

Supplementary Figure Legends:

Supplementary Figure 1: Effect on mouse body weights of three different schedules by metronomic oral dosing of LY2334737 in the human colon HCT-116 xenograft model. Body weights are the mean \pm SEM and are from the efficacy study in Figure 2. **Panel A:** Mouse body weights for once-a-day oral administration of LY2334737 for 14 days. Mice (10 per group) were dosed by oral gavage with vehicle (\blacktriangle), 1.89 mg/kg (O), 3.77 mg/kg (\blacksquare), or 7.55 mg/kg LY2334737 (\triangle) or 160 mg/kg gemcitabine HCl (\blacksquare) IP Q3D x 4. One animal died in the highest dose group. **Panel B:** Mouse body weights of every-other-day dosing for 7 doses. Mice (9 per group) were treated with vehicle (\blacktriangle), 6.5 mg/kg (O), 13 mg/kg (\blacksquare), or 26 mg/kg LY2334737 (\triangle). **Panel C:** Body weights of mice treated once-a-day dosing for one week, followed by a week of rest and then once-a-day dosing for the next week. Mice (8 per group) were dosed by oral gavage with vehicle (\blacktriangle), 6.0 mg/kg (O), 7.2 mg/kg (\blacksquare), or 10.5 mg/kg LY2334737 (data not presented). Each mouse received a total of 14 doses. In the highest dose group (10.5 mg/kg LY2334737), all mice either died or were taken off study due to poor health within the first 7-10 days of treatment.

Supplementary Figure 2: Effect of LY2334737, capecitabine and dual therapy on mouse body weights in human colon cancer xenograft models. Body weights are the mean \pm SEM and are from the efficacy study in Figure 5. All therapies were given QD x14 by oral gavage. **Panel A:** HCT-116 xenograft model. Mice (8 per group) were treated with vehicle (\blacktriangle), 4 mg/kg LY2334737 (\bullet), 175 mg/kg capecitabine (MTD, O) or both (\blacksquare). Dual therapy resulted in significant (14%) weight loss on day 8, however complete recovery occurred over the next 7 days. There were no deaths. **Panel B:** HT-29 xenograft model. Mice (7 per group) were treated with vehicle (\blacktriangle), 4 mg/kg LY2334737 (\bullet), 150 mg/kg capecitabine (MTD, O) or dual therapy (\blacksquare). All drug treatments resulted in significant weight loss on Day 7 of $\leq 13\%$ ($p \leq 0.05$); no mortalities in the drug treatment groups and two in the vehicle group. **Panel C:** Efficacy in patient-derived colon tumor CXF 676 xenograft. Mice (7 per group) were treated with vehicle (\blacktriangle), 4 mg/kg LY2334737 (\bullet), 150 mg/kg capecitabine (MTD, O) or dual therapy (\blacksquare). There was one death in the vehicle group and one in the dual therapy group on Day 17.