**Supplemental Figure Legends**

**Supplemental Figure 1.****Phenotypic characterization of CSPG4-CAR.CIK**

Representative flow-cytometry dot-plots showing that patient-derived CAR.CIK express the CSPG4-CAR as compared to paired control unmodified CIK **(A).** CSPG4-CAR.CIK were mostly composed by effector memory (EM), followed by central memory and naive cells. Cell subset composition of CSPG4-CAR.CIK was comparable with that of unmodified NTD.CIK (paired t test, p>0.05) **(B).**

Abbreviations: CIK, Cytokine Induced Killer cells; CSPG4, Chondroitin Sulfate Proteoglycan 4; Chimeric Antigen Receptor (CAR); Not Transduced (NTD); Effector Memory (EM: CD45RA−/CD62 L-); Central Memory (CM: CD45RA−/CD62 L+); NAÏVE: CD45RA+/CD62L+.

**Supplemental Figure 2.** **CSPG4-CAR.CIK *in vitro* cytolytic activity against 12 distinct STS histotypes**

Patient-derived CSPG4-CAR.CIK show superior *in vitro* cytolytic activity against multiple STS (red symbols) as compared to paired unmodified NTD.CIK (blue symbols). Each symbol represents a specific STS sample. \*S061 is a STS sample that expresses CSPG4 but lacks NKG2D ligands **(A)**. In two cases (S1 e S172) we performed cytotoxicity assays in the autologous setting against S1 e S172 STS. The S1 and S172 CSPG4-CAR.CIK and paired unmodified NTD.CIK showed comparable cytotoxic activity in autologous and allogeneic settings (n=2) **(B)**.

Abbreviations: CIK, Cytokine Induced Killer cells; CSPG4, Chondroitin Sulfate Proteoglycan 4; Chimeric Antigen Receptor (CAR); Not Transduced (NTD).

**Supplemental Figure 3.** **Phenotype characterization of CSPG4-CAR.CIK and CSPG4-CAR.T**

Representative flow-cytometry plots showing the expression of CSPG4.CAR in paired CIK and T lymphocytes **(A)**. The immunophenotype of paired patient-derived CSPG4-CAR.CIK, CSPG4-CAR.T and respective unmodified NTD controls is reported in the table **(B)**.

Abbreviations: CIK, Cytokine Induced Killer cells; CSPG4, Chondroitin Sulfate Proteoglycan 4;Chimeric Antigen Receptor (CAR); Not Transduced (NTD); Effector Memory (EM: CD45RA−/CD62 L-); Central Memory (CM: CD45RA−/CD62 L+); NAÏVE: CD45RA+/CD62L+.

**Supplemental Figure 4. Th1 and Th2 cytokine production by CSPG4-CAR.CIK and CSPG4-CAR.T**

Cytokine production by CSPG4-CAR.CIK and CSPG4-CAR.T was measured with and without engagement with the STS targets. The M14 melanoma cell line that lacks CSPG4 expression was used as control. CSPG4-CAR.CIK (IL-2 300U/ml) **(A, B)** and CSPG4-CAR.T lymphocytes, minimally activated with IL-2 (50U/ml), **(D, C)** produced higher baseline amounts of IFNγ, IL1β, TNFα, GM-CSF, IL-8, IL-6, IL-4, IL-10 and granzyme B as compared with paired unmodified NTD.CIK or NTD.T. In both cases the cytokine production increased following engagement with STS CSPG4-positive targets. Each sample was measured in duplicate and results are reported as pg/ml (according to manufacturer instructions). Statistics were calculated using unpaired t-test and statistical significance is reported as \* P ≤ 0.05; \*\* P ≤ 0.01; \*\*\* P ≤ 0.001; \*\*\*\* P ≤ 0.0001.

Abbreviations: CIK, Cytokine Induced Killer cells; CSPG4, Chondroitin Sulfate Proteoglycan 4;Chimeric Antigen Receptor (CAR); Not Transduced (NTD).

**Supplemental Figure 5. CSPG4-CAR.CIK show antitumor activity in STS xenografts models**

Schematic illustration of the treatment plan of STS xenografts with CSPG4-CAR.CIK (red arrows) and NTD.CIK (blue arrows). Vehicle-treated mice were infused with PBS (grey arrows). CIK were infused intravenously (3x106 cells/infusion) twice at day 0 and day 3 via tail vein in NOD/SCID mice. Tumor growth was monitored up to day 14 after the last dose of CIK **(A).** Antitumor activity by CSPG4-CAR.CIK (n=5) was observed in the HT1080 fibrosarcoma (23% CSPG4+ and 521 molecule/cell) model (n=5). CSPG4-CAR.CIK delayed tumor growth up to 11 days after the end of treatments (p<0.0001). The antitumor effect was superior to that observed with paired unmodified NTD.CIK (n=5). In 1 out of 5 mice bearing the HT1080 fibrosarcoma (20%) and receiving CSPG4-CAR.CIK the tumor regressed **(B).** CSPG4-CAR.CIK resulted in significant reduction of S172 leiomyosarcoma (72% CSPG4+ and 262 molecule/cell) growth (n=4) as compared NTD.CIK (n=4, p<0.05) or vehicle treatment (n=4; p<0.05) up to day 8. In the following period CSPG4-CAR.CIK delayed tumor growth more efficiently as compared with unmodified NTD.CIK or vehicle-treated controls (p<0.0001). In 2 out of 4 mice nearing the S172 leiomyosarcoma (50%) and treated with CSPG4-CAR.CIK the tumor regressed **(C).** All results were analyzed by two way ANOVA and Bonferroni’s post test analysis, statistical significance is reported as \* P ≤ 0.05; \*\* P ≤ 0.01; \*\*\* P ≤ 0.001; \*\*\*\* P ≤ 0.0001. **(D).**

Abbreviations: CIK, Cytokine Induced Killer cells; CSPG4, Chondroitin Sulfate Proteoglycan 4; CAR Chimeric Antigen Receptor; NTD, Not Transduced; NOD/SCID, Non obese diabetic/severe combined immunodeficiency mice.