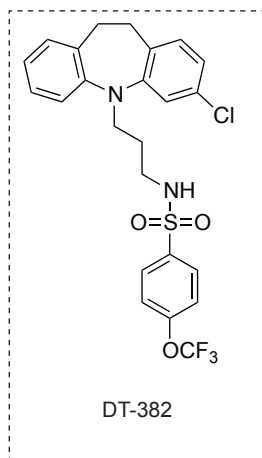
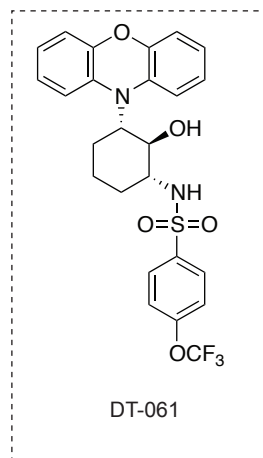


A

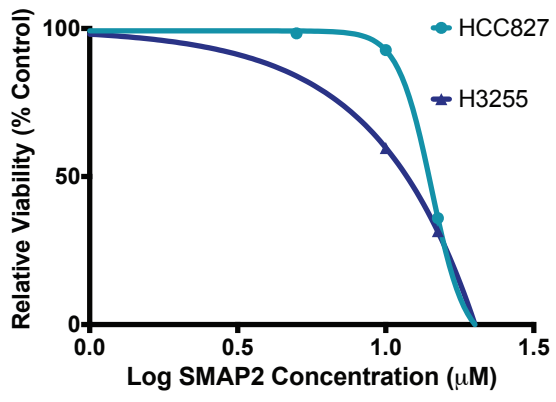


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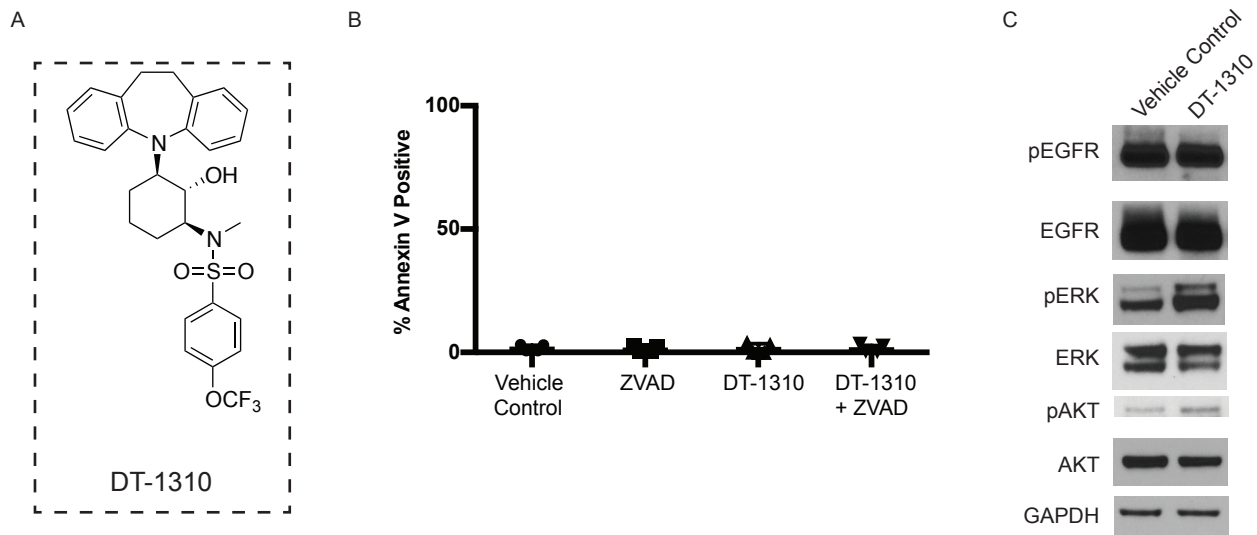


Supplementary Figure 1. SMAPs chemical structures. A, Chemical structure for DT-382. B, Chemical structure for DT-061

Supplemental Figure 2:

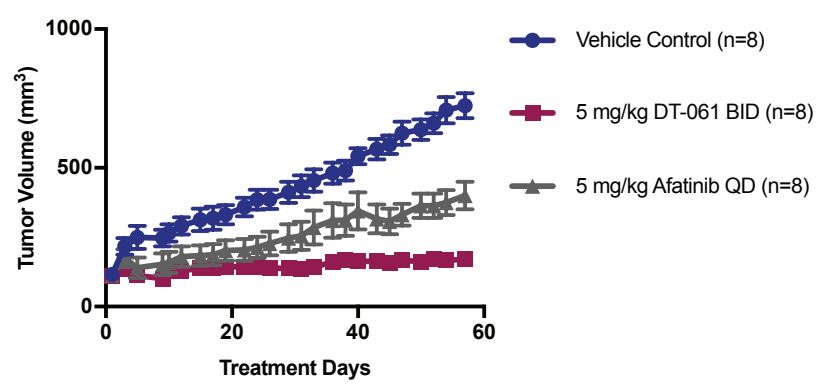


Supplementary Figure 2. PP2A activation induces cell death in EGFR-driven TKI-sensitive NSCLC cell lines. HCC827 and H3255 cell lines were treated with various concentrations of SMAP DT-061 for 48 hours, cell viability assay by cell counting.



Supplementary Figure 3. A, Chemical structure for DT-1310. B, Annexin V positivity at 24 hours in H1975 cells treated with 20  $\mu$ M of DT-1310 in combination with ZVAD. Three independent experiments represented as mean  $\pm$  SD. \*,  $P < 0.05$ ; \*\*,  $P < 0.01$ ; \*\*\*,  $P < 0.001$ ; \*\*\*\*,  $P < 0.0001$ . C, Western blot analysis for pEGFR, EGFR, pAKT, AKT, pERK, ERK in H1975 treated with 20  $\mu$ M of DT-1310 at 24 hours.

Supplemental Figure 4:



Supplementary Figure 4. A, TM00199 PDX model has low sensitivity to TKI afatinib. Tumor volume (mm<sup>3</sup>) in function of time in a PDX mouse model treated with either vehicle control, afatinib (5mg/kg) or SMAP DT-061 (5 mg/kg).