CLAIMS

1. A liquid pharmaceutical composition comprising an IL-15/IL-15Rα complex and about 0.0001% to Q about 1% (w/v) of a surfactant.

2. The composition according to claim 1, wherein:

(i) the composition further comprises about 1 mM to about 100 mM of a buffering agent providing a pH in the range of from about 4.5 to about 8.5(ii) the composition further comprises about 1 mM to about 500 mM of at least one stabilizer;

(iii) the surfactant is a poloxamer, optionally wherein the poloxamer is poloxamer 188 and/or optionally wherein the poloxamer is present at a concentration of about 0.05% to about 0.5% (w/v); and/or

(iv) the surfactant is a polysorbate, optionally wherein the polysorbate is polysorbate 20 or polysorbate 80, and/or

(v) the surfactant is at a concentration of about 0.01% to about 0.1% (w/v).

3. The composition according to claim 2, wherein:

(i) the buffering agent is an acetate buffer, a succinate buffer, a citrate buffer, or a histidine buffer, optionally wherein the buffering agent is an acetate buffer, optionally wherein the acetate buffer is Na-acetate buffer, and/or

(ii) the buffering agent is at a concentration of about 10 mM to about 50 mM, optionally wherein the buffering agent is at a concentration of about 15 mM to about 30 mM;

optionally wherein the buffering agent is at a concentration of about 20 mM, optionally wherein the buffering agent provides a pH of about 4.7 to about 5.5.

4. The composition according to claim 2 or 3, wherein:

(i) the at least one stabilizer is a polyol or a sugar;

(ii) the at least one stabilizer is a sugar, wherein the sugar is sucrose; and/or

(iii) the at least one stabilizer is present at a concentration of about 100 mM to about 350 mM, optionally wherein:

(a) the at least one stabilizer is present at a concentration of about 220 mM to about 300 mM, and/or

(b) the at least one stabilizer is present at a concentration of about 260 mM.

5. The composition according to any one of the preceding claims, wherein:

(i) the concentration of the IL-15/IL-15Rα complex is about 0.1 mg/mL to about 50 mg/mL, optionally wherein the concentration of the IL-15/IL-15Rα complex is about 0.1 mg/mL to about 10 mg/mL; and/or

(ii) the composition comprises about 1 mg/mL of the IL-15/IL-15Rα complex, about 0.2% (w/v) of the surfactant, wherein the surfactant is Poloxamer 188, and further comprising about 260 mM Sucrose, and about 20 mM Na-acetate buffer, wherein the composition has a pH of about 5.0.

6. The composition of any one of the preceding claims, comprising:

(a) about 1 mg/mL of the IL-15/IL-15Rα complex and about 0.2% (w/v) of the surfactant, wherein the surfactant is Poloxamer 188, and further comprising about 260 mM Sucrose and about 20 mM Na-acetate buffer, wherein the composition has a pH of about 4.7; or

(b) about 0.1 mg/mL to about 10 mg/ml of IL-15/IL-15Rα complex and about 0.1% to about 0.5% (w/v) of the surfactant, wherein the surfactant is Poloxamer 188, and further comprising about 180 mM to about 260 mM sucrose and about 10 mM to about 30 mM Na-acetate buffer, wherein the composition has a pH of about 4.5 to about 5.5; optionally wherein the pH is about 4.7 or 5.0.

7. The liquid pharmaceutical composition of any one of the preceding claims, wherein the surfactant is poloxamer 188, and further comprising sucrose and Na-acetate buffer, wherein the pH of the composition is from about 4.5 to about 5.5;
optionally wherein the pH is about 4.7 or 5.0.

8. The composition according to any one of the preceding claims, comprising:

(a) about 1 mg/mL of the IL-15/IL-15Rα complex, about 0.2% (w/v) of the surfactant, wherein the surfactant is Poloxamer 188, and further comprising about 260 mM Sucrose and about 20 mM Na-acetate buffer; or

(b) about 0.1 mg/mL to about 10 mg/ml of IL-15/IL-15Rα complex, about 0.1% to about 0.5% (w/v) of the surfactant, wherein the surfactant is Poloxamer 188, and further comprising about 180 mM to about 260 mM sucrose and about 10 mM to about 30 mM Na-acetate buffer.

9. A solid pharmaceutical composition comprising an IL-15/IL-15Rα complex and about 10 mM to about 50 mM of a buffering agent providing a pH in the range of from about 6.5 to about 8.5, about 1 mM to about 500 mM of at least one stabilizer and about 0.1 mM to about 50 mM of at least one tonicity agent.

10. The composition according to claim 9, wherein:

(i) the buffering agent is a phosphate buffer, an acetate buffer, a succinate buffer, a citrate buffer, or a histidine buffer, optionally wherein the buffering agent is Na/K phosphate buffer;

(ii) the composition comprises about 1 mM to about 50 mM of the buffering agent, optionally wherein the composition comprises about 1 mM to about 5 mM of the buffering agent;

(iii) the pH of the composition is about 6.5 to about 7.5, optionally wherein the pH of the composition is about 7.3;

(iv) the composition further comprises about 1 mM to about 500 mM of at least two stabilizers;

(v) the composition comprises about 1 mM to about 500 mM sucrose and about 1 mM to about 500 mM mannitol;

(vi) the composition comprises about 5 mM to about 50 mM sucrose and about 100 mM to about 300 mM mannitol.;

(vii) the composition comprises about 30 mM sucrose and about 220 mM mannitol;

(viii) the composition further comprises about 0.1 mM to about 50 mM of at least two tonicity agents;

(ix) the composition comprises about 0.1 mM to about 50 mM KCl and about 0.1 mM to about 50 mM NaCl;

(x) the composition comprises about 0.1 mM to about 1 mM KCl and about 10 mM to about 50 mM NaCl, optionally wherein the composition comprises about 0.375 mM KCl and about 20 mM NaCl;

(xi) the composition comprises about 0.1 mg/mL to about 50 mg/mL of IL-15/IL-15Rα complex, optionally wherein:

(a) the composition comprises about 0.1 mg/mL to about 10 mg/mL of IL-15/IL-15Rα complex, and/or

(b) the composition comprises about 0.1 mg/mL to about 0.5 mg/mL of IL-15/IL-15Rα complex;

(xii) the composition is lyophilized

; and/or

(xiii) the composition comprises about 0.24 mg/mL IL-15/IL-15Rα complex, about 30 mM sucrose, about 220 mM mannitol, about 0.375 mM potassium chloride, about 20 mM NaCl, about 1.35 mM Na/K phosphate buffer at pH of about 7.3.

11. The composition according to any one of the preceding claims, wherein:

(i) the IL-15/IL-15Rα complex comprises IL-15 comprising SEQ ID NO: 2;

(ii) the IL-15/IL-15Rα complex comprises IL-15Rα comprising SEQ ID NO: 5; and/or

(iii) the IL-15/IL-15Rα complex comprises IL-15 comprising SEQ ID NO: 2 and IL-15Rα comprising SEQ ID NO: 5.

12. Use of the composition according to any one of claims 1-11 in the manufacture of a medicament for treating a disorder in a subject, wherein the disorder is selected from the group consisting of cancer, lymphopenia, immunodeficiencies, infectious diseases, and wounds.

13. The use according to claim 12, wherein the disorder is cancer, optionally wherein:
(a) the cancer is selected from the group consisting of: bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, anal cancer, gastro-esophageal, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Merkel cell cancer, Hodgkin lymphoma, non-Hodgkin lymphoma, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, solid tumors of childhood, lymphocytic lymphoma, cancer of the bladder, multiple myeloma, myelodysplastic syndromes, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers, and combinations of said cancers;
(b) the cancer is melanoma, renal cancer, colon cancer, or prostate cancer
; and/or
(c) the cancer is metastatic.

14. A dosage form comprising the composition of any one of claims 1 to 11.

15. A vial comprising the composition according to any one of claims 1 to 11.

16. A syringe comprising the composition according to any one of claims 1 to 11.

17. An autoinjector comprising the syringe of claim 16.

18. An autoinjector comprising the composition according to any one of claims 1-11.

19. The composition according to any one of claims 1-8 or 11, wherein the liquid composition maintains:

a. about 0.1% to about 0.25% sum of aggregates upon storage at 2-8°C for 24 weeks;

b. about 0.15% to about 0.35% sum of aggregates upon storage at 25 ºC for 12 weeks;

c. about 0.3% to about 0.6% sum of aggregates upon storage at 40ºC for 6 weeks;

d. about 0.25% to about 0.75% sum of fragments upon storage at 2-8°C for 24 weeks;

e. about 1.5% to about 2.0% sum of fragments upon storage at 25 ºC for 12 weeks;

f. about 2.5% to about 3.5% sum of fragments upon storage at 40ºC for 6 weeks;

g. about 42.5% to about 45% sum of basic variants upon storage at 2-8°C for 24 weeks;

h, about 55% to about 57.5% sum of acid variants storage at 2-8°C for 24 weeks;

i about 38% to about 42% sum of basic variants upon storage at 25ºC for 12 weeks;

j. about 55% to about 60% of acidic variants upon storage at 25ºC for 12 weeks;

k. about 65% to about 67% of IL-15Rα by CE-SDS upon storage at 2-8°C for 24 weeks;

l. about 17% to about 19% of IL-15 by CE-SDS upon storage at 2-8°C for 24 weeks;

m. about 7% to about 8% of IL-15 HMW by CE-SDS upon storage at 2-8°C for 24 weeks;

n. about 5% to about 6% aglycosylated IL-15 by CE-SDS upon storage at 2-8°C for 24 weeks;

o. about 2% to about 4% sum of impurities by RP-HPLC upon storage at 2-8°C for 24 weeks;

p. about 3% to about 5% sum of impurities by RP-HPLC upon storage at 25ºC for 12 weeks;

q. below 5% sum of impurities by RP-HPLC upon storage at 40ºC for 6 weeks;

r. substantially no SVP >2μm by PAMAS upon storage at 2-8°C for 24 weeks;

s. substantially no SVP >10μm by PAMAS upon storage at 2-8°C for 24 weeks;

t. below 1.0 NTU turbidity upon storage at 2-8°C for 24 weeks;

u. below 0.25% sum of aggregates assessed by SEC after being subjected to five freeze/thaw cycles or overnight shaking; or

v, below 0.35% sum of fragment assessed by SEC after being subjected to five freeze/thaw cycles or overnight shaking.