CLAIMS

What is claimed is:

1. A humanized anti-CD19 antibody or antigen binding fragment thereof comprising a light chain variable (VL) region and a heavy chain variable (VH) region wherein

the VL region has an amino acid sequence of SEQ ID NO: 14, and the VH region has an amino acid sequence of SEQ ID NO: 15; or

the VL region has an amino acid sequence of SEQ ID SEQ ID NO: 17 and the VH region has an amino acid sequence of SEQ ID NO: 18.

2. The humanized anti-CD19 antibody or antigen binding fragment thereof of claim 1, wherein the antibody or the antigen binding fragment thereof is selected from the group consisting of an IgG, an Fab, an Fab′, an $F(ab')_2$, an Fv, and an scFv.

3. A polypeptide comprising the humanized anti-CD19 antibody or antigen binding fragment thereof of claim 1 or 2.

4. A chimeric antigen receptor (CAR), comprising: (i) an antigen binding domain, (ii) a costimulatory domain, and (iii) an activating domain,

wherein the costimulatory domain comprises an extracellular domain, a transmembrane domain, and an intracellular domain, and

wherein the antigen binding domain comprises at least the polypeptide of claim 3.

5. The CAR of claim 4, wherein the costimulatory domain is from or is derived from CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3),

CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll ligand receptor, and fragments or combinations thereof.

6. The CAR of claim 4 or claim 5, wherein the transmembrane domain is from or is derived from 4-1BB/CD137, an alpha chain of a T cell receptor, a beta chain of a T cell receptor, CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll ligand receptor, and combinations thereof.

7. The CAR of any one of claims 4 to 6, wherein the intracellular domain is from or is derived from 4-1BB/CD137, activating NK cell receptors, B7-H3, BAFFR, BLAME (SLAMF8), BTLA, CD100 (SEMA4D), CD103, CD160 (BY55), CD18, CD19, CD19a, CD2, CD247, CD27, CD276 (B7-H3), CD28, CD29, CD3 delta, CD3 epsilon, CD3 gamma, CD30, CD4, CD40, CD49a, CD49D, CD49f, CD69, CD7, CD84, CD8alpha, CD8beta, CD96 (Tactile), CDl la, CDl lb, CDl lc, CDl ld, CDS, CEACAM1, CRT AM, cytokine receptors, DAP-10, DNAM1 (CD226), Fc gamma receptor, GADS, GITR, HVEM (LIGHTR), IA4, ICAM-1, ICAM-1, Ig alpha (CD79a), IL2R beta, IL2R gamma, IL7R alpha, Immunoglobulin-like proteins, inducible T cell costimulator (ICOS), integrins, ITGA4, ITGA4, ITGA6, ITGAD, ITGAE, ITGAL, ITGAM, ITGAX, ITGB2, ITGB7, ITGBl, KIRDS2, LAT, LFA-1, LFA-1, a ligand that specifically binds with CD83, LIGHT, LIGHT (tumor necrosis factor superfamily member 14; TNFSF14), LTBR, Ly9 (CD229), lymphocyte function-associated antigen-1 (LFA-1 (CDl la/CD18), MHC class I molecule, NKG2C, NKG2D, NKp30, NKp44, NKp46, NKp80 (KLRF1), OX-40, PAG/Cbp, programmed death-1 (PD-1), PSGL1, SELPLG (CD162), signaling lymphocytic activation molecules (SLAM proteins), SLAM (SLAMF1; CD150; IPO-3), SLAMF4 (CD244; 2B4), SLAMF6 (NTB-A; Lyl08), SLAMF7, SLP-76, TNF receptor proteins, TNFR2, a Toll ligand receptor, TRANCE/RANKL, VLA1, or VLA-6, or a combination thereof.

8. The CAR of any one of claims 4 to 7, wherein the extracellular domain is from or is derived from CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352

(SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll ligand receptor, and fragments or combinations thereof.

9. The CAR of any one of claims 4 to 8, wherein the activating domain is from or is derived from CD3-zeta or CD3-episilon.

10. A vector encoding the humanized anti-CD19 antibody or antigen binding fragment thereof of claim 1 or 2, the polypeptide of claim 3, or the CAR of any one of claims 4 to 9.

11. A cell comprising the humanized anti-CD19 antibody or antigen binding fragment thereof of claim 1 or 2, the polypeptide of claim 3, the vector of claim 10, or the chimeric antigen receptor (CAR) of any one of claims 4 to 9.

12. A composition comprising a plurality of the cell of claim 11.

13. A method for manufacturing a cell expressing a chimeric antigen receptor (CAR), comprising a step of transducing a cell with the vector of claim 10.

14. Use of the humanized anti-CD19 antibody or antigen binding fragment thereof of claim 1 or 2, the polypeptide of claim 3, the CAR of any one of claims 4 to 9, the vector of claim 10, the cell of claim 11, or the composition of claim 12, in the manufacture of a medicament for treating a B-cell lymphoma.

15. The use of claim 14, wherein the B-cell lymphoma is selected from the group consisting of Acute Lymphoblastic Leukemia (ALL), AIDS-related lymphoma, ALK-positive large B-cell lymphoma, Burkitt's lymphoma, Chronic lymphocytic leukemia, CLL), Classical Hodgkin lymphoma, Diffuse large B-cell lymphoma (DLBCL), Follicular lymphoma, Intravascular large B-cell lymphoma, Large B-cell lymphoma arising in HHV8-associated multicentric Castleman's disease, Lymphomatoid granulomatosis, Lymphoplasmacytic lymphoma, Mantle cell lymphoma (MCL), Marginal zone B-cell lymphoma (MZL), Mucosa-Associated Lymphatic Tissue lymphoma (MALT), Nodal

marginal zone B cell lymphoma (NMZL), Nodular lymphocyte predominant Hodgkin's lymphoma, Non-Hodgkin’s lymphoma, Plasmablastic lymphoma, Primary central nervous system lymphoma, Primary effusion lymphoma, Splenic marginal zone lymphoma (SMZL), and Waldenström's macroglobulinemia.

16. The use of claim 15, wherein the B-cell lymphoma is selected from the group consisting of Acute Lymphoblastic Leukemia (ALL), Chronic lymphocytic leukemia, CLL), Diffuse large B-cell lymphoma (DLBCL), Follicular lymphoma, Mantle cell lymphoma (MCL), Marginal zone B-cell lymphoma (MZL), Mucosa-Associated Lymphatic Tissue lymphoma (MALT), and Non-Hodgkin’s lymphoma.

17. The use of claim 16, wherein the B-cell lymphoma is Non-Hodgkin’s lymphoma.