Supplementary Figure Legends

Supplementary Figure 1. Compound I has a cytostatic effect on cells. Compound I was compared to staurosporine in a proliferation assay in NIH3T3 TPR-Met cells. 5 000 cells/well were plated in a 96-well plate and allowed to attach for 2 hours. Culture media where then replaced by media containing increasing concentrations of Compound I or staurosporine. An ATP-lite assay was performed just prior to treatment to establish the baseline counts (red circle) and 24 hours after the initiation of treatment to assess the effects of Compound I and staurosporine. There was a 3-fold increase in luminescence counts after 24 hours, reflecting cell proliferation during that period of time. Compound I inhibited cell proliferation at concentrations above 1 000 nM. The remaining cells looked healthy at all concentrations (data not shown). No further decrease in counts were observed at later time points (data not shown). In contrast, staurosporine, a known cytotoxic, inhibited cell proliferation at all concentrations tested and caused cell death as judged by cell morphology (data not shown) and by the dramatic decrease in luminescence counts.

Supplementary Figure 2. Selective inhibition of c-Met with SU11274 has no effect of ERK1/2 phosphorylation in HT-29 cells. *A*, SU11274 inhibits c-Met enzymatic activity (left panel) and HGF-mediated c-Met phosphorylation in cells (right panel). *B*, To test the effect of SU11274 on RON, NIH3T3 RON cells were treated with SU11274 followed by stimulation with MSP. The effects of SU11274 were analyzed by western blotting. Phospho-RON was detected with the RON C-20 antibody as a single band of 150 kDa after immunoprecipitation with the 4G10 antibody. The phosphorylation of signaling molecules downstream of RON were analyzed by western blotting. SU11274 is not a RON inhibitor. *C*, HT-29 cells were treated with increasing concentrations of SU11274 and the effects of treatment on ERK1/2 were determined by western blotting.

Supplementary Figure 3. Compound I has no direct inhibitory effect on Src phosphorylation in cells or *in vivo*. *A*, A431 cells were either untreated or treated with 1 μM Iressa or increasing concentrations of Compound I for 1 hour followed by 100 ng/ml of EGF for 5 minutes. Levels of Src phosphorylation were then monitored by western blotting. Total Src protein levels served as a loading control. B, Colo205 xenografts were treated with vehicle or with 100 mg/kg of Compound I for 3 hours, a dose and time-point that correspond to the highest levels of Compound I achieved in the xenograft experiments (see figure 5C of the manuscript). Tumor lysates were used to monitor the effect of Compound I on Src phosphorylation levels by western blotting (Y416 – Cell Signaling # 2101). N=3 mice/group.