CLAIMS

I claim:

1. A method of inducing PARP1-mediated tumor necrosis in a tumor in a patient, the method comprising administering a therapeutically effective amount of a Zn(II) salt and a γ-polyglutamic acid carrier in a dosage form to the patient with the tumor;

wherein said γ-polyglutamic acid carrier comprises γ-polyglutamic acid and/or a tumor-targeting γ-polyglutamic acid derivative and/or a charge-modified γ-polyglutamic acid derivative and/or a tumor-targeting charge-modified γ-polyglutamic acid derivative.

2. The method according to claim 1, wherein said tumor has a drug-resistant phenotype.

3. The method according to claim 2, wherein said drug-resistance phenotype is dysfunctional p53.

4. The method according to claim 2, wherein said drug-resistance phenotype is MDR1 overexpression.

5. The method according to claim 2, wherein said drug-resistance phenotype is MRP1 overexpression.

6. The method according to any one of claims 1-5, wherein said Zn(II) salt and said γ-polyglutamic acid carrier in said dosage form are administered in a

therapeutic amount in combination with a therapeutic amount of an NF-κB inhibitor.

7. The method according to any one of claims 1-6, wherein said dosage form is a solid dosage form or a liquid dosage form.

8. The method according to claim 7, wherein said dosage form is a solid dosage form, and is selected from a tablet, a minitab, a hard capsule, a soft capsule, a caplet, a gelcap, an oral disintegrating films, granules, pellets, a paste, and a powder sachet.

9. The method according to claim 7, wherein said dosage form is a liquid dosage form, and is selected from a liquid solution, a liquid suspension, a syrup, and an oral spray.

10. The method according to claim 7, wherein said administering step is selected from an oral administration and an injection administration.

11. A pharmaceutical composition comprising (i) a pharmaceutically acceptable Zn(II) salt, and (ii) γ-polyglutamic acid carrier comprising a tumor-targeting moiety and/or a charge-modifying moiety.

12. The pharmaceutical composition according to claim 11, wherein said tumor-targeting moiety is selected from folic acid, ^{5}N, ^{10}N-dimethyl

tetrahydrofolate, and RGD peptide, and any combination of said moieties are covalently joined to γ-polyglutamic acid.

13. The pharmaceutical composition according to claim 11 or 12, wherein said charge-modifying moiety is selected from citric acid, ethylenediamine tetraacetic acid, 1,4,7,10-tetracyclododecane-N,N',N'',N'''-tetraacetic acid, and diethylenetriamine pentaacetic acid, and any combination of said moieties are covalently joined to γ-polyglutamic acid.

14. The pharmaceutical composition according to any of claims 11-13, further comprising (iii) γ-polyglutamic acid.

15. The pharmaceutical composition according to any one of claims 11-14, wherein a substantial portion of said Zn(II) salt is a bound complex of the Zn(II) ion with γ-polyglutamic acid and/or said tumor-targeting moiety and/or said charge-modifying moiety.

16. The pharmaceutical composition according to any one of claims 11-14, wherein (i) said Zn(II) salt and (ii) said γ-polyglutamic acid carrier are mixed together in a solid mixture.

17. The pharmaceutical composition according to any one of claims 11-16, wherein said composition further comprises an NF-κB inhibitor.

18. The pharmaceutical composition according to any one of claims 11-17, wherein said composition is formulated as a solid dosage form.

19. The pharmaceutical composition according to claim 18, wherein said solid dosage form further comprises a gastro-resistant binder and/or a gastro-resistant outer coating.

20. The pharmaceutical composition according to any one of claims 11-17, wherein said composition is formulated as a liquid dosage form.

21. The pharmaceutical composition according to claim 20, wherein said liquid dosage form is suitable for injection.

22. The pharmaceutical composition according to claim 20 or 21, wherein said liquid dosage form is a suspension of a pharmaceutical composition that further comprises a gastro-resistant material.

23. A method for treating a tumor in a patient, the method comprising administering a therapeutically effective amount of the pharmaceutical composition according to any one of claims 11-22 to the patient with the tumor.

24. The method according to claim 23, wherein said tumor has a drug-resistant phenotype selected from dysfunctional p53, MDR1 overexpression, and MRP1 overexpression.

CLAIMS

I claim:

1. Use of a therapeutically effective amount of Zn(II) and a γ-polyglutamic acid carrier in the preparation of a dosage form for inducing tumor necrosis in a tumor in a patient;

wherein said γ-polyglutamic acid carrier comprises one or more carrier selected from γ-polyglutamic acid, a tumor-targeting γ-polyglutamic acid derivative, a charge-modified γ-polyglutamic acid derivative, and a tumor-targeting charge-modified γ-polyglutamic acid derivative;

wherein a substantial portion of said Zn(II) is complexed to a carboxylate moiety of γ-polyglutamic acid in said γ-polyglutamic acid carrier.

2. The use according to claim 1, wherein said tumor has a drug-resistant phenotype.

3. The use according to claim 2, wherein said drug-resistance phenotype is dysfunctional p53.

4. The use according to claim 2, wherein said drug-resistance phenotype is MDR1 overexpression.

5. The use according to claim 2, wherein said drug-resistance phenotype is MRP1 overexpression.

6. The use according to any one of claims 1-5, wherein said Zn(II) complexed with said γ-polyglutamic acid in said γ-polyglutamic acid carrier in said dosage form are to be administered in a therapeutic amount in combination with a therapeutic amount of an NF-κB inhibitor.

7. The use according to any one of claims 1-6, wherein said dosage form is a solid dosage form or a liquid dosage form.

8. The use according to claim 7, wherein said dosage form is a solid dosage form, and is selected from a tablet, a minitab, a hard capsule, a soft capsule, a caplet, a gelcap, an oral disintegrating films, granules, pellets, a paste, and a powder sachet.

9. The use according to claim 7, wherein said dosage form is a liquid dosage form, and is selected from a liquid solution, a liquid suspension, a syrup, and an oral spray.

10. The use according to claim 6, wherein said administration step is selected from an oral administration and an injection administration.

11. A pharmaceutical composition comprising (i) Zn(II) complexed to (ii) a carboxylate moiety of γ-polyglutamic acid in a γ-polyglutamic acid carrier comprising γ-polyglutamic acid modified with a tumor-targeting moiety and/or a charge-modifying moiety.

12. The pharmaceutical composition according to claim 11, wherein said tumor-targeting moiety is selected from folic acid, ^{5}N, ^{10}N-dimethyl tetrahydrofolate, and RGD peptide, and any combination of said moieties are covalently joined to γ-polyglutamic acid.

13. The pharmaceutical composition according to claim 11 or 12, wherein said charge-modifying moiety is selected from citric acid, ethylenediamine tetraacetic acid, 1,4,7,10-tetracyclododecane-N,N',N'',N'''-tetraacetic acid, and diethylenetriamine pentaacetic acid, and any combination of said moieties are covalently joined to γ-polyglutamic acid.

14. The pharmaceutical composition according to any of claims 11-13, further comprising (iii) γ-polyglutamic acid.

15. The pharmaceutical composition according to any one of claims 11-14, wherein said composition further comprises an NF-κB inhibitor.

16. The pharmaceutical composition according to any one of claims 11-15, wherein said composition is formulated as a solid dosage form.

17. The pharmaceutical composition according to claim 16, wherein said solid dosage form further comprises a gastro-resistant binder and/or a gastro-resistant outer coating.

18. The pharmaceutical composition according to any one of claims 11-15, wherein said composition is formulated as a liquid dosage form.

19. The pharmaceutical composition according to claim 18, wherein said liquid dosage form is suitable for injection.

20. The pharmaceutical composition according to claim 18 or 19, wherein said liquid dosage form is a suspension of a pharmaceutical composition that further comprises a gastro-resistant material.

21. Use of a therapeutically effective amount of the pharmaceutical composition according to any one of claims 11-20 in the preparation of a medicament for treating a tumor in a patient, wherein the medicament is to be administered to the patient with the tumor.

22. The use according to claim 21, wherein said tumor has a drug-resistant phenotype selected from dysfunctional p53, MDR1 overexpression, and MRP1 overexpression.