

CLAIMS

What Is Claimed Is:

1. Use of a TUSC2 therapy in the manufacture of a medicament for treating a subject having a cancer, wherein the subject has been or is being treated with at least one immune checkpoint inhibitor.
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2. The use of claim 1, further comprising at least one immune checkpoint inhibitor to be administered to the subject.
3. The use of claim 2, wherein the at least one immune checkpoint inhibitor is to be administered to the subject before the TUSC2 therapy.
- 10 4. The use of claim 2, wherein the at least one immune checkpoint inhibitor is to be administered to the subject after or concomitantly with the TUSC2 therapy.
5. The use of claim 1, wherein the subject had been administered the at least one immune checkpoint inhibitor no more than two weeks before the TUSC2 therapy.
6. The use of claim 1, wherein the at least one immune checkpoint inhibitor comprises
15 an anti-PD1 agent.
7. The use of claim 6, wherein the anti-PD1 agent comprises an anti-PD1 antibody, anti-PDL1 antibody, or an anti-PDL2 antibody.
- 20 8. The use of claim 6, wherein the anti-PD1 agent is nivolumab, pembrolizumab, pidilizumab, KEYTRUDA®, AMP-514, REGN2810, CT-011, BMS 936559, MPDL3280A or AMP-224.
9. The use of claim 1, wherein the at least one immune checkpoint inhibitor is selected
25 from an inhibitor of CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, BTLA, B7H3, B7H4, TIM3, KIR, or A2aR.
10. The use of claim 1, wherein the at least one immune checkpoint inhibitor is an anti-CTLA-4 antibody.

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11. The use of claim 10, wherein the anti-CTLA-4 antibody is tremelimumab, YERVOY®, or ipilimumab.
12. The use of claim 1, wherein the at least one immune checkpoint inhibitor is an anti-killer-cell immunoglobulin-like receptor (KIR) antibody.
13. The use of claim 12, wherein the anti-KIR antibody is lirilumab.
14. The use of claim 1, wherein the subject has been or is to be treated with two immune checkpoint inhibitors.
15. The use of claim 14, wherein the two immune checkpoint inhibitors are an anti-PD1 antibody and an anti-CTL4 antibody.
16. The use of claim 1, wherein the TUSC2 therapy comprises a TUSC2 expression vector to be administered.
17. The use of claim 16, wherein the TUSC2 expression vector is plasmid DNA.
18. The use of claim 17, wherein the plasmid is pLJ143/KGB2/FUS1.
19. The use of claim 16, wherein the TUSC2 expression vector is provided in a liposome.
20. The use of claim 19, wherein the liposome is a DOTAP:cholesterol liposome.
21. The use of claim 20, wherein the DOTAP:cholesterol ratio is between about 1.5:1 and 1:1.5.
22. The use of claim 20, wherein the DOTAP:cholesterol ratio is about 10:9.
23. The use of claim 20, wherein the TUSC2 expression vector and DOTAP:cholesterol liposome are administered in a dose of from about 0.01 mg/kg to about 0.10 mg/kg.
24. The use of claim 1, wherein the TUSC2 therapy is to be administered two or more times.
25. The use of claim 1, further comprising an anti-inflammatory agent to be administered.

26. The use of claim 1, wherein the TUSC2 therapy comprises a TUSC2 polypeptide to be administered.
27. The use of claim 26, wherein the TUSC2 polypeptide is myristoylated.
28. The use of claim 26, wherein the TUSC2 polypeptide is comprised in a nanoparticle.
- 5 29. The use of claim 28, wherein the nanoparticle is a lipid-based nanoparticle, a superparamagnetic nanoparticle, a nanoshell, a semiconductor nanocrystal, a quantum dot, a polymer-based nanoparticle, a silicon-based nanoparticle, a silica-based nanoparticle, a metal-based nanoparticle, a fullerene or a nanotube.
- 10 30. The use of claim 1, further comprising a further anti-cancer therapy to be administered to the subject.
31. The use of claim 30, wherein the further anti-cancer therapy is chemotherapy, radiotherapy, gene therapy, surgery, hormonal therapy, anti-angiogenic therapy or cytokine therapy.
- 15 32. The use of claim 31, wherein the further anti-cancer therapy is an EGFR inhibitor.
33. The use of claim 1, wherein the cancer is oral cancer, oropharyngeal cancer, nasopharyngeal cancer, respiratory cancer, urogenital cancer, gastrointestinal cancer, central or peripheral nervous system tissue cancer, an endocrine or neuroendocrine cancer or
20 hematopoietic cancer, glioma, sarcoma, carcinoma, lymphoma, melanoma, fibroma, meningioma, brain cancer, oropharyngeal cancer, nasopharyngeal cancer, renal cancer, biliary cancer, pheochromocytoma, pancreatic islet cell cancer, Li-Fraumeni tumors, thyroid cancer, parathyroid cancer, pituitary tumors, adrenal gland tumors, osteogenic sarcoma tumors, multiple neuroendocrine type I and type II tumors, breast cancer, lung cancer, head
25 and neck cancer, prostate cancer, esophageal cancer, tracheal cancer, liver cancer, bladder cancer, stomach cancer, pancreatic cancer, ovarian cancer, uterine cancer, cervical cancer, testicular cancer, colon cancer, rectal cancer or skin cancer.
34. The use of claim 33, wherein the cancer is a lung cancer.
35. The use of claim 34, wherein the lung cancer is a non-small cell lung cancer.

36. The use of claim 34, wherein the cancer is a metastatic lung cancer.
37. The use of claim 1, wherein the cancer is resistant to a least a first chemotherapy.
38. The use of claim 37, wherein the cancer is resistant to a platinum-based chemotherapy.
- 5 39. The use of claim 2, wherein the TUSC2 therapy and at least one immune checkpoint inhibitor to be administered results in an increase of NK and/or CD8⁺ T cell density in the tumor.
- 10 40. The use of claim 39, wherein the CD8⁺ T cell density increases by at least 3-fold.
41. The use of claim 2, wherein the TUSC2 therapy and at least one immune checkpoint inhibitor to be administered results in CcL3, CcL4, CcL21a, and/or CcL19 serum levels.
42. A kit comprising a TUSC2 therapeutic and an immune checkpoint inhibitor.
- 15 43. The kit of claims 42, wherein the immune checkpoint inhibitor is an anti-PD1 antibody.
44. The use of claim 32, wherein the EGFR inhibitor is a tyrosine kinase inhibitor.
45. The use of claim 32, wherein the EGFR inhibitor is an EGFR binding antibody or aptamer.
- 20 46. The use of claim 32, wherein the EGFR inhibitor is gefitinib, erlotinib, cetuximab, matuzumab, panitumumab, AEE788; CI-1033, HKI-272, HKI-357 or EKB-569.
47. A composition comprising a TUSC2 therapeutic and an immune checkpoint inhibitor in a therapeutically effective amount to treat a cancer.