Supplementary Figure Legends and Supplementary Table 1:

Supplementary Figure 1. Inhibition of a panel of protein kinases *in vitro* by 10 μM CCT128930. Data are from a kinase profile against 50 different human kinases carried out using 10 μmol/L CCT128930 with an ATP concentration equivalent to the Km for each enzyme (Millipore).

Supplementary Figure 2 CCT128930 induces PARP cleavage in *PTEN*-null U87MG human glioblastoma cells *in vitro*.

Cells were treated with CCT128930 (16 μM) for the indicated durations of time and immunoblotted for the AKT substrates shown and for PARP cleavage. GAPDH was used as a loading control. ∅ no treatment, - DMSO treated control, + CCT128930 treated samples, LY is a positive control for AKT pathway inhibition (LY294002 30μM x 1 hour) and OA is a positive control for apoptosis (Okadaic acid 100nM x 24h).

Supplementary Figure 3. Effect of CCT128930 concentration on the cell cycle distribution of *PTEN*-null U87MG human glioblastoma cells *in vitro*. Cells were treated with the indicated concentrations of CCT128930 for 24 hours and the cell cycle distribution determined using BrdUrd incorporation and PI staining. Cont refers to a no treatment control, and DMSO is the vehicle control. Similar results were obtained in a repeat experiment.

Supplementary Figure 4. Effects of CCT128930 on pThr246 and total PRAS40 expression in *PTEN*-null U87MG human glioblastoma cells *in vitro*. A, Expression of pThr246 and total PRAS40 in *PTEN*-null U87MG

human glioblastoma cells following CCT128390 expression at different concentrations for 24 hours. Panel **1** shows pThr246 PRAS40 expression in control treated cells. Panel **2** shows pThr246 PRAS40 in cells treated with 18.9 μM CCT128390 for 24 hours (3 x GI_{50}). Panels **3** and **4** show the corresponding total PRAS40 signals from control and CCT128930-treated cells, respectively. Magnification was x500. **B,** Quantification of pThr246 PRAS40 changes relative to control in U87MG human glioblastoma cells treated with different concentrations of CCT128390 for 24 hours. The within run precision (%CV) ranged between 16 to 36% for eight separate determinations. Data are mean ± SE for 3 values determined in independent experiments. Statistics: * P<0.05, ** P<0.01 and *** P<0.001 significantly different from vehicle treatment.

Supplementary table 1. Summary of the pharmacokinetic parameters of CCT128930 (25 mg/kg) in CrTacNCr-*Fox1nu* mice

Tissue	Route	T1/2 (h)	Tmax (h)	Cmax (μM)	Vss (L)	Cl (L/h)	$AUC_{0-\infty}$ (μMh)	Bioavailability (%)
Plasma	i.v.	0.95	0.083	6.36	0.25	0.325	4.62	100
Plasma	i.p.	2.33	0.5	1.28	N/A	0.372	1.33	28.8
Tumor	i.p.	3.89	1	8.02	N/A	0.06*	25.8	N/A
Plasma	p.o.	0.57	0.5	0.432	N/A	0.317	0.392	8.5

Non-parametric PK parameters were determined using WinNonlin software with 7 to 8 time points and 3 to 5 mice per time point. *Apparent clearance. N/A not applicable.