

Figure 1. Inhibitors of DNA damage response

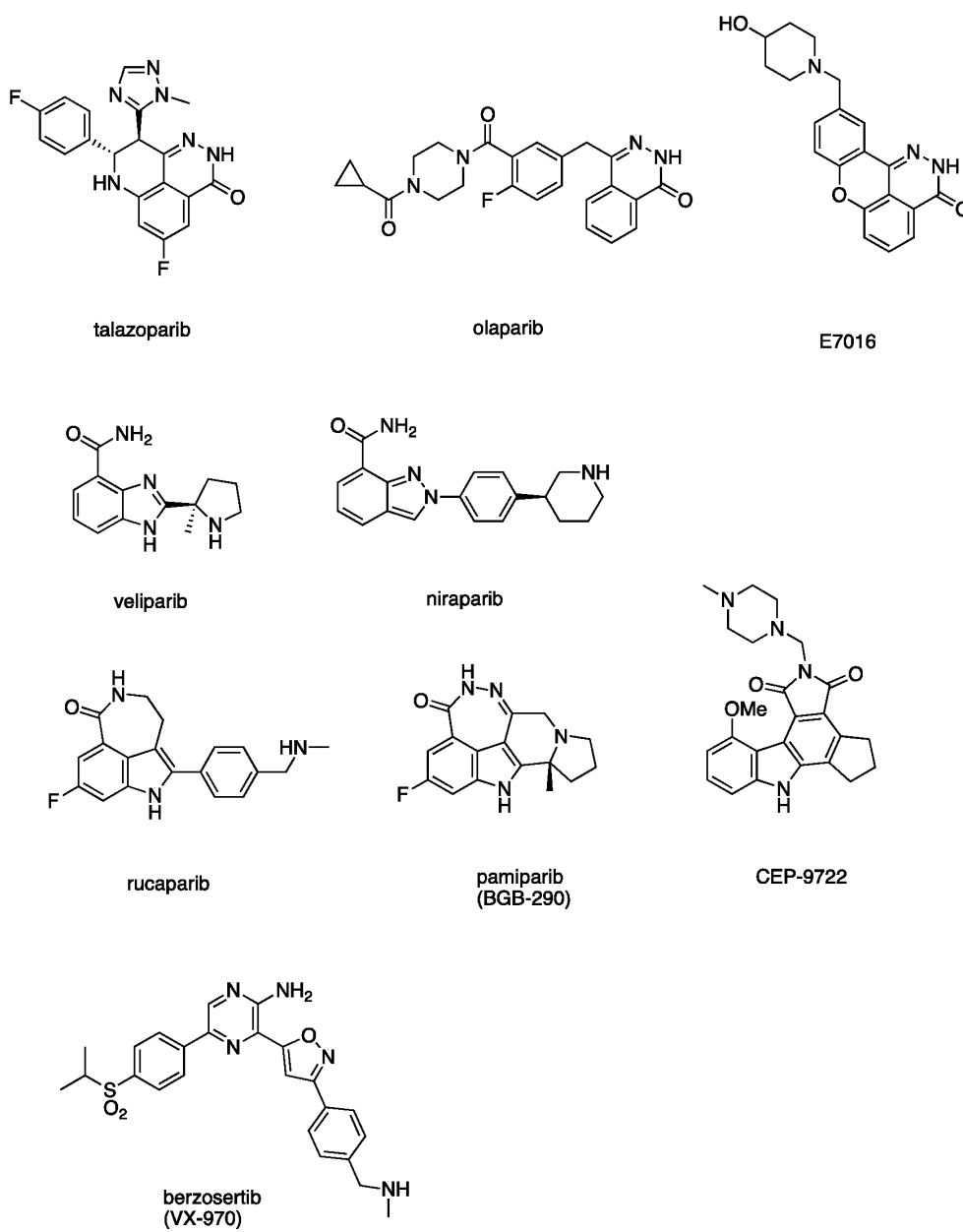
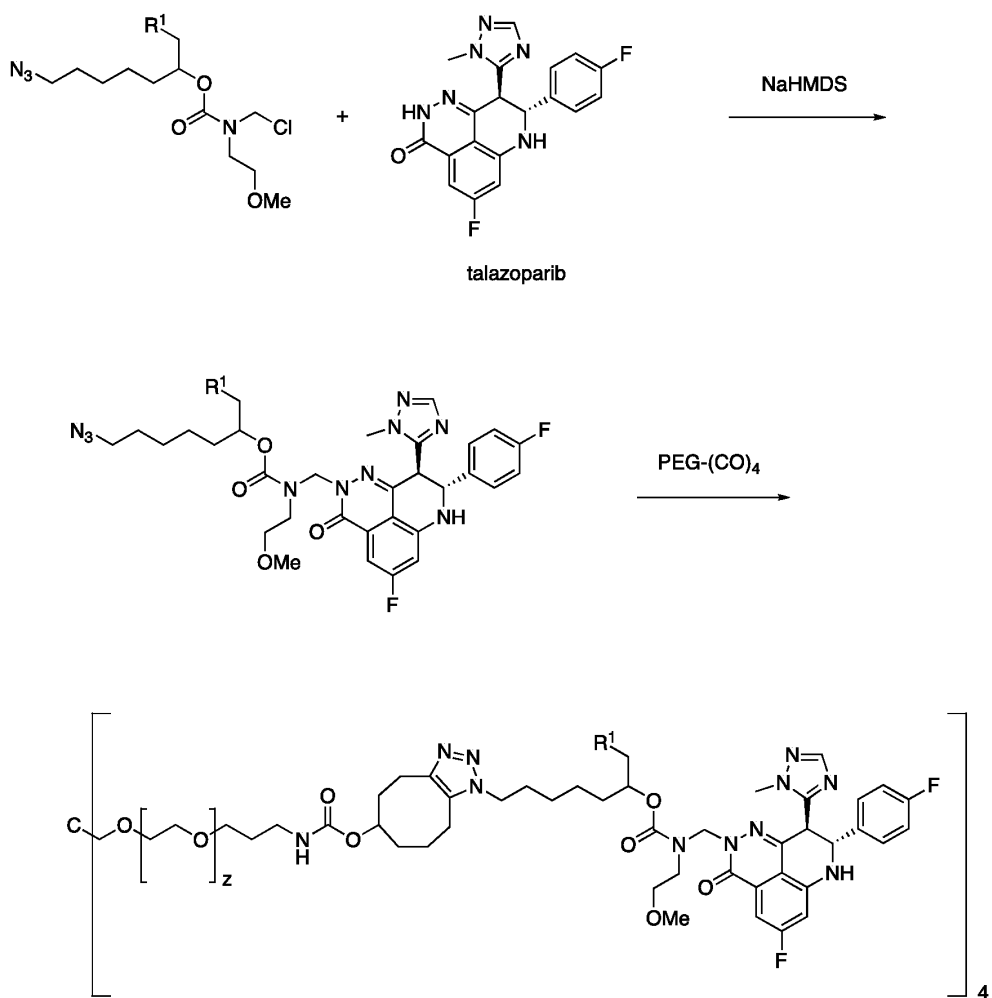
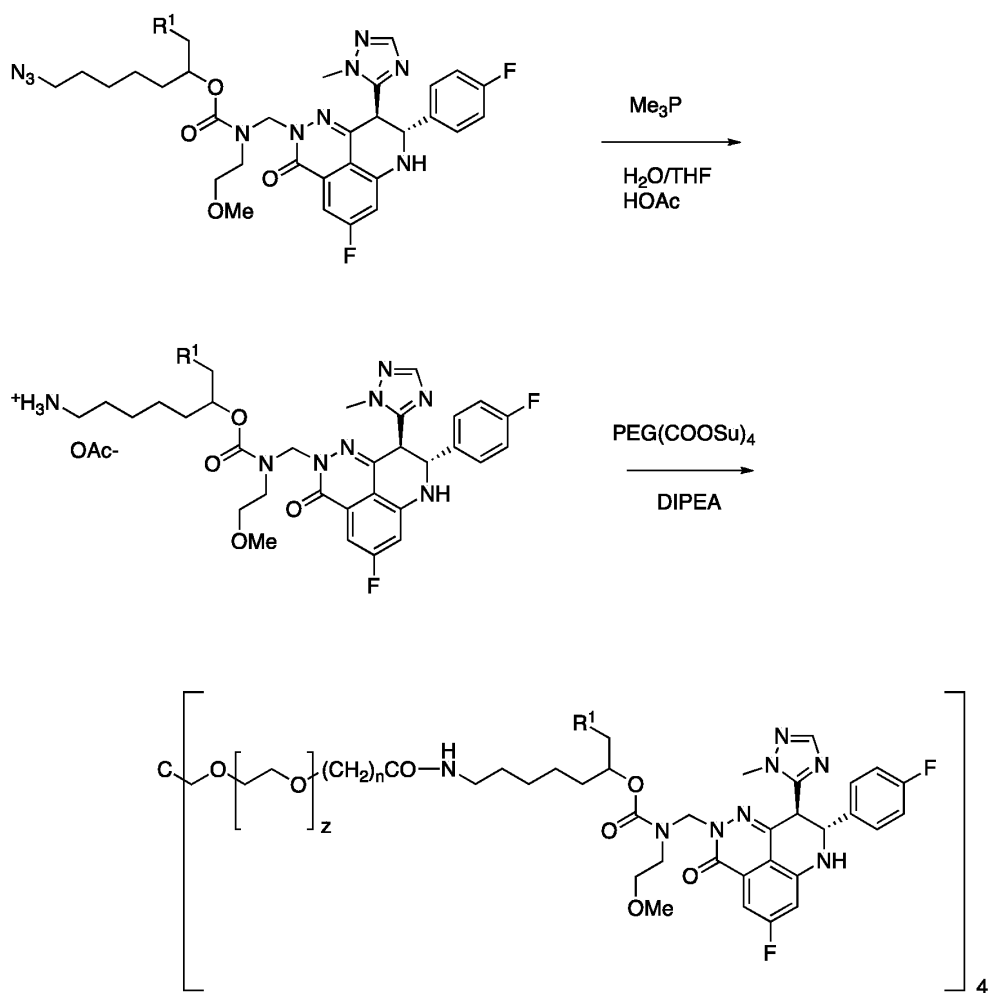


Figure 2. Preparation of releasable PEG-talazoparibs



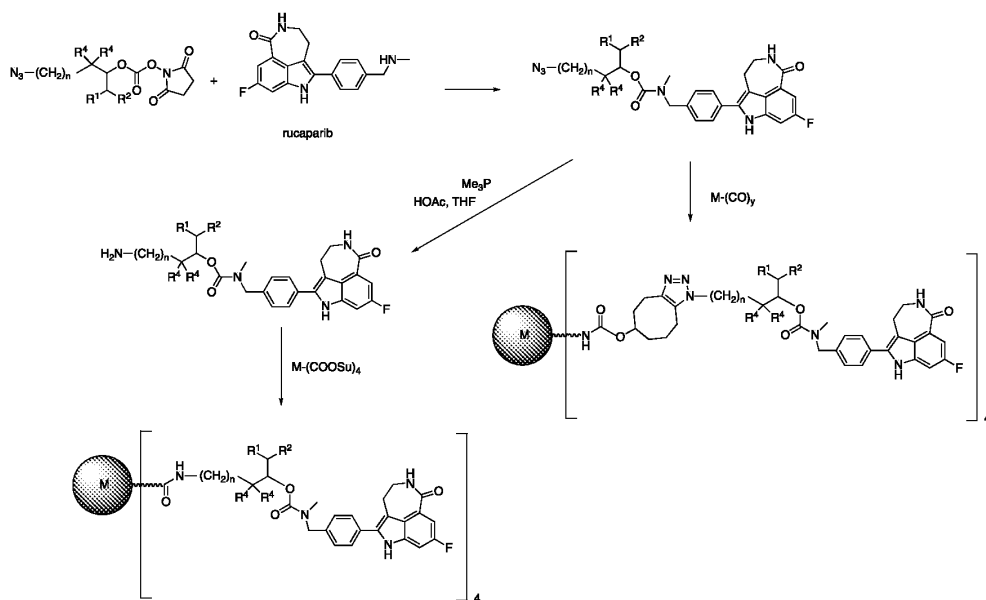
3/12

Figure 3. Alternate synthesis of conjugated talazoparib



4/12

Figure 4. Preparation of conjugated Rucaparib



5/12

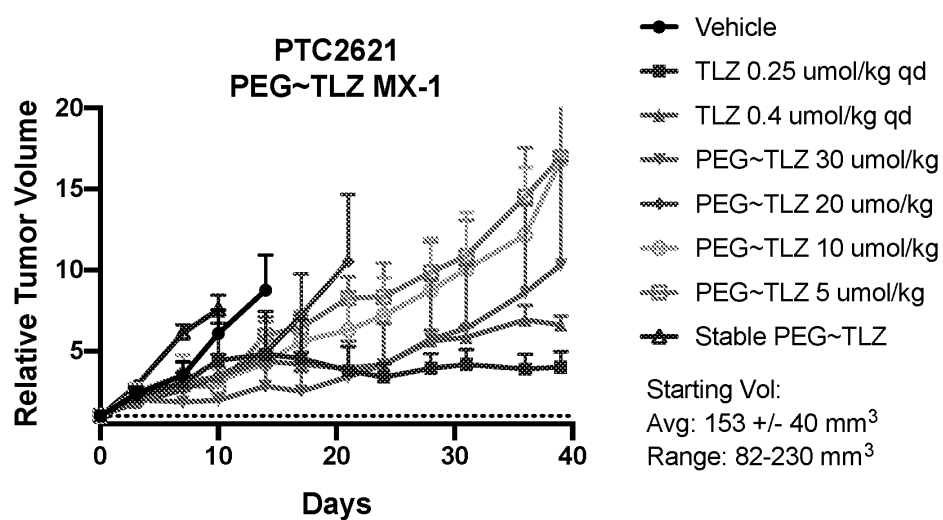


Figure 5. Relative tumor volume versus time. Mice bearing MX-1 xenografts were treated on day 0 with vehicle (●), daily oral TLZ at 0.25 (■) or 0.4 $\mu\text{mol/kg}$ (▲), a single ip dose of releasable PEG~TLZ at 30 (▼), 20 (◆), 10 (○), 5 (□) or a single ip dose of 30 $\mu\text{mol/kg}$ stable PEG~TLZ (△). Relative tumor volumes are plotted as average $\pm$ SEM.

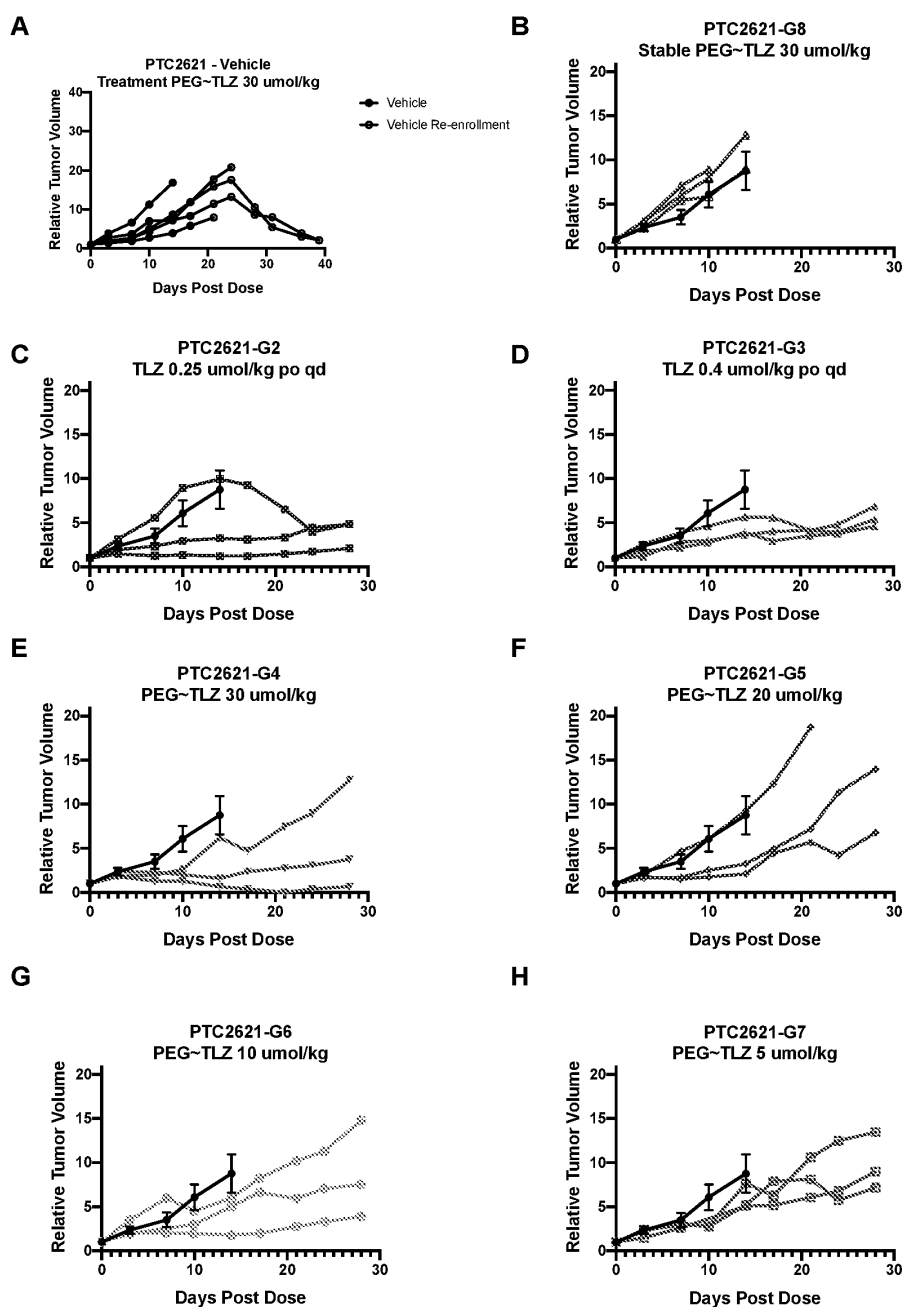
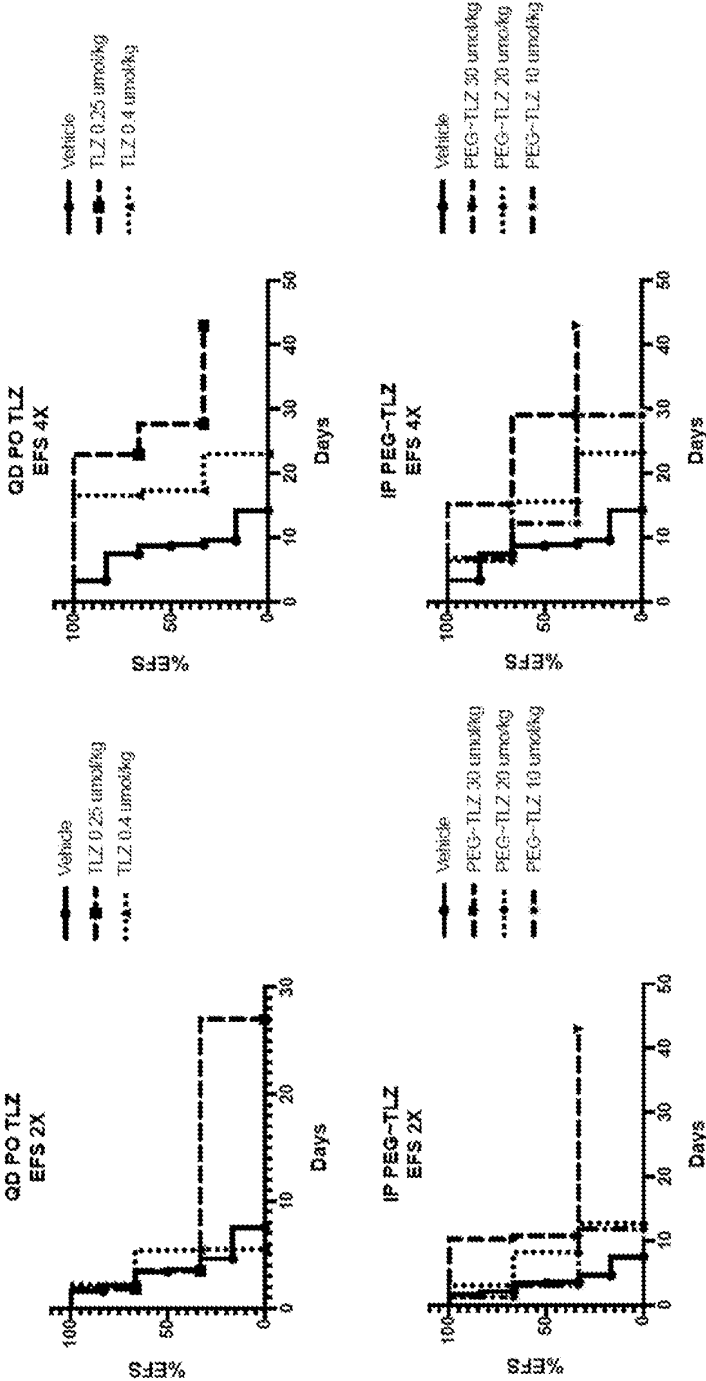


Figure 6. Individual relative tumor volume for: vehicle (●), daily oral TLZ at 0.25 (⊗) or 0.4 $\mu\text{mol/kg}$ (⊠), a single ip dose of PEG~TLZ at 30 (▼), 20 (◆), 10 (○), 5 (◐) or a single ip dose of 30 $\mu\text{mol/kg}$ stable PEG~TLZ (Δ). Relative tumor volumes are plotted as average $\pm$ SEM.

Figure 7



8/12

Figure 8

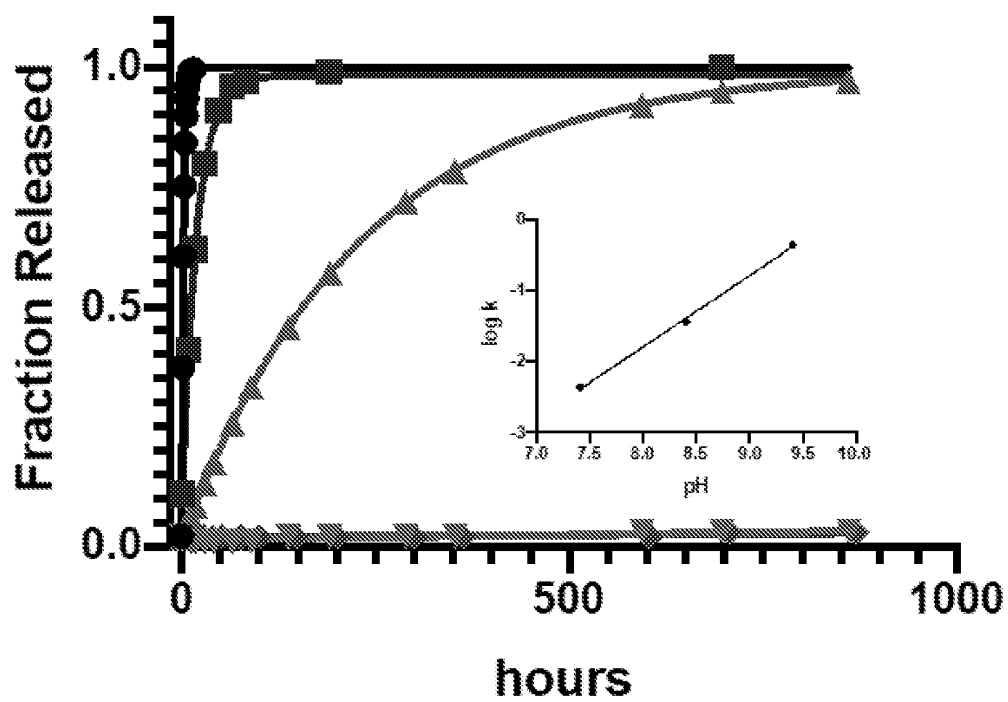
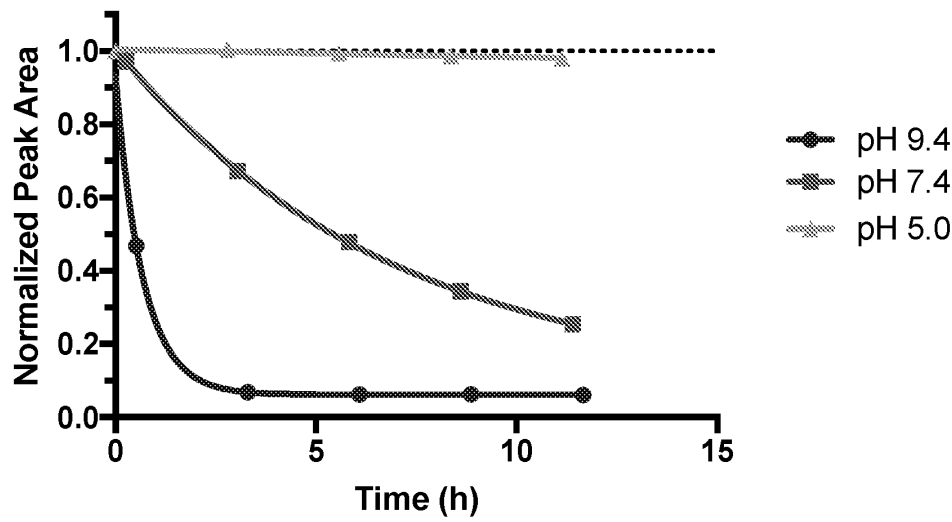
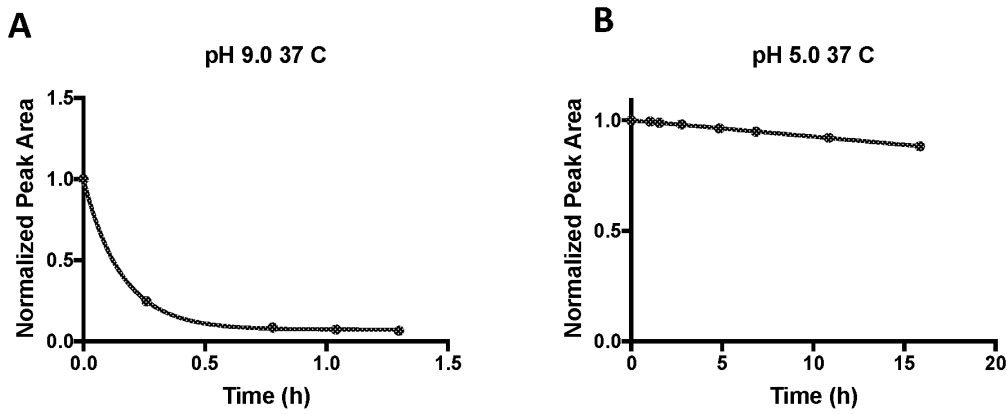


Figure 9A



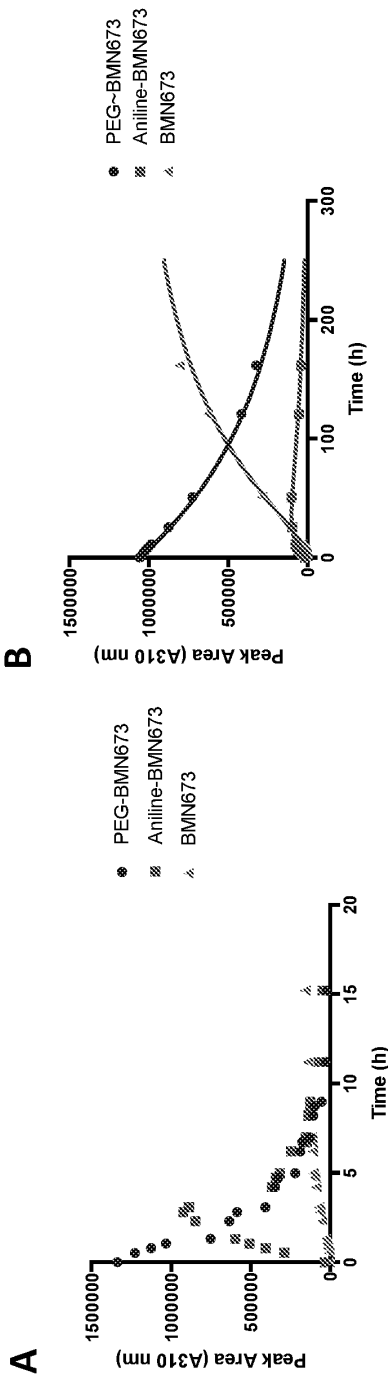
Stability of non-releasable acylated conjugate (Mod = H).

Figure 9B



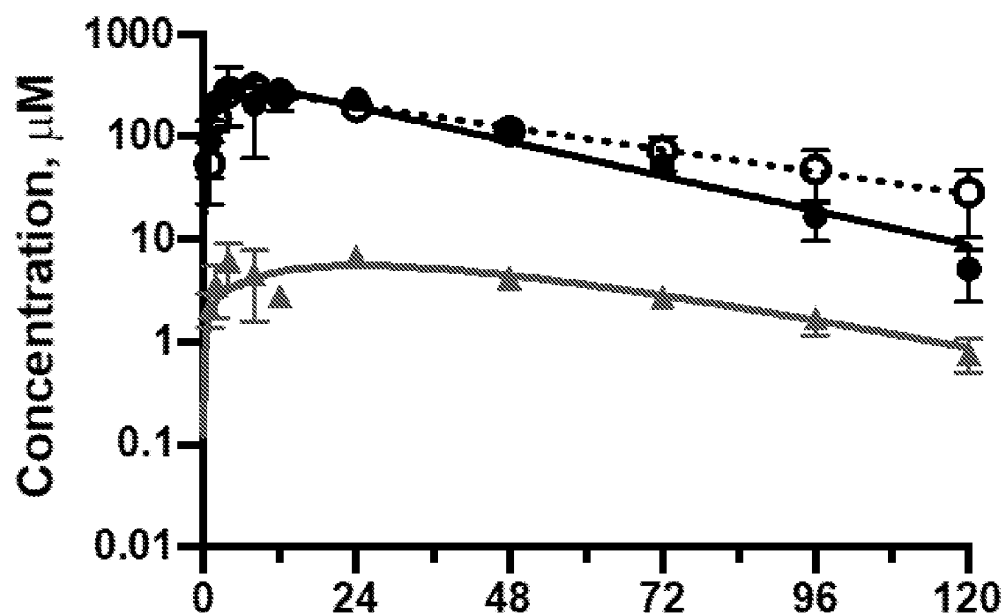
Release kinetics and stability of releasable conjugate (Mod = SO₂Me).

Figure 10



11/12

Figure 11



Plasma concentration versus time plot for non-releasable PEG-talazoparib conjugate (Mod = H) (○), releasable PEG-talazoparib conjugate (Mod = SO₂Me) (●), and talazoparib released from releasable PEG-talazoparib conjugate (▲) in mice.

Figure 12

