Supplemental Figures

Sup Fig 1. Verification of renal origins and confirmation of patient tissue match for RWV-366T ccRCC cell line. **(A)** STR analysis of patient ccRCC tissue and matched RWV-366T cell line. **(B)** IHC staining of RVW-366T cell line for renal cell markers including Podocin, PAX2, and GGT.

Sup Fig 2. Inhibition of SCD1 activity in ccRCC induces endoplasmic reticulum stress response in ccRCC. **(A)** Representation of the chemical structure of A939572. **(B)** Table depicting ER stress response genes upregulated in response to A939572 treatment in ccRCC cell lines from gene array analysis. Fold change represents combined average of A498, Caki1, Caki2, and ACHN cells. **(C)** A939572 dose response in K359N and K360N NRE cells. **(D)** QPCR for ER stress markers *CHOP, HERPUD1, GADD45a*, and *BiP* in K359N and K360N cells (100nM A939572 or lentiviral (shSCD780) SCD1 inhibition at 48Hr).

Sup Fig 3. ATF6 is activated in response to SCD1 inhibition in ccRCC. Relative luciferase activity of ATF6 ER stress p5xATF6-GL3 (UPR) luciferase reporter transfected in Caki1 and A498 cells treated with A939572 (75nM) or shSCD lentivirus +/-OA-BSA supplementation was measured after 48Hr. Fold change inductions of 1.6, 1.7, 3.8, and 2.0 were observed in Caki1 A939572+BSA, Caki1 shSCD780+BSA, A498 A939572+BSA, and A498 shSCD780+BSA cells respectively.

Sup Fig 4. Monotherapeutic dose out of pazopanib and sunitinib, and combinatorial effects with SCD1 inhibitor in ccRCC cells. **(A)** Dose out of pazopanib in ccRCC cell lines A498, Caki1, Caki2, and ACHN. **(B)** Growth response to combinatorial treatment of Caki1 and A498 with pazopanib and A939572. **(C)** Dose out of sunitinib in ccRCC cell lines A498, Caki1, Caki2, and

ACHN. **(D)** Growth response to combinatorial treatment of Caki1 and A498 with sunitinib and A939572.

Sup Fig 5. Monotherapeutic Dose out of the mTOR inhibitor temsirolimus in ccRCC cell lines. Dose out of Temsirolimus in ccRCC cell lines A498, Caki1, Caki2, and ACHN. Y-axis values are plotted as percent of DMSO control for each respective cell line.

Sup Fig 6. Treatment of ccRCC cells with SCD1 inhibitor in combination with the mTOR inhibitor temsirolimus synergistically inhibits tumor cell growth *in vitro*. Proliferation, Synergy curves, and combination index (CI) of **(A)** Caki1 **(B)** A498 **(C)** Caki2 and **(D)** ACHN cells treated with A939572 (SCDi) and a fixed concentration of 0.1, 1, and 10nM Temsirolimus. Y-axis values are plotted as percent of DMSO control for each respective cell line. Drug synergy was analyzed using CalcuSyn® (19) based on the Chou-Talalay Method where CI values >1 represent an antagonistic effect and values <1 represent synergy. Individual dose CI values are provided in the adjacent tables.

Sup Fig 7. Treatment of ccRCC cells with A939572 in combination with the mTOR inhibitor Temsirolimus synergistically inhibits tumor cell growth in soft agar. Soft agar colony formation assay was performed on A498 cells grown in the presence of A939572 or Tem alone or in combination. Drug was refreshed every week throughout the course of the treatment which was 3 weeks (3x total).