

Supplementary Figure S1. Relationship between oral doses and average plasma concentrations of PD-0325901 in athymic nu/nu mice. Shaded area represents average plasma concentrations of PD-0325901 in patients of Phase I trial (17). Average concentrations (C_{ave}) were calculated by the area under plasma concentration-time curve from time 0 to end of dosing interval divided by dosing interval period.

Supplementary Figure S2. PD-0325901 reverses body weight loss due to PF-04880594 administration in nude mice. Changes in body weight over a 2-week period were measured in nude mice treated with 40 mg/kg PF-04880594 alone or with 40 mg/kg PF-04880594 co-administered with 0.3, 1.0, or 2.5 mg/kg PD-0325901. Mice treated with PF-04880594 alone were euthanized on Day 7 due to the onset of moribundity. Mice co-treated with PD-0325901 maintained higher body weights by Day 15 and survived to the end of the study.

Supplementary Figure S3. Photographs of canine muzzles showing skin flushing following PF-04880594 treatment. Canines treated with PF-04880594 exhibited a noticeable flushing of the skin, visible through the fur, approximately 30 minutes after dosing.