Fig. S8.

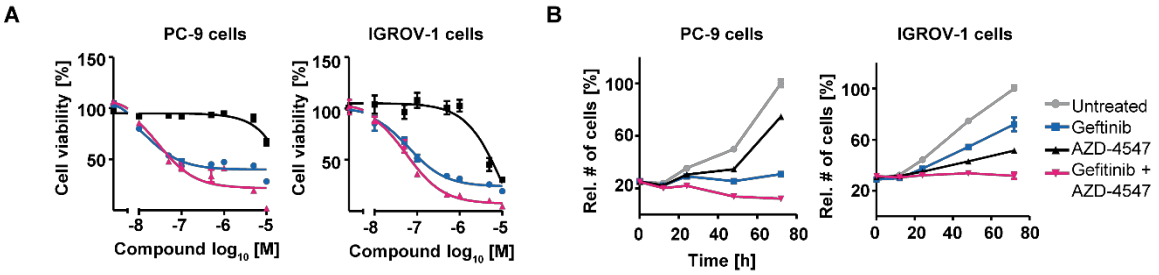

Fig. S8 | From target to pathway engagement – combination treatment. (A) Viability assays of drug combination treatment in lung (PC-9) and ovarian (IGROV-1) cancer cell lines. **(B)** Proliferation assays (from left to right) for PC-9 and IGROV-1 with single and drug combination treatment with Gefitinib and AZD-4547. Combination treatment of Gefitinib and AZD-4547 was more effective than any single drug. Experiments were performed in technical triplicates and error bars depict standard deviation.

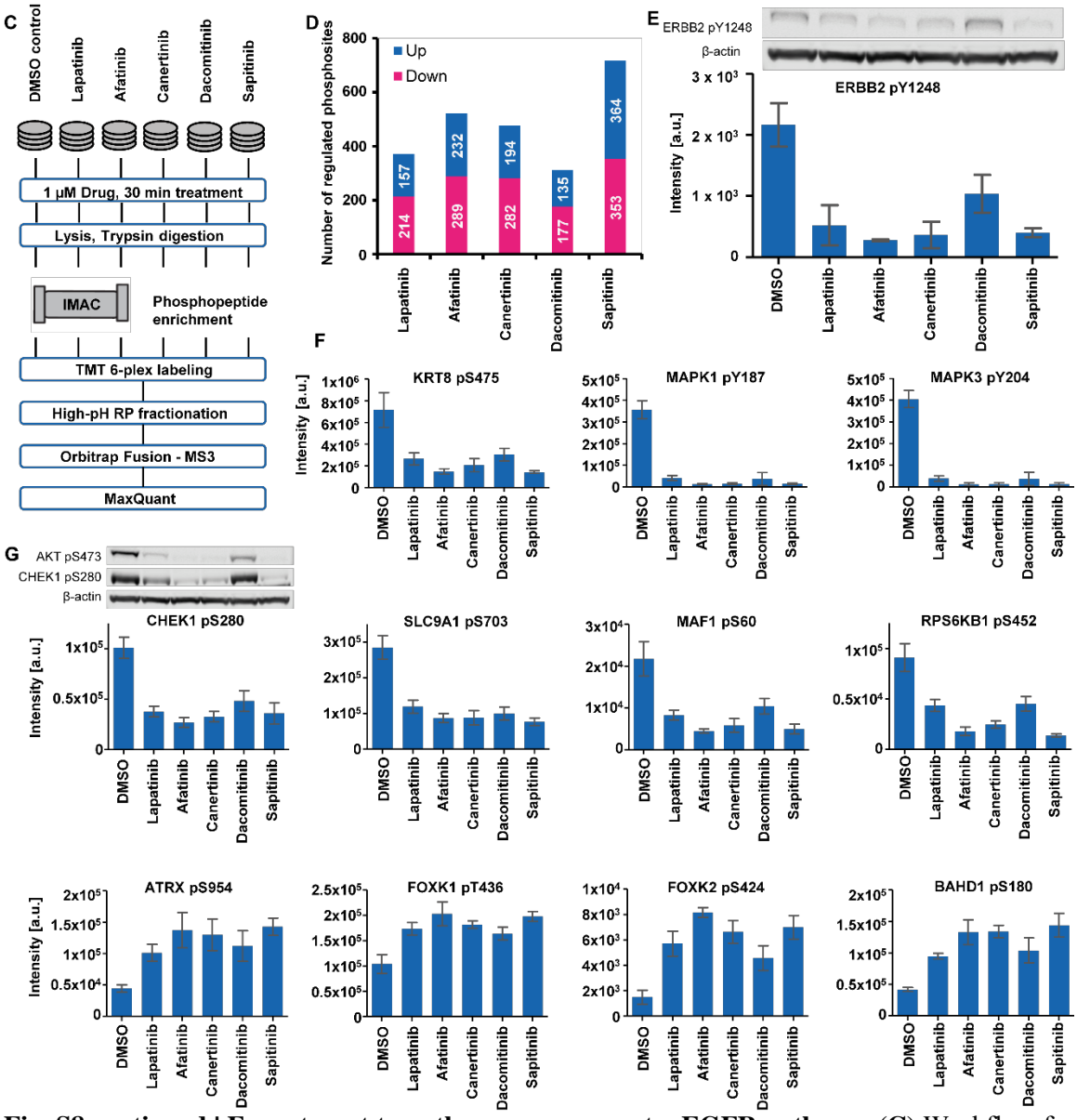

Fig. S8 continued | From target to pathway engagement – EGFR pathway. **(C)** Workflow for quantitative phosphoproteomics in BT-474 cell lines treated with different EGFR/ERBB2 inhibitors (in four replicates). **(D)** Number of reproducible (at least 3 from 4 biological replicates) significantly up- (blue) and down-regulated (pink) phosphorylated sites observed for each drug (two-sided t-test, $p<0.01$). **(E)** Down-regulation of the ERBB2 autophosphorylation site pY1248 can be used as a target engagement marker in cells for all drugs shown. **(F-G)** Up- and down-regulated phosphorylated sites for **(F)** known and **(G)** novel members of the ERBB2 network. Error bars depict the standard deviation.