CLAIMS

1. A pharmaceutical composition comprising:

substantially spherical particles formed of PLGA-PEG block co-polymers, the particles having a size in the range of about 100 to 200 nm, a surface charge of about 0 to -20 mV, and from about 100 to 1500 protein ligands per particle, the protein ligands optionally coupled through a sulfhydryl-maleimide chemistry;

wherein the protein ligands are covalently coupled to said PLGA-PEG block co-polymers through surface functional groups at the end of the PEG portion of the polymer that faces outwards away from the surface of the particle;

the protein-ligands comprising:

a population of anti-CD28 antibody ligands;

a population of HLA ligands;

with one or more antigenic peptides bound to the HLA ligands for presentation to T cells; and a pharmaceutically acceptable carrier for intravenous, intra-arterial, subcutaneous, intradermal, intralymphatic, or intra-tumoral administration.

2. The pharmaceutical composition of claim 1, wherein the PLGA is a polymer of about 50% lactic acid (LA) and 50% glycolic acid (GA).

3. The pharmaceutical composition of claims 1 or 2, wherein the PLGA polymer has a molecular weight of from about 25K to about 35K, and the PEG has a molecular weight of from about 3K to about 10K.

4. The pharmaceutical composition of any one of claims 1 to 3, having from 400 to 1000 ligands per particle.

5. The pharmaceutical composition of any one of claims 1 to 4, wherein the anti-CD28 antibody ligands comprise a human IGHV4-59 germline framework optionally having from 5 to 15 murine framework residues, a IGKV4-01 germline framework optionally having from 3 to 15 murine framework residues, and wherein the anti-CD28 antibody ligands optionally comprise a murine 9.3 monoclonal antibody variable region.

6. The pharmaceutical composition of any one of claims 1 to 4, wherein the anti-CD28 antibody ligand is an antigen-binding antibody fragment.

7. The pharmaceutical composition of claim 6, wherein the anti-CD28 ligand comprises a scFv.

8. The pharmaceutical composition of any one of claims 1 to 7, wherein the HLA ligand is dimeric.

9. The pharmaceutical composition of claim 8, wherein the HLA ligands is HLA-A*02:01.

10. The pharmaceutical composition of claim 8 or 9, wherein the HLA comprises an immunoglobulin fusion.

11. The pharmaceutical composition of claim 10, wherein the anti-CD28 antibody ligand and the HLA-A*02:01 immunoglobulin fusion have an IgG4 constant region with mutations at S241 and L248, and a Cysteine at codon 473.

12. The pharmaceutical composition of claim 11, wherein the anti-CD28 antibody ligands and/or the HLA ligands are conjugated to the particles through the Cysteine at codon 473 of the immunoglobulin heavy chain.

13. The pharmaceutical composition of claim 11 or 12, wherein the HLA ligands are conjugated to the particles through the Cysteine at codon 473 of the immunoglobulin heavy chain.

14. The pharmaceutical composition of claim 1, wherein the HLA ligands comprise an extracellular domain of HLA, and are HLA monomers linked to the particle through a peptide or chemical linker attached to the C-terminus of the HLA extracellular domain, and wherein the HLA is optionally HLA-A2.

15. The pharmaceutical composition of claim 1, wherein the HLA ligands comprise an extracellular domain of HLA, and are HLA monomers linked to both a scFv of an anti-CD28 ligand and the particle through one or more peptide or chemical linkers, and wherein the HLA is optionally HLA-A2.

16. The pharmaceutical composition of any one of claims 1 to 15, wherein the composition is lyophilized.

17. The pharmaceutical composition of any one of claims 1 to 16, wherein the protein ligands comprise an antigen present complex having two humanized or human immunoglobulin heavy chain amino acid sequences joined by disulfide bonds, each heavy chain being fused above the hinge region to an HLA amino acid sequence, wherein the constant region of each heavy chain comprises an unpaired cysteine directly coupled to the particle, wherein the antigen presenting complex does not contain an immunoglobulin light chain or an immunoglobulin heavy chain variable domain sequence.

18. The pharmaceutical composition of any one of claims 1 to 17, wherein the one or more antigenic peptides are tumor associated antigens.

19. The pharmaceutical composition of any one of claims 1 to 17, wherein the one or more antigenic peptides are of an infectious disease.

20. Use of the pharmaceutical composition of any one of claims 1 to 19 for the manufacture of a medicament for inducing the formation of antigen-specific cytotoxic T cells in a patient.

21. The use of claim 20, wherein the patient is a cancer patient.

22. The use of claim 20 or 21, wherein the patient is undergoing or has undergone therapy with one or more checkpoint inhibitors.

23. The use of claim 20, wherein the patient has a solid tumor.

24. The use of claim 20, wherein the patient has a hematological tumor.