the multispecific antibody comprises SEQ ID NO. 49 and SEQ ID NO. 67, or variants thereof.

44. The use according to any one of claims 34-41, wherein the multispecific antibody comprises CDR 1, 2 and 3 of MF6783 and CDRs 1, 2 and 3 of MF5542, or variants thereof.

45. The use according to claim 44, wherein the multispecific antibody comprises SEQ ID NO. 1 and SEQ ID NO. 92, or variants thereof.

46. The use according to any one of claims 34-41, wherein the multispecific antibody comprises CDR 1, 2 and 3 of MF6754 and CDRs 1, 2 and 3 of MF5561, or variants thereof.

47. The use according to claim 46, wherein the multispecific antibody comprises SEQ ID NO. 20 and SEQ ID NO. 100, or variants thereof.

48. The use according to any one of claims 34-41, wherein the multispecific antibody comprises CDR 1, 2 and 3 of MF6785 and CDRs 1, 2 and 3 of MF5439, or variants thereof.

49. The use according to claim 48, wherein the multispecific antibody comprises SEQ ID NO. 31 and SEQ ID NO. 89, or variants thereof.

50. The use according to any one of claims 34-41, wherein the multispecific antibody comprises CDR 1, 2 and 3 of MF6795 and CDRs 1, 2 and 3 of MF5442, or variants thereof.

51. The use according to claim 50, wherein the multispecific antibody comprises SEQ ID NO. 9 and SEQ ID NO. 92, or variants thereof.

52. The use according to any one of claims 1-51, wherein the antibody comprises a common light chain variable domain having an amino acid sequence as set forth in SEQ ID NO: 110, or a common light chain having an amino acid sequence as set forth in SEQ ID NO: 109, or variants thereof.

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53. The use according to any one of claims 1-52, wherein the antibody comprises a heavy chain constant domain 1 (CH1) having an amino acid sequence as set forth in SEQ ID NO: 112, a heavy chain constant domain 2 (CH2) having an amino acid sequence as set forth in SEQ ID NO: 114, a heavy chain constant domain 3 (CH3) having an amino acid sequence as set forth in SEQ ID NO: 115, and a heavy chain constant domain 3 (CH3) having an amino acid sequence as set forth in SEQ ID NO: 116, or variants thereof.

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54. A kit of parts comprising a multispecific antibody as defined in any one of the preceding claims and instructions for use of the multispecific antibody at a dose, or flat dose, of between 25-75 mg or between 25-50 mg or between 25-40 mg or between 25-30 mg, or at 25 mg or 30 mg or 40 mg or 50 mg or 60 mg or 70 mg or 75 mg.

15

55. The kit of parts according to claim 54, wherein the kit comprises instructions for use of the multispecific antibody in any one the indications selected from the group consisting of:

20

any solid tumor harboring MSI-high alterations;

cervical cancer, in particular PD-L1 positive cervical cancer, more in particular cervical cancer with high expression of PD-L1;

endometrial cancer, in particular MSI-high endometrial cancer;

25

lung cancer, in particular non-small cell lung cancer (NSCLC), more in particular PD-L1 positive NSCLC, more in particular NSCLC with high expression of PD-L1;

brain cancer, in particular glioblastoma; and

breast cancer, in particular metastatic breast cancer and triple negative breast cancer (TNBC).

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