

CLAIMS

1. Use of a binding agent comprising a first binding region binding to human CD137 and a second binding region binding to human PD-L1 in the manufacture of a medicament for reducing or preventing progression of a tumor or for treating cancer in a human subject, wherein a combined treatment with the binding agent and a taxane chemotherapeutic agent is to be administered to said subject.

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2. The use according to claim 1, wherein the binding agent and the taxane chemotherapeutic agent are to be administered to said subject in at least one treatment cycle.
3. The use according to any one of the preceding claims, wherein

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 - a) 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
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 - b) 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.
4. The use according to any one of the preceding claims, wherein

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 - 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
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 - 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.
5. The use according to any one of the preceding claims, wherein the binding agent is an antibody, a multispecific antibody, such as a bispecific antibody.
6. The use according to any one of the preceding claims, wherein the binding agent is in the format of a full-length antibody or an antibody fragment.

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7. 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) comprising the amino acid sequence set forth in SEQ ID NO: 19 or SEQ ID NO: 20, and
 - 5 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) comprising the amino acid sequence set forth in SEQ ID NO: 20 or SEQ ID NO: 19.
8. The use according to any one of the preceding claims, which comprises
- 10 i) a polypeptide comprising said first light chain variable region (VL) and further comprising a first light chain constant region (CL) comprising the amino acid sequence set forth in SEQ ID NO: 21 or SEQ ID NO: 22, and
 - ii) a polypeptide comprising said second light chain variable region (VL) and further comprising a second light chain constant region (CL) comprising the amino acid sequence set forth in SEQ ID NO: 22 or SEQ ID NO: 21.
- 15 9. The use according to any one of the preceding claims, wherein said antibody is acasunlimab or a biosimilar thereof.
10. The use according to any one of the preceding claims, wherein the taxane chemotherapeutic agent is selected from the group consisting of: Docetaxel, paclitaxel, cabazitaxel and tesetaxel, preferably the taxane chemotherapeutic agent is docetaxel.
- 20 11. The use according to any one of the preceding claims, wherein the amount of binding agent to be administered in each dose and/or in each treatment cycle is
- a) about 0.3-15 mg/kg body weight or about 25-1200 mg in total; and/or
 - b) about $2.1 \times 10^{-9} - 1.2 \times 10^{-7}$ mol/kg body weight or about $1.7 \times 10^{-7} - 8.1 \times 10^{-6}$ mol in total.
- 25 12. The use according to any one of the preceding claims, wherein the amount of binding agent to be administered in each dose and/or in each treatment cycle is
- a) about 0.3-10 mg/kg body weight or about 25-800 mg in total; and/or
 - b) about $2.1 \times 10^{-9} - 6.8 \times 10^{-8}$ mol/kg body weight or about $1.7 \times 10^{-7} - 5.4 \times 10^{-6}$ mol in total.

13. The use according to any one of the preceding claims, wherein the amount of binding agent to be administered in each dose and/or in each treatment cycle is
- a) about 0.3-5 mg/kg body weight or about 25-400 mg in total; and/or
 - b) about $2.1 \times 10^{-9} - 3.4 \times 10^{-8}$ mol/kg body weight or about $1.7 \times 10^{-7} - 2.7 \times 10^{-6}$ mol in total.
14. The use according to any one of the preceding claims, wherein the amount of binding agent 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 8.5×10^{-9} mol/kg body weight or about 6.8×10^{-7} mol in total.
15. The use according to any one of the preceding claims, wherein the amount of taxane chemotherapeutic agent to be administered in each dose and/or in each treatment cycle is about 10-200 mg/m², such as 20-40 mg/m², 30-50 mg/m², 40-100 mg/m², 50-100 mg/m², 50-80 mg/m², 50-70 mg/m², 50-60 mg/m², 50-110 mg/m², 60-100 mg/m², 60-100 mg/m², 60-90 mg/m², 70-80 mg/m², 80-200 mg/m², 90-180 mg/m², 90-110 mg/m², 100-175 mg/m², or such as a bout 170-180 mg/m².
16. The use according to any one of the preceding claims, wherein the taxane chemotherapeutic agent is docetaxel and the amount to be administered in each dose and/or in each treatment cycle is about 50-60 mg/m², such as about 55 mg/m², or the amount to be administered in each dose and/or in each treatment cycle is about 70-80 mg/m², such as about 75 mg/m².
17. The use according to any one of the preceding claims, wherein the binding agent and/or the taxane chemotherapeutic agent is/are to be administered by systemic administration, preferably by intravenous injection or infusion.
18. The use according to any one of the preceding claims, wherein at least one dose of said binding agent and at least one dose of said taxane chemotherapeutic drug are to be administered in each treatment cycle, preferably each treatment cycle is three weeks (21 days), more preferably said binding agent and said taxane chemotherapeutic agent are to be administered on the same day.
19. The use according to any one of the preceding claims, wherein one dose of said binding agent is to be administered every third week (1Q3W), such as on day 1 on each three-week treatment cycle, and/or one dose of said taxane chemotherapeutic agent is to be administered every third week (1Q3W), such as on day 1 on each three-week treatment cycle.

20. The use according to any one of the preceding claims, wherein each dose of taxane chemotherapeutic agent is preceded by steroid premedication, such as premedication with an oral corticosteroid; e.g. administration of about 8 mg dexamethasone 2 times a day for 3 days starting 1 day prior to administration of the taxane chemotherapeutic agent.
- 5 21. The use according to any one of the preceding claims, wherein the tumor or cancer is a solid tumor, preferably 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
- 10 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, more preferably the tumor or cancer is selected from the group consisting of lung cancer (e.g. non-small cell lung
- 15 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.
22. The use according to any one of the preceding claims, wherein the tumor or cancer is a lung
- 20 cancer, preferably the lung cancer is a non-small cell lung cancer (NSCLC), such as a squamous or non-squamous NSCLC, more preferably the NSCLC does not have an epidermal growth factor (EGFR)-sensitizing mutation and/or anaplastic lymphoma (ALK) translocation / ROS1 rearrangement.
23. The use according to claim 22, wherein the subject has received up to four prior systemic
- 25 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.
24. The use according to claim 23, wherein the subject has received platinum-based
- 30 chemotherapy or the subject is not eligible for platinum-based therapy and has received alternative chemotherapy, e.g., a treatment with gemcitabine-containing regimen.

- 5 25. 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, preferably 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.
26. The use according to any one of claims 23-25, wherein the subject has experienced disease progression on or after last prior systemic treatment, such as disease progression determined by radiography.
- 10 27. The use according to any one of the preceding claims, 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.
28. The use according to any one of the preceding claims, wherein the tumor or cancer is an endometrial cancer, preferably the subject has epithelial endometrial histology including: endometrioid, serous, squamous, clear-cell carcinoma, or carcinosarcoma.
- 15 29. The use according to claim 28, 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.
- 20 30. The use according to claim 28 or 29, 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.
31. The use according to any one of the preceding claims, wherein the tumor or cancer is an urothelial cancer, including cancer of the bladder, ureter, urethra, or renal pelvis.
- 25 32. The use according to claim 31, 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.
33. The use according to claim 31 or 32, 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.

34. The use according to claim 31 or 32, wherein the subject has received platinum-based chemotherapy, or the subject is not eligible for platinum-based therapy and has received alternative chemotherapy, e.g., a treatment with gemcitabine-containing regimen.
- 5 35. The use according to any one of the preceding claims, wherein the tumor or cancer is a breast cancer, such as a triple negative breast cancer (TNBC).
36. The use according to claim 35, 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, preferably 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.
- 10 37. The use according to claim 35 or 36, 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, preferably the subject has experienced disease progression on or after said prior treatment with checkpoint inhibitor(s), such as disease progression determined by radiography.
- 15 38. The use according to claim 35 or 36, 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.
- 20 39. The use according to any one of the preceding claims, wherein the tumor or cancer is a head and neck cancer, such as a squamous cell carcinoma of the head and neck (SCCHN), preferably the tumor or cancer is recurrent or metastatic SCCHN.
40. The use according to claim 39, 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.
- 25 41. The use according to claim 40, wherein the subject has received platinum-based chemotherapy or the subject is not eligible for platinum-based therapy and has alternative chemotherapy.

- 5 42. The use according to any one of claims 39-41, 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, preferably the subject has experienced disease progression on or after said prior treatment with checkpoint inhibitor(s), such as disease progression determined by radiography.
43. The use according to any one of claims 39-41, 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.
- 10 44. The use according to any one of the preceding claims, wherein the tumor or cancer is a cervical cancer, preferably the cervical cancer is of squamous cell, adenocarcinoma or adenosquamous histology.
- 15 45. The use according to claim 44, 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, preferably 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.
- 20 46. The use according to claim 44 or 45, 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.
- 25 47. A composition comprising a taxane chemotherapeutic agent and a binding agent comprising a first binding region binding to human CD137, and a second binding region binding to human PD-L1.
48. A binding agent comprising a first binding region binding to human CD137, and a second binding region binding to human PD-L1 for use in treatment of cancer or for use in reducing or preventing progression of a tumor, wherein the binding agent is used in combination with a taxane chemotherapeutic agent.

49. A taxane chemotherapeutic agent for use in treatment of cancer or for use in reducing or preventing progression of a tumor, wherein the taxane chemotherapeutic agent is used in combination with a binding agent comprising a first binding region binding to human CD137, and a second binding region binding to human PD-L1.
- 5 50. The composition according to claim 47, the binding agent for use according to claim 48, the taxane chemotherapeutic agent for use according to claim 49, wherein the binding agent is as defined in any one of claims 3-9, and/or the taxane chemotherapeutic agent is as defined in claim 10.