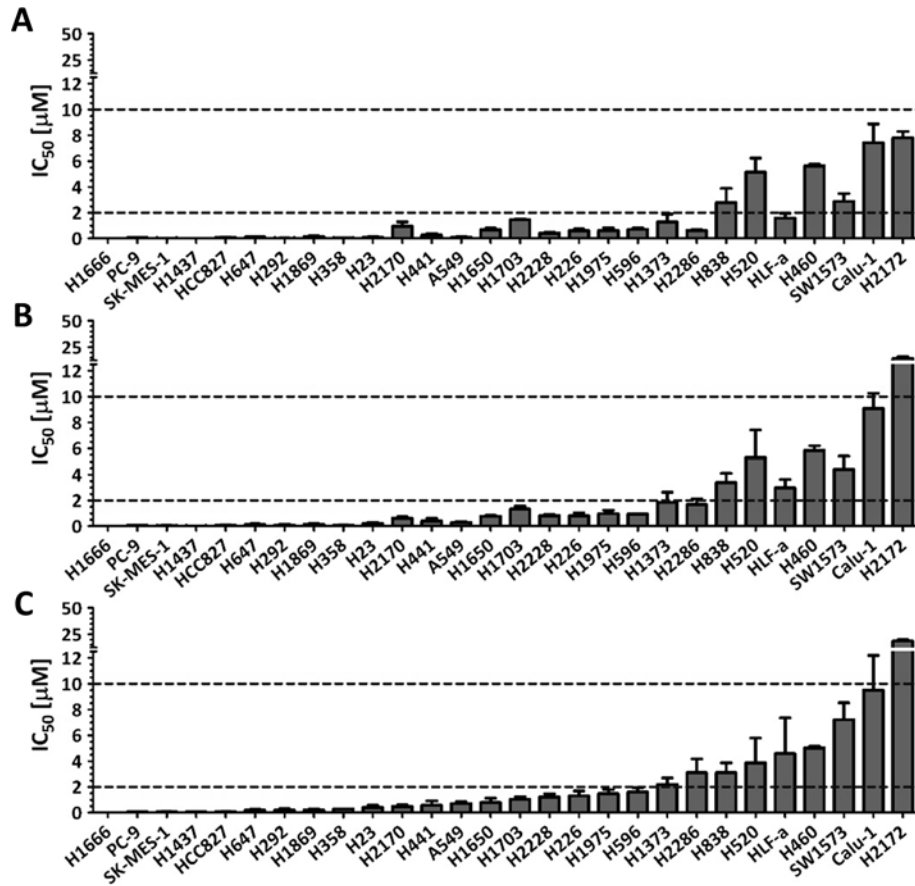
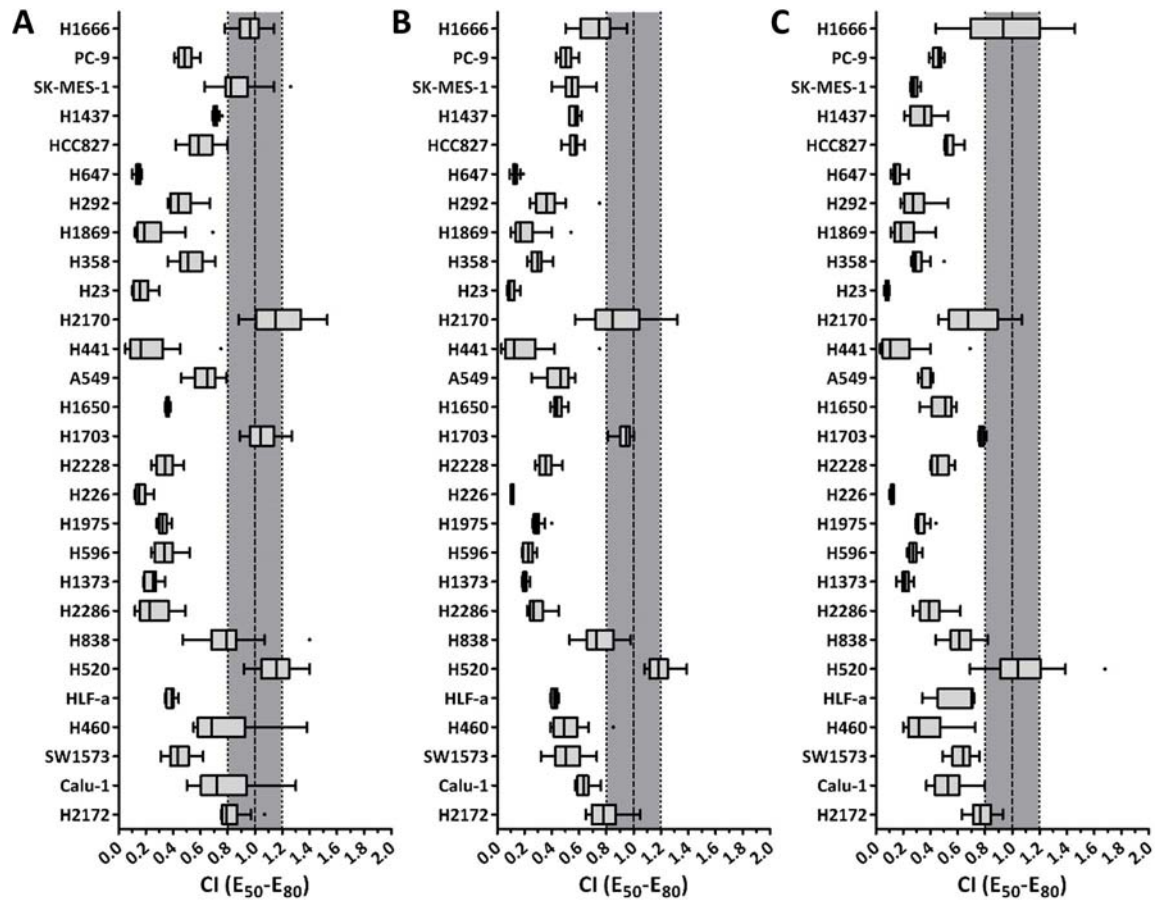


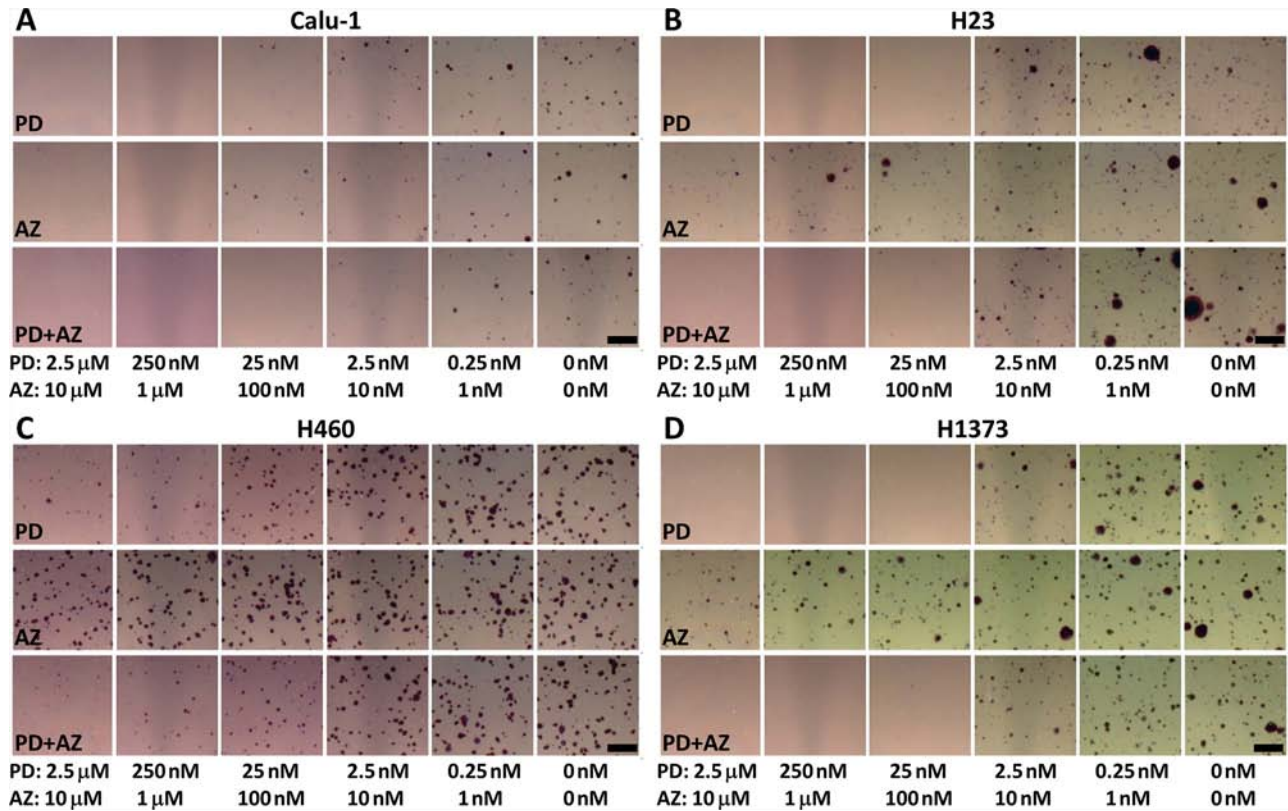
SUPPLEMENTARY FIGURES, TABLE AND LEGENDS



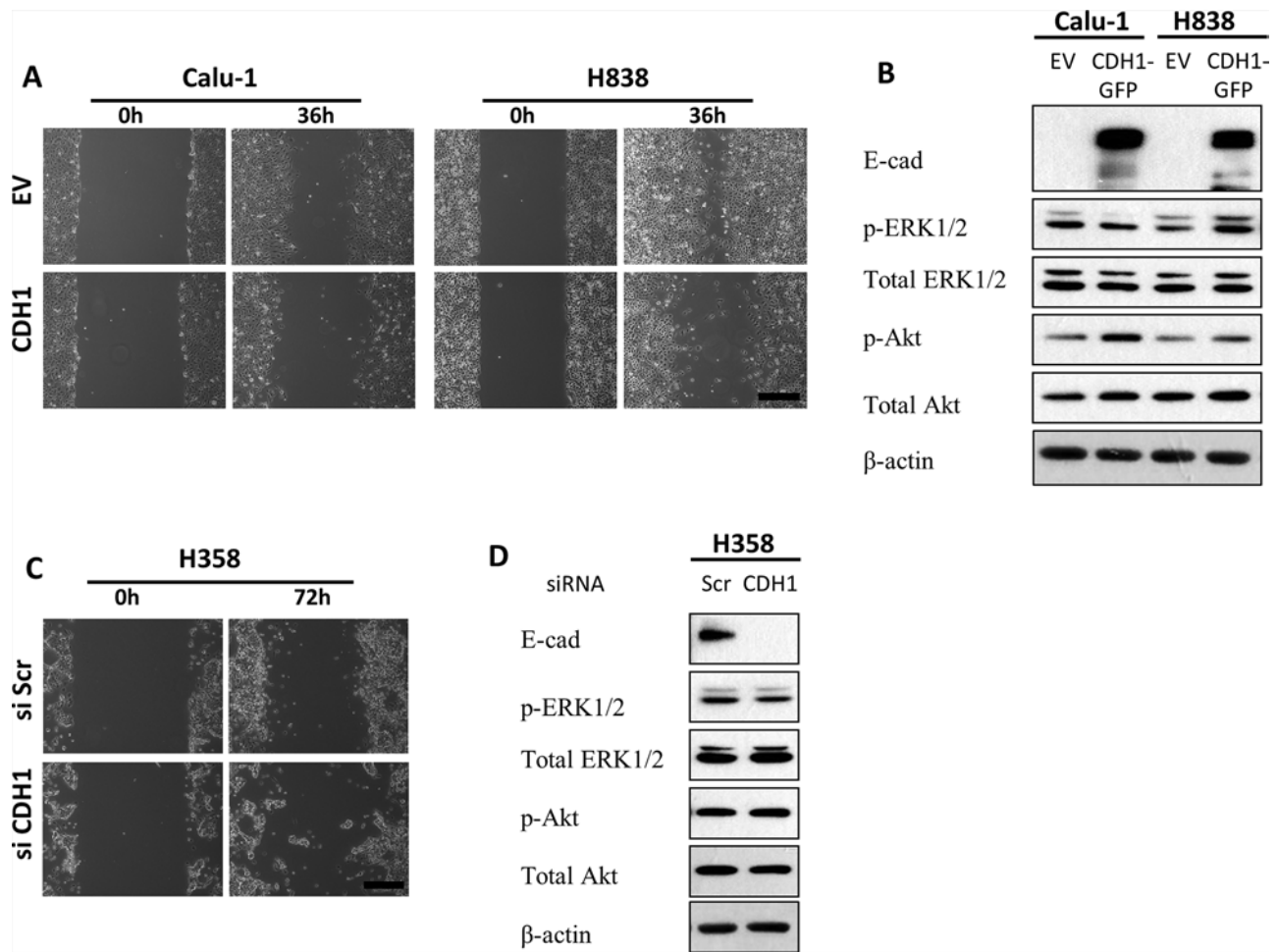
Supplementary Figure S1: Cell proliferation IC<sub>50</sub> plots (mean ± SD) for a panel of 28 NSCLC cell lines treated at fixed PD0325901 to Saracatinib ratios of 4:1 A. 1:1 B. and 0.25:1 C. for 72 h. Data were tabulated from three independent experiment sets.



**Supplementary Figure S2: Combination index (CI) box plots of PD0325901 and Saracatinib co-treatment at the ratios of 4:1 A, 1:1 B, and 0.25:1 C on the panel of 28 NSCLC cell lines.** Data were tabulated from three independent experiment sets. Combination index of CI < 0.8 indicates synergism, CI from 0.8 to 1.2 indicates additive effect, and CI = 1.2 indicates antagonism.



**Supplementary Figure S3: Suppression of anchorage-independent growth by PD0325901 and Saracatinib combination treatment.** NSCLC lines were grown in soft agar in the presence of various concentrations of PD, AZ or their combination at a fixed ratio of 0.25:1. Representative images shown highlighted the dose-dependent colony inhibitory effect of the various treatments on Calu-1 **A**, H23 **B**, H460 **C**, and H1373 **D**. Scale bars: 1 mm.



**Supplementary Figure S2: E-cadherin expression reduced migratory activity and did not promote tumor progression in NSCLC cells.** Calu-1 and H838 cells were transfected with CDH1-GFP or pCMV-entry plasmids (1 ug plasmid in each reaction) **A.** and **B.** H358 cells were transfected with CDH1 or negative control siRNA (50 nM of siRNA in each reaction) **C.** and **D.** Cell migration assays were conducted 24 h after transfections. The wounded areas were imaged at 0 h and 36 h (**A.**, for Calu-1 and H838) or 72 h (**B.**, for H358) after the monolayer cultures were scratched. Representative images were shown. Scale bar: 500  $\mu$ m. Westernblot was performed to validate the efficiency of overexpression (**B.**) and siRNA knockdown (**D.**). Effects of the transfection on phospho-ERK1/2 and phospho-Akt were also shown. ( $n = 3$  per group).  $\beta$ -actin shown as loading control.

**Supplementary Table S1: Anchorage-independent cell colony formation IC<sub>50</sub> data of the cell lines treated with PD, AZ or PD+AZ combination**

Cell line	Single compound treatment		PD + AZ combination treatment		PD + AZ combination index range
	PD IC <sub>50</sub> (μM)	AZ IC <sub>50</sub> (μM)	PD IC <sub>50</sub> (μM)	AZ IC <sub>50</sub> (μM)	
Calu-1	0.0053 ± 0.0016	0.038 ± 0.016	0.0024 ± 0.0009	0.0095 ± 0.0035	0.48 – 0.71
H23	0.0066 ± 0.0059	4.6 ± 2.1	0.0060 ± 0.0009	0.024 ± 0.004	0.59 – 1.08
H460	0.33 ± 0.04	29.8 ± 2.5	0.19 ± 0.05	0.75 ± 0.18	0.35 – 0.78
H1373	0.0037 ± 0.0002	13.5 ± 0.4	0.0037 ± 0.0001	0.015 ± 0.001	1.01 – 1.07

Note: NSCLC lines were grown in soft agar in the presence of various concentrations of PD, AZ or their combination at a fixed ratio of 0.25:1 for a period of 2–4 weeks. IC<sub>50</sub> data (mean ± SD) were tabulated from at least two independent experiment sets. The combination index range for between 50% to 80% colony formation inhibition effect was tabulated for the drug combination treatment on each cell line. Combination index of CI < 0.8 indicates synergism, CI from 0.8 to 1.2 indicates additive effect, and CI > 1.2 indicates antagonism.