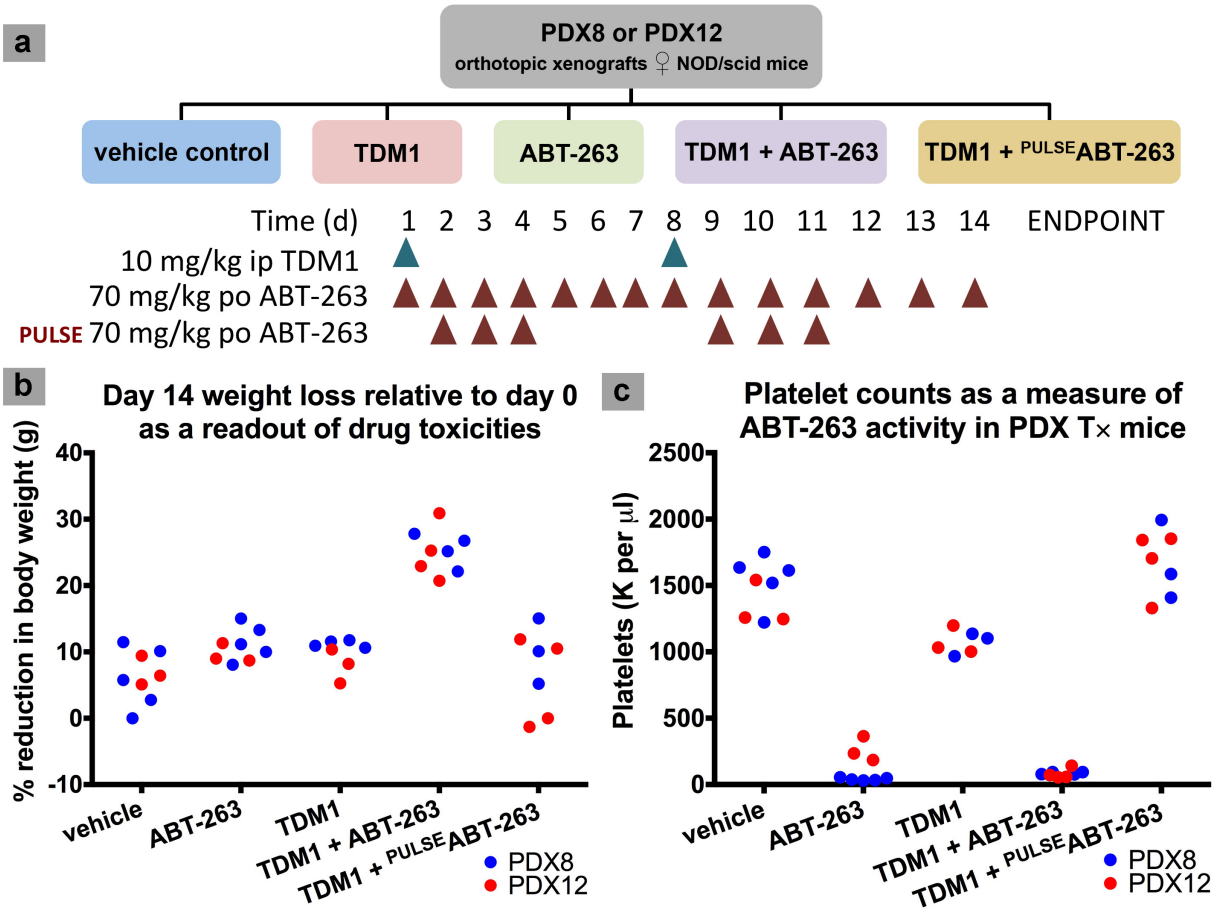

Supplementary Figure 2. Comparison of continuous versus pulsatile combination treatments. Female NOD/scid mice bearing either PDX8 or PDX12 orthotopic xenografts were randomized into one of the five treatment arms shown (**a**). T-DM1 and ABT-263 were administered as indicated (**a**). Body weight measurements were recorded on day 0 and at the experimental endpoint on day 14. Changes in body weights are graphed (**b**) as percent weight loss relative to individual day 0 measurements for PDX8 and PDX12 mice in each treatment group (Mann-Whitney one-tail test PDX8: vehicle versus T-DM1 + ABT-263; *p* value = 0.0079, T-DM1 + ABT-263 versus T-DM1 + ^{PULSE}ABT-263; *p* value = 0.0286 and PDX12: vehicle versus T-DM1 + ABT-263; *p* value = 0.0286, T-DM1 + ABT-263 versus T-DM1 + ^{PULSE}ABT-263; *p* value = 0.0143). Note greater tolerability of the pulsatile treatment compared to continuous treatment (**b**). Platelet counts are graphed (**c**) for PDX8 and PDX12 (Welch's one-tail *t* test PDX8: vehicle versus ABT-263; *p* value < 0.0001, ABT-263 versus T-DM1 + ^{PULSE}ABT-263; *p* value = 0.0056, T-DM1 + ABT-263 versus T-DM1 + ^{PULSE}ABT-263; *p* value = 0.0059 and PDX12: vehicle versus ABT-263; *p* value = 0.0009, ABT-263 versus T-DM1 + ^{PULSE}ABT-263; *p* value = 0.0002, T-DM1 + ABT-263 versus T-DM1 + ^{PULSE}ABT-263; *p* value = 0.0004). Note blood samples were collected from ABT-263-treated animals 3-6 h post-treatment. Note continuous ABT-263 treatment induces thrombocytopenia (**c**), whereas pulsatile ABT-263 treatment eliminates platelet side effects (**c**). Note blood clotting, at the time of sample collection, prevented accurate assessment of platelet counts in one of the four PDX8 mice treated with T-DM1 (**c**). Female non-tumor bearing NOD/scid mice, treated with T-DM1 and ABT-263 according to the dose and schedule presented here, exhibited no evidence of cardiac fibrosis or cardiomyocyte apoptosis.