

Supplementary Methods

Plasma stability assay

STA-12-8666 and irinotecan were incubated with mouse, dog, and human plasma at four different time points (0, 15, 30, and 60 minutes). The final concentration of the test articles was 10 μ M with a DMSO concentration of 1% in plasma. At each time point, 50 μ L aliquots of plasma were sampled in triplicate and precipitated with 0.5% formic acid in acetonitrile containing isotope labeled internal standards for the test articles. The samples were centrifuged and the resultant supernatant was evaporated under nitrogen at 40°C. The remaining residue was reconstituted with 150 μ L of 1% formic acid in 50:50 acetonitrile:water and analyzed by LC-MS/MS. A Waters SymmetryShield RP18 column (5 μ m, 2.1x100mm) was used with a run time of 5 minutes per sample. The percentage of test article remaining at the individual time points was calculated relative to the 0 minute sample, and error is presented as \pm SD.