CLAIMS

I claim:

1. Use of a therapeutically effective amount of a Zn(II) agent comprising Zn(II)/γ-polyglutamic acid conjugated to a tumor-targeting moiety and/or a charge-carrying moiety and/or Zn(II)/α-polyglutamic acid conjugated to a tumor-targeting moiety and/or a charge-carrying moiety, and an immune checkpoint inhibitor in the preparation of a medicament for combination therapy for the treatment of a tumor in a patient, wherein the immune checkpoint inhibitor is a programmed cell death-1 (PD-1) antibody or an antigen-binding portion thereof that binds specifically to a PD-1 receptor and inhibits PD-1 activity.

2. The use according to claim 1, wherein said tumor includes tumor cells that have genetic instability mutations and/or genetic instability due to gene overexpression.

3. The use according to claim 2, wherein said genetic instability mutations are dysfunctional mutations in one or more genes selected from ATM; ATR; PAXIP1; BRCA1; BRCA2; WRN; RFC1; RPA1; ERCC1; ERCC4; ERCC6; MGMT; PARP1; PARP2; NEIL3; XRCC1; MLH1; PMS2; TP53; CREBBP; JAK1; NFKB1; MSH2; MSH3; MSH6; and MLH3.

4. Use of a therapeutically effective amount of a Zn(II) agent comprising Zn(II)/γ-polyglutamic acid conjugated to a tumor-targeting moiety and/or a charge-carrying moiety and/or Zn(II)/α-polyglutamic acid conjugated to a tumor-targeting moiety and/or a charge-carrying moiety, and an immune checkpoint inhibitor in the preparation of a medicament for combination therapy for increasing the tumor infiltrating leukocyte population of CD4+T cells and CD8+T cells in a tumor in a patient, wherein the immune checkpoint inhibitor is a programmed cell death-1 (PD-1) antibody or an antigen-binding portion thereof that binds specifically to a PD-1 receptor and inhibits PD-1 activity.

5. The use of claim 1, wherein the molecular weight of said γ-polyglutamic acid prior to conjugation with a tumor-targeting moiety and/or a charge-carrying moiety, and said α-polyglutamic acid prior to conjugation with a tumor-targeting moiety and/or a charge-carrying moiety, is in the range of about 2.5 kDa to about 60 kDa.

6. The use according to claim 3, wherein said genetic instability due to overexpression is caused by overexpression of APOBEC3B.

7. The use of claim 4, wherein the molecular weight of said γ-polyglutamic acid prior to conjugation with a tumor-targeting moiety and/or a charge-carrying moiety, and said α-polyglutamic acid prior to conjugation with a tumor-targeting moiety and/or a charge-carrying moiety, is in the range of about 2.5 kDa to about 60 kDa.

8. The use of claim 1, wherein the tumor-targeting moiety is folic acid, N^5, N^{10}-dimethyl tetrahydrofolate (DMTHF), RGD peptide or combinations thereof.

9. The use of claim 1, wherein the charge-carrying moiety is citric acid, ethylenediamine tetraacetic acid (EDTA), 1,4,7,10-tetracyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA), and diethylenetriamine pentaacetic acid (DTPA) or combinations thereof.

10. The use of claim 1, wherein the Zn(II) agent comprises Zn(II)/γ-polyglutamic acid conjugated to folate-PEG4-NH2 and cRGDfK-PEG4-NH2; and wherein the molecular weight of said γ-polyglutamic acid prior to conjugation is 45 kDa.

11. The use of claim 4, wherein the tumor-targeting moiety is folic acid, N^5, N^{10}-dimethyl tetrahydrofolate (DMTHF), RGD peptide or combinations thereof.

12. The use of claim 4, wherein the charge-carrying moiety is citric acid, ethylenediamine tetraacetic acid (EDTA), 1,4,7,10-tetracyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA), and diethylenetriamine pentaacetic acid (DTPA) or combinations thereof.

13. The use of claim 4, wherein the Zn(II) agent comprises Zn(II)/γ-polyglutamic acid conjugated to folate-PEG4-NH2 and cRGDfK-PEG4-NH2; and wherein the molecular weight of said γ-polyglutamic acid prior to conjugation is 45 kDa.