

**Supplementary Figure S1.** Effects of combination treatments on membrane permeability. T24 cells subjected to combination treatments as described in Figure 5 were stained with trypan blue. Combination treatments resulted in an increased percentage of cells staining positive for trypan blue, most notably in the sequentially dosed combination regimens.

**Supplementary Figure S2.** Cell cycle analysis of MLN8237/paclitaxel and MLN8237/gemcitabine combination treatments. Propidium iodide staining with flow cytometry was performed to assess cell cycle changes. Simultaneous MLN8237/paclitaxel and MLN8237/gemcitabine treatments appeared to have little, if any, additional effect on cell cycle arrest compared to MLN8237 alone. Sequential treatments of MLN8237 followed by either paclitaxel or gemcitabine produced the greatest degree of cell cycle derangement.