Plasma concentrations of AUY922 and docetaxel in nanoparticle formulation are more than 2-4 orders of magnitude greater than conventional IV formulation

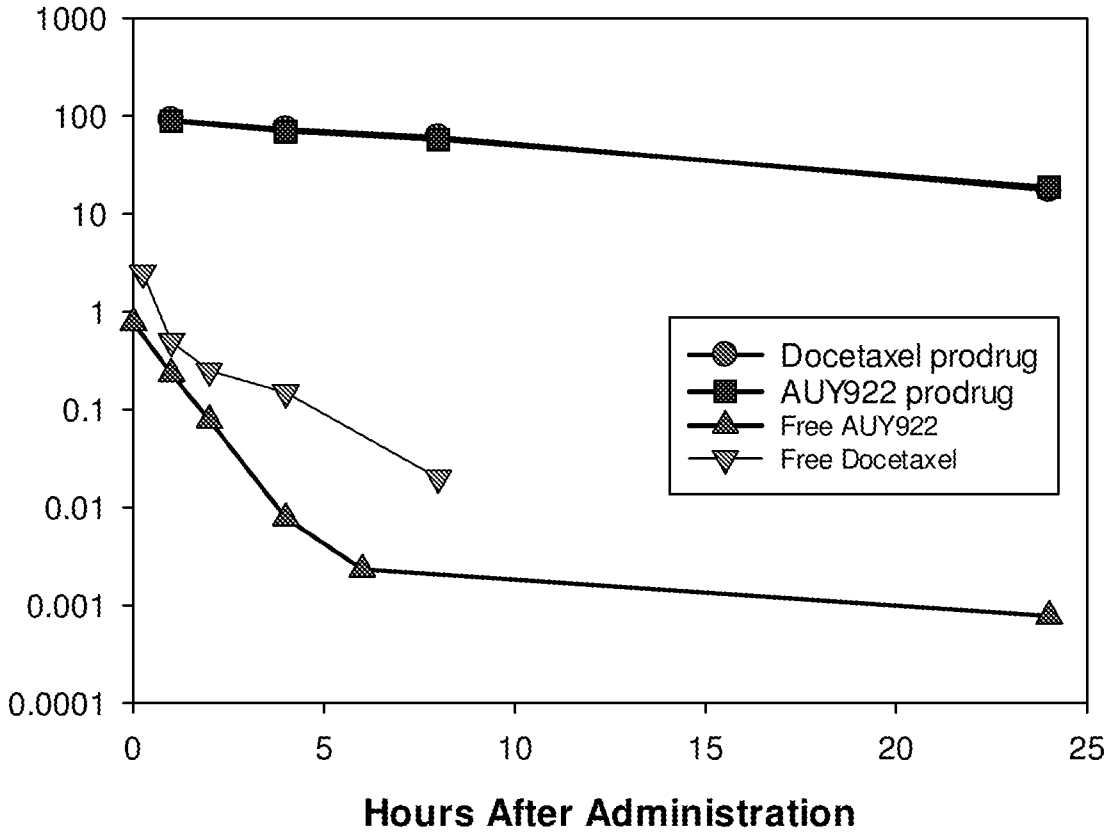


Figure 1

Relative tolerability of Docetaxel and AUY922 administered as a combination was compared to the MTD of free drugs administered individually

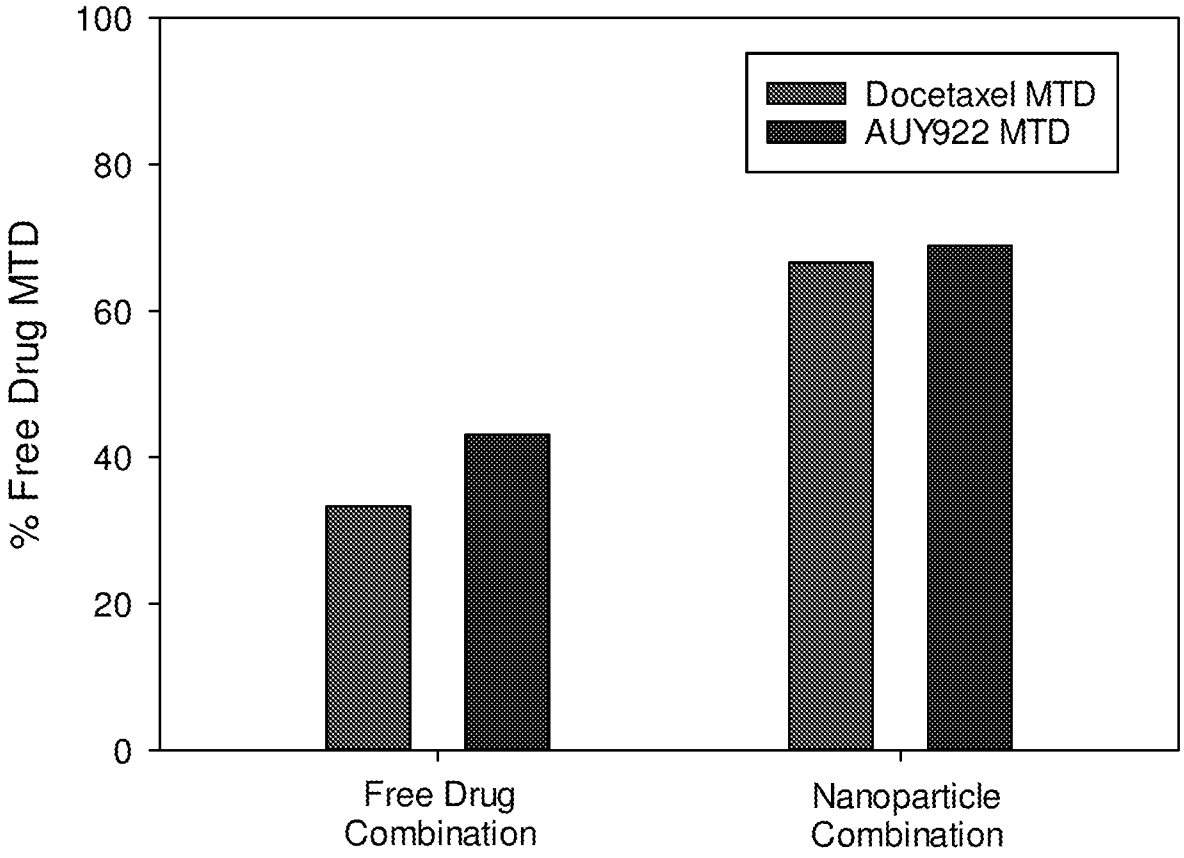
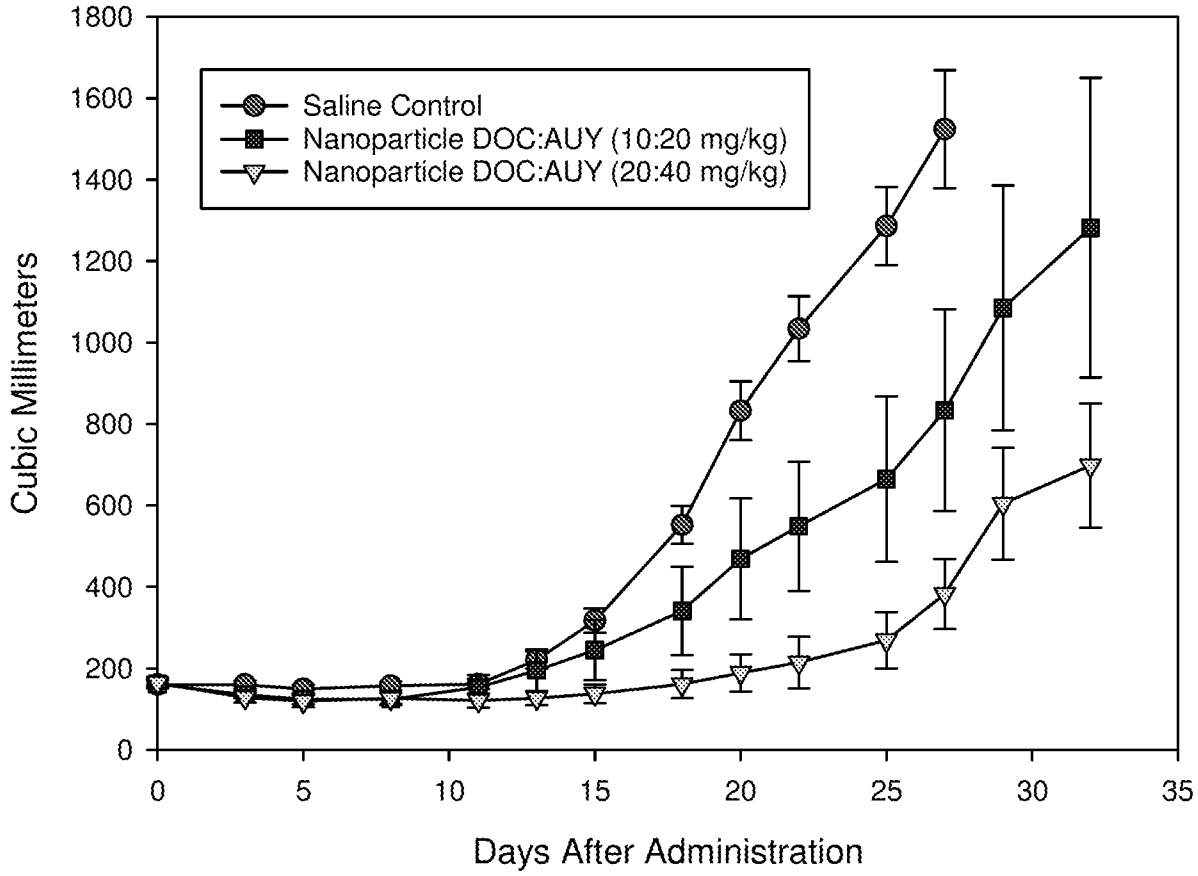


Figure 2

Prodrugs of Docetaxel and AUY922 formulated in PLA-PEG nanoparticles at a 1:2 drug ratio



Note: lowest free drug combination dose using 10 mg/kg docetaxel was excessively toxic (>25% body wt loss)

Figure 3

Combination of Docetaxel and AUY922 formulated in PLA-PEG nanoparticles is more efficacious than the free drug combination

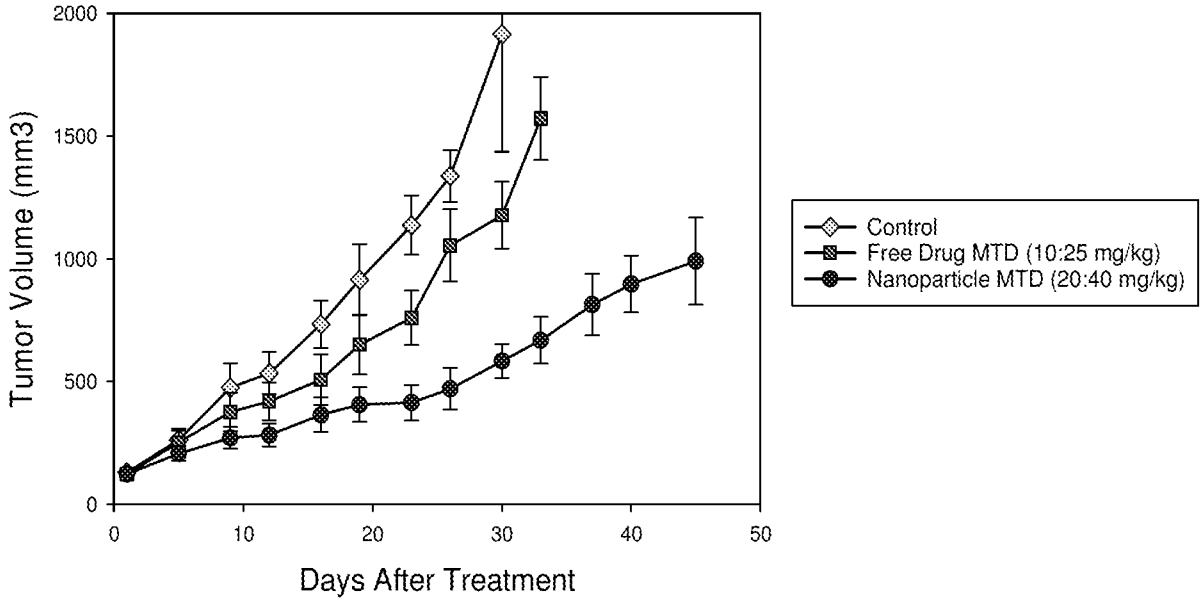


Figure 4

Prodrugs of Selumetinib and Ipatasertib formulated in PS:PEG nanoparticles (PS (10k) – PEG (5k)) at a 1:1 or 1:2 drug ratio

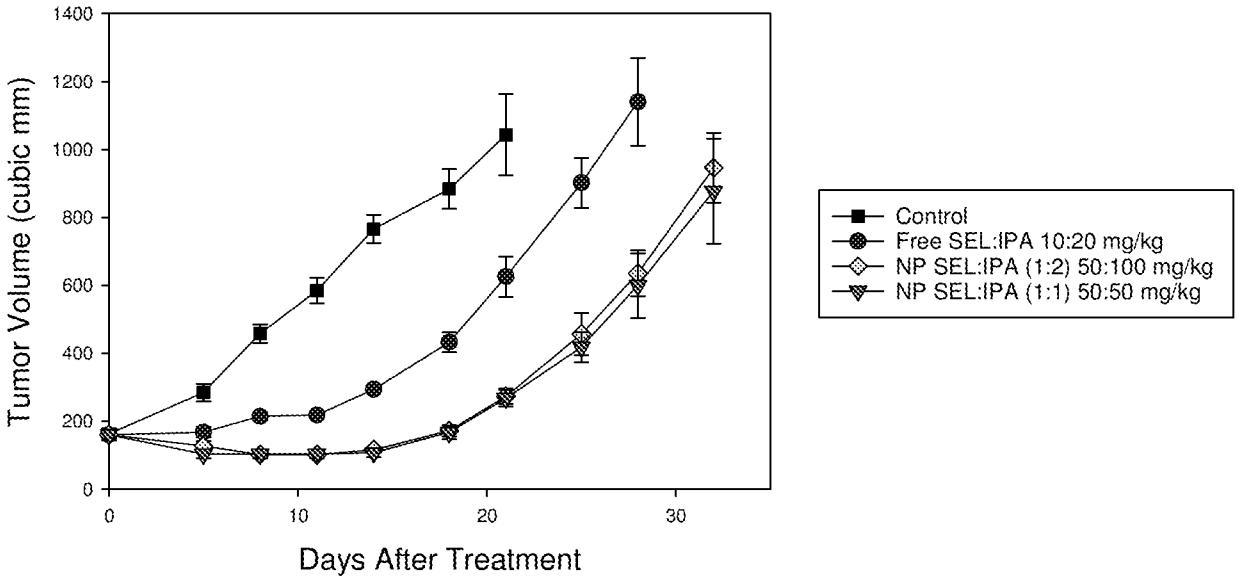


Figure 5A

Prodrugs of Selumetinib and Ipatasertib formulated in PS:PEG nanoparticles (PS (10k) – PEG (5k)) at a 1:1 or 1:2 drug ratio

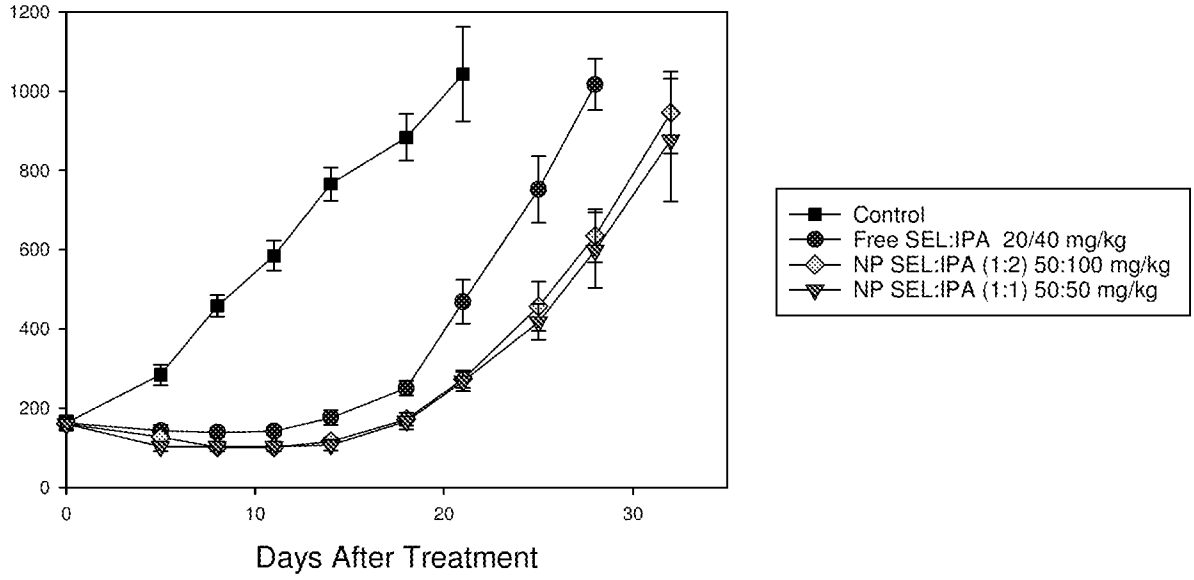


Figure 5B

Combination of Selumetinib and Ipatasertib formulated in PS:PEG nanoparticles is more efficacious than the free drug combination

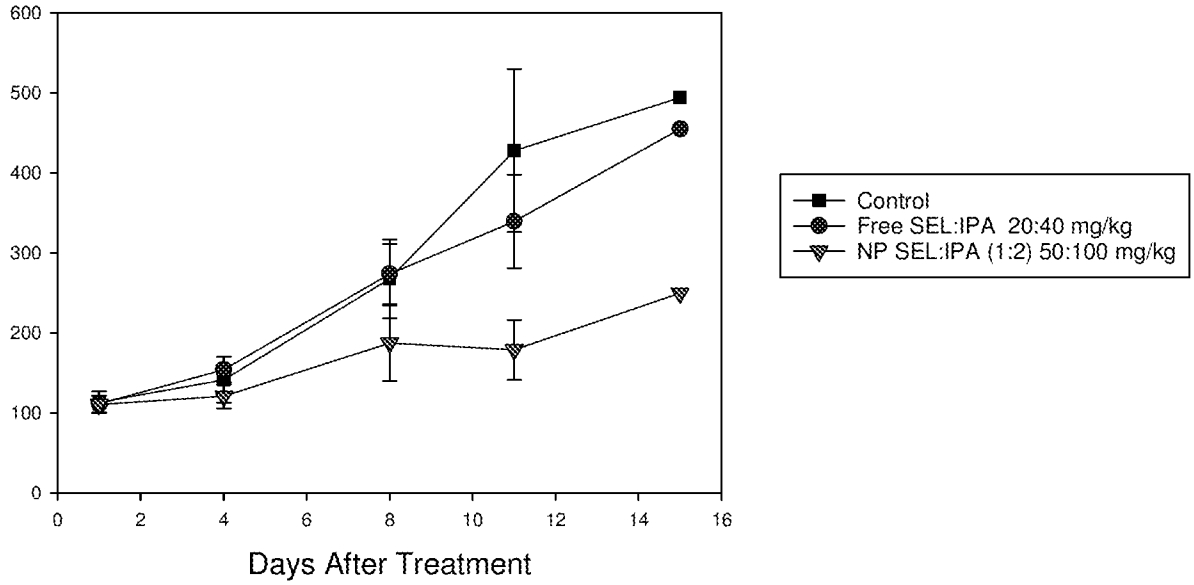


Figure 6