Claims

We claim:

1. A composition comprising:

i) a phosphorylated form of a fusion polypeptide comprising:

a) an immunomodulatory polypeptide comprising an interleukin-12 immune agonist moiety; and

b) a metal hydroxide-binding polypeptide,

whose amino acid sequence includes a plurality of phosphorylation sites, so that the fusion polypeptide can adopt phosphorylated and unphosphorylated forms;

ii) Tris buffer;

iii) salt;

iv) sucrose;

v) L-methionine; and

vi) a surfactant,

wherein the pH of the composition is within the range of about 6.5 and about 8.

2. The composition according to claim 1, wherein the fusion polypeptide, when exposed to a metal-hydroxide, forms a complex therewith, optionally wherein the metal hydroxide is an aluminum hydroxide.

3. The composition according to claim 1 or 2, wherein the pH is within the range about 6.5 and about 7.8, or about 7 and about 7.6, or about 7.3 to about 7.4.

4. The composition according to any of claims 1-3, wherein the concentration of the fusion polypeptide is within the range of about 0.1 g/L and about 15 g/L, or about 0.5 g/L and about 5 g/L, or about 1 g/L and about 3 g/L, or wherein the concentration of the fusion polypeptide is about 2 g/L.

5. The composition according to any of the preceding claims, wherein the concentration of Tris buffer is within the range of about 1 mM and about 50 mM, or about 10 mM and about 25 mM;

wherein the concentration of salt is within the range of about 1 mM and about 750 mM, or about 10 mM and about 100 mM, optionally wherein the salt is NaCl or Na_2SO_4;

wherein the concentration of L-methionine is within the range of about 1 mM and about 20 mM, or about 5 mM and about 15 mM, or about 10 mM;

wherein the concentration of polysorbate is within the range of about 0.005% w/v and about 0.1% w/v, or about 0.01% w/v and about 0.05% w/v, or about 0.02% w/v, optionally wherein the surfactant is a polysorbate, and further optionally polysorbate 20 or polysorbate 80; and/or

wherein the concentration of sucrose is within the range of about 100 mM and about 200 mM, or about 150 mM.

6. The composition according to any of the preceding claims, wherein the composition comprises 2 mg/mL fusion polypeptide, 20 mM Tris buffer, 50 mM NaCl, 10 mM L-methionine, 0.02% polysorbate 20, and 150 mM sucrose, and wherein the pH of the composition is within the range of 6.5 and 8.

7. A pharmaceutical formulation comprising

i) a fusion polypeptide metal-hydroxide complex comprising:

(a) a phosphorylated form of a fusion polypeptide comprising:

ai) an immunomodulatory polypeptide comprising an interleukin-12 immune agonist moiety; and

aii) a metal hydroxide-binding polypeptide

wherein the fusion polypeptide metal-hydroxide complex amino acid sequence includes a plurality of phosphorylation sites, so that it can adopt phosphorylated and unphosphorylated forms; and

(b) a metal hydroxide

ii) Tris buffer;

iii) salt;

iv) sucrose;

v) L-methionine; and

vi) a surfactant,

wherein the pH of the composition is within the range of about 6.5 and about 8.

8. The pharmaceutical formulation of claim 7, wherein the metal hydroxide is an aluminum hydroxide, optionally wherein the concentration of the aluminum hydroxide is within the range of about 0.5 mg/mL and about 10 mg/mL, or about 1 mg/mL and about 5 mg/mL, or wherein the concentration of the aluminum hydroxide is about 2.5 mg/mL.

9. The pharmaceutical formulation of claims 7 or 8, wherein the concentration of Tris buffer is within the range of about 1 mM and about 50 mM, or about 10 mM and about 40 mM, or about 15 mM and about 20 mM;

wherein the concentration of salt is within the range of about 1 mM and about 100 mM, or about 20 mM and about 60 mM, or about 38 mM and about 50 mM, optionally wherein the salt is NaCl or Na_2SO_4;

wherein the concentration of L-methionine is within the range of about 1 mM and about 20 mM, or about 5 mM and about 15 mM, or about 7.5 mM and about 10 mM;

wherein the concentration of polysorbate is within the range of about 0.005% w/v and about 0.1% w/v, or about 0.01% w/v and about 0.05% w/v, or about 0.015% w/v, optionally wherein the surfactant is a polysorbate, further optionally polysorbate 20 or polysorbate 80; and/or

wherein the concentration of sucrose is within the range of about 100 mM and about 200 mM, or about 113 mM.

10. The pharmaceutical formulation of claims 7-9, wherein the composition comprises 0.25 mg/mL fusion polypeptide, 15 mM Tris buffer, 38 mM NaCl, 7.5 mM L-methionine, 0.015% polysorbate 20, and 113 mM sucrose, 2.5 mg/mL aluminum hydroxide and wherein the pH of the composition is within the range of 6.5 and 8.

11. The pharmaceutical formulation of claims 7-10, wherein the formulation is formulated for parenteral delivery, optionally for intratumoral injection, peritumoral injection, or into a tumor-draining lymph node.

12. The composition of claim 1 or the pharmaceutical formulation according to claim 7 for use as a medicament.

13. The composition of claim 1 or the pharmaceutical formulation according to claim 7 for use in treating cancer in a subject, optionally wherein the cancer is associated with a tumor.

14. A method of manufacturing a composition of claim 1, the method comprising combining the phosphorylated form of the fusion polypeptide with a Tris buffer, salt, sucrose, L-methionine and a surfactant.

15. A method of manufacturing a pharmaceutical formulation of claim 6, the method comprising contacting the composition of claim 1 with a metal-hydroxide.

16. A method of characterizing a composition of claim 1, the method comprising assessing degree of phosphorylation of the fusion polypeptide, and optionally assessing the purity of the fusion polypeptide in the composition.