

## **SUPPLEMENTARY FIGURE LEGENDS**

**Supplementary Figure S1.** **A)** STRING protein-protein interaction analysis for the top-fifteen genes is represented. Gene enrichment analysis of the top-fifteen genes by FunRich (Functional Enrichment Analysis Tool) software indicating the key **B)** biological pathways, and **C)** biological processes mediated by these genes. **D)** RNA expression of KIF11, AURKA, KIF15 and TPX2 from EWS patients were accessed from BioGPS.

**Supplementary Figure S2 (related to Figure 1B & C).** **A)** Quantification of Wes blots data are shown.

**Supplementary Figure S3.** Dose-response curves, dose-response matrix, and heat map indicating synergy scores in different EWS cell lines. Combination treatment resulted in the following synergy scores in **A)** CHLA-9 (27.45), **B)** CHLA-32 (38.97), and **C)** TC-32 (31.28).

**Supplementary Figure S4.** Dose-response curves, dose-response matrix, and heat map indicating synergy scores in different cancer cell lines and control. Combination treatment resulted in the following synergy scores in **A)** U2-OS (17.91), **B)** CRL-2061 (13.16), and **C)** BMD-MSCs - control (13.04).

**Supplementary Figure S5 (related To Figure 6).** Quantification of Wes blot data for Figure 6 is shown.

**Supplementary Figure S6.** **A)** Timeline of in vivo study is represented. SB-743921 (2.5 mg/kg) and VIC-1911 (37.5 mg/kg) were dosed intraperitoneally and orally respectively. Mice were treated with these drugs every other day for 20 days (11 treatments) and monitored until end-point criteria were met. We observed significant **B)** tumor regression (control vs combination, VIC-

1911 vs combination,  $p \leq 0.001^{***}$  as assessed by one-way ANOVA) and **C)** overall survival.  $p \leq 0.001^{***}$ ,  $p \leq 0.001^{***}$  and  $p\text{-value}^{**} \leq 0.01$  is determined by logrank (Mantel-cox) test and indicated on the graph.

**Supplementary Figure S7.** The body weights of mice are represented for the tumor efficacy **A)** efficacy Study 1 and **B)** efficacy Study 2.  $p \leq 0.0001^{****}$ ,  $p \leq 0.001^{***}$ ,  $p \leq 0.01^{**}$  and  $p \leq 0.05$  as measured by one-way ANOVA.