What is claimed is:

1. A nucleic acid comprising a sequence that encodes a first chimeric antigen receptor (CAR), wherein the first CAR comprises:

an extracellular domain comprising a first antigen recognition domain consisting of a fully human single variable heavy (VH) domain that binds a first epitope on B-cell maturation antigen (BCMA);

a transmembrane domain; and

an intracellular domain comprising a signaling domain.

2. The nucleic acid of claim 1, wherein the extracellular domain further comprises a second antigen recognition domain consisting of a fully human single variable heavy (VH) domain that binds a second epitope on BCMA, wherein the first and second BCMA epitopes are different.

3. The nucleic acid of claim 2, wherein the first or the second antigen recognition domain has an amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 9, SEQ ID NO: 17 or SEQ ID NO: 25; or

wherein the first or the second antigen recognition domain comprises a variant of any of SEQ ID NO: 1, SEQ ID NO: 9, SEQ ID NO: 17 or SEQ ID NO: 25 that binds BCMA; or

wherein the first or the second antigen recognition domain comprises a variant of any of SEQ ID NO: 1, SEQ ID NO: 9, SEQ ID NO: 17 or SEQ ID NO: 25 that binds BCMA, and wherein the variant of the first or the second antigen recognition domain has an amino acid sequence having at least about 95% identity or at least 98% with any one of SEQ ID NOs: 1, 9, 17, or 25.

4. The nucleic acid of claim 2, wherein the first and second antigen recognition domains are connected by a linker, optionally wherein the linker comprises an amino acid sequence of GGGX (SEQ ID NO: 33), GGGGX (SEQ ID NO: 34), GSSGSX (SEQ ID NO: 35), GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 36), GSTSGSGKPGSGEGSTKG (SEQ ID NO: 37), KESGSVSSEQLAQFRSLD (SEQ ID NO: 38), EGKSSGSGSESKST (SEQ ID NO: 39), or GSAGSAAGSGEF (SEQ ID NO: 40), wherein X is either C or S.

5. The nucleic acid of claim 1, wherein the transmembrane domain is derived from CD3, CD8α, CD28, or CD137; or

wherein the extracellular domain further comprises a hinge domain disposed between the first antigen recognition domain and the transmembrane domain; optionally wherein the hinge domain is derived from IgG1 or IgG4; or

wherein the first CAR further comprises a signal peptide; optionally wherein the signal peptide is derived from albumin, CD8α, EPO, IgGκ, or IL-2; or

wherein the signaling domain comprises a primary signaling domain, a co-stimulatory signaling domain, or both a primary signaling domain and a co-stimulatory signaling domain

6. The nucleic acid of claim 5, wherein the intracellular domain comprises a) a CD3ζ primary signaling domain and a 4-1BB co-stimulatory signaling domain, b) a CD3ζ primary signaling domain and a CD28 co-stimulatory signaling domain, or c) a CD3ζ primary signaling domain and both a 4-1BB and a CD28 co-stimulatory signaling domain.

7. The nucleic acid of claim 1, which is codon-optimized for expression in a human immune cell; or .

wherein the nucleic acid does not comprise a stretch of 20 or more base pairs of direct or inverted repeat sequences; or

wherein the nucleic acid does not comprise alternate splice sites.

8. An expression vector encoding the nucleic acid of claim 1, which is encapsulated in a lipid-based carrier; or

wherein the vector is a viral vector; or

wherein the vector is a non-viral vector, optionally wherein the non-viral vector is a plasmid.

9. An immune cell or hematopoietic cell comprising the nucleic acid of claim 1.

10. The cell of claim 9, wherein the immune cell is a T cell, optionally wherein the T cell is a central memory T cell, a cell-like central memory T cell, or a CD8+ T cell, a NK cell, a macrophage or a dendritic cell, or wherein the immune cell or the hematopoietic cell is derived from a hematopoietic stem cell or an induced pluripotent stem cell.

11. The cell of claim 9, further comprising a second CAR, wherein the second CAR comprises an extracellular domain comprising an antigen recognition domain, a transmembrane domain, and an intracellular signaling domain; wherein the antigen recognition domain consists of a fully human single VH domain that binds a third BCMA epitope, wherein the first and third BCMA epitopes are different.

12. A pharmaceutical composition comprising a therapeutically effective number of the immune cells or hematopoietic cells of claim 9.

13. Use of the pharmaceutical composition of claim 12 in the manufacture of a medicament for treating cancer or autoimmune disease that involves aberrant BCMA activity in a subject in need thereof.

14. The use of claim 13, wherein the immune cells or hematopoietic cells are allogeneic and have a complete or partial HLA-match with the subject; or .
wherein the immune cells or hematopoietic cells are autologous.

15. The use of claim 13, wherein the cancer is a hematological cancer, optionally wherein the hematological cancer is multiple myeloma.

16. The use of claim 15, wherein the use further comprises co-administration of a pharmaceutical composition comprising a therapeutically effective amount of an additional active agent that binds a surface antigen on a myeloma cell,

optionally wherein the additional active agent binds CD3, CD16, CD38, CD44, CD138, CD229, SLAMF7, integrin β7 (ITGB7), Natural Killer Group 2D (NKG2D), NKp44, NKp46, or cereblon E3 ligase; or

further optionally wherein the additional active agent is one or more of bortezomib, carfilzomib, ixazomib, lenalidomide, pomalidomide, thalidomide, dexamethasone, prednisone, elotuzumab, daratumumab, isatuximab, and mezigdomide, iberdomide, talquetamab, monalizumab, AMG420, and AMG701.

17. The use of claim 15, wherein the cancer is lymphoma, optionally wherein the use further comprises co-administration of a pharmaceutical composition comprising a

therapeutically effective amount of an additional active agent that binds a surface antigen on a lymphoma cell, and optionally wherein the additional active agent is one or more of rituximab, mosunetuzumab, and blinatumomab.

18. The use of claim 13, wherein the autoimmune disease comprises lupus, systemic lupus erythematosus (SLE), myasthenia graves, immune thrombocytopenia (ITP), scleroderma, immune nephritis, Sjogren's syndrome, POEMS syndrome, pemphigus vulgaris, amyloidosis, autoimmune hemolytic anemia, or vasculitis; optionally wherein the use further comprises co-administration of a pharmaceutical composition comprising a therapeutically effective amount of a gamma secretase inhibitor, optionally wherein the gamma secretase inhibitor comprises one or more of Avagacestat, Begacestat, Crenigacestat, Iminostilbene, Itanapraced, Nirogacestat, L-685458, Semagacestat, and Tarenflurbil.

19. The use of claim 13, wherein the cancer is relapsed or refractory.

20. The use of claim 13, wherein the pharmaceutical composition is to be administered after lymphodepletion chemotherapy, optionally wherein the lymphodepletion chemotherapy agent comprises a therapeutically effective amount of melphalan.