



**Figure S3. Inhibition of ERK phosphorylation by AZD6244 and of AKT phosphorylation by BEZ235.** Melanoma cells from three different cell lines were cultured for 18 hr in the presence of AZD6244 (0.05  $\mu$ M) or of BEZ235 (0.02  $\mu$ M). Antibodies against p-ERK 1/2 and p-AKT (s473) as well as against total ERK1/2 and AKT were used.

**Figure S4**

**Figure S4.** Drug interaction analysis by Chou and Talalay method in two groups of melanoma cell lines with different responsiveness to AZD6244 (resistant lines: IC<sub>50</sub> ≥ 0.2 μM, n=7; susceptible lines: IC<sub>50</sub> ≤ 0.2 μM, n=14) treated with the association of AZD6244, BEZ235 and TRAIL (a), or AZD6244 and TRAIL (b), or BEZ235 and TRAIL (c). Combination indexes (CI, upper panel), and fraction affected (FA, lower panel) by a color code as in Figure 2. Susceptibility to TRAIL, AZD6244 and BEZ235 and main molecular features of all cell lines summarized in the right hand side panel (m: mutant; wt: wild type; +, -: expression/lack of expression of PTEN by western blot). Numbers at the bottom of the upper and lower panels: median CI values and mean FA values, respectively, for each combination of drugs and TRAIL doses.