**Supplementary figure 1.** NVP-BEZ235 regulates Thr308-P-Akt. High concentrations of NVP-BEZ235 are required to decrease Akt Thr308-phosphorylation. Moreover, low concentrations of NVP-BEZ235 dramatically increased Thr-308-P-Akt over time.

**Supplementary figure 2.** Suboptimal doses of NVP-BEZ235 induce P-Akt. Western blot of total lysates showing increase in Akt phosphorylation in BT474 (and MDA-468) cells treated with NVP-BEZ235 at 10 (and 100nM) for 48h. 50nM everolimus (24h) slightly increased P-Akt in BT474 cells. 1µM AEW-541 did not prevent the NVP-BEZ235-dependent increase in the phosphorylation of Akt. 100nM NVP-BEZ235 in BT474 (and 500nM in MDA-468, not shown) fully decreased P-Akt. Similar data was obtained immunoprecipitating Akt1.

**Supplementary figure 3.** NVP-BEZ235 inhibits cell proliferation. WST-1 assay showing sensitivity of cancer cells to NVP-BEZ235 and everolimus at increasing concentrations for 72h, as in figure 2A.

**Supplementary figure 4.** NVP-BEZ235 inhibits the growth of cancer cells. GI50 values (the concentration required to achieve 50% growth inhibition) of 27 cell lines treated with NVP-BEZ235. Treatment with NVP-BEZ235 effectively inhibited growth in the low nanomolar range in all cell lines tested, regardless of tissue type of origin or genetic aberration present. Those cell lines harboring either a K-Ras mutation, B-Raf mutation and / or overexpressing EGFR were significantly less sensitive to NVP-BEZ235 induced growth inhibition than those cell lines without any of these changes, irrespective of the presence or absence of p110-α mutations or PTEN loss (p < 0.01).