CLAIMS

1. A pharmaceutical composition comprising a first population of ~~T cells, wherein the population comprises a population of cells~~ T-cells comprising a chimeric antigen receptor (CAR) and a mutated endogenous CD5 gene and a second population of T-cells comprising a mutated endogenous CD5 gene, wherein the second population does not comprise the CAR.

2. The pharmaceutical composition of claim 1, wherein the mutated endogenous CD5 gene comprises a mutation in exon 2 of the CD5 gene.

3. The pharmaceutical composition of claim 1, wherein the mutated endogenous CD5 gene comprises an exon 2 deletion of a nucleotide sequence of SEQ ID NO: 23.

~~4. The pharmaceutical composition of any one of claims 1-3, wherein the population comprises a first population of cells comprising a chimeric antigen receptor (CAR) and a second population of cells comprising a mutated endogenous CD5 gene.~~

4~~5~~. The pharmaceutical composition of any one of claims 1-3 ~~1-4~~, wherein the first and second population of T-cells comprising the mutated endogenous CD5 gene has a decrease in expression of endogenous CD5 protein.

5~~6~~. The pharmaceutical composition of any one of claims 1-4 ~~1-5~~, wherein the chimeric antigen receptor comprises an antigen binding domain that binds to CD5, CD 19, CD2, CD7, a tumor-specific antigen (TSA), a tumor associated antigen (TAA), a glioma-associated antigen, carcinoembryonic antigen (CEA), b-human chorionic gonadotropin, alphafetoprotein (AFP), lectin-reactive AFP, thyroglobulin, RAGE-1, MN-CA IX, human telomerase reverse transcriptase, RU1, RU2 (AS), intestinal carboxyl esterase, mut hsp70-2, M-CSF, prostase, prostate-specific antigen (PSA), PAP, NY-ESO-1, LAGE-la, p53, prostein, PSMA, Her2/neu, survivin, telomerase, prostate-carcinoma tumor antigen- 1 (PCTA-1), MAGE, ELF2M, neutrophil elastase, ephrinB2, CD22, insulin growth factor (IGF)-I, IGF-II, IGF-I receptor, mesothelin, MART - 1 /Mel an A (MART -I), gplOO (Pmel 17), tyrosinase, TRP-1, TRP-2, MAGE-1, MAGE-3, BAGE, GAGE-1, GAGE-2, pl5, Ras, BCR-ABL, E2A-PRL, H4-RET, IGH-IGK, MYL-RAR, EBVA, HPV antigen E6, HPV antigen E7, TSP-180, MAGE-4, MAGE-5, MAGE-6, RAGE, NY-ESO, pl85erbB2, pl80erbB-3, c-met, nm-23Hl, PSA, TAG-

72, CA 19-9, CA 72-4, CAM 17.1, NuMa, K-ras, beta-Catenin, CDK4, Mum-1, p 15, p 16, 43-9F, 5T4, 791Tgp72, alpha-fetoprotein, beta-HCG, BCA225, BTAA, CA 125, CA 15-3\CA 27.29\BCAA, CA 195, CA 242, CA-50, CAM43, CD68\P1, CO-029, FGF-5, G250, Ga733\EpCAM, HTgp-175, M344, MA-50, MG7- Ag, MOV18, NB/70K, NY-CO-1, RCAS1, SDCCAG16, TA-90\Mac-2 binding protein\cyclophilin C-associated protein, TAAL6, TAG72, TLP, or TPS.

67. The pharmaceutical composition of any one of claims 1-5 ~~1-6~~, wherein the chimeric antigen receptor comprises an antigen binding domain that binds to CD5.

7. The pharmaceutical composition of claim 1, wherein the first population of T-cells comprises more than one chimeric antigen receptor.

8. The pharmaceutical composition of claim 1, wherein the mutated CD5 gene is a CRISPR mutated CD5 gene.

98. The pharmaceutical composition of any one of claims 1-4 ~~claim 7~~, wherein the antigen binding domain of the CAR comprises a complementarity determining region (CDR) comprising the amino acid sequence selected from the group consisting of SEQ ID NOs: 31-36, 43-48, 53-58, 65-70, 83-88, and 95-100.

109. The pharmaceutical composition of any one of claims 1-4 ~~claim 7~~, wherein the antigen binding domain of the CAR comprises a scFv comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 27, 28, 39, 40, 50, 61, 62, 73, 74, 79, 80, 91, and 92.

1110. The pharmaceutical composition of claim 1 ~~any one of claims 1-5~~, wherein the CAR comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 25, 26, 37, 38, 49, 59, 60, 71, 72, 77, 78, 89, and 90.

1211. ~~A~~ The pharmaceutical composition of claim 5 ~~any one of claims 1-10~~ for treating cancer in a subject, wherein the mutated endogenous CD5 gene is a knock-out of the endogenous CD5 gene.

13~~12~~. The pharmaceutical composition of claim 12~~ 11~~, wherein the cancer is a T cell lymphoma or a T cell leukemia.

14~~13~~. The pharmaceutical composition of claim 12 ~~11~~, wherein the cancer is acute myeloid leukemia (AML), T-cell acute lymphoblastic leukemia (T-ALL), acute lymphoblastic leukemia (ALL), or chronic lymphocytic leukemia (CLL).

15~~14~~. A pharmaceutical composition of claim 5 ~~any one of claims 1-10~~ for enhancing the efficacy of a T-cell comprising a chimeric antigen receptor for treating cancer in a subject, wherein the mutated endogenous CD5 gene is a knock-out of the endogenous CD5 gene.