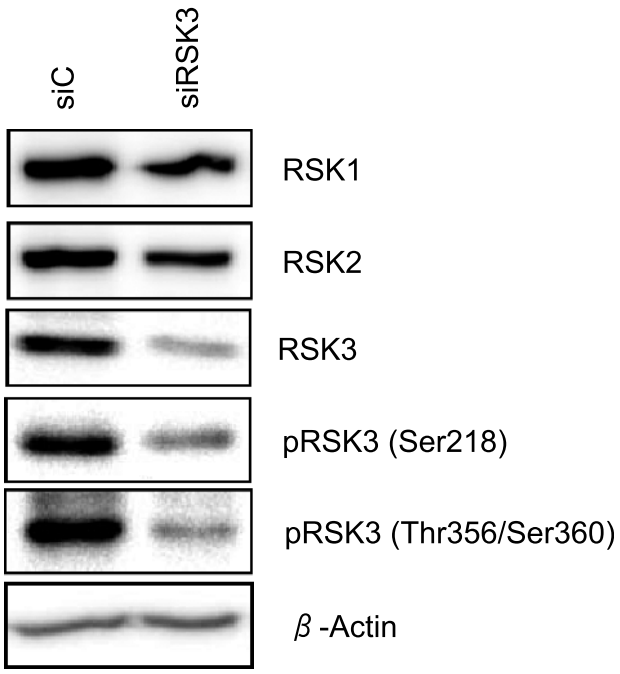

Figure W1. Validation of RSK3 antibodies. Protein levels of RSKs and phospho-RSKs were determined in PaTu8988t 48 hours after transient transfection with siRSK3 and siC.

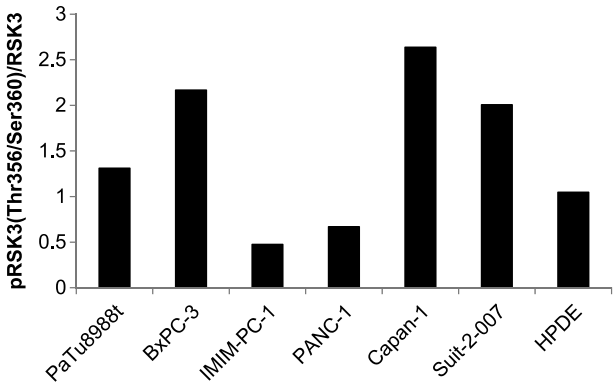

Figure W2. Densitometric quantification of Figure 2*A* shows phospho-RSK3 (Thr^{356}) expression normalized to total RSK3 protein expression in various pancreatic cancer cell lines and the pancreatic ductal epithelial cell line HPDE.

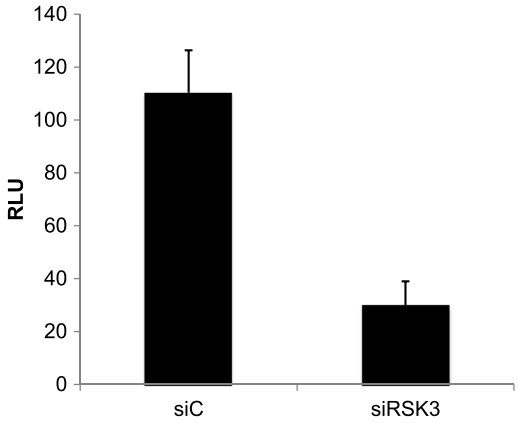

Figure W3. Knockdown of RSK3 affects cell viability in PaTu-8988t cells in the presence of erlotinib. PaTu-8988t cells were transfected with siRSK3 and incubated with erlotinib. Cell viability was measured using an MTT assay 48 hours after transfection. Results are representative for three independent experiments.

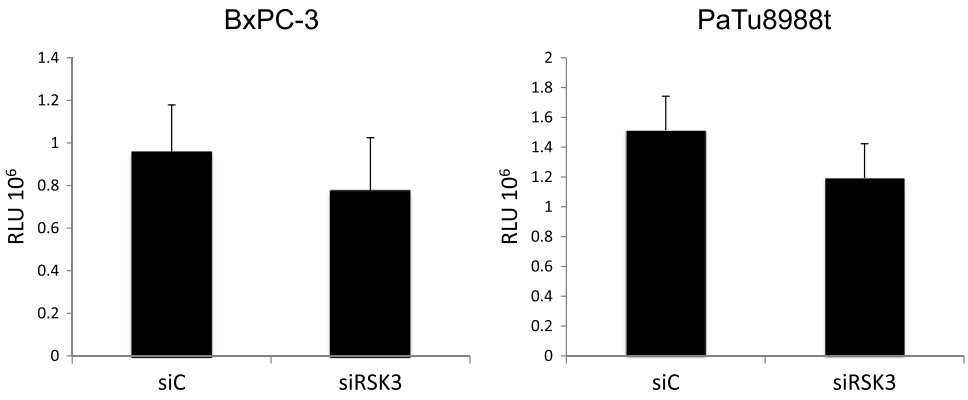

Figure W4. Knockdown of RSK3 has no significant effects on tumor cell proliferation in the presene of erlotinib. BxPC-3 and PaTu-8988t cells were transiently transfected with siRSK3 or siC and incubated with erlotinib. Proliferation was measured by BrdU incorporation. Results are representative for three independent experiments.

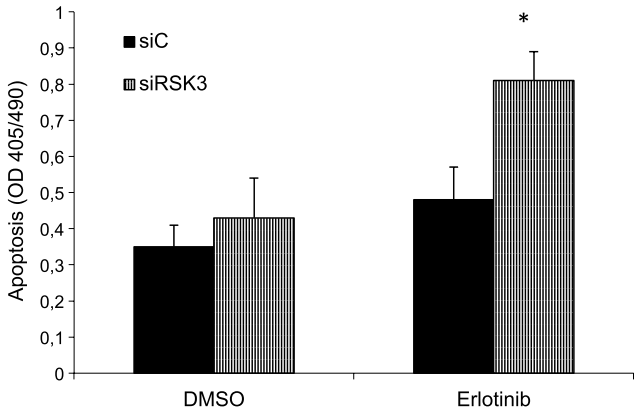

Figure W5. RSK3 inhibition induces apoptosis synergistically with erlotinib. BxPC-3 cells were transiently transfected with siRSK3 or siC and treated with erlotinib or solvent DMSO. Apoptosis was determined by a DNA fragmentation assay. *$P < .05$ compared to siC. Results are representative for three independent experiments.

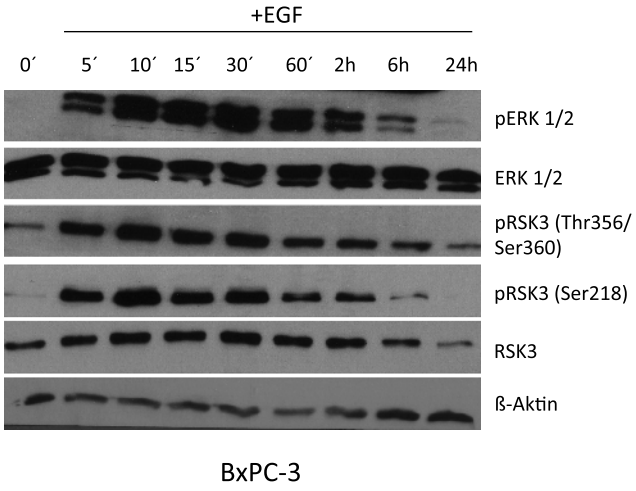

Figure W6. Time course of RSK3 activation by recombinant human EGF. BxPC-3 cells were serum starved for 24 hours before EGF treatment (5 ng/ml), and indicated proteins were detected by specific antibodies.

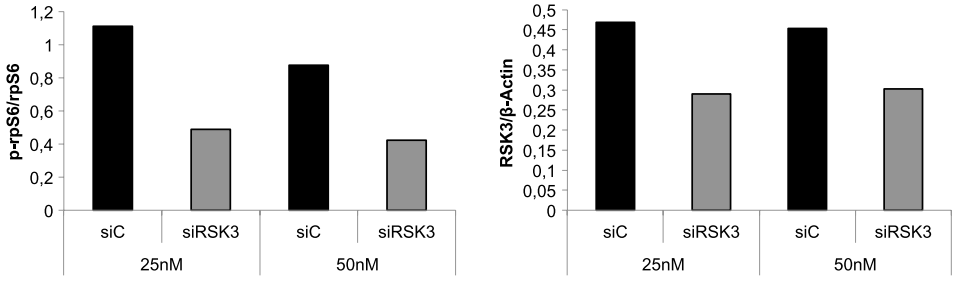

Figure W7. Densitometric quantification of Figure 5*A* demonstrates that RSK3 phosphorylates rpS6. PaTu-8988t cells were transiently transfected with siRSK3 or siC at different siRNA concentrations. Phosphorylated rpS6 normalized to total rpS6 (left panel) or β-actin (right panel), as detected with specific antibodies, was quantified by densitometry.

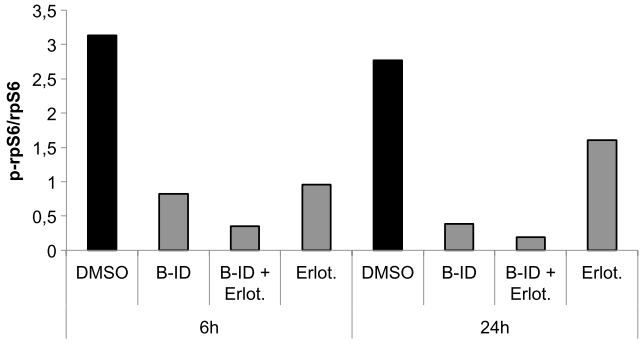

Figure W8. Densitometric quantification of Figure 5*B* demonstrates the effect of the RSK inhibitor BI-D1870 (5 μM) and/or erlotinib (10 μM) for the indicated time points on phospho-rpS6 that was quantified by densitometry and shown as normalized to total rpS6.

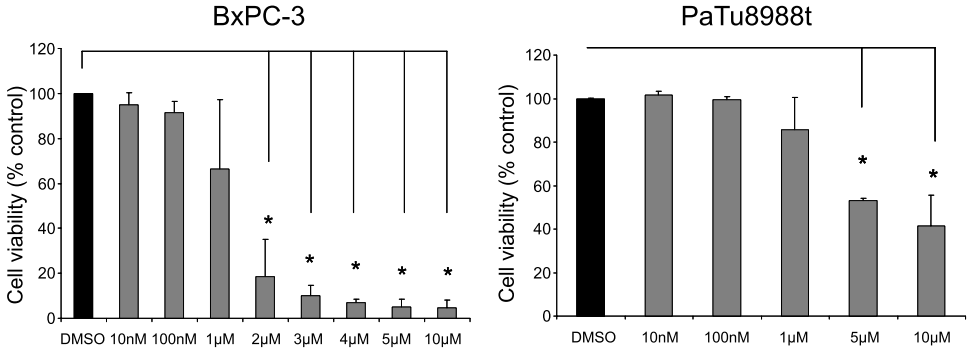

Figure W9. Dose-response curve of BI-D1870 in PaTu-8988t and BxPC-3 cells. Cells were incubated with BI-D1870 or the solvent DMSO at the indicated concentrations for 24 hours, and cell viability was measured by MTT assay. *$P < .05$ compared to DMSO-treated control.

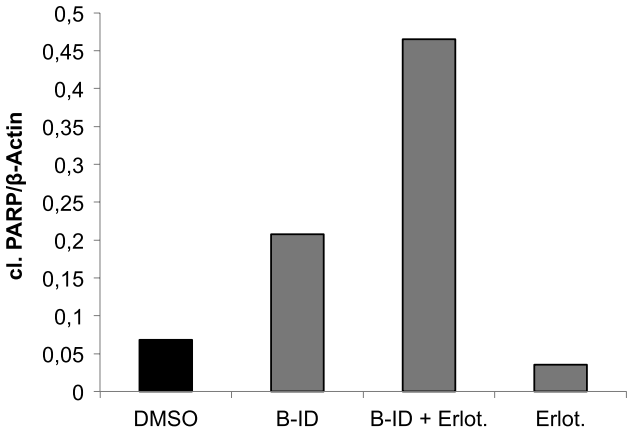

Figure W10. Densitometric quantification of Figure 7*A* demonstrates the synergistic effect of RSK inhibition by BI-D1870 and EGFR inhibition by erlotinib on apoptosis in PaTu-8988t cells, as determined by PARP cleavage. PARP cleavage was quantified by densitometry and shown as normalized to β-actin.