**Supplemental Figure Legends**

**Supplemental Figure S1. Clinical strategy to pharmacologically inhibit Akt during *ex vivo* expansion of tumor-infiltrating lymphocytes (TIL).** Illustration showing conventional approach to isolating and expanding TIL using high-dose interleukin-2 (IL-2) promotes T cell senescence, differentiation, and effector function—qualities that have previously been shown to negatively correlate with therapeutic efficacy. Simple supplementation of Akt inhibitor to TIL culture media throughout *ex vivo* clinical expansion enhances cell-intrinsic features of TIL that are associated with complete and durable regression of metastatic disease. Ontogeny of T cell differentiation is showed as naïve T cells differentiation into distinct antigen-experienced subsets: stem cell memory (TSCM), central memory (TCM), effector memory (TEM), and terminal effector T cells.

**Supplemental Figure S2. CD8+ tumor-infiltrating lymhphocytes (TIL) isolated from patient with melanoma have reduced phosphorylation of Akt T308 and GSK3βS9  in presence of Akt inhibitor.** Immunoblot of AKT threonine 308 residue and GSK3β serine 9 residue at indicated time points after CD3 stimulation in the presence and absence of Akti.

**Supplemental Figure S3. Surface phenotype of Akti-treated and vehicle TIL isolated from patient with melanoma and expanded to clinical scale for 30 days prior to adoptive-transfer into humanized mouse model.** FACS analysis gated on live, singlet lymphocytes and indicated surface markers.

**Supplemental Figure S4. Akti-treated tumor-specific Pmel CD8+ T cell have reduced phosphorylation of Akt and substrates in presence of pharmacologic inhibition of Akt.** FACS histogram and quantification of phosphorylation events at indicated residues during acute time points after CD3 stimulation either in presence or absence of pharmacologic inhibition of Akt. Grey shading represents unstimulated T cells.

**Supplemental Figure S5. Akti-treated murine CD8+ T cells have enhanced expression of “naïve/memory”-associated genes (e.g. *Klf2, Tcf7, Lef1, Foxo1, and Sell*) and decreased expression of “effector”-associated genes (e.g. *Eomes, Prf1, GzmB, and Klrg1*). (a)** Bar graph showing mRNA levels of the indicated transcription factors after a primary and secondary stimulation of CD8+ T cells. Stimulated Pmel CD8+ T cells were expanded over 5 days (primary) followed by peptide restimulation and culture for additional 5 days (secondary) in presence or absence of Akti. mRNA abundance relative to *Actb* mRNA. Asterisks are used to indicate following P values: \* = P<0.05, \*\* P<0.01, \*\*\* P<0.001, \*\*\*\* P<0.0001. Center bar indicates mean and error bars indicate SEM.

**Supplemental Figure S6. Akt inhibition of murine CD8+ T cells increased expression of CD62L and CD27, and decreased expression of CD44. (a)** FACS analysis at day 5 of Pmel splenocytes stimulated with cognate peptide and cultured in IL-2 in the presence and absence of Akti.

**Supplemental Figure S7. Pharmacologic inhibition of Akt modulates global metabolic profile and key lipid metabolites of antigen-experienced murine CD8+ T cells.** **(A)** Principle component analysis and unsupervised hierarchical clustering of metabolome (346 biochemicals) of Pmel T cells cultured in indicated doses of Akt inhibitor for 10 days. 5 replicates per treatment group. (**B)** Relative abundance of key metabolites in lipid metabolism. 5 replicates per treatment group. G-3-P, glucose-3-phosphate; GPC glycerophosphorylcholine. Box plot legend: open circles, extreme data point; plus sign, mean value; center line, median value; box represents limit of upper and lower quartile.