CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising a population of human T cells, wherein the population of human T cells include human T cells that comprise a nucleic acid molecule comprising:

a first nucleic acid sequence that encodes modified programmed cell death protein 1 (PD-1), which comprises the amino acid sequence of SEQ ID NO: 13, and

a second nucleic acid sequence that encodes a chimeric antigen receptor (CAR) comprising:

an extracellular domain that recognizes a tumor antigen, a transmembrane domain, and

an intracellular domain comprising a CD3-zeta signaling domain and one or more signaling domains of one or more costimulatory molecules, wherein the modified PD-1 and the CAR are expressed as gene products that are separate polypeptides.

2. The pharmaceutical composition of claim 1, wherein an inhibitory effect induced by a target cell on cytokine production of the human T cells is reduced as compared to human T cells that express the CAR and lack the modified PD-1, and the target cell express the tumor antigen and programmed death ligand 1 (PD-L1).

3. The pharmaceutical composition of claim 1, wherein the tumor antigen is CD19.

4. The pharmaceutical composition of claim 1, wherein the one or more costimulatory molecules include 4-1 BB.

5. A method of reducing an inhibitory effect induced by a target cell on cytokine production of human T cells that express a chimeric antigen receptor (CAR), the method comprising introducing a nucleic acid molecule into the human T cells, wherein:

the nucleic acid molecule that encodes modified programmed cell death protein 1 (PD-1), which comprises the amino acid sequence of SEQ ID NO: 13,

the CAR comprising:

an extracellular domain that recognizes a tumor antigen,

a transmembrane domain, and

an intracellular domain comprising a CD3-zeta domain and one or more signaling domains of one or more costimulatory molecules, the target cell express the tumor antigen and programmed death ligand 1 (PD-L1), and the modified PD-1 and the CAR are expressed as gene products that are separate polypeptides.

6. The method of claim 4, wherein the tumor antigen is CD19.

7. The method of claim 4, wherein the one or more costimulatory molecules include 4-1 BB.