

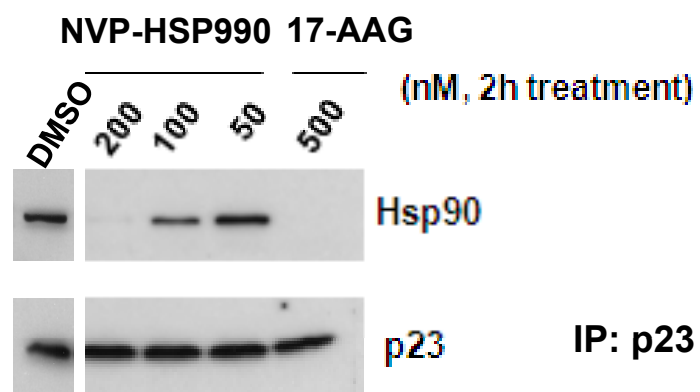
Supplementary Figure Legends:

Supplementary Figure 1. *In vitro* mechanistic effects of NVP-HSP990 on p23-Hsp90 complex. GTL-16 cells were treated with DMSO, 17-AAG (500 nM) or NVP-HSP990 at various concentrations (50, 100, 200 nM) for two hours. The amount of p23 bound to hsp90 was determined by immunoprecipitation/Western blot analysis

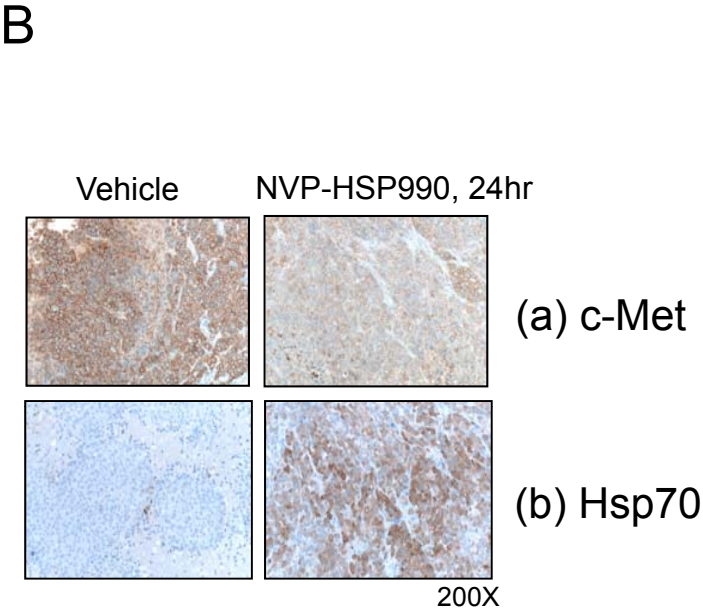
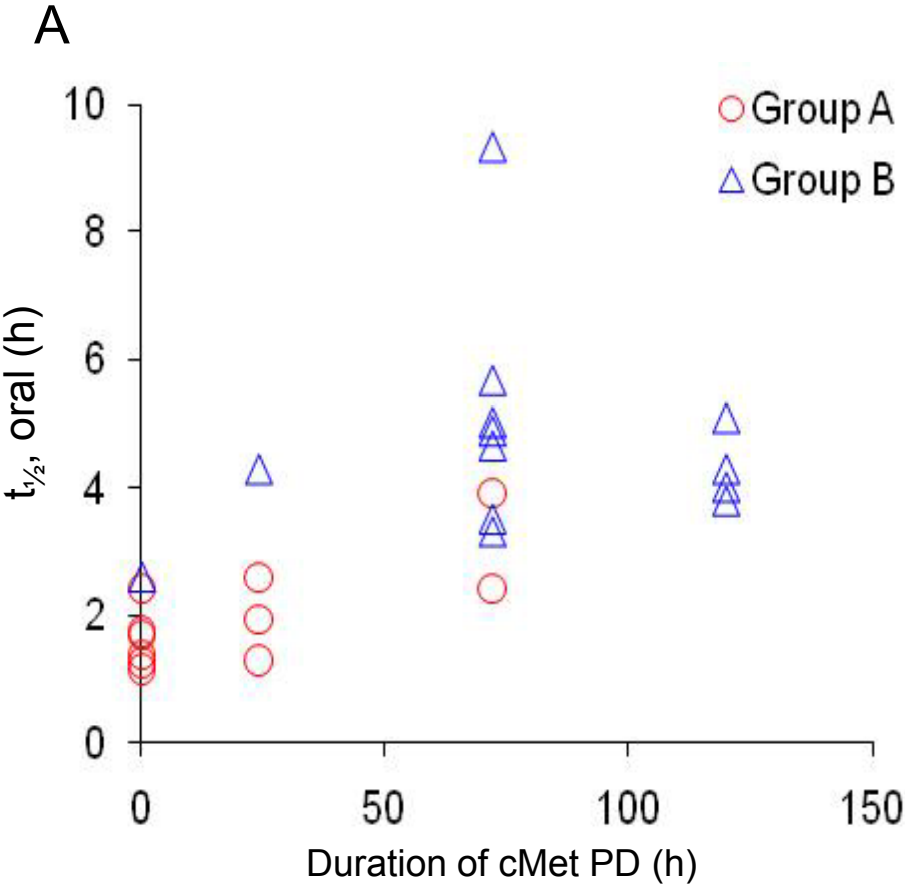
Supplementary Figure 2. PK-PD relationship of various Hsp90 inhibitors *in vivo*. (A) Correlation of mouse $t_{1/2, \text{oral}}$ with duration of c-Met PD. Data illustrates PD modulation in hours $\geq 50\%$ c-Met inhibition relative to vehicle, assessed in the GTL-16 tumor xenograft model in nude mice. (B) Immunohistochemistry of c-Met (a) or Hsp70 (b). GTL-16 tumored nude mice were administered with a single oral treatment of vehicle or NVP-HSP990 (15 mg/kg). Tumors were harvested at 24 h post-dose. Magnification: 200x.

Supplementary Figure 3. Efficacy of NVP-HSP990 in the GTL-16 (c-Met overexpressing) tumor xenograft model. (A) Nude mice bearing GTL-16 xenografts were treated orally with vehicle or NVP-HSP990 at various dose/schedules: daily/qd (0.5 mg/kg), twice weekly/q2w (2.5 or 5 mg/kg) or weekly/qw (5, 10, or 15 mg/kg). Tumor inhibition was defined by percent treatment/control (T/C) values as described in Methods. Negative values for tumor inhibition indicate percent tumor regression. * $p < 0.05$ versus vehicle (Kruskal-Wallis One Way ANOVA on Ranks; Dunn's); ns, not significant. Data computed from $n=2$ studies. (B) Quantitation of proliferation index. GTL-16 tumored mice were treated with vehicle or NVP-HSP990 at indicated dose/schedules. Percent Ki67-positive tumor cells were determined by quantitative image analysis of immunohistochemical staining of tumor tissues collected on day 14, 24h post-dose last dose ($n=3$). * $p < 0.05$ versus vehicle (One Way ANOVA; Tukey test), ns, not significant

Supplementary Figure 1

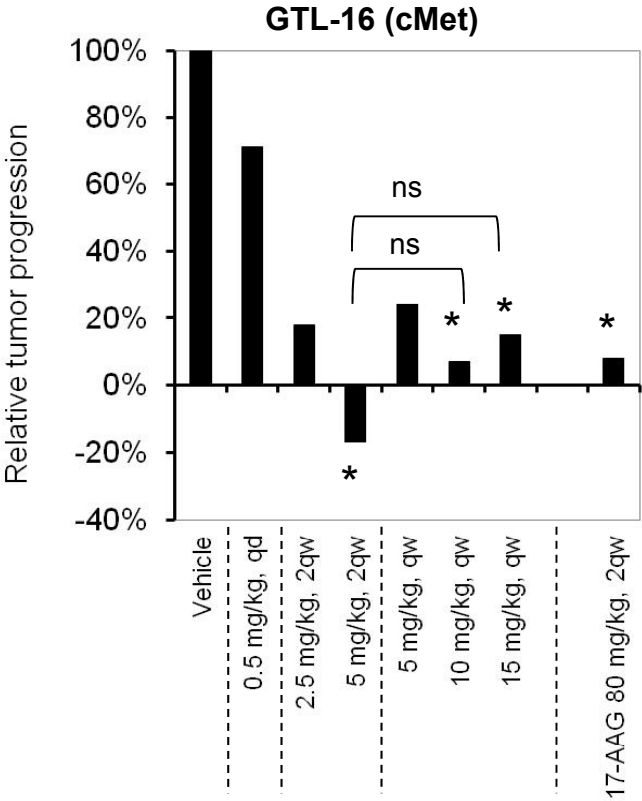


Supplementary Figure 2:



Supplementary Figure 3:

A



B

