

CLAIMS

What is claimed is:

- 5 1. A method of treating cancer in a patient in need thereof, the method comprising:
- i) administering to the patient a therapeutically effective amount of the fusion
 protein of SEQ ID NO: 1, or a variant thereof; and
- ii) administering to the patient a therapeutically effective amount of an immune
 checkpoint inhibitor;
- 10 wherein step (i) is carried out before, after or simultaneously with step (ii),
 wherein the patient has previously failed to achieve complete or partial response to prior
 treatment or to ongoing treatment with an immune checkpoint inhibitor, and
 wherein the variant fusion protein is at least 80% identical to full length SEQ ID NO: 1.
- 15 2. The method of claim 1, wherein the patient has previously failed to achieve complete or
 partial response to prior treatment or to ongoing treatment with an immune checkpoint
 inhibitor as determined by RECIST (Response Evaluation Criteria In Solid Tumors)
 criteria or according to the irRECIST (immune- related Response Evaluation Criteria In
 Solid Tumors) criteria.
- 20 3. The method of claim 1, wherein the patient has previously failed to achieve complete
 response to prior treatment or to ongoing treatment with an immune checkpoint inhibitor
 as determined by RECIST (Response Evaluation Criteria In Solid Tumors) criteria or
 according to the irRECIST (immune- related Response Evaluation Criteria In Solid
- 25 Tumors) criteria.
4. The method of any one of the preceding claims, wherein the immune checkpoint inhibitor
 is an anti-PD-1 antibody or an anti PD-L1 antibody.
- 30 5. The method of any one of the preceding claims, wherein the immune checkpoint inhibitor
 is pembrolizumab.

6. The method of any one of claims 1-3, wherein the immune checkpoint inhibitor is an anti-CTLA4 antibody.
- 5 7. The method of any one of claims 1-3, wherein the immune checkpoint inhibitor is ipilimumab.
8. The method of any one of claims 1-7, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered parenterally to the patient.
- 10 9. The method of any one of claims 1-7, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered intravenously to the patient.
- 15 10. The method of any one of claims 1-7, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient.
11. The method of any one of the preceding claims, wherein a therapeutically effective amount of the fusion protein of SEQ ID NO: 1 or variant thereof is a dose of the fusion protein of SEQ ID NO: 1 or variant thereof of about 0.1 µg/kg, 0.3 µg/kg, 1 µg/kg, 3 µg/kg, 3.5 µg/kg, 4 µg/kg, 4.5 µg/kg, 5 µg/kg, 5.5 µg/kg, 6 µg/kg, 6.5 µg/kg, 7 µg/kg, 7.5 µg/kg, 8 µg/kg, 8.5 µg/kg, 9 µg/kg, 9.5 µg/kg, 10 µg/kg, 10.5 µg/kg, 11 µg/kg, 11.5 µg/kg, 12 µg/kg, 12.5 µg/kg, 13 µg/kg, 13.5 µg/kg, 14 µg/kg, or 14.5 µg/kg.
- 20 12. The method of any one of the preceding claims, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered to the patient at a dose of about 3 µg/kg.
- 25 13. The method of any one of the preceding claims, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered intravenously to the patient at a dose of about 3 µg/kg.

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14. The method of any one of the preceding claims, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered to the patient daily for five consecutive days.
- 5 15. The method of any one of claims 1-10, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered to the patient at a dose of about 0.3 mg, about 0.6 mg, about 1 mg, about 3 mg, or about 10 mg.
- 10 16. The method of any one of claims 1-10, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient at a dose of about 0.3 mg, about 0.6 mg, about 1 mg, about 3 mg, or about 10 mg.
- 15 17. The method of any one of claims 15 or 16, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered to the patient once every week, once every two weeks, or once every three weeks.
18. The method of claim 5, wherein the pembrolizumab is administered to the patient at a dose of 200 mg.
- 20 19. The method of any one of the preceding claims, wherein pembrolizumab is administered intravenously to the patient at a dose of 200 mg.
20. The method of any one of the preceding claims, wherein pembrolizumab is administered to the patient once every three weeks.
- 25 21. The method of claim 5, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered intravenously to the patient at a dose of about 3 µg/kg daily for five consecutive days, every three weeks, and wherein the pembrolizumab is administered intravenously to the patient at a dose of about 200 mg once every three weeks.

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22. The method of claim 5, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient at a dose of about 0.3 mg once every week and the pembrolizumab is administered intravenously to the patient at a dose of about 200 mg once every three weeks, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient as a monotherapy at a dose of about 0.3 mg once every week for 6 weeks prior to administration of the pembrolizumab.
23. The method of claim 5, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient at a dose of about 0.6 mg once every week and the pembrolizumab is administered intravenously to the patient at a dose of about 200 mg once every three weeks, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient as a monotherapy at a dose of about 0.6 mg once every week for 6 weeks prior to administration of the pembrolizumab.
24. The method of claim 5, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient at a dose of about 1 mg once every week and the pembrolizumab is administered intravenously to the patient at a dose of about 200 mg once every three weeks, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient as a monotherapy at a dose of about 1 mg once every week for 6 weeks prior to administration of the pembrolizumab.
25. The method of claim 5, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient at a dose of about 3 mg once every week and the pembrolizumab is administered intravenously to the patient at a dose of about 200 mg once every three weeks, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient as a monotherapy at a dose of about 3 mg once every week for 6 weeks prior to administration of the pembrolizumab.
26. The method of claim 5, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient at a dose of about 1 mg once every three weeks and the pembrolizumab is administered intravenously to the patient at a dose of about 200

mg once every three weeks, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient as a monotherapy at a dose of about 1 mg once every three weeks for 6 weeks prior to administration of the pembrolizumab.

- 5 27. The method of claim 5, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient at a dose of about 3 mg once every three weeks and the pembrolizumab is administered intravenously to the patient at a dose of about 200 mg once every three weeks, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient as a monotherapy at a dose of about 3 mg
10 once every three weeks for 6 weeks prior to administration of the pembrolizumab.
28. The method of claim 5, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient at a dose of about 10 mg once every three weeks and the pembrolizumab is administered intravenously to the patient at a dose of
15 about 200 mg once every three weeks, wherein the fusion protein of SEQ ID NO: 1 or variant thereof is administered subcutaneously to the patient as a monotherapy at a dose of about 10 mg once every three weeks for 6 weeks prior to administration of the pembrolizumab.
- 20 29. The method of any one of the preceding claims, wherein the patient failed to achieve complete remission (CR) following prior immune checkpoint inhibitor therapy.
30. The method of any one of the preceding claims, wherein the patient has stable disease (SD), or partial response (PR) with no further reduction in tumor size or response,
25 following prior immune checkpoint inhibitor therapy.
31. The method of claims 29 and 30, wherein the prior immune checkpoint inhibitor therapy comprises one or more of anti-PD-1 therapy, anti-PD-L1 therapy, and anti-CTLA-4 therapy.

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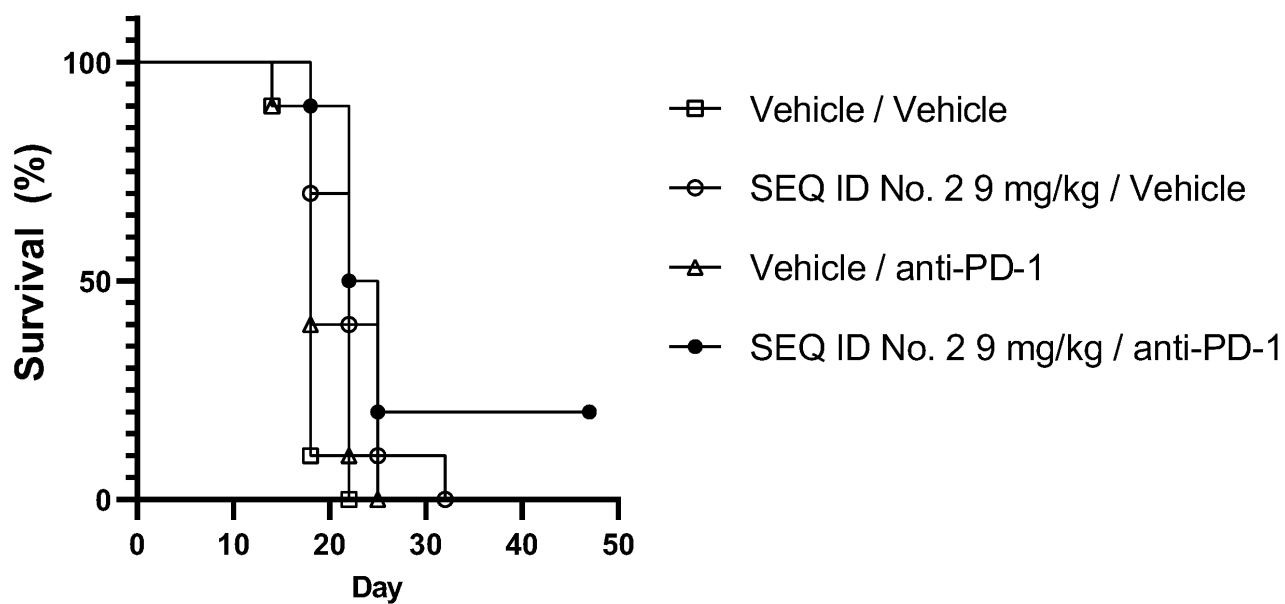


Fig. 5B