CLAIMS

1. Use of a bispecific antibody in a suitable amount, comprising a first binding region binding to human CD137, such as human CD137 having the sequence set forth in SEQ ID NO: 24, and a second binding region binding to human PD-L1, such as human PD-L1 having the sequence set forth in SEQ ID NO: 26, in the manufacture of a medicament for reducing or preventing progression of a tumor or treating cancer in a subject, wherein said medicament is to be administered to said subject, in at least one treatment cycle, wherein the first binding region comprises a heavy chain variable region (VH) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 2, 3, and 4, respectively, and a light chain variable region (VL) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 6, GAS, 7, respectively; and the second antigen-binding region comprises a heavy chain variable region (VH) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 9, 10, 11 respectively, and a light chain variable region (VL) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 13, DDN, 14, respectively; wherein the amount of bispecific antibody administered in each dose and/or in each treatment cycle is a) 0.3-2.5 mg/kg body weight or 25-200 mg in total; and/or b) $2.1 \times 10^{-9} – 1.7 \times 10^{-8}$ mol/kg body weight or $1.7 \times 10^{-7} – 1.4 \times 10^{-6}$ mol in total.

2. The use according to claim 1, wherein the amount of bispecific antibody is to be administered in each dose and/or treatment cycle leads to the proliferation, cytokine production, maturation and prolonged survival of T-cells and renders such T cells unsusceptible for inhibition by PD-L1.

3. The use according to any one of the preceding claims, wherein the amount of bispecific antibody is to be administered in each dose and/or treatment cycle is in a range wherein more than 5%, preferably more than 10%, more preferably more than 15%, even more preferably more than 20%, even more preferably more than 25%, even more preferably more than 30%, even more preferably more than 35%, even more preferably more than 40%, even more preferably more than 45%, most preferably more than 50% of said bispecific antibodies bind to both, CD137 and PD-L1.

4. The use according to any one of the preceding claims, wherein the amount of bispecific antibody is to be administered in each dose and/or in each treatment cycle is

    a) about 1.25 mg/kg body weight or about 100 mg in total; and/or

b) about 8.5 x 10^{-9} mol/kg body weight or about 6.8 x 10^{-7} mol in total.

5. The use according to any one of the preceding claims, wherein the bispecific antibody activates human CD137 when bound thereto and inhibits the binding of human PD-L1 to human PD-1 when bound to PD-L1.

6. The use according to any one of the preceding claims, wherein

a) The first binding region comprises a heavy chain variable region (VH) comprising an amino acid sequence having at least 90%, at least 95%, at least 97%, at least 99%, or 100% sequence identity to SEQ ID NO: 1 and a light chain variable region (VL) region comprising an amino acid sequence having at least 90%, at least 95%, at least 97%, at least 99%, or 100% sequence identity to SEQ ID NO: 5;

and

b) the second binding region comprises a heavy chain variable region (VH) comprising an amino acid sequence having at least 90%, at least 95%, at least 97%, at least 99%, or 100% sequence identity to SEQ ID NO: 8 and a light chain variable region (VL) region comprising an amino acid sequence having at least 90%, at least 95%, at least 97%, at least 99%, or 100% sequence identity to SEQ ID NO: 12.

7. The use according to any one of the preceding claims, wherein

a) The first binding region comprises a heavy chain variable region (VH) comprising the amino acid sequence set forth in SEQ ID NO: 1 and a light chain variable region (VL) region comprising the amino acid sequence set forth in SEQ ID NO: 5;

and

b) the second binding region comprises a heavy chain variable region (VH) comprising the amino acid sequence set forth in SEQ ID NO: 8 and a light chain variable region (VL) region comprising the amino acid sequence set forth in SEQ ID NO: 12.

8. The use according to any one of the preceding claims, wherein the bispecific antibody is in the format of a full-length antibody or an antibody fragment.

9. The use according to any one of the preceding claims, wherein each variable region comprises three complementarity determining regions (CDR1, CDR2, and CDR3) and four framework regions (FR1, FR2, FR3, and FR4).

10. The use according to claim 9, wherein said complementarity determining regions and said framework regions are arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4.

11. The use according to any one of the preceding claims, which comprises

i) a polypeptide comprising, consisting of or consisting essentially of, said first heavy chain variable region (VH) and a first heavy chain constant region (CH), and

ii) a polypeptide comprising, consisting of or consisting essentially of, said second heavy chain variable region (VH) and a second heavy chain constant region (CH).

12. The use according to any one of the preceding claims, which comprises

i) a polypeptide comprising said first light chain variable region (VL) and further comprising a first light chain constant region (CL), and

ii) a polypeptide comprising said second light chain variable region (VL) and further comprising a second light chain constant region (CL).

13. The use according to any one of the preceding claims, wherein the bispecific antibody is an antibody comprising a first binding arm and a second binding arm, wherein

the first binding arm comprises

i) a polypeptide comprising said first heavy chain variable region (VH) and said first heavy chain constant region (CH), and

ii) a polypeptide comprising said first light chain variable region (VL) and said first light chain constant region (CL);

and the second binding arm comprises

iii) a polypeptide comprising said second heavy chain variable region (VH) and said second heavy chain constant region (CH), and

iv) a polypeptide comprising said second light chain variable region (VL) and said second light chain constant region (CL).

14. The use according to any one of the preceding claims, which comprises

i) a first heavy chain and light chain comprising said antigen-binding region capable of binding to CD137, and

ii) a second heavy chain and light chain comprising said antigen-binding region capable of binding PD-L1.

15. The use according to any one of the preceding claims, wherein said bispecific antibody comprises

    i) a first heavy chain and light chain comprising said antigen-binding region capable of binding to CD137, the first heavy chain comprising a first heavy chain constant region and the first light chain comprising a first light chain constant region; and

    ii) a second heavy chain and light chain comprising said antigen-binding region capable of binding PD-L1, the second heavy chain comprising a second heavy chain constant region and the second light chain comprising a second light chain constant region.

16. The use according to any one of claims 11-15, wherein each of the first and second heavy chain constant regions (CH) comprises one or more of a constant heavy chain 1 (CH1) region, a hinge region, a constant heavy chain 2 (CH2) region and a constant heavy chain 3 (CH3) region, preferably at least a hinge region, a CH2 region and a CH3 region.

17. The use according to any one of claims 11-16, wherein each of the first and second heavy chain constant regions (CHs) comprises a CH3 region and wherein the two CH3 regions comprise asymmetrical mutations.

18. The use according to any one of claims 11-17, wherein in said first heavy chain constant region (CH) at least one of the amino acids in a position corresponding to a position selected from the group consisting of T366, L368, K370, D399, F405, Y407, and K409 in a human IgG1 heavy chain according to EU numbering has been substituted, and in said second heavy chain constant region (CH) at least one of the amino acids in a position corresponding to a position selected from the group consisting of T366, L368, K370, D399, F405, Y407, and K409 in a human IgG1 heavy chain according to EU numbering has been substituted, and wherein said first and said second heavy chains are not substituted in the same positions.

19. The use according to claim 18, wherein (i) the amino acid in the position corresponding to F405 in a human IgG1 heavy chain according to EU numbering is L in said first heavy chain constant region (CH), and the amino acid in the position corresponding to K409 in a human IgG1 heavy chain according to EU numbering is R in said second heavy chain constant region (CH), or (ii) the amino acid in the position corresponding to K409 in a human IgG1 heavy chain according to EU numbering is R in said first heavy chain, and the amino acid in the position corresponding to F405 in a human IgG1 heavy chain according to EU numbering is L in said second heavy chain.

20. The use according to any of the preceding claims, wherein said bispecific antibody induces Fc-mediated effector function to a lesser extent compared to another antibody comprising the same first and second antigen binding regions and two heavy chain constant regions (CHs) comprising human IgG1 hinge, CH2 and CH3 regions.

21. The use according to claim 20, wherein said first and second heavy chain constant regions (CHs) are modified so that the antibody induces Fc-mediated effector function to a lesser extent compared to an antibody which is identical except for comprising non-modified first and second heavy chain constant regions (CHs).

22. The use according to claim 21, wherein each of said non-modified first and second heavy chain constant regions (CHs) comprises the amino acid sequence set forth in SEQ ID NO: 15.

23. The use according to any of claims 21-22, wherein said Fc-mediated effector function is measured by binding to Fcγ receptors, binding to C1q, or induction of Fc-mediated cross-linking of Fcγ receptors.

24. The use according to claim 23, wherein said Fc-mediated effector function is measured by binding to C1q.

25. The use according to any one of claims 20-24, wherein said first and second heavy chain constant regions have been modified so that binding of C1q to said antibody is reduced compared to a wild-type antibody, preferably reduced by at least 70%, at least 80%, at least 90%, at least 95%, at least 97%, or 100%, wherein C1q binding is preferably determined by ELISA.

26. The use according to any one of the preceding claims, wherein in at least one of said first and second heavy chain constant regions (CH), one or more amino acids in the positions corresponding to positions L234, L235, D265, N297, and P331 in a human IgG1 heavy chain according to EU numbering, are not L, L, D, N, and P, respectively.

27. The use according to claim 26, wherein the positions corresponding to positions L234 and L235 in a human IgG1 heavy chain according to EU numbering are F and E, respectively, in said first and second heavy chains.

28. The use according to claim 26 or 27, wherein the positions corresponding to positions L234, L235, and D265 in a human IgG1 heavy chain according to EU numbering are F, E, and A, respectively, in said first and second heavy chain constant regions (HCs).

29. The use according to any one of claims 26-28, wherein the positions corresponding to positions L234 and L235 in a human IgG1 heavy chain according to EU numbering of both the first and second heavy chain constant regions are F and E, respectively, and wherein (i) the position corresponding to F405 in a human IgG1 heavy chain according to EU numbering of the first heavy chain constant region is L, and the position corresponding to K409 in a human IgG1 heavy chain according to EU numbering of the second heavy chain is R, or (ii) the position corresponding to K409 in a human IgG1 heavy chain according to EU numbering of the first heavy chain constant region is R, and the position corresponding to F405 in a human IgG1 heavy chain according to EU numbering of the second heavy chain is L.

30. The use according to any one of claims 26-29, wherein the positions corresponding to positions L234, L235, and D265 in a human IgG1 heavy chain according to EU numbering of both the first and second heavy chain constant regions are F, E, and A, respectively, and wherein (i) the position corresponding to F405 in a human IgG1 heavy chain according to EU numbering of the first heavy chain constant region is L, and the position corresponding to K409 in a human IgG1 heavy chain according to EU numbering of the second heavy chain constant region is R, or (ii) the position corresponding to K409 in a human IgG1 heavy chain according to EU numbering of the first heavy chain is R, and the position corresponding to F405 in a human IgG1 heavy chain according to EU numbering of the second heavy chain is L.

31. The use according to any one of claims 11-30, wherein the constant region of said first and/or second heavy chain comprises or consists essentially of or consists of an amino acid sequence selected from the group consisting of

    a) the sequence set forth in SEQ ID NO: 15 or SEQ ID NO: 30 [IgG1-FC],
    b) a subsequence of the sequence in a), such as a subsequence wherein 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 consecutive amino acids has/have deleted, starting from the N-terminus or C-terminus of the sequence defined in a); and
    c) a sequence having at the most 10 substitutions, such as at the most 9 substitutions, at the most 8, at the most 7, at the most 6, at the most 5, at the most 4, at the most 3, at the most 2 or at the most 1 substitution compared to the amino acid sequence defined in a) or b).

32. The use according to any one of claims 11-31, wherein the constant region of said first or second heavy chain, such as the second heavy chain, comprises or consists essentially of or consists of an amino acid sequence selected from the group consisting of

    a) the sequence set forth in SEQ ID NO: 16 or SEQ ID NO: 31 [IgG1-F405L],
    b) a subsequence of the sequence in a), such as a subsequence wherein 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 consecutive amino acids has/have deleted, starting from the N-terminus or C-terminus of the sequence defined in a); and
    c) a sequence having at the most 9 substitutions, such as at the most 8, at the most 7, at the most 6, at the most 5, at the most 4, at the most 3, at the most 2 or at the most 1 substitution compared to the amino acid sequence defined in a) or b).

33. The use according to any one of claims 11-32, wherein the constant region of said first or second heavy chain, such as the first heavy chain comprises or consists essentially of or consists of an amino acid sequence selected from the group consisting of

    a) the sequence set forth in SEQ ID NO: 17 or SEQ ID NO: 32 [IgG1-F409R]
    b) a subsequence of the sequence in a), such as a subsequence wherein 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 consecutive amino acids has/have deleted, starting from the N-terminus or C-terminus of the sequence defined in a); and
    c) a sequence having at the most 10 substitutions, such as at the most 9 substitutions, at the most 8, at the most 7, at the most 6, at the most 5, at the most 4 substitutions, at the most 3, at the most 2 or at the most 1 substitution compared to the amino acid sequence defined in a) or b).

34. The use according to any one of claims 11-33, wherein the constant region of said first and/or second heavy chain comprises or consists essentially of or consists of an amino acid sequence selected from the group consisting of

    a) the sequence set forth in SEQ ID NO: 18 or SEQ ID NO: 33 [IgG1-Fc_FEA],
    b) a subsequence of the sequence in a), such as a subsequence wherein 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 consecutive amino acids has/have deleted, starting from the N-terminus or C-terminus of the sequence defined in a); and
    c) a sequence having at the most 7 substitutions, such as at the most 6 substitutions, at the most 5, at the most 4, at the most 3, at the most 2 or at the most 1 substitution compared to the amino acid sequence defined in a) or b).

35. The use according to any one of claims 11-34, wherein the constant region of said first and/or second heavy chain, such as the second heavy chain, comprises or consists essentially of or consists of an amino acid sequence selected from the group consisting of

    a) the sequence set forth in SEQ ID NO: 19 or SEQ ID NO: 34 [IgG1-Fc_FEAL],
    b) a subsequence of the sequence in a), such as a subsequence wherein 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 consecutive amino acids has/have deleted, starting from the N-terminus or C-terminus of the sequence defined in a); and
    c) a sequence having at the most 6 substitutions, such as at the most 5 substitutions, at the most 4 substitutions, at the most 3, at the most 2 or at the most 1 substitution compared to the amino acid sequence defined in a) or b).

36. The use according to any one of claims 11-35, wherein the constant region of said first and/or second heavy chain, such as the first heavy chain, comprises or consists essentially of or consists of an amino acid sequence selected from the group consisting of

    a) the sequence set forth in SEQ ID NO: 20 or SEQ ID NO: 35 [IgG1-Fc_FEAR]
    b) a subsequence of the sequence in a), such as a subsequence wherein 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 consecutive amino acids has/have deleted, starting from the N-terminus or C-terminus of the sequence defined in a); and
    c) a sequence having at the most 6 substitutions, such as at the most 5 substitutions, at the most 4, at the most 3, at the most 2 or at the most 1 substitution compared to the amino acid sequence defined in a) or b).

37. The use according to any one of the preceding claims, wherein said bispecific antibody comprises a kappa (κ) light chain constant region.

38. The use according to any one of the preceding claims, wherein said bispecific antibody comprises a lambda (λ) light chain constant region.

39. The use according to any one of the preceding claims, wherein said first light chain constant region is a kappa (κ) light chain constant region.

40. The use according to any one of the preceding claims, wherein said second light chain constant region is a lambda (λ) light chain constant region.

41. The use according to any one of the preceding claims, wherein said first light chain constant region is a lambda (λ) light chain constant region.

42. The use according to any one of the preceding claims, wherein said second light chain constant region is a kappa (κ) light chain constant region.

43. The use according to any one of claims 37-42, wherein the kappa (κ) light chain comprises an amino acid sequence selected from the group consisting of

    a) the sequence set forth in SEQ ID NO: 21,

    b) a subsequence of the sequence in a), such as a subsequence wherein 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 consecutive amino acids has/have been deleted, starting from the N-terminus or C-terminus of the sequence defined in a); and

    c) a sequence having at the most 10 substitutions, such as at the most 9 substitutions, at the most 8, at the most 7, at the most 6, at the most 5, at the most 4 substitutions, at the most 3, at the most 2 or at the most 1 substitution, compared to the amino acid sequence defined in a) or b).

44. The use according to any one of claims 38-43, wherein the lambda (λ) light chain comprises an amino acid sequence selected from the group consisting of

    a) the sequence set forth in SEQ ID NO: 22,

    b) a subsequence of the sequence in a), such as a subsequence wherein 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 consecutive amino acids has/have been deleted, starting from the N-terminus or C-terminus of the sequence defined in a); and

    c) a sequence having at the most 10 substitutions, such as at the most 9 substitutions, at the most 8, at the most 7, at the most 6, at the most 5, at the most 4 substitutions, at the most 3, at the most 2 or at the most 1 substitution, compared to the amino acid sequence defined in a) or b).

45. The use according to any one of the preceding claims, wherein the bispecific antibody is of an isotype selected from the group consisting of IgG1, IgG2, IgG3, and IgG4.

46. The use according to any one of the preceding claims, wherein the bispecific antibody is a full-length IgG1 antibody.

47. The use according to any one of the preceding claims, wherein said antibody is of the IgG1m(f) allotype.

48. The use according to any one of the preceding claims, wherein the subject is a human subject.

49. The use according to any one of the preceding claims, wherein the tumor or cancer is a solid tumor.

50. The use according to any one of the preceding claims, wherein the tumor or cancer is selected from the group consisting of melanoma, ovarian cancer, lung cancer (e.g. non-small cell lung cancer (NSCLC), colorectal cancer, head and neck cancer, gastric cancer, breast cancer, renal cancer, urothelial cancer, bladder cancer, esophageal cancer, pancreatic cancer, hepatic cancer, thymoma and thymic carcinoma, brain cancer, glioma, adrenocortical carcinoma, thyroid cancer, other skin cancers, sarcoma, multiple myeloma, leukemia, lymphoma, myelodysplastic syndromes, ovarian cancer, endometrial cancer, prostate cancer, penile cancer, cervical cancer, Hodgkin's lymphoma, non-Hodgkin's lymphoma, Merkel cell carcinoma and mesothelioma.

51. The use according to any one of the preceding claims, wherein the tumor or cancer is selected from the group consisting of lung cancer (e.g. non-small cell lung cancer (NSCLC), urothelial cancer (cancer of the bladder, ureter, urethra, or renal pelvis), endometrial cancer (EC), breast cancer (e.g. triple negative breast cancer (TNBC)), squamous cell carcinoma of the head and neck (SCCHN) (e.g. cancer of the oral cavity, pharynx or larynx) and cervical cancer.

52. The use according to any one of the preceding claims, wherein the tumor or cancer is a lung cancer.

53. The use according to claim 52, wherein the lung cancer is a non-small cell lung cancer (NSCLC), such as a squamous or non-squamous NSCLC.

54. The use according to claim 53, wherein the NSCLC does not have an epidermal growth factor (EGFR)-sensitizing mutation and/or anaplastic lymphoma (ALK) translocation / ROS1 rearrangement.

55. The use according to any one of claims 52-54, wherein the subject has received up to four prior systemic treatment regimens for advanced/metastatic disease and has experienced disease progression on or after last prior systemic treatment, such as disease progression determined by radiography.

56. The use according to claim 55, wherein the subject has received platinum-based chemotherapy.

57. The use according to claim 55, wherein the subject is not eligible for platinum-based therapy and has alternative chemotherapy, e.g., a treatment with gemcitabine-containing regimen.

58. The use according to any one of the preceding claims, wherein the subject has received prior treatment with checkpoint inhibitor(s), such as agent(s) targeting PD-1/PD-L, such as a PD-1/PD-L1 inhibitor.

59. The use according to any one of the preceding claims, wherein the subject has experienced disease progression on or after treatment with checkpoint inhibitor(s), such as agent(s) targeting PD-1/PD-L, such as a PD-1/PD-L1 inhibitor.

60. The use according to any one of the preceding claims, wherein the subject has experienced disease progression on or after last prior treatment with checkpoint inhibitor(s), such as agent(s) targeting PD-1/PD-L, such as a PD-1/PD-L1 inhibitor.

61. The use according to any one of claim 55-60, wherein the subject has experienced disease progression on or after last prior systemic treatment, such as disease progression determined by radiography.

62. The use according to any one of claims 1-57, wherein the subject has not received prior treatment with checkpoint inhibitor(s), such as agent(s) targeting PD-1/PD-L, such as a PD-1/PD-L1 inhibitor.

63. The use according to any one of claims 1-51, wherein the tumor or cancer is an endometrial cancer.

64. The use according to claim 63, wherein the subject has epithelial endometrial histology including: endometrioid, serous, squamous, clear-cell carcinoma, or carcinosarcoma.

65. The use according to claim 63 or 64, wherein the subject has received up to four prior systemic treatment regimens for advanced/metastatic disease and has experienced disease progression on or after last prior systemic treatment, such as disease progression determined by radiography.

66. The use according to any one of claims 63-65, wherein the subject has not received prior treatment with checkpoint inhibitor(s), such as agent(s) targeting PD-1/PD-L, such as a PD-1/PD-L1 inhibitor.

67. The use according to any one of claims 1-51, wherein the tumor or cancer is an urothelial cancer, including cancer of the bladder, ureter, urethra, or renal pelvis.

68. The use according to claim 67, wherein the subject has received up to four prior systemic treatment regimens for advanced/metastatic disease and has experienced disease progression on or after last prior systemic treatment, such as disease progression determined by radiography.

69. The use according to claim 67 or 68, wherein the subject has received prior treatment with checkpoint inhibitor(s), such as agent(s) targeting PD-1/PD-L, such as a PD-1/PD-L1 inhibitor.

70. The use according to claim 67 or 68, wherein the subject has received platinum-based chemotherapy.

71. The use according to any one of claims 67 or 68, wherein the subject is not eligible for platinum-based therapy and has received alternative chemotherapy, e.g., a treatment with gemcitabine-containing regimen.

72. The use according to any one of claims 1-51, wherein the tumor or cancer is a breast cancer, such as a triple negative breast cancer (TNBC).

73. The use according to claim 72, wherein the TNBC is HER2 negative, such as determined by Fluorescence in situ hybridization (FISH) or determination of protein expression by immunohistochemistry.

74. The use according to claim 72 or 73, wherein the subject has received at least one prior systemic treatment regimen for locally advanced/metastatic disease, such as at least one prior systemic treatment regimen including anthracycline-, taxane-, antimetabolite- or microtubule inhibitor-containing regimens.

75. The use according to claim 74, wherein the subject has received at the most 4 prior systemic treatment regimens for locally advanced/metastatic disease, such including as at least one prior systemic treatment regimen including anthracycline-, taxane-, antimetabolite- or microtubule inhibitor-containing regimens.

76. The use according to any one of claims 72-75, wherein the subject has received prior treatment with checkpoint inhibitor(s), such as agent(s) targeting PD-1/PD-L, such as a PD-1/PD-L1 inhibitor.

77. The use according to claim 76, wherein the subject has experienced disease progression on or after said prior treatment with checkpoint inhibitor(s), such as disease progression determined by radiography.

78. The use according to any one of claims 72-75, wherein the subject has not received prior treatment with checkpoint inhibitor(s), such as agent(s) targeting PD-1/PD-L, such as a PD-1/PD-L1 inhibitor.

79. The use according to any one of claims 1-51, wherein the tumor or cancer is a head and neck cancer, such as a squamous cell carcinoma of the head and neck (SCCHN).

80. The use according to claim 79, wherein the tumor or cancer is recurrent or metastatic SCCHN.

81. The use according to claim 79 or 80, wherein the tumor or cancer is cancer of the oral cavity, pharynx or larynx.

82. The use according to any one of claims 79-81, wherein the subject has received up to four prior systemic treatment regimens for recurrent/metastatic disease and has experienced disease progression on or after last prior systemic treatment, such as disease progression determined by radiography.

83. The use according to claim 82, wherein the subject has received platinum-based chemotherapy.

84. The use according to claim 82, wherein the subject is not eligible for platinum-based therapy and has alternative chemotherapy.

85. The use according to any one of claims 79-84, wherein the subject has received prior treatment with checkpoint inhibitor(s), such as agent(s) targeting PD-1/PD-L, such as a PD-1/PD-L1 inhibitor.

86. The use according to claim 85, wherein the subject has experienced disease progression on or after said prior treatment with checkpoint inhibitor(s), such as disease progression determined by radiography.

87. The use according to any one of claims 79-84, wherein the subject has not received prior treatment with checkpoint inhibitor(s), such as agent(s) targeting PD-1/PD-L, such as a PD-1/PD-L1 inhibitor.

88. The use according to any one of claims 1-51, wherein the tumor or cancer is a cervical cancer.

89. The use according claim 88, wherein the cervical cancer is of squamous cell, adenocarcinoma or adenosquamous histology.

90. The use according to claim 88 or 89, wherein the subject has received at least one prior systemic treatment regimen for recurrent/metastatic disease, such as chemotherapy in combination with treatment targeting vascular endothelial growth factor A, such as treatment with bevacizumab, and has experienced disease progression on or after last prior systemic treatment, such as disease progression determined by radiography.

91. The use according to claim 90, wherein the subject has received at the most 4 prior systemic treatment regimens for recurrent/metastatic disease, including chemotherapy in combination with treatment targeting vascular endothelial growth factor A, such as treatment with bevacizumab.

92. The use according to claim 88 or 89, wherein the subject has not received prior treatment with checkpoint inhibitor(s), such as agent(s) targeting PD-1/PD-L, such as a PD-1/PD-L1 inhibitor.

93. The use according to any one of the preceding claims, wherein the bispecific antibody is to be administered by systemic administration.

94. The use according to any one of the preceding claims, wherein the bispecific antibody is to be administered by intravenous injection or infusion.

95. The use according to any one of the preceding claims, wherein each treatment cycle is three weeks (21 days).

96. The use according to any one of the preceding claims, wherein one dose is to be administered every third week (1Q3W).

97. The use according to any one of the preceding claims, wherein one dose is to be administered on day 1 of each treatment cycle.

98. The use according to any one of the preceding claims, wherein each dose is infused over a minimum of 30 minutes, such as over a minimum of 60 minutes, a minimum of 90 minutes, a minimum of 120 minutes or a minimum of 240 minutes.

99. A composition comprising a bispecific antibody comprising a first binding region binding to human CD137 and a second binding region binding to human PD-L1, wherein the first binding

region comprises a heavy chain variable region (VH) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 2, 3, and 4, respectively, and a light chain variable region (VL) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 6, GAS, 7, respectively; and the second antigen-binding region comprises a heavy chain variable region (VH) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 9, 10, 11 respectively, and a light chain variable region (VL) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 13, DDN, 14, respectively; wherein the amount of bispecific antibody in the composition is between 25-200 mg or $1.7 \times 10^{-7} – 1.4 \times 10^{-6}$ mol.

100. The composition according to claim 99, comprising about 100 mg of said bispecific antibody.

101. The composition according to any one of claims 99-100, wherein the bispecific antibody is as defined in any one of claims 1-98.

102. The composition according to any one of claims 99-101, wherein the composition is for systemic administration.

103. The composition according to any one of claims 99-102, wherein the composition is for injection or infusion, such as intravenous injection or infusion.

104. The composition according to any one of claims 99-103, wherein the bispecific antibody is in aqueous solution, such in 0.9% NaCl (saline), at a volume of 50-500 mL, such as 100-250 mL.

105. The composition according to any one of claims 99-104, said composition being a dosage unit form.

106. A composition comprising a bispecific antibody comprising a first binding region binding to human CD137 and a second binding region binding to human PD-L1, wherein the first binding region comprises a heavy chain variable region (VH) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 2, 3, and 4, respectively, and a light chain variable region (VL) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 6, GAS, 7, respectively; and the second antigen-binding region comprises a heavy chain variable region (VH) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 9, 10, 11 respectively, and a light chain variable region (VL) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 13, DDN, 14, respectively; wherein the amount of bispecific

antibody in the composition is between 25-200 mg or 1.7×10^{-7} – 1.4×10^{-6} mol, for use as a medicament.

107. A bispecific antibody in a suitable amount, comprising a first binding region binding to human CD137, such as human CD137 having the sequence set forth in SEQ ID NO: 24, and a second binding region binding to human PD-L1, such as human PD-L1 having the sequence set forth in SEQ ID NO: 26, for use as a medicament for reducing or preventing progression of a tumor or treating cancer in a subject, wherein said medicament is to be administered to said subject, in at least one treatment cycle; wherein the first binding region comprises a heavy chain variable region (VH) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 2, 3, and 4, respectively, and a light chain variable region (VL) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 6, GAS, 7, respectively; and the second antigen-binding region comprises a heavy chain variable region (VH) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 9, 10, 11 respectively, and a light chain variable region (VL) comprising the CDR1, CDR2, and CDR3 sequences set forth in: SEQ ID NO: 13, DDN, 14, respectively; wherein the amount of bispecific antibody administered in each dose and/or in each treatment cycle is a) 0.3-2.5 mg/kg body weight or 25-200 mg in total; and/or b) 2.1×10^{-9} – 1.7×10^{-8} mol/kg body weight or 1.7×10^{-7} – 1.4×10^{-6} mol in total.