**Supplemental Figure 1**

Sequences of CAR T cells with mCD8 signal peptide annotated in orange, scFv annotated in red, myc tag annotated in highlighted gray, mCD28 transmembrane and intracellular annotated in purple, mZeta annotated in green, IRES annotated in pink, mIL12 annotated in black, and m4-1BB annotated in yellow.

**Supplemental Figure 2**

1. Media from *in vitro* co-culture of CAR T cells with EL4mCD19 tumor cells was assessed for IL12p70 on day 7 after CAR T cell treatment. Data shown is mean +/- s.e.m. of two independent experiments.
2. EL4mCD19 tumor bearing C57BL/6 mice, pretreated with 250mg/kg per mouse of cyclophosphamide day -3, treated i.v. with CAR T cells day 0. Significance determined bylong-rank Mantel-Cox Test, with 95% confidence interval (n=3 per group). \*p=0.0224 m1928 compared to m1928 + cyclophosphamide and \*p=0.0295 m19 compared to m19 + cyclophosphamide
3. Flow cytometry demonstrating CD25 expression on CAR T cells prior to injection in terms of percentage and representative flow cytometry plot (ns by ordinary one-way ANOVA). Data shown is mean +/- s.e.m. of three independent experiments (n=3 per group).
4. CAR T cells were co-cultured with EL4mCD19 tumor cells and assessed for cytotoxicity 4 hours later, using a luciferase killing assay. m1928, m19IL-12, and m1928IL-12 CAR T cells showed significantly increased cytotoxicity compared to m19 CAR T cells at E:T ratios of 2:1, 1:1, and 0.5:1. There was no difference in tumor lysis between 1912 and m1928IL-12 CAR T cells (\*p=<0.001 by two-way ANOVA). Data shown is mean +/- s.e.m. of three independent experiments.

Serum was obtained through retro-orbital bleeds and assessed for IL12p70 through luminex on day 7 after CAR T cell treatment. Data shown is mean +/- s.e.m. of three independent experiments.

**Supplemental Figure 3**

1. CAR T cells were co-cultured with EL4mCD19 tumor cells and then assessed for cytotoxicity 4 hours later, using a luciferase killing assay. There was no difference in tumor lysis between CAR T cells and vex-GFP tagged CAR T cells (two-way ANOVA). Data shown is representative of two independent experiments.
2. Flow cytometry gating strategy to determine CD8+ and CD4+ ratio and PD-1, TIM-3, and LAG-3 inhibitory receptor expression.

**Supplemental Figure 4**

1. CAR T cells, day 5 after infusion, were characterized by flow cytometry in terms of percentage and representative plots. m1928IL-12 CAR T cells expressed higher levels of inhibitory receptors, PD-1 (\*p=0.0015) and LAG-3 (\*p=0.0491) and showed a trend toward higher levels of TIM-3 (\*p=0.1715). Data obtained is mean +/- s.e.m. of three independent experiments analyzed by unpaired t test.
2. Representative flow cytometry plots of PD-1, LAG-3, and TIM-3 inhibitory receptor expression of CAR T cells referenced in Figure 2B.

**Supplemental Figure 5**

1. CAR T cells, day 0 before infusion, were characterized by flow cytometry. Data shown is mean +/- s.e.m. of three independent experiments. “ns” (not significant) by unpaired t test.
2. Representative flow cytometry plots of CAR T cell CD8+ and CD4+ ratios day 5 after infusion referenced in Figure 2D.
3. Representative flow cytometry plots of PD-1, LAG-3, and TIM-3 inhibitory receptor expression of CD8+ CAR T cells referenced in Figure 2E.
4. CAR T cells, day 5 after infusion, were characterized by flow cytometry. m1928IL-12 CAR T cells, gated on CD8+ T cells, expressed higher levels of double positive inhibitory receptors, LAG-3;TIM-3 (\*p=0.0397) and LAG-3;PD-1 (\*p=0.001), and showed a trend toward higher levels of TIM-3;PD-1 (\*p=0.0563). Data obtained is mean +/- s.e.m. of three independent experiments analyzed by unpaired t test.

**Supplemental Figure 6**

1. B cells were assessed for CD80 expression by flow cytometry through peripheral blood. \*p=0.048 unpaired t test of BM and \*p=0.0233 unpaired t test of spleen. Data shown is mean +/- s.e.m. of two independent experiments.
2. Luminex data showing IL-4 secreting from EL4mCD19 tumor cells. Data shown is mean +/- s.e.m. of two independent experiments. \*p=0.002 by unpaired t test.
3. Flow cytometry demonstrating lack of CD28 expression on CD28-/- T cells. Data shown is representative of two independent experiments.
4. CAR T cells were co-cultured with EL4mCD19 tumor cells and then assessed for cytotoxicity 4 hours later, using a luciferase killing assay. There was no difference in tumor lysis between CD28-/- or wildtype transduced CAR T cells. Data shown is mean +/- s.e.m. of two independent experiments.