SUPPLEMENTAL INFORMATION: FIGURE LEGENDS

S1. Further representative sections of normal right kidney (RK) and tumor tissues were subjected to immunohistochemical analysis for NRF2 (see Fig. 1D and accompanying legend).

S2. Glucose (Glu), glutamine (Gln), glutathione (GSH), and cell viability in RCC cells

A. 786-0 cells were incubated with 1 μM CB-839 for 24 h. The cells and conditioned media were obtained and analyzed by LC-MS/MS for the metabolites indicated as described in Materials and Methods. Error bars are ±SD. * $p<0.05$ as compared to DMSO treated cells

B: Incubation of RCC cells with CB-839 for 72 h at various concentrations gave a cell viability IC50 of 740 nM for SN12 cells and 970 nM for 786-0.

S3. Apoptosis flow data

SN12 cells were grown to 70% confluence and incubated with CB-839 at the concentrations indicated for 20 h followed by H_2O_2 (where indicated) for 4 h. Total apoptosis was measured using the MUSE Annexin V and Dead Cell Assay.

S4. Bioluminescence imaging, measurements, and animal weights

A: SN12 cells (0.5 million cells) were injected under the left kidney capsule of SCID mice (n=8 per condition; third animal experiment). After 3 weeks of xenograft tumor growth, the mice were randomly assigned to two treatment groups and dosed orally twice a day with vehicle or 200 mg/kg CB-839 for 2 weeks. Weekly whole body bioluminescence imaging (BLI) with luciferase signal quantitation was performed to monitor tumor progression. *In vivo* bioluminescent images for all mice per before and after CB-839 treatment are shown demonstrating reduction in tumor growth with CB-839 after 2 weeks. Color scale for all images was set on a minimum of 500 and a maximum of 6000 counts

B: Average weight of animals (n=8 per group) in CB-839 and vehicle treated animals over the entire treatment period in the third animal experiment.

S5. Coronal PET MIP images overlaid with CT images. PET scans were obtained at day 0 (three weeks after SN12 cells were injected under the renal capsule) and day 14, immediately following two weeks of orally dosing mice twice daily with vehicle or 200 mg/kg CB-839.