CLAIMS

What is claimed is:

1. Use of the fusion protein of SEQ ID NO: 1 in the manufacture of a medicament for treating cancer in a patient, wherein the fusion protein is to be administered at a dose of at least about 6 µg/kg/day to about 15 µg/kg per day.

2. The use of claim 1, wherein:

the dose is 6 µg/kg/day, 8 µg/kg/day, 10 µg/kg/day, 12 µg/kg/day, 14 µg/kg/day, or 15 µg/kg/day;

the patient has an improved safety profile as compared to a patient receiving high dose recombinant human IL-2 (rhIL-2) treatment, optionally wherein the patient has a lower risk of capillary leak syndrome or cytokine release syndrome;

the dose is to be administered by intravenous (I.V.) injection or infusion;

the dose is a fixed dose based on a 60-70 kg human;

the dose is a fixed dose and wherein the patient is a child, optionally wherein the child weighs about 15 kg to about 50 kg;

the use results in at least a partial response in the patient;

the use further comprises repeated administration of the fusion protein if the cancer reoccurs, or a new cancer develops in the patient; or

the mean fold change from baseline (FCB) in IFNγ present in a patient's peripheral blood, serum or plasma is at least about 2-fold, at least about 3-fold, at least about 4-fold, or at least about 5-fold.

3. The use of claim 1, wherein administration results in a dose dependent increase in circulating NK cells and CD8+ cells in a patient in the absence of a dose dependent increase in T regulatory (Treg) cells, optionally wherein:

the increase in circulating NK cells and CD8+ cells is at least 2 fold over baseline;

the increase in circulating NK cells and CD8+ cells is greater relative to the increase in circulating Treg cells;

an increase in circulating NK cells and CD8+ cells is greater relative to the increase in circulating Treg cells as compared to the increase in circulating NK cells

and CD8+ cells relative to the increase in circulating Treg cells in a patient receiving high dose rhIL-2 treatment; and/or

the patient has a lower risk of capillary leak syndrome.

4. The use of claim 1, wherein the cancer being treated is a solid tumor or a blood cancer, optionally wherein:

the solid tumor is a carcinoma, sarcoma or lymphoma;

the cancer being treated is renal cell carcinoma (RCC), melanoma, breast cancer, pancreatic cancer, prostate cancer, non-small cell lung cancer, liver cancer, colon and rectal cancer, bladder cancer, cervical cancer, thyroid cancer, esophageal cancer, oral cancer, mesothelioma, and non-melanoma skin cancer;

the blood cancer is leukemia, non-Hodgkin lymphoma, Hodgkin lymphoma and multiple myeloma; and/or

the size of the solid tumor is reduced.

5. The use of claim 1, wherein the fusion protein of SEQ ID NO: 1 is to be administered by intravenous injection or infusion at a dose of at least about 6 µg/kg to about 15 µg/kg per day as a once a day administration for about 1 day to about 5 days, optionally wherein:

the fusion protein is to be administered once a day for at least about 2 consecutive days, at least about 3 consecutive days, at least about 4 consecutive days, or at least about 5 consecutive days;

the fusion protein is to be administered once a day on non-consecutive days for no more than about 5 total non-consecutive of days of administration; and/or

the fusion protein is to be administered followed by a rest period of at least about 9 consecutive days, optionally wherein the rest period is at least about 16 consecutive days.

6. The use of claim 1, wherein the fusion protein of SEQ ID NO: 1 is to be administered in at least two courses of treatment, the first course of treatment comprising administration by intravenous injection or infusion at a dose of at least about 6 µg/kg to about 15 µg/kg per day for a period of about 1 to about 5 consecutive or non-consecutive days followed by a rest period of at least about 9 consecutive days

followed by a second course of treatment wherein the fusion protein of SEQ ID NO: 1 is to be administered by intravenous injection or infusion at a dose of at least about 6 µg/kg to about 15 µg/kg per day for a period of at least about 1 to at least about 5 consecutive or nonconsecutive days, followed by a rest period of at least about 9 consecutive days, optionally wherein:

administration of the fusion protein for the first course of treatment and for the second course of treatment is for a period of 5 consecutive days or 5 non-consecutive days prior to a rest period of at least about 9 days, optionally wherein the rest period is at least about 16 days or wherein the rest period during the first course of treatment is about 9 consecutive days and wherein the rest period for the second course of treatment is about 16 or more consecutive days;

the second course of treatment begins at least about 24 hours or more after completion of the first course of treatment; and/or

the use further comprises a third course of treatment following the second course of treatment, optionally wherein:

the third course of treatment begins within about 24 hours or more after completion of the second course of treatment;

the use further comprises a fourth course of treatment following the third course of treatment, optionally wherein the fourth course of treatment begins about 24 hours or more after completion of the third course of treatment; and/or

wherein subsequent courses of treatment begin about 24 hours or more after completion of the prior course of treatment until the cancer is treated or until the patient is no longer benefitting from the treatment.

7. The use of claim 1, wherein a therapeutically effective amount of a therapeutic agent is to be further co-administered to the patient, optionally wherein the therapeutic agent is a PARP inhibitor, a cytotoxic agent, a chemotherapeutic agent, or an immune checkpoint inhibitor, optionally wherein the immune checkpoint inhibitor inhibits the interaction of PD-1 and PD-L1, optionally wherein the immune checkpoint inhibitor is pembrolizumab.

8. The use of claim 7, wherein the fusion protein of SEQ ID NO: 1 is to be administered in at least two courses of treatment, the first course of treatment comprising

administration by intravenous injection or infusion at a dose of at least about 6 µg/kg to about 15 µg/kg per day once a day for 1 to 5 days followed by a rest period of at least about 16 consecutive days followed by a second course of treatment wherein a dose of at least about 6 µg/kg to about 15 µg/kg per day is to be administered by intravenous injection or infusion for a period 1 to 5 consecutive days, followed by a rest period of at least about 16 consecutive days and wherein pembrolizumab is to be co-administered once during the 1 to 5 days of administration during the first course and second course of treatment.

9. The use of claim 7, wherein:

the fusion protein is to be administered once a day for at least about 2 consecutive days, at least about 3 consecutive days, at least about 4 consecutive days, or at least about 5 consecutive days;

the fusion protein of SEQ D NO: 1 is to be administered once a day on non-consecutive days for no more than about 5 total non-consecutive of days of administration;

the second course of treatment begins at least about 24 hours or more after completion of the first course of treatment; and/or

the use further comprises a third course of treatment following the second course of treatment, optionally wherein:

the third course of treatment begins within about 24 hours or more after completion of the second course of treatment;

the use further comprises a fourth course of treatment following the third course of treatment, optionally wherein the fourth course of treatment begins about 24 hours or more after completion of the third course of treatment; and/or

wherein subsequent courses of treatment begin about 24 hours or more after completion of the prior course of treatment until the cancer is treated or until the patient is no longer benefitting from the treatment.

10. The use of claim 8, wherein the pembrolizumab is to be co-administered prior to, simultaneously with, or subsequent to, administration of the fusion protein of SEQ ID NO:1, optionally wherein:

the pembrolizumab is to be co-administered in a separate composition from the fusion protein of SEQ ID NO: 1;

the pembrolizumab is to be co-administered in an amount of 200 mg by I.V. injection or infusion;

the pembrolizumab is to be administered on the first day of administration of the fusion protein of SEQ ID NO: 1 during the first course of treatment;

the pembrolizumab is to be administered on the first day of administration of the fusion protein of SEQ ID NO: 1 during the second course of treatment; and/or

the pembrolizumab is to be administered on the first day of administration of the fusion protein of SEQ ID NO: 1 during subsequent courses of treatment.

11. The use of claim 7 resulting in a dose dependent increase in circulating NK cells and CD8+ cells in a patient in the absence of a dose dependent increase in T regulatory (Treg) cells, optionally wherein:

the dose dependent increase in circulating NK cells and CD8+ cells is greater than the non-dose dependent increase in Treg cells;

the patient has an improved safety profile as compared to a patient receiving high dose recombinant human IL-2 (rhIL-2) treatment;

the patient has a lower risk of cytokine release syndrome as compared to a patient receiving high dose recombinant human IL-2 (rhIL-2) treatment; and/or

the patient has a lower risk of capillary leak syndrome as compared to a patient receiving high dose recombinant human IL-2 (rhIL-2) treatment.

12. Use of the fusion protein of SEQ ID NO: 1 in the manufacture of a medicament for treating cancer in a patient, wherein the fusion protein is to be administered to the patient at a dose of at least about 40 µg/kg to about 70 µg/kg per day once weekly.

13. The use of claim 12, wherein the daily dose is about 50 µg/kg to about 60 µg/kg.

14. Use of the fusion protein of SEQ ID NO: 1 in the manufacture of a medicament for treating cancer in a patient, wherein the fusion protein is to be administered to the patient at a dose of at least about 50 µg/kg to about 60 µg/kg per day once weekly, resulting in a dose dependent increase in circulating NK cells and CD8+ cells in a patient in the absence of a dose dependent increase in circulating T regulatory (Treg)

cells and wherein the increase in circulating NK cells and CD8+ cells relative to the increase in circulating T regulatory (Treg) is greater compared to the increase in circulating NK cells and CD8+ cells relative to the increase in circulating T regulatory (Treg) in a patient receiving high dose recombinant human IL-2 (rhIL-2) treatment, and wherein the patient has a lower risk of capillary leak syndrome as compared to a patient receiving high dose recombinant human IL-2 (rhIL-2) treatment, optionally wherein the dose is to be administered by intravenous injection or infusion.

15. A pharmaceutical composition comprising about 0.4 to about 1 mg of the fusion protein of SEQ ID NO: 1.

16. Use of the fusion protein of SEQ ID NO: 1 in the manufacture of a medicament for treating cancer in a patient, wherein the fusion protein is to be administered to the patient at a daily dose of at least about 3 µg/kg to about 5.5 µg/kg, wherein administration results in a dose dependent increase in circulating NK cells and CD8+ cells in a patient in the absence of a dose dependent increase in circulating T regulatory (Treg) cells and wherein the increase in circulating NK cells and CD8+ cells is greater relative to the increase in circulating T regulatory cells (Treg).

17. Use of the fusion protein of SEQ ID NO: 1 in the manufacture of a medicament for treating cancer in a patient, wherein a dose of at about 16 µg/kg/day to about 70 µg/kg/day or a corresponding fixed dose based on an about 60-70 kg adult or about 12 kg to 50 kg or more child is to be intravenously administered to the patient.

18. The use of claim 17, wherein the dose is about 16 µg/kg/day to about 50 µg/kg/day of the fusion protein of SEQ ID NO: 1 or a corresponding fixed dose based on an about 60-70 kg adult or about 12 kg to 50 kg or more child, optionally wherein the corresponding fixed dose is about 5 µg to about 3 mg;

the mean fold change from baseline (FCB) in IFNγ present in a patient's peripheral blood, serum or plasma is at least about 2-fold, at least about 3-fold, at least about 4-fold, or at least about 5-fold; and/or

the fusion protein of SEQ ID NO: 1 is to be administered on non-consecutive days, optionally wherein:

the fusion protein of SEQ ID NO: 1 is to be administered once every 7 days, once every 14 days or once every 21 days of a treatment cycle;

the fusion protein of SEQ ID NO: 1 is to be administered on days 1, 7, 14 and 21 of a treatment cycle;

the fusion protein of SEQ ID NO: 1 is to be administered on days 1 and 14 of a treatment cycle; or

the fusion protein of SEQ ID NO: 1 is to be administered on days 1 and 21 of a treatment cycle.

19. The use of claim 2, wherein: the mean fold change from baseline in IL-6 is less than 4-fold; and/or the dose of the fusion protein of SEQ ID NO: 1 is about 6 µg/kg/day or about 8 µg/kg/day.

20. The use of claim 17 wherein: the mean fold change from baseline in IL-6 is less than 4-fold; and/or the dose of the fusion protein of SEQ ID NO: 1 is about 30 µg/kg/day or about 50 µg/kg/day.