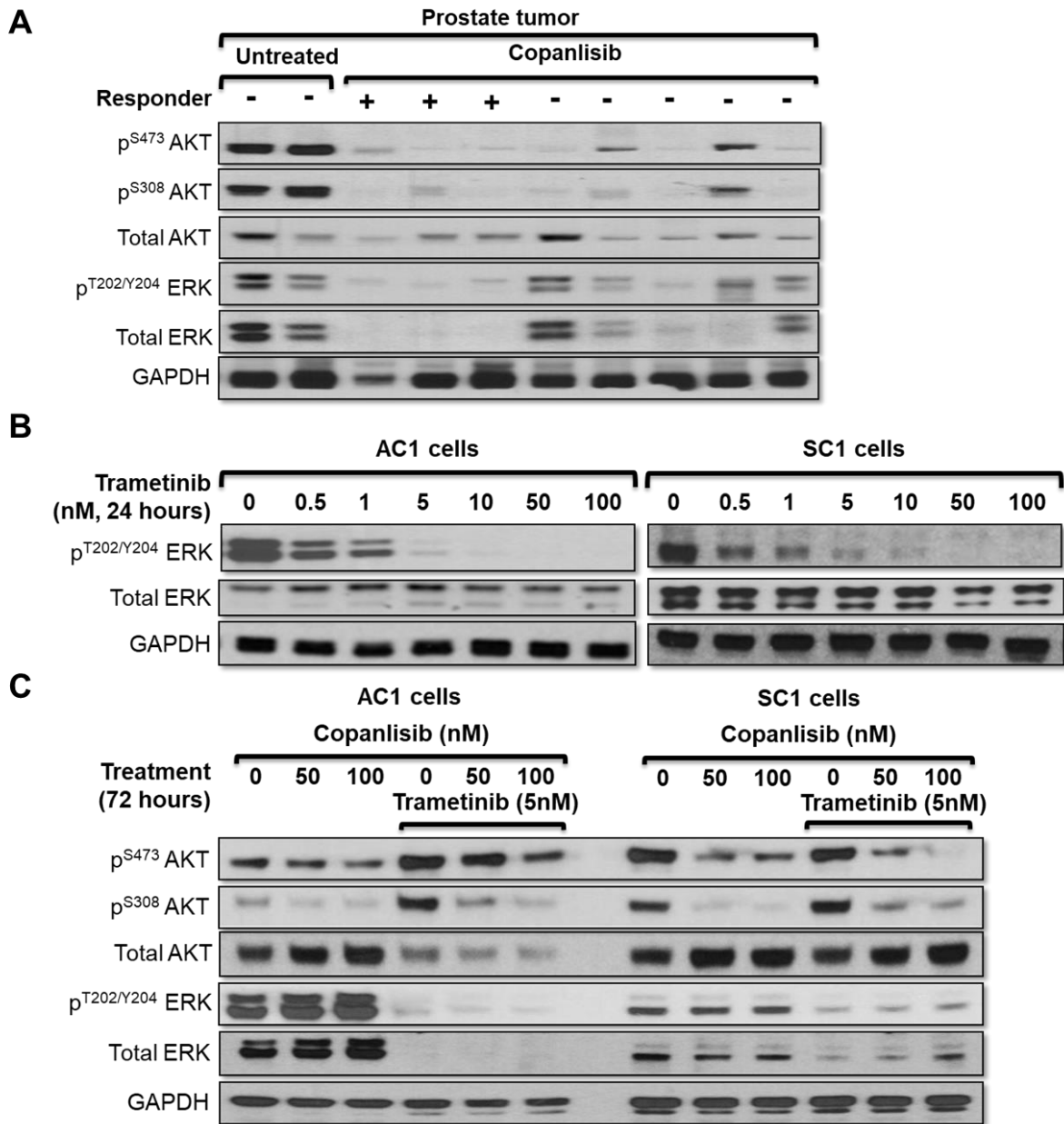


Supplementary Figure S1



Supplementary Figure S1. Persistent MEK signaling in PTEN/p53-deficient GEM tumors

resistant to PI3Ki monotherapy. (A) Pb-Cre;PTEN^{fl/fl}Trp53^{fl/fl} mice with established prostate

tumors were treated with copanlisib (14 mg/kg, *iv*, every alternate day) for 28 days. Western blot

analyses were performed for indicated protein markers on prostate tumor extracts. (B-C)

PTEN/p53-deficient GEM tumor-derived PC cells, AC1 and SC1 were treated with trametinib (B),

copanlisib and their combination (C) at mentioned amounts/time points. Western blot analyses were performed for indicated proteins. For *in vivo* studies, n=6-8 mice per group (experimental male mice with the correct genotype were obtained following screening of 42 littermates derived from 6 breeding pairs and randomized until the indicated number of mice achieved in each group). For *in vitro* experiments, n=2 independent biological experiments.