

What is claimed is:

1. ~~A method of~~ Use of an antibody drug conjugate (ADC) in the manufacture of a medicament for preventing or treating cancer in a human subject, comprising administering to the subject wherein an effective amount of an antibody drug conjugate the ADC is to be administered to the subject,

wherein the ~~antibody drug conjugate~~ ADC comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE);

wherein the subject has urothelial or bladder cancer;

wherein the subject has received an immune checkpoint inhibitor (CPI) therapy;

wherein the subject is ineligible to receive cisplatin treatment (cisplatin ineligible).

2. The ~~method~~ use of claim 1, wherein the cisplatin ineligible subject is a platinum-naïve subject.

3. The ~~method~~ use of claim 1 or 2, wherein the platinum-naïve subject is:
(i) a subject that received platinum in the adjuvant or neoadjuvant setting and did not progress within 12 months of completion of the platinum treatment; or
(ii) a subject that has not received prior platinum-containing or other chemotherapy in the locally advanced or metastatic setting.

4. ~~The method of claim 1 or 2, wherein the platinum-naïve subject is a subject that has not received prior platinum-containing or other chemotherapy in the locally advanced or metastatic setting.~~

54. The ~~method~~ use of any one of claims 1 to 43, wherein the cisplatin ineligible subject has one or more of the conditions selected from the group consisting of: ECOG

performance status score of 2, impaired renal function, and no less than Grade 2 hearing loss; optionally wherein:

(i) the impaired renal function is determined by creatinine clearance (CrCl) less than 60 mL/min;

(ii) the impaired renal function is determined by CrCl less than 60 but no less than 30 mL/min; or

(iii) the impaired renal function is determined by CrCl less than 30 but no less than 15 mL/min.

~~6. — The method of claim 5, wherein the impaired renal function is determined by creatinine clearance (CrCl) less than 60 mL/min.~~

~~7. — The method of claim 5, wherein the impaired renal function is determined by CrCl less than 60 but no less than 30 mL/min.~~

~~8. — The method of claim 5, wherein the impaired renal function is determined by CrCl less than 30 but no less than 15 mL/min.~~

~~95. The method use of any one of claims 1 to 84, wherein:~~

~~(i) the cisplatin ineligible subject had progression or recurrence of the cancer during or following most recent therapy; or~~

~~(ii) the cisplatin ineligible subject had progression or recurrence of the cancer during or following the CPI therapy.~~

~~10. — The method of any one of claims 1 to 8, wherein the cisplatin ineligible subject had progression or recurrence of the cancer during or following the CPI therapy.~~

~~116.~~ The ~~method~~ use of any one of claims 1 to ~~105~~, wherein the subject has a primary site of tumor in the lower urinary tract or in the upper urinary tract.

~~12.~~ The ~~method~~ of any one of claims 1 to 10, wherein the subject has a primary site of tumor in the upper urinary tract.

~~137.~~ The ~~method~~ use of any one of claims 1 to ~~126~~, wherein the subject has visceral metastases; optionally wherein the subject has liver metastases; further optionally wherein the subject has at least 1 Bellmunt risk factor.

~~14.~~ The ~~method~~ of any one of claims 1 to 13, wherein the subject has liver metastases.

~~15.~~ The ~~method~~ of any one of claims 1 to 14, wherein the subject has at least 1 Bellmunt risk factor.

~~168.~~ The ~~method~~ use of any one of claims 1 to ~~157~~, wherein the subject has one or more of the conditions selected from the group consisting of:

- (i) absolute neutrophil count no less than $1.0 \times 10^9/L$,
 - (ii) platelet count no less than $100 \times 10^9/L$,
 - (iii) hemoglobin no less than 9 g/dL,
 - (iv) serum bilirubin no more than either of 1.5 times of upper limit of normal (ULN) or 3 times ULN for patients with Gilbert's disease,
 - (v) CrCl no less than 30 mL/min, and
 - (vi) alanine aminotransferase and aspartate aminotransferase no more than 3 fold of ULN;
- optionally wherein the subject has all of conditions (i) to (vi).

~~17. The method of claim 16, wherein the subject has all of conditions (i) to (vi) of claim 16.~~

~~189. The method use of any one of claims 6 to 8, 16 and 17 claim 4 or claim 8, wherein the CrCl is measured by 24 hour urine collection or estimated by the Cockcroft-Gault criteria.~~

~~1910. The method use of any one of claims 1 to 189, wherein:~~
~~(i) the subject has no more than Grade 2 sensory or motor neuropathy;~~
~~(ii) the subject has no active central nervous system metastases; and/or~~
~~(iii) the subject has no uncontrolled diabetes.~~

~~20. The method of any one of claims 1 to 19, wherein the subject has no active central nervous system metastases.~~

~~21. The method of any one of claims 1 to 20, wherein the subject has no uncontrolled diabetes.~~

~~2211. The method use of claim 2110, wherein the uncontrolled diabetes is determined by hemoglobin A1c (HbA1c) no less than 8% or HbA1c between 7 and 8% with associated diabetes symptoms that are not otherwise explained; optionally wherein the associated diabetes symptoms comprise or consist of polyuria, polydipsia, or both polyuria and polydipsia.~~

~~23. The method of claim 22, wherein the associated diabetes symptoms comprise or consist of polyuria, polydipsia, or both polyuria and polydipsia.~~

~~2412. The method use of any one of claims 1 to 2311, wherein:~~
~~(i) the subject has locally advanced or metastatic urothelial cancer; or~~

(ii) the subject has locally advanced or metastatic bladder cancer.

~~25.—The method of any one of claims 1 to 23, wherein the subject has locally advanced or metastatic bladder cancer.~~

~~26~~13. The ~~method~~ use of any one of claims 1 to ~~25~~12, wherein:

(i) the CPI therapy is a therapy of programmed death receptor-1 (PD-1) inhibitor; optionally wherein the PD-1 inhibitor is nivolumab or pembrolizumab; or

(ii) the CPI therapy is a therapy of programmed death-ligand 1 (PD-L1) inhibitor; optionally wherein the PD-L1 inhibitor is selected from a group consisting of atezolizumab, avelumab, and durvalumab.

~~27.—The method of any one of claims 1 to 25, wherein the CPI therapy is a therapy of programmed death ligand 1 (PD-L1) inhibitor.~~

~~28.—The method of claim 26, wherein PD-1 inhibitor is nivolumab or pembrolizumab.~~

~~29.—The method of claim 27, wherein PD-L1 inhibitor is selected from a group consisting of atezolizumab, avelumab, and durvalumab.~~

~~30~~14. The ~~method~~ use of any one of claims 1 to ~~29~~13, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23.

~~31~~15. The ~~method~~ use of any one of claims 1 to ~~30~~14, wherein the antibody or antigen binding fragment thereof comprises CDR-H1 comprising the amino acid sequence of SEQ ID NO:9, CDR-H2 comprising the amino acid sequence of SEQ ID NO:10, CDR-H3 comprising the amino acid sequence of SEQ ID NO:11; CDR-L1 comprising the amino acid sequence of SEQ ID NO:12, CDR-L2 comprising the amino acid sequence of SEQ ID NO:13, and CDR-L3 comprising the amino acid sequence of SEQ ID NO:14, or

wherein the antibody or antigen binding fragment thereof comprises CDR-H1 comprising the amino acid sequence of SEQ ID NO:16, CDR-H2 comprising the amino acid sequence of SEQ ID NO:17, CDR-H3 comprising the amino acid sequence of SEQ ID NO:18; CDR-L1 comprising the amino acid sequence of SEQ ID NO:19, CDR-L2 comprising the amino acid sequence of SEQ ID NO:20, and CDR-L3 comprising the amino acid sequence of SEQ ID NO:21.

~~32~~16. The ~~method~~ use of any one of claims 1 to ~~30~~14, wherein the antibody or antigen binding fragment thereof comprises CDR-H1 consisting of the amino acid sequence of SEQ ID NO:9, CDR-H2 consisting of the amino acid sequence of SEQ ID NO:10, CDR-H3 consisting of the amino acid sequence of SEQ ID NO:11; CDR-L1 consisting of the amino acid sequence of SEQ ID NO:12, CDR-L2 consisting of the amino acid sequence of SEQ ID NO:13, and CDR-L3 consisting of the amino acid sequence of SEQ ID NO:14, or

wherein the antibody or antigen binding fragment thereof comprises CDR-H1 consisting of the amino acid sequence of SEQ ID NO:16, CDR-H2 consisting of the amino acid sequence of SEQ ID NO:17, CDR-H3 consisting of the amino acid sequence of SEQ ID NO:18; CDR-L1 consisting of the amino acid sequence of SEQ ID NO:19, CDR-L2 consisting of the amino acid sequence of SEQ ID NO:20, and CDR-L3 consisting of the amino acid sequence of SEQ ID NO:21.

~~33~~17. The ~~method~~ use of any one of claims 1 to ~~32~~16, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising the amino acid

sequence of SEQ ID NO:22 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:23.

~~3418~~. The ~~method~~ use of any one of claims 1 to ~~3317~~, wherein the antibody comprises a heavy chain comprising the amino acid sequence ranging from the 20th amino acid (glutamic acid) to the 466th amino acid (lysine) of SEQ ID NO:7 and a light chain comprising the amino acid sequence ranging from the 23rd amino acid (aspartic acid) to the 236th amino acid (cysteine) of SEQ ID NO:8.

~~3519~~. The ~~method~~ use of any one of claims 1 to ~~3317~~, wherein:
(i) the antigen binding fragment is an Fab, F(ab)2, Fv or scFv; and/or
(ii) the antigen binding fragment is recombinantly produced.

~~3620~~. The ~~method~~ use of any one of claims 1 to ~~3418~~, wherein:
(i) the antibody is a fully human antibody;
(ii) the antibody is an IgG1 and light chain is a kappa light chain; and/or
(iii) the antibody is recombinantly produced.

~~37. The method of any one of claims 1 to 34 and 36, wherein the antibody is an IgG1 and light chain is a kappa light chain.~~

~~38. The method of any one of claims 1 to 37, wherein the antibody or antigen binding fragment thereof is recombinantly produced.~~

~~3921~~. The ~~method~~ use of any one of claims 1 to ~~3820~~, wherein the antibody or antigen binding fragment is conjugated to each unit of MMAE via a linker.

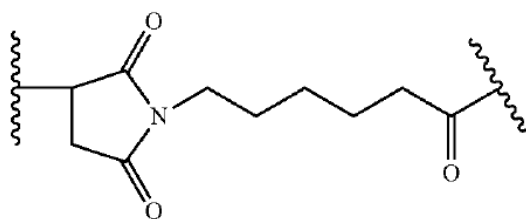
~~4022~~. The ~~method~~ use of claim ~~3921~~, wherein:

(i) the linker is an enzyme-cleavable linker, and wherein the linker forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof; and/or

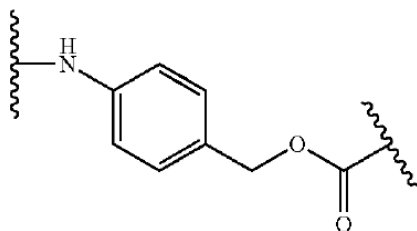
(ii) the linker has a formula of: $-Aa-Ww-Yy-$; wherein $-A-$ is a stretcher unit, a is 0 or 1; $-W-$ is an amino acid unit, w is an integer ranging from 0 to 12; and $-Y-$ is a spacer unit, y is 0, 1, or 2.

~~41. The method of claim 39 or 40, wherein the linker has a formula of: $-Aa-Ww-Yy-$; wherein A is a stretcher unit, a is 0 or 1; W is an amino acid unit, w is an integer ranging from 0 to 12; and Y is a spacer unit, y is 0, 1, or 2.~~

~~4223.~~ The ~~method~~ use of claim ~~4122~~, wherein the stretcher unit has the structure of Formula (1) below; the amino acid unit is valine-citrulline; and the spacer unit is a PAB group comprising the structure of Formula (2) below:



Formula (1)



Formula (2).

~~4324.~~ The ~~method~~ use of claim ~~4122~~ or ~~4223~~, wherein the stretcher unit forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof; and wherein the spacer unit is linked to MMAE via a carbamate group.

~~4425.~~ The ~~method~~ use of any one of claims 1 to ~~4324,~~ wherein:

(i) the ADC comprises from 1 to 20 units of MMAE per antibody or antigen binding fragment thereof;

(ii) the ADC comprises from 1 to 10 units of MMAE per antibody or antigen binding fragment thereof;

(iii) the ADC comprises from 2 to 8 units of MMAE per antibody or antigen binding fragment thereof; or

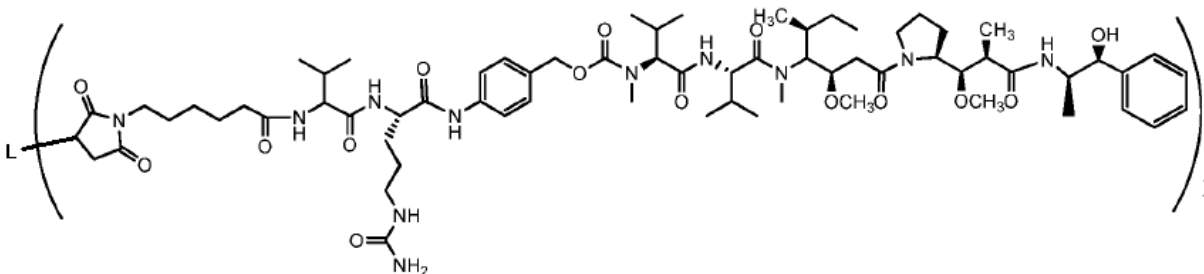
(iv) the ADC comprises from 3 to 5 units of MMAE per antibody or antigen binding fragment thereof .

~~45. The method of any one of claims 1 to 44, wherein the ADC comprises from 1 to 10 units of MMAE per antibody or antigen binding fragment thereof.~~

~~46. The method of any one of claims 1 to 45, wherein the ADC comprises from 2 to 8 units of MMAE per antibody or antigen binding fragment thereof.~~

~~47. The method of any one of claims 1 to 46, wherein the ADC comprises from 3 to 5 units of MMAE per antibody or antigen binding fragment thereof.~~

~~4826.~~ The ~~method~~ use of any one of claims 1 to ~~4525,~~ wherein the ADC has the following structure:



wherein L- represents the antibody or antigen binding fragment thereof and p is from 1 to 10.

~~49~~27. The ~~method~~ use of claim ~~48~~26, wherein:

(i) p is from 2 to 8;

(ii) p is from 3 to 5;

(iii) p is from 3 to 4;

(iv) p is about 4; or

(v) the average p value of the effective amount of the antibody drug conjugates is about

3.8.

~~50. The method of claim 48 or 49, wherein p is from 3 to 5.~~

~~51. The method of any one of claims 48 to 50, wherein p is from 3 to 4.~~

~~52. The method of any one of claims 48 to 51, wherein p is about 4.~~

~~53. The method of any one of claims 48 to 51, wherein the average p value of the effective amount of the antibody drug conjugates is about 3.8.~~

~~54~~28. The ~~method~~ use of any one of claims 1 to ~~53~~27, wherein:

(i) the ADC is to be administered at a dose of about 1 to about 10 mg/kg of the subject's body weight, about 1 to about 5 mg/kg of the subject's body weight, about 1 to about 2.5 mg/kg of the subject's body weight, or about 1 to about 1.25 mg/kg of the subject's body weight;

(ii) the ADC is to be administered at a dose of about 0.25 mg/kg, about 0.5 mg/kg, about 0.75 mg/kg, about 1.0 mg/kg, about 1.25 mg/kg, about 1.5 mg/kg, about 1.75 mg/kg, about 2.0 mg/kg, about 2.25 mg/kg, or about 2.5 mg/kg of the subject's body weight;

(iii) the ADC is to be administered at a dose of about 1 mg/kg of the subject's body weight; or

(iv) the ADC is to be administered at a dose of about 1.25 mg/kg of the subject's body weight.

~~55. The method of any one of claims 1 to 54, wherein the ADC is administered at a dose of about 0.25 mg/kg, about 0.5 mg/kg, about 0.75 mg/kg, about 1.0 mg/kg, about 1.25 mg/kg, about 1.5 mg/kg, about 1.75 mg/kg, about 2.0 mg/kg, about 2.25 mg/kg, or about 2.5 mg/kg of the subject's body weight.~~

~~56. The method of any one of claims 1 to 55, wherein the ADC is administered at a dose of about 1 mg/kg of the subject's body weight.~~

~~57. The method of any one of claims 1 to 55, wherein the ADC is administered at a dose of about 1.25 mg/kg of the subject's body weight.~~

5829. The method use of any one of claims 1 to 5728, wherein the ADC is to be administered by:

(i) an intravenous (IV) injection or infusion;

(ii) an IV injection or infusion three times every four-week cycle;

(iii) an IV injection or infusion on Days 1, 8 and 15 of every four-week cycle;

(iv) an IV injection or infusion over about 30 minutes three times every four-week cycle;
and/or

(v) an IV injection or infusion over about 30 minutes on Days 1, 8 and 15 of every four-week cycle.

~~59. The method of any one of claims 1 to 58, wherein the ADC is administered by an IV injection or infusion three times every four-week cycle.~~

~~60. The method of any one of claims 1 to 59, wherein the ADC is administered by an IV injection or infusion on Days 1, 8 and 15 of every four week cycle.~~

~~61. The method of any one of claims 1 to 60, wherein the ADC is administered by an IV injection or infusion over about 30 minutes three times every four week cycle.~~

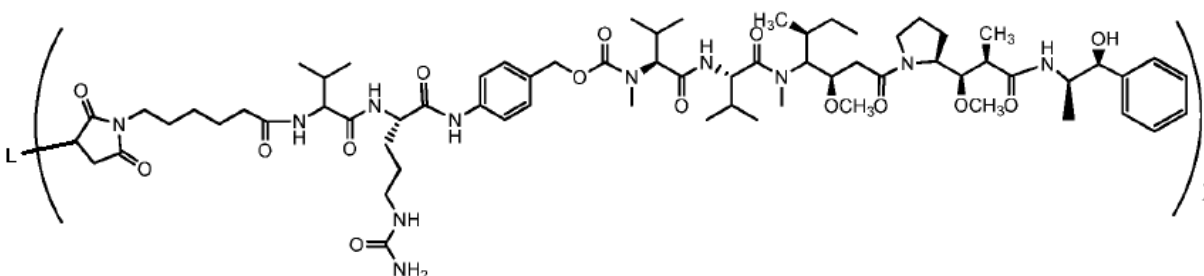
~~62. The method of any one of claims 1 to 61, wherein the ADC is administered by an IV injection or infusion over about 30 minutes on Days 1, 8 and 15 of every four week cycle.~~

~~6330. The method use of any one of claims 1 to 6229, wherein:~~
~~(i) the ADC is formulated in a pharmaceutical composition comprising L-histidine, polysorbate-20 (TWEEN-20), and trehalose dehydrate;~~
~~(ii) the ADC is formulated in a pharmaceutical composition comprising about 20 mM L-histidine, about 0.02% (w/v) TWEEN-20, about 5.5% (w/v) trehalose dihydrate, and hydrochloride, and wherein the pH of the pharmaceutical composition is about 6.0 at 25°C; or~~
~~(iii) the ADC is formulated in a pharmaceutical composition comprising about 9 mM histidine, about 11 mM histidine hydrochloride monohydrate, about 0.02% (w/v) TWEEN-20, and about 5.5% (w/v) trehalose dihydrate, and wherein the pH of the pharmaceutical composition is about 6.0 at 25°C.~~

~~64. The method of any one of claims 1 to 63, wherein the ADC is formulated in a pharmaceutical composition comprising about 20 mM L-histidine, about 0.02% (w/v) TWEEN-20, about 5.5% (w/v) trehalose dihydrate, and hydrochloride, and wherein the pH of the pharmaceutical composition is about 6.0 at 25°C.~~

~~65. The method of any one of claims 1 to 63, wherein the ADC is formulated in a pharmaceutical composition comprising about 9 mM histidine, about 11 mM histidine hydrochloride monohydrate, about 0.02% (w/v) TWEEN 20, and about 5.5% (w/v) trehalose dihydrate, and wherein the pH of the pharmaceutical composition is about 6.0 at 25°C.~~

~~6631. The method use of any one of claims 1 to 6530, wherein the ADC has the following structure:~~



wherein L- represents the antibody or antigen binding fragment thereof and p is from about 3 to about 4, the antibody comprises a heavy chain comprising the amino acid sequence ranging from the 20th amino acid (glutamic acid) to the 466th amino acid (lysine) of SEQ ID NO:7 and a light chain comprising the amino acid sequence ranging from the 23rd amino acid (aspartic acid) to the 236th amino acid (cysteine) of SEQ ID NO:8, wherein the ADC is to be administered at a dose of about 1.25 mg/kg of the subject's body weight, and wherein the dose is to be administered by an IV injection or infusion over about 30 minutes on Days 1, 8 and 15 of every four-week cycle.

~~6732. The method use of any one of claims 1 to 6631, whereby wherein:~~

- ~~(i) the subject has a complete response following the treatment;~~
- ~~(ii) the subject has a partial response following the treatment; or~~
- ~~(iii) the subject has a stable disease following the treatment.~~

~~68. The method of any one of claims 1 to 66, wherein the subject has a partial response following the treatment.~~

~~69. The method of any one of claims 1 to 66, wherein the subject has a complete response or a partial response following the treatment.~~

~~70. The method of any one of claims 1 to 66, wherein the subject has a stable disease following the treatment.~~

7133. The ~~method~~ use of any one of claims 1 to ~~66~~31, wherein:
(i) the subject has a duration of response of at least or about 10 months following the treatment; or
(ii) the subject has a duration of response ranging from 5 to 22 months following the treatment.

~~72. The method of any one of claims 1 to 66, wherein the subject has a duration of response ranging from 5 to 22 months following the treatment.~~

7334. The ~~method~~ use of any one of claims 1 to ~~66~~31, wherein:
(i) the subject has a progression free survival of at least or about 5 months following the treatment; or
(ii) the subject has a progression free survival ranging from 5 to 9 months following the treatment.

~~74. The method of any one of claims 1 to 66, wherein the subject has a progression free survival ranging from 5 to 9 months following the treatment.~~

7535. The ~~method~~ use of any one of claims 1 to ~~66~~31, wherein:
(i) the subject has an overall survival of at least or about 14 months following the treatment; or

(ii) the subject has an overall survival ranging from 10 to 19 months following the treatment.

~~76. — The method of any one of claims 1 to 66, wherein the subject has an overall survival ranging from 10 to 19 months following the treatment.~~

~~77~~36. The ~~method~~ use of any one of claims 1 to ~~66~~31, wherein a population of the subjects is to be treated by the ~~methods~~ medicament, and wherein:

(i) the percentage of the subjects having complete response in the treated population is at least or about 20%;

(ii) the percentage of the subjects having partial response in the treated population is at least or about 31%;

(iii) the objective response rate in the treated population is at least or about 51%;

(iv) the objective response rate in the treated population ranges from 40% to 63%; or

(v) the percentage of the subjects having stable disease in the treated population is at least or about 30%.

~~78. — The method of any one of claims 1 to 66, wherein a population of the subjects is treated by the methods, and wherein percentage of the subjects having partial response in the treated population is at least or about 31%.~~

~~79. — The method of any one of claims 1 to 66, wherein a population of the subjects is treated by the methods, and wherein objective response rate in the treated population is at least or about 51%.~~

~~80. — The method of any one of claims 1 to 66, wherein a population of the subjects is treated by the methods, and wherein objective response rate in the treated population ranges from 40% to 63%.~~

~~81. — The method of any one of claims 1 to 66, wherein a population of the subjects is treated by the methods, and wherein percentage of the subjects having stable disease in the treated population is at least or about 30%.~~

~~8237. The method use of any one of claims 1 to 6631, wherein a population of the subjects is to be treated by the methods medicament, and wherein:~~

~~(i) the median duration of response in the treated population is at least or about 10 months;~~

~~(ii) the duration of response in the treated population ranges from 5 to 22 months;~~

~~(iii) the median progression free survival in the treated population is at least or about 5 months;~~

~~(iv) the progression free survival in the treated population ranges from 5 to 9 months;~~

~~(v) the median overall survival in the treated population is at least or about 14 months; or~~

~~(vi) the overall survival in the treated population ranges from 10 to 19 months.~~

~~83. — The method of any one of claims 1 to 66, wherein a population of the subjects is treated by the methods, and wherein duration of response in the treated population ranges from 5 to 22 months.~~

~~84. — The method of any one of claims 1 to 66, wherein a population of the subjects is treated by the methods, and wherein median progression free survival in the treated population is at least or about 5 months.~~

~~85. — The method of any one of claims 1 to 66, wherein a population of the subjects is treated by the methods, and wherein progression free survival in the treated population ranges from 5 to 9 months.~~

~~86. — The method of any one of claims 1 to 66, wherein a population of the subjects is treated by the methods, and wherein median overall survival in the treated population is at least or about 14 months.~~

~~87. — The method of any one of claims 1 to 66, wherein a population of the subjects is treated by the methods, and wherein overall survival in the treated population ranges from 10 to 19 months.~~

~~88~~38. The ~~method~~ use of any one of claims 1 to ~~67~~32 and ~~69~~, wherein:

(i) the subject has a complete response following the treatment, and wherein the complete response rate is at least or about 20% for a population of subjects treated with the method medicament; or

(ii) the subject has a partial response following the treatment, and wherein the partial response rate is at least or about 31% for a population of subjects treated with the medicament.

~~89. — The method of any one of claims 1 to 66, 68, and 69, wherein the partial response rate is at least or about 31% for a population of subjects treated with the method.~~

~~90~~39. The ~~method~~ use of any one of claims 1 to ~~69~~32, wherein:

(i) objective response rate is at least or about 51% for a population of subjects treated with the method medicament; or

(ii) objective response rate is from 40% to 63% for a population of subjects treated with the medicament.

~~91. — The method of any one of claims 1 to 69, wherein objective response rate is from 40% to 63% for a population of subjects treated with the method.~~

9240. The ~~method~~ use of any one of claims 1 to ~~66 and 70~~ 32, wherein the stable disease rate is at least or about 30% for a population of subjects treated with the ~~method~~ medicament.

9341. The ~~method~~ use of any one of claims 1 to ~~66~~31, ~~71 and 72~~, wherein:

(i) the median duration of response is at least or about 10 months for a population of subjects treated with the ~~method~~ medicament; or

(ii) the duration of response is from 5 to 22 months for a population of subjects treated with the medicament.

~~94. — The method of any one of claims 1 to 66, 71 and 72, wherein the duration of response is from 5 to 22 months for a population of subjects treated with the method.~~

9542. The ~~method~~ use of any one of claims 1 to ~~66~~31 and ~~34~~ 73 and 74, wherein:

(i) the median progression free survival is at least or about 5 months for a population of subjects treated with the ~~method~~ medicament; or

(ii) the progression free survival is from 5 to 9 months for a population of subjects treated with the medicament.

~~96. — The method of any one of claims 1 to 66, 73 and 74, wherein the progression free survival is from 5 to 9 months for a population of subjects treated with the method.~~

9743. The ~~method~~ use of any one of claims 1 to ~~66~~31 and ~~35~~ 75 and 76, wherein:

(i) the median overall survival is at least or about 14 months for a population of subjects treated with the ~~method~~ medicament; or

(ii) the overall survival is from 10 to 19 months for a population of subjects treated with the medicament.

98. — ~~The method of any one of claims 1 to 66, 75 and 76, wherein the overall survival is from 10 to 19 months for a population of subjects treated with the method.~~