CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising a plurality of genetically modified CD62L-positive Type I human natural killer T (NKT) cells comprising at least one chimeric antigen receptor (CAR) expression construct wherein said CD62L-positive Type I human NKT cells comprise the majority of the NKT Type I human NKT cells in said composition.

2. The pharmaceutical composition of claim 1, wherein said composition comprises a dose of said plurality of genetically modified Type I CD62L-positive Type I NKT cells that is between 1×10^7 to 2×10^8 cells per square meter of patient surface area.

3. The pharmaceutical composition of claims 1 or 2, wherein said composition comprises a therapeutically effective amount of said CD62L-positive Type I human natural killer T (NKT) cells.

4. The pharmaceutical composition of any one of claims 1 to 3, wherein said NKT cells are at least 12 day old *in vitro* expanded primary human CD62L-positive NKT cells.

5. The pharmaceutical composition of any one of claims 1 to 4, wherein the CAR expression construct comprises an antigen recognition domain directed to at least one tumor-associated antigen.

6. The pharmaceutical composition of claim 5, wherein said at least one tumor-associated antigen is selected from the group consisting of melanoma-associated antigen (MAGE), expressed antigen of melanoma (PRAME), CD19, CD20, CD22, K-light chain, CD30, CD33, CD123, CD38, CD138, ROR1, ErbB2, ErbB3/4, EGFRvIII, carcinoembryonic antigen, EGP2, EGP40, HER2, mesothelin, TAG72, PSMA, NKG2D ligands, B7-H6, IL-13 receptor α2, MUC1, MUC16, CA9, GD2, GD3, HMW-MAA, CD171, Lewis Y, G250/CAIX, HLA-AI MAGE AI, HLA-A2 NY-ESO-1, PSCI, folate receptor-α, CD44v6, CD44v7/8, 8H9, NCAM, VEGF receptors, 5T4, Fetal AchR, NKG2D ligands, CD44v6, GPC3, CSPG4, CEA, or combinations thereof.

7. The pharmaceutical composition of claims 5 or 6, wherein said at least one antigen is CD19.

8. The pharmaceutical composition of claims 5 or 6, wherein said at least one antigen is GD2.

9. The pharmaceutical composition of claims 5 or 6, wherein said at least one antigen is GPC3.

10. The pharmaceutical composition of any one of claims 1 to 9, wherein the CAR expression construct comprises an ectodomain that includes an antigen recognition domain, and a transmembrane domain that links the antigen recognition domain to the transmembrane domain.

11. The pharmaceutical composition of claim 10, further comprising a spacer that links the antigen recognition domain to the transmembrane domain, wherein the spacer is selected from a group consisting of a CH2CH3 region of immunoglobulin, a hinge region from IgG1, and at least portions of CD3.

12. The pharmaceutical composition of claims 10 or 11, wherein the transmembrane domain comprises a CD28 transmembrane region.

13. The pharmaceutical composition of any one of claims 5 to 12, wherein the antigen recognition domain comprises a single-chain variable fragment (scFv).

14. The pharmaceutical composition of any one of claims 1 to 13, wherein the CAR expression construct comprises at least a portion of a cytoplasmic signaling domain.

15. The pharmaceutical composition of claim 14, wherein the cytoplasmic signaling domain is derived from a T cell receptor CD3zeta-chain.

16. The pharmaceutical composition of any one of claims 1 to 15, wherein the CAR expression construct comprises a costimulatory endodomain.

17. The pharmaceutical composition of claim 16, wherein the costimulatory endodomain is selected from CD28, OX40, 4-1BB, ICOS, CD40, CD30, CD27, or combinations thereof.

18. The pharmaceutical composition of claims 16 or 17, wherein the costimulatory endodomain is 4-1BB.

19. The pharmaceutical composition of claims 16 or 17, wherein the costimulatory endodomain is CD28.

20. The pharmaceutical composition of any one of claims 1 to 19, wherein the CAR expression construct comprises a scFv from a CD19-specific antibody FMC-63 which is connected, via a spacer derived from the IgG1 hinge region, to a transmembrane domain derived from CD8a, and a signaling endodomain sequence of 4-1BB fused with a CD3-zeta-chain.

21. The pharmaceutical composition comprising a plurality of genetically modified CD62L-positive Type I human natural killer T (NKT) cells of any one of claims 1 to 20, wherein said cells exhibit in vivo persistence and are detectable at day 10 when transferred into NOD/SCID/IL2RY(null) (NSG) mice having $CD19^{+}$ Daudi lymphoma cells.

22. Use of a pharmaceutical composition in the manufacture of a medicament for immunotherapy of a subject in need thereof, wherein the composition comprises a dose of genetically modified CD62L-positive Type I human natural killer T (NKT) cells expressing at least one chimeric antigen receptor (CAR) expression construct, and wherein said dose comprises between 1×10^7 to 2×10^8 said NKT cells per square meter of said subject surface area and said NKT cells are the majority of Type I NKT cells in said composition.

23. Use of claim 22, wherein said composition comprises a pharmaceutically acceptable carrier.

24. Use of claims 22 or 23, wherein said composition is a composition for parenteral administration.

25. Use of any one of claims 22 to 24, wherein said composition is a composition for intravenous administration.

26. Use of any one of claims 23 to 25, wherein said pharmaceutically acceptable carrier is saline or a buffered media.

27. Use of any one of claims 22 to 26, wherein said subject is a cancer patient.

28. Use of claim 27, wherein said cancer is neuroblastoma, lymphoma, leukemia, or liver cancer.