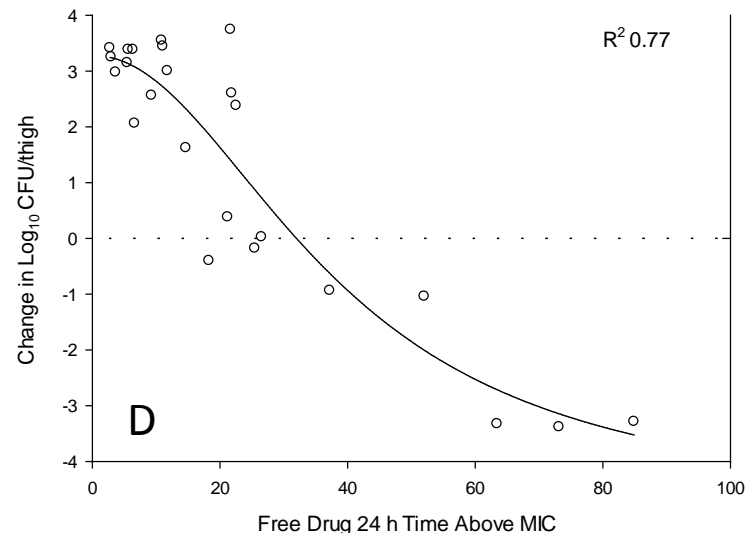
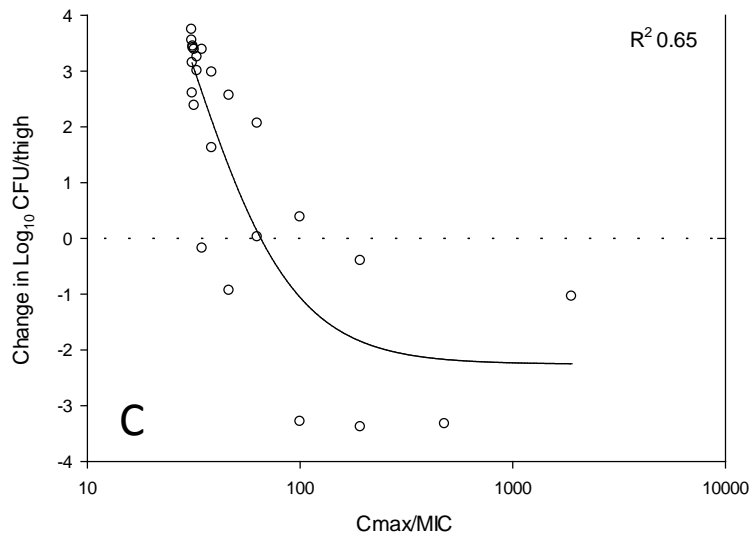
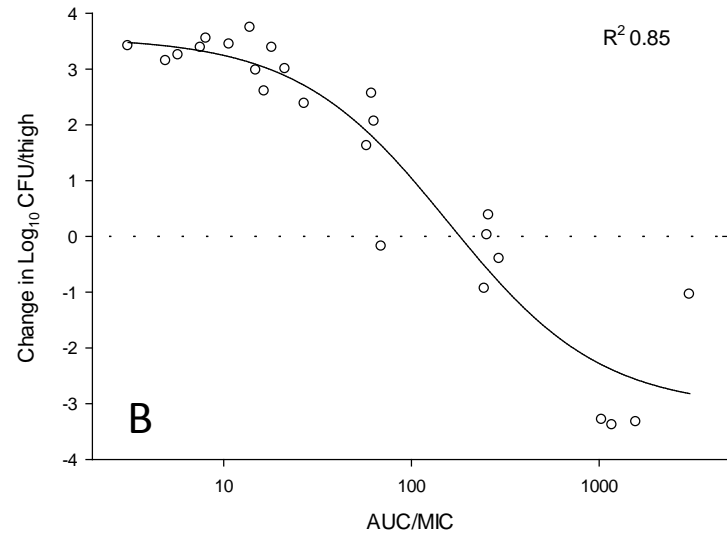
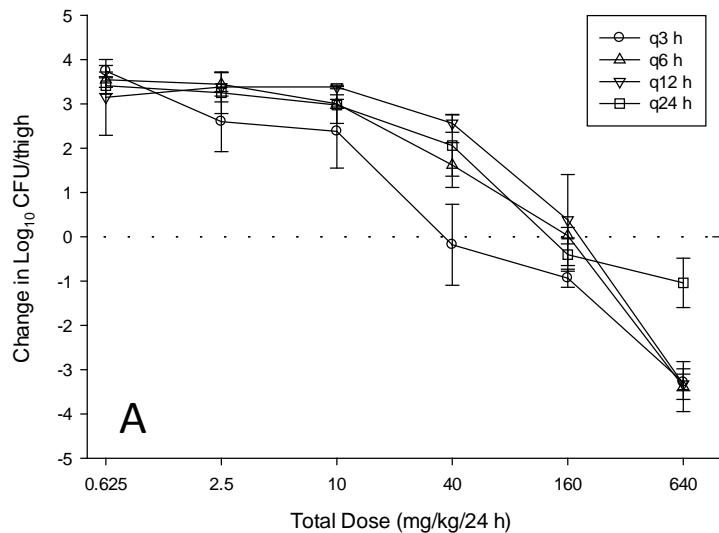


**Supplemental Figure 1.** Plasma ACT-387042 AUC<sub>0-∞</sub> values for each of the four doses administered in the pharmacokinetic experiments. The relationship between AUC and dose was non-linear and best described by an exponential, single, 3 parameter model as shown in the figure legend.



**Supplemental Figure 2.** *In vivo* dose fractionation study with ACT-387042 against *S. pneumoniae* ATCC 10813 (Panel **A**). Each symbol represents the result from six thighs. Total dose ranged from 0.625 to 640 mg/kg/24 h fractionated into every 3-, 6-, 12-, and 24-hourly regimens. The association between the PK/PD index 24 h AUC/MIC on treatment effect is shown in **B**, the association between PK/PD index Cmax/MIC on treatment effect is shown in **C**, and the association between the PK/PD index percent time free drug levels exceed the MIC on treatment effect is shown in **D**. The  $R^2$  represents the coefficient of determination. The curved, solid line drawn through the data points is the best fit line based upon the sigmoid Emax formula. The dashed horizontal line represents net stasis of organism burden over the 24 h treatment period. Data points below the line represent killing and points above the line represent growth.