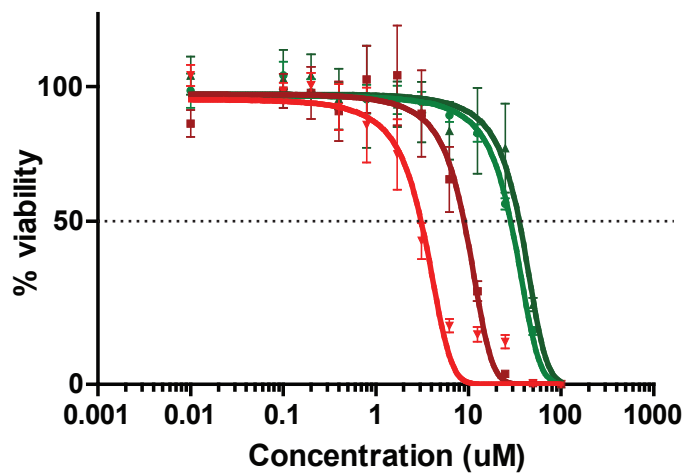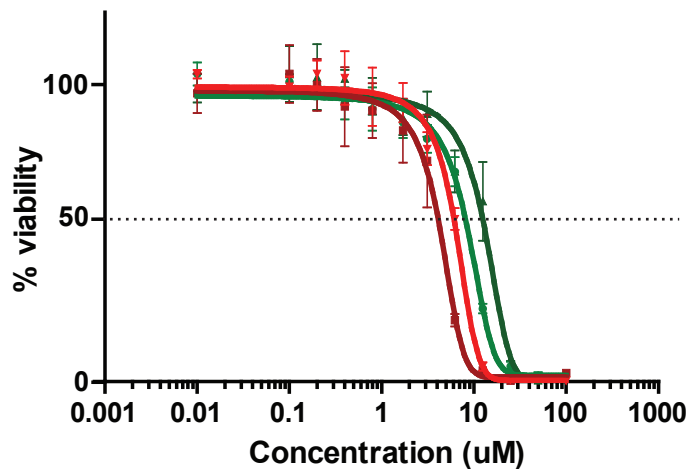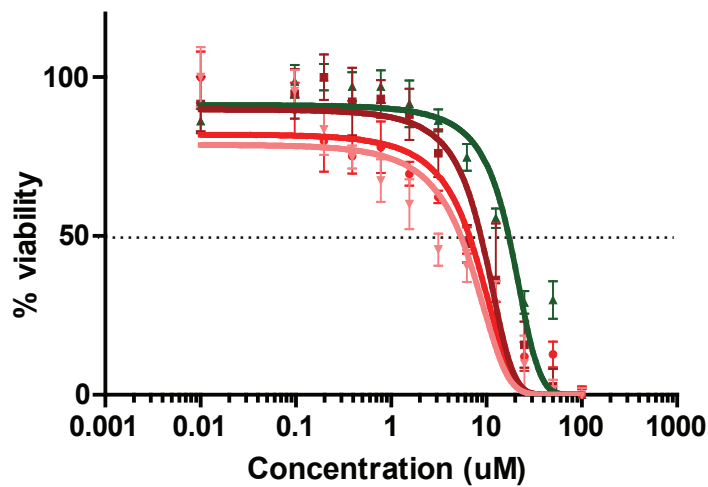**Supplementary Figure S5. qPCR analysis of target knockdown efficiencies.** (A) shRNA-mediated knockdown of *ERBB2*, *RPS6KB1*, and *FGFR4* in breast cancer cell lines. (B) Western blot of *FGFR4* levels after shRNA-mediated knockdown in MDA-MB-361 and MDA-MB-453 breast cancer cell lines. The bar graphs show siRNA-mediated knockdown of *AKT2* (C), *AXL* (D), *EGFR* (E), *MET* (F), and *PLK2* (G) and shRNA-mediated knockdown of *KRAS* (H) in pancreatic cancer cell lines. Expression levels are measured as relative quantity (RQ) compared to siNTC or shNTC.

A PD173074

	IC$_{50}$ (uM)
▲ L3.3	37.03
● MDA-MB-231	29.95
■ BxPC-3	9.384
▼ MDA-MB-453	3.241

B Dovitinib

	IC$_{50}$ (uM)
▲ L3.3	13.04
● MDA-MB-231	8.379
▼ MDA-MB-453	6.308
■ BxPC-3	4.244

C XL184

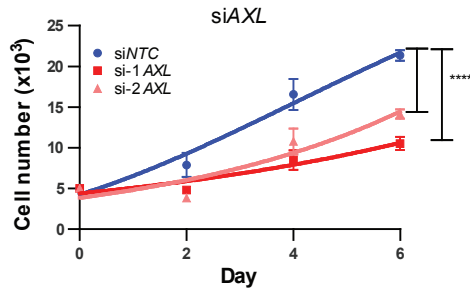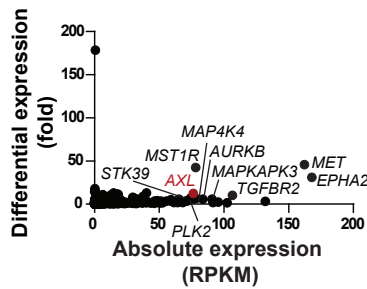|	IC$_{50}$ (uM)
▲ L3.3	17.15
■ BxPC-3	8.765
● AsPC-1	6.626
▼ PANC-1	5.363

Supplementary Figure S6. Inhibition of sample-specific outlier kinases. Dose-response curves for *FGFR* inhibitors PD173074 (A) and Dovitinib (B) in cells with (red shades) and without (green shades) outlier expression of *FGFR* . Dose-response curve for *MET* inhibitor XL184 (C) in cells with (red shades) and without (green) outlier expression of *MET*. IC$_{50}$ values are displayed.
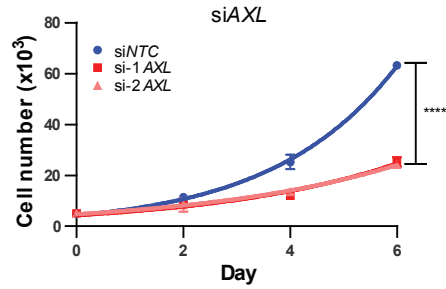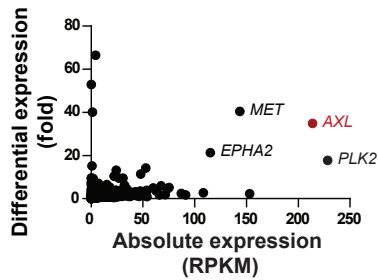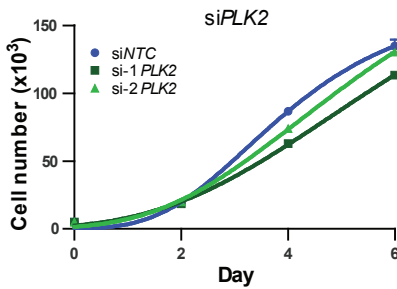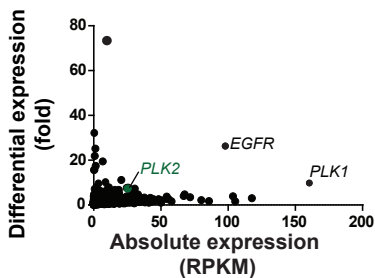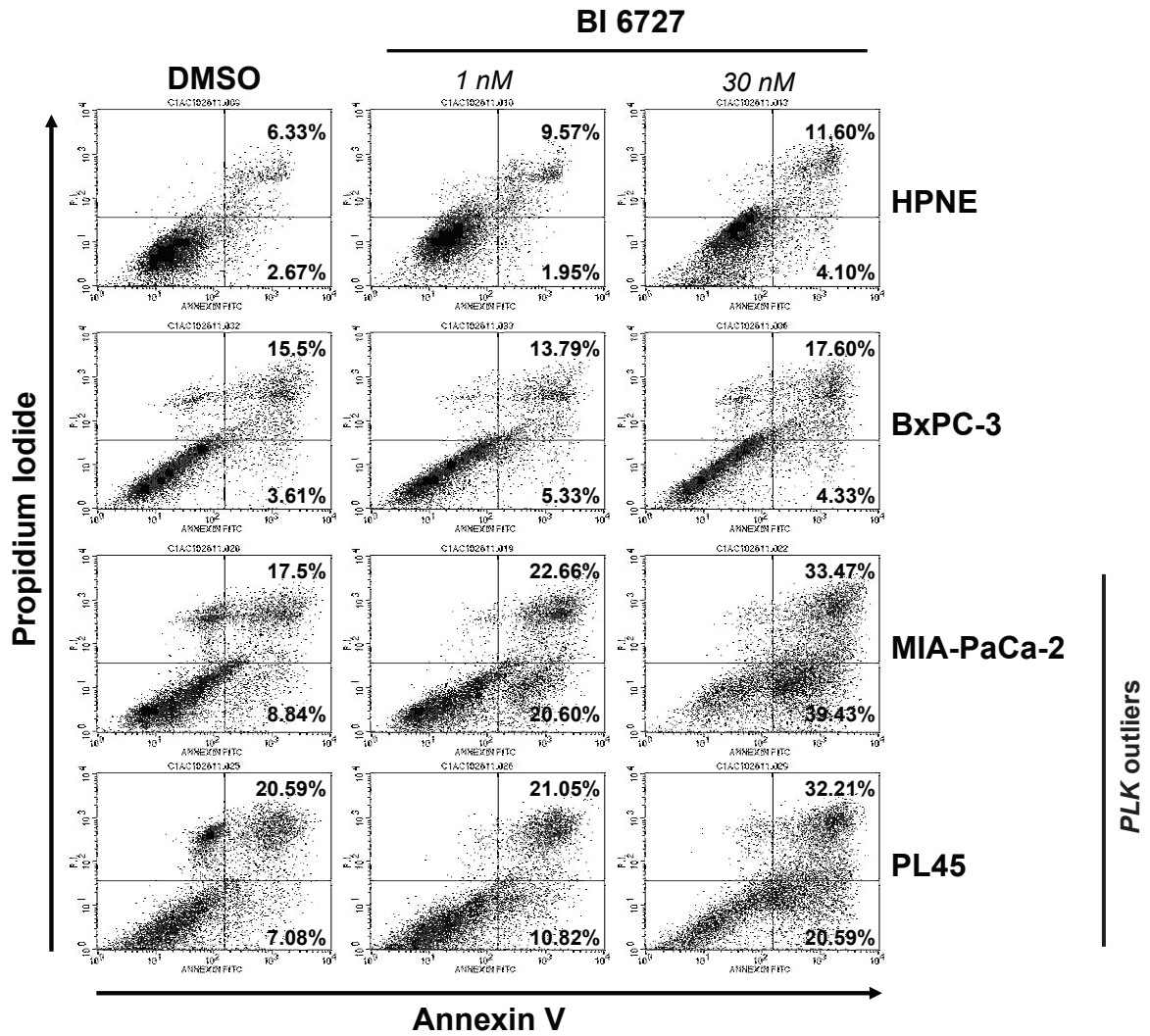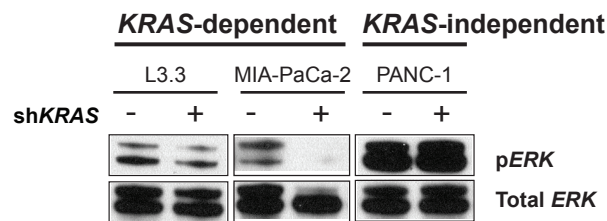
Supplementary Figure S7. Pancreatic cancer cell lines are sensitive to knockdown of outlier kinases. (Left) Scatter plots display kinome expression profiles of select pancreatic cancer cell lines. Kinases targeted for siRNA knockdown are shown in color. Labels in black denote additional kinases with outlier expression. (Right) Growth curves of indicated cell lines after knockdown of sample-specific outliers (in HPAC, Panc-08.13, and PL45) and non-outliers (in L3.3) are displayed. Values represent mean ± SD. ****, $P < 0.0001$.

A

B

Supplementary Figure S8. (A) BI 6727 treatment increases apoptosis in pancreatic cancer cell lines with *PLK* outlier expression. Early (Annexin V-positive/PI-negative) and late (Annexin V-positive/PI-positive) apoptotic cells were measured by flow cytometry in cell lines without *PLK* outlier expression (HPNE, BxPC-3) and those with *PLK* outlier expression (MIA-PaCa-2, PL45) after 48 hours of BI 6727 treatment. (B) Western blot shows levels of phospho-*ERK* (p*ERK*) and total *ERK* after doxycycline-induction of *KRAS* shRNA in *KRAS*-dependent (L3.3, MIA-PaCa-2) and *KRAS*-independent (PANC-1) cell lines.