

CLAIMS

What Is Claimed Is:

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

11. The method of claim 10, wherein the anti-CTLA-4 antibody is tremelimumab, YERVOY®, or ipilimumab.
- 5 12. The method of claim 1, wherein the at least one immune checkpoint inhibitor is an anti-killer-cell immunoglobulin-like receptor (KIR) antibody.
13. The method of claim 12, wherein the anti-KIR antibody is lirilumab.
- 10 14. The method of claim 1, wherein the subject has been or is being treated with two immune checkpoint inhibitors.
- 15 15. The method of claim 14, wherein the two immune checkpoint inhibitors are an anti-PD1 antibody and an anti-CTLA4 antibody.
16. The method of claim 1, wherein the TUSC2 therapy comprises administration of a TUSC2 expression vector.
17. The method of claim 16, wherein the TUSC2 expression vector is plasmid DNA.
18. The method of claim 17, wherein the plasmid is pLJ143/KGB2/FUS1.
- 20 19. The method of claim 16, wherein the TUSC2 expression vector is provided in a liposome.
20. The method of claim 19, wherein the liposome is a DOTAP:cholesterol liposome.
21. The method of claim 20, wherein the DOTAP:cholesterol ratio is between about 1.5:1 and 1:1.5.
- 25 22. The method of claim 20, wherein the DOTAP:cholesterol ratio is about 10:9.
23. The method 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 method of claim 1, wherein the TUSC2 therapy is administered two or more times.

25. The method of claim 1, further comprising administering an anti-inflammatory agent.
26. The method of claim 1, wherein the TUSC2 therapy comprises administration of a TUSC2 polypeptide.
27. The method of claim 26, wherein the TUSC2 polypeptide is myristoylated.
- 5 28. The method of claim 26, wherein the TUSC2 polypeptide is comprised in a nanoparticle.
29. The method 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-
- 10 based nanoparticle, a fullerene or a nanotube.
30. The method of claim 1, further comprising administering a further anti-cancer therapy to the subject.
31. The method of claim 30, wherein the further anti-cancer therapy is chemotherapy, radiotherapy, gene therapy, surgery, hormonal therapy, anti-angiogenic therapy or cytokine
- 15 therapy.
32. The method of claim 31, wherein the further anti-cancer therapy is an EGFR inhibitor.
33. The method 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 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,
- 20 parathyroid cancer, pituitary tumors, adrenal gland tumors, osteogenic sarcoma tumors, multiple neuroendocrine type I and type II tumors, breast cancer, lung cancer, head 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 method of claim 33, wherein the cancer is a lung cancer.
35. The method of claim 34, wherein the lung cancer is a non-small cell lung cancer.
36. The method of claim 34, wherein the cancer is a metastatic lung cancer.
37. The method of claim 1, wherein the cancer is resistant to a least a first chemotherapy.
- 5 38. The method of claim 37, wherein the cancer is resistant to a platinum-based chemotherapy.
39. The method of claim 2, wherein administering the TUSC2 therapy and at least one immune checkpoint inhibitor results in an increase of NK and/or CD8⁺ T cell density in the tumor.
- 10 40. The method of claim 39, wherein the CD8⁺ T cell density increases by at least 3-fold.
41. The method of claim 2, wherein administering the TUSC2 therapy and at least one immune checkpoint inhibitor results in CcL3, CcL4, CcL21a, and/or CcL19 serum levels.
- 15 42. A kit comprising a TUSC2 therapeutic and an immune checkpoint inhibitor.
43. The kit of claims 42, wherein the immune checkpoint inhibitor is an anti-PD1 antibody.
44. The method of claim 32, wherein the EGFR inhibitor is a tyrosine kinase inhibitor.
45. The method of claim 32, wherein the EGFR inhibitor is an EGFR binding antibody or
20 aptamer.
46. The method 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.