CLAIMS

1. A pharmaceutical composition comprising a population of T-cells comprising a chimeric antigen receptor (CAR) and a mutated endogenous CD5 gene, wherein the mutated endogenous CD5 gene comprises a mutation in exon 2 of the CD5 gene.

2. The pharmaceutical composition of claim 1, wherein the population of T-cells comprising the mutated endogenous CD5 gene has a decrease in expression of endogenous CD5 protein.

3. The pharmaceutical composition of any one of claims 1-2, 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.

4. The pharmaceutical composition of any one of claims 1-3, wherein the chimeric antigen receptor comprises an antigen binding domain that binds to CD5.

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

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

7. The pharmaceutical composition of any one of claims 1-2, 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.

8. The pharmaceutical composition of any one of claims 1-2, 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.

9. The pharmaceutical composition of claim 1, 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.

10. The pharmaceutical composition of claim 3 for treating cancer in a subject, wherein the mutated endogenous CD5 gene is a knock-out of the endogenous CD5 gene.

11. The pharmaceutical composition of claim 10, wherein the cancer is a T cell lymphoma or a T cell leukemia.

12. The pharmaceutical composition of claim 10, wherein the cancer is acute myeloid leukemia (AML), T-cell acute lymphoblastic leukemia (T-ALL), acute lymphoblastic leukemia (ALL), or chronic lymphocytic leukemia (CLL).

13. A pharmaceutical composition of claim 3 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.

14. A pharmaceutical composition comprising a population of T cells, wherein the population comprises a population of T cells comprising a chimeric antigen receptor (CAR) and a mutated endogenous CD5 gene,

wherein the CAR comprises an antigen binding domain that binds to CD5, and wherein the mutated endogenous CD5 gene comprises a mutation in exon 2 of the CD5 gene.

15. The pharmaceutical composition according to claim 14, wherein the antigen binding domain comprises a variable heavy chain region (VH) and a variable light chain region (VL), wherein the VH comprises an amino acid sequence having at least 90% identity to an amino acid sequence of SEQ ID NO: 75 and wherein the VL comprises an amino acid sequence having at least 90% identity to an amino acid sequence of SEQ ID NO: 76.

16. The pharmaceutical composition of claim 15, wherein the VH comprises the amino acid sequence of SEQ ID NO: 75 and the VL comprises the amino acid sequence of SEQ ID NO: 76.

17. The pharmaceutical composition according to claim 14, wherein the antigen binding domain comprises a scFv comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 73, 74, 79, 80, 91, and 92.

18. The pharmaceutical composition according to claim 14, wherein the antigen binding domain comprises a scFv comprising an amino acid sequence of SEQ ID NO: 74.

19. The pharmaceutical composition according to claim 14, wherein the CAR comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 71, 72, 77, 78, 89, and 90.

20. The pharmaceutical composition according to claim 14, wherein the CAR comprises an amino acid sequence having at least 90% identity to an amino acid sequence of SEQ ID NO: 72.

21. The pharmaceutical composition according to claim 14, wherein the CAR comprises an amino acid sequence of SEQ ID NO: 72.