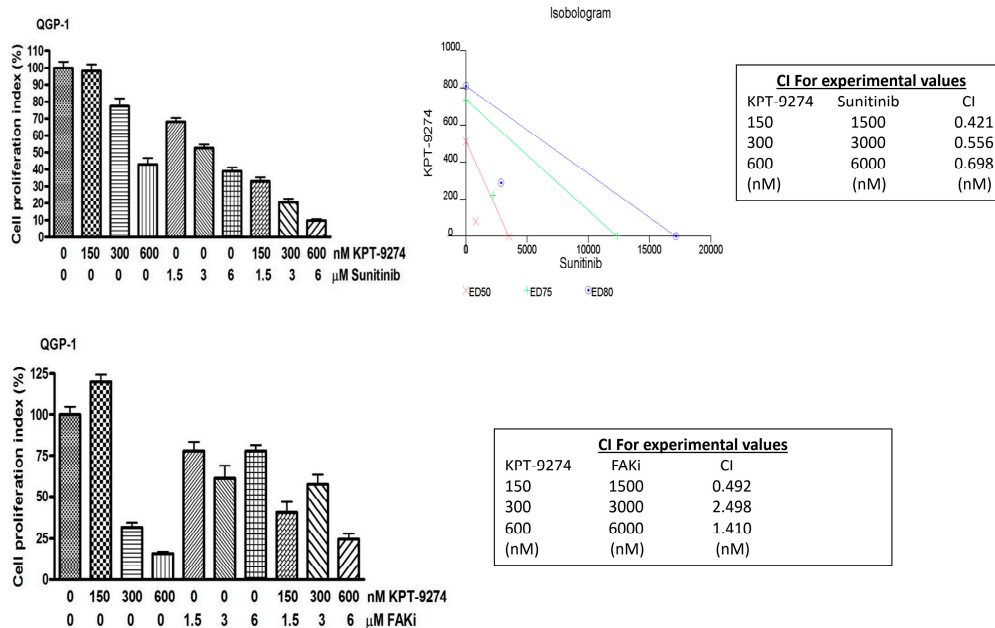
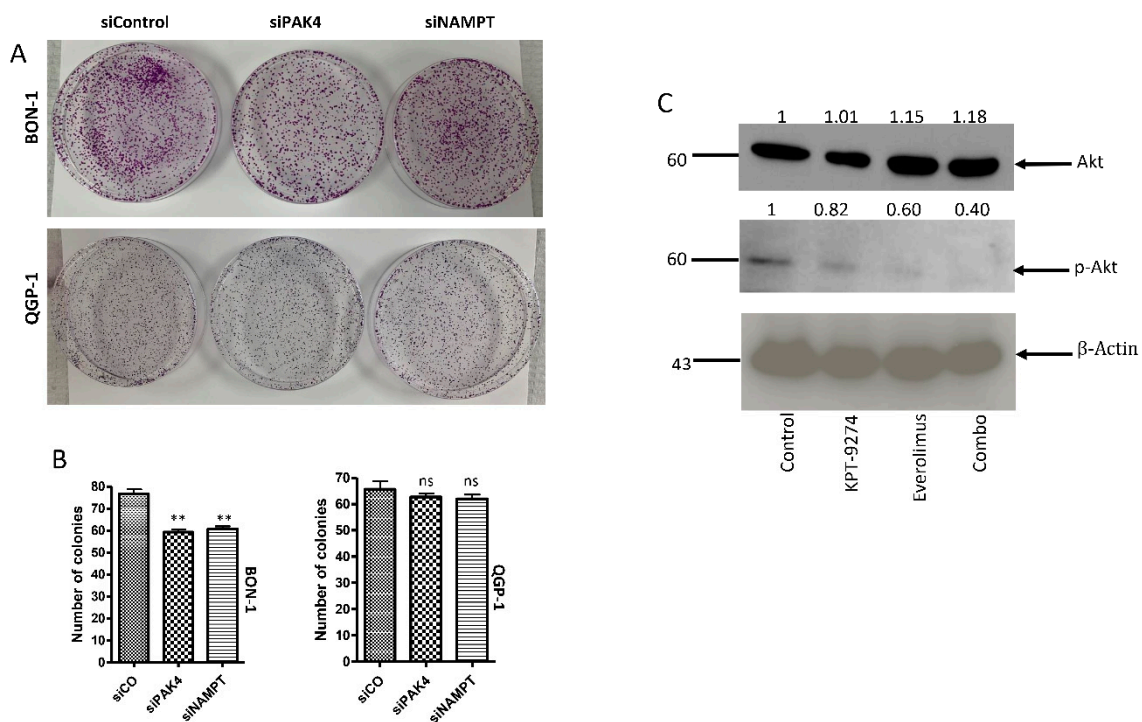


**Figure S1.** (A) PNET cells are inherently resistant to mTOR inhibitors. Bon-1 and QGP-1 cells were grown in 96 well plates overnight and exposed to increasing concentrations of everolimus (EV) for 72 h, (EV1 and EV2 represent two biological replicates). At the end of the treatment period, standard MTT assay was performed. Growth curves were developed using GraphPad Prism software. (B) KPT-9274 synergize with mTOR inhibitor INK-128. QGP-1 cells were grown at a density of 30,000 cell/well in six well plate overnight followed by incubation with either KPT-9274 (600 nM) or INK-128 (6  $\mu$ M) or their combination for 72 h followed by Apoptosis analysis using standard protocol (Biovisions Danver MA).



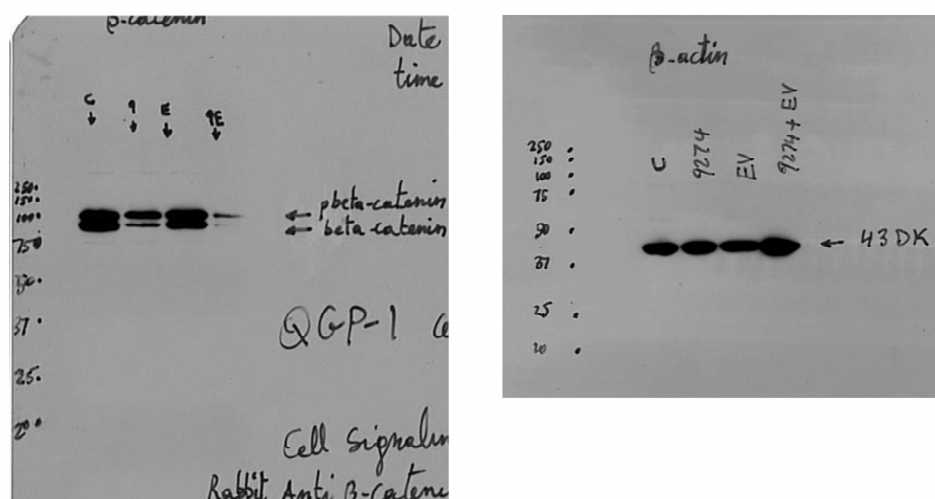
**Figure S2.** KPT-9274 synergy analysis. QGP-1 cell were grown in 96 well plate at a density of 5000 cells per well overnight and exposed to indicated concentrations of either KPT-9274 in the absence or presence of equimolar ratio concentrations of sunitinib or FAKi/Defactinib (VS-6063, PF-04554878) for 72 hrs. MTT assay was performed according to standard procedure. Raw data was analyzed for synergy using CalcuSyn software. Graphs were plotted using GraphPad Prism software.





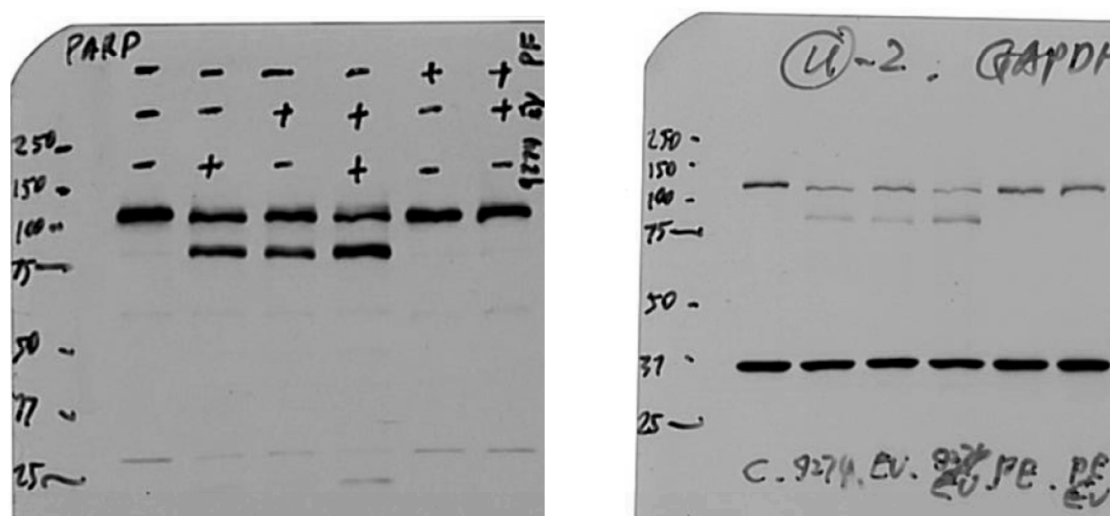
**Figure S4.** Targeting PAK4-NAMPT axis suppresses PNET tumor growth. **(A)** Colony formation post single siPAK4 and single siNAMPT. **(B)** Graphical representation of number of colonies. \*  $p < 0.05$ ; \*\*  $p < 0.01$  siPAK4  $p = 0.008$ ; siNAMPT  $p = 0.0025$ . **(C)** Western blot analyses of proteins extracted from QGP-1 post treatment with 600 nM of KPT-9274, 6 $\mu$ M everolimus and combination.

Figure 5F full blot

Relative protein expression (Normalized to  $\beta$ -actin)

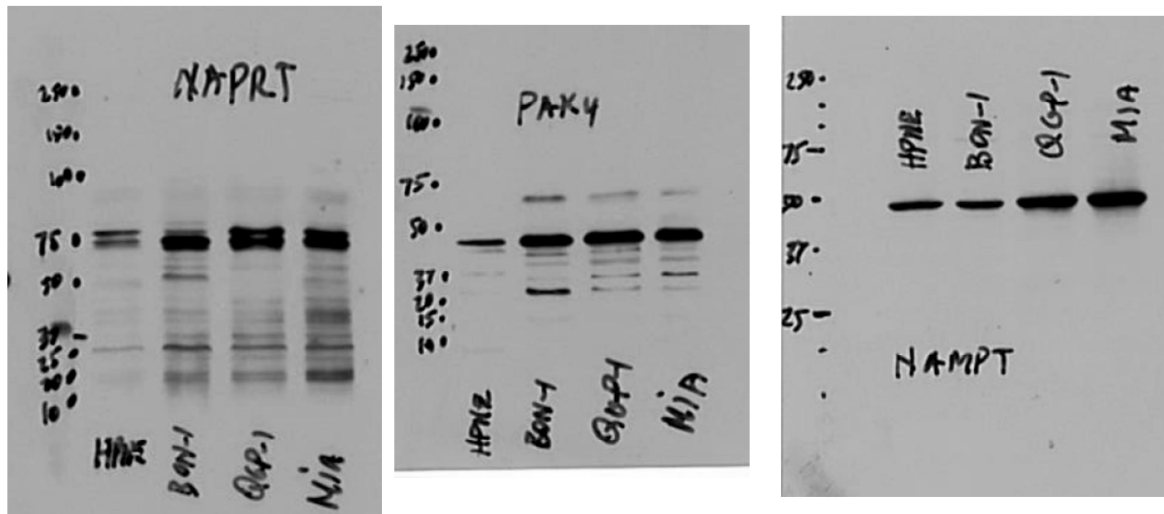
	Control	KPT-9274	Everolimus	Combo
Phospho $\beta$ -catenin	1	0.88	0.87	0.41
$\beta$ -catenin	1	0.63	0.93	0.06

Figure 4E full blot

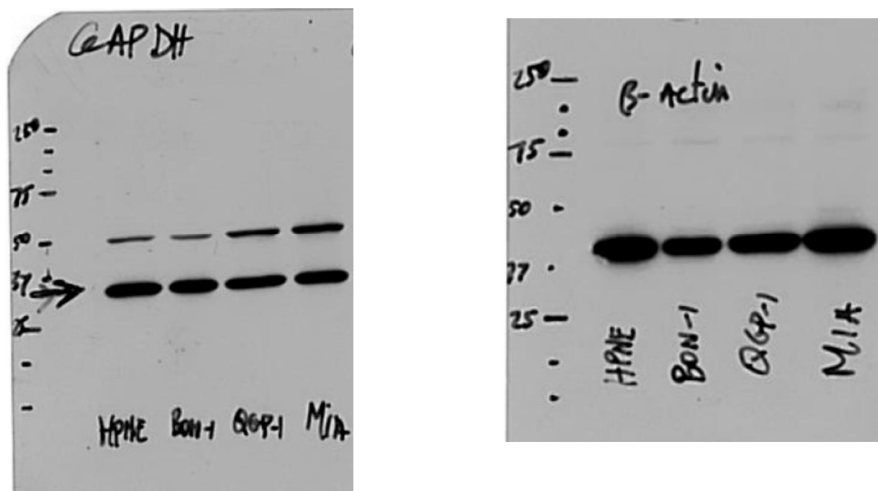
Relative protein expression (Normalized to  $\beta$ -actin)

	Control	9274	EV	9274 + Ev	PF	PF + Ev
PARP	1	0.89	1.12	0.78	1.26	0.84
CLEAVED PARP	0.03	0.45	0.41	0.77	0.02	0.02

Figure 1C full blot

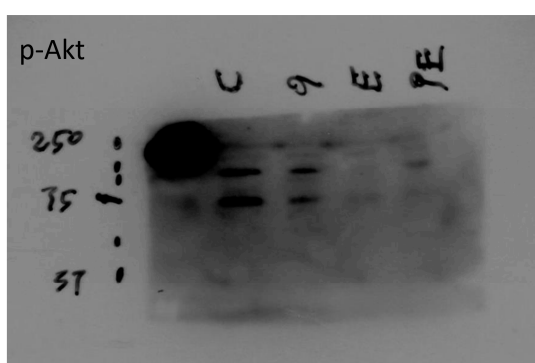
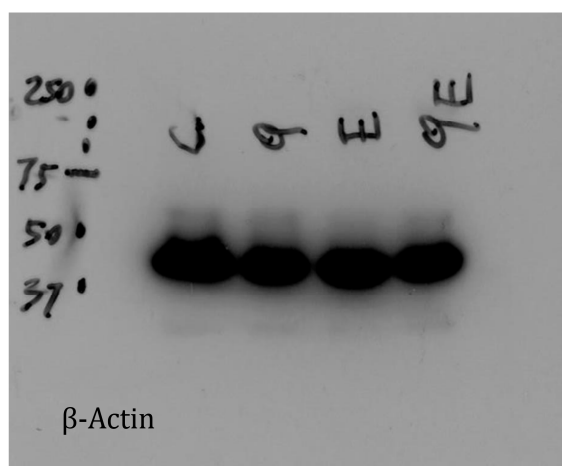
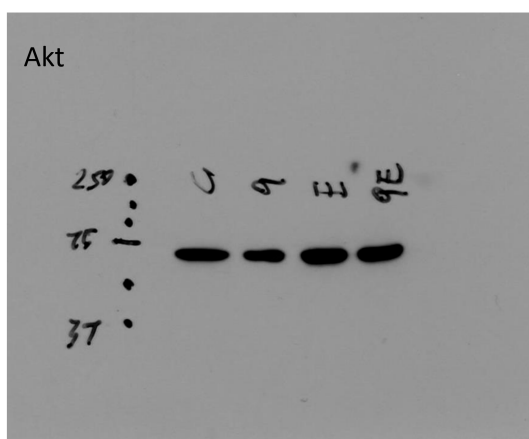


Base line expression loading control (beta-Actin and GAPDH)

Relative protein expression (Normalized to  $\beta$ -actin)

	HPNE	BON-1	QGP-1	MiaPaca-2
PAK4	0.46	1.08	1.01	0.81
NAMPT	0.73	0.89	1.05	0.92
NAPRT	0.30	0.83	0.71	0.61

Supplemental figure 4C full blot



Control	KPT-9274	Everolimus	Combo
Akt	1	1.1	1.18
P-Akt	1	0.60	0.40