CLAIMS

1. A fusion protein comprising:

(a) an extended recombinant polypeptide characterized in that:

i) it comprises at least 12 amino acid residues;

ii) at least 90% of the amino acid residues of the extended recombinant polypeptide are selected from glycine (G), alanine (A), serine (S), threonine (T), glutamate (E) and proline (P); and

iii) it has 4–6 different amino acid residues selected from G, A, S, T, E and P; and

(b) a cytokine; and

(c) a linker joining the cytokine and the extended recombinant polypeptide, wherein the linker comprises a release segment (RS).

2. The fusion protein of claim 1, wherein said fusion protein comprises 1, 2, 3, 4 or more extended recombinant polypeptides.

3. The fusion protein of claim 1, wherein said fusion protein further comprises a tumor targeting domain.

4. The fusion protein of claim 1, wherein saidRS is capable of being cleaved by at least one mammalian protease.

5. The fusion protein of claim 1, wherein the fusion protein has a structural arrangement, from N- to C-terminus of XTEN-RS-cytokine or cytokine-RS-XTEN.

6. The fusion protein of claim 1, wherein the cytokine is selected from a group consisting of interleukins, chemokines, interferons, tumor necrosis factors, colony-stimulating factors, or TGF-Beta superfamily members.

7. The fusion protein of claim 6, wherein the cytokine is IL-12 or an IL-12 variant.

8. The fusion protein of claim1, wherein the cytokine comprises a first cytokine fragment (Cy1) and a second cytokine fragment (Cy2).

9. The fusion protein of claim 8, wherein Cy1 comprises an IL-12 p35 subunit.

10. The fusion protein of claim 9, wherein Cy2 comprises IL-12 p40 subunit.

11. The fusion protein of any one of claim 8, wherein the cytokine comprises a linker positioned between the first cytokine fragment (Cy1) and the second cytokine fragment (Cy2).

12. The fusion protein of claim 11, wherein said fusion protein comprises a Cy1 fragment that comprises an extended recombinant polypeptide at the C-terminus.

13. The fusion protein of claim 11, wherein said fusion protein comprises a Cy2 fragment that comprises an extended recombinant polypeptide at the N terminus and an extended recombinant polypeptide at the C-terminus.

14. The fusion protein of any one of claims 1-13, wherein the extended recombinant polypeptide sequence consists of multiple non-overlapping sequence motifs, wherein the sequence motifs are selected from the sequence motifs of Table 1.

15. A pharmaceutical composition, comprising the fusion protein of any one of the claims 1-14 and at least one pharmaceutically acceptable carrier.

16. Use of the fusion protein of any one of claims 1-14 or the pharmaceutical composition of claim 15 in the manufacture of a medicament for treating or preventing a disease or condition in a subject.

17. The use of claim 16, wherein the disease or condition is a cancer or a cancer-related disease or condition.

18. The use of claim 16 or claim 17, wherein the medicament further comprises at least one immune checkpoint inhibitor.

19. A fusion protein comprising a disulfide-linked heterodimer,

wherein the disulfide-linked heterodimer comprises a first subunit and a second subunit,

wherein the first subunit comprises the following elements in a N-to-C terminal or a C-to-N terminal orientation:

(a) an extended recombinant polypeptide characterized in that:

i) it comprises at least 12 amino acid residues;

ii) at least 90% of the amino acid residues of the extended recombinant polypeptide are selected from glycine (G), alanine (A), serine (S), threonine (T), glutamate (E) and proline (P); and

iii) it has 4–6 different amino acid residues selected from G, A, S, T, E and P;

(b) a release segment (RS); and

(c) a first cytokine fragment (Cy1);

wherein the second subunit comprises the following elements in a N-to-C terminal or a C-to-N terminal orientation:

(d) an extended recombinant polypeptide characterized in that:

i) it comprises at least 12 amino acid residues;

ii) at least 90% of the amino acid residues of the extended recombinant polypeptide are selected from glycine (G), alanine (A), serine (S), threonine (T), glutamate (E) and proline (P); and

iii) it has 4–6 different amino acid residues selected from G, A, S, T, E and P;

(e) a release segment (RS); and

(f) a second cytokine fragment (Cy2).

20. The fusion protein of claim 35, wherein Cy1 is an IL-12 p35 subunit.

21. The fusion protein of claim 35, wherein Cy2 is an IL-12 p40 subunit.

22. A kit comprising at least a first container, the first container comprising:

(a) an amount of a fusion protein sufficient to treat a disease, condition, or disorder upon administration to a subject in need thereof,

(b) an amount of a pharmaceutically acceptable carrier, together in a formulation

ready for injection or for reconstitution with sterile water, buffer, or dextrose.

23. The kit of claim 35, wherein the kit further comprises:

(a) a label identifying the fusion protein, storage and handling conditions,

(b) a sheet of the approved indications for the fusion protein,

(c) instructions for the reconstitution and/or administration of the fusion protein for the use for the prevention and/or treatment of an approved indication,

(d) appropriate dosage and safety information,

(e) information identifying the lot and expiration of the drug, or

(f) any combination of (a)-(e).