



Figure S8. Drug profiling on PDAC patient derived tumor organoids (PDTOs). **A.** PDAC patient-derived tumor organoids; brightfield images, scale 1000µm; disease characterization, diagnosis, histological assessment. **B.** Heatmap of drug profiling results using the CTD² network informer set (CNIS) drug library by performed on 4 KRAS mutant PDAC PDTOs; potency shown in AUC; x indicates no data; drug target group curation of top 50 agents ranked by both AUC and IC₅₀ values (right). **C.** Representative brightfield images of the normal pancreas organoid (NPO) and 5 KRAS mutant PDAC PDTOs used in preclinical organoid screening platform; scale 1000 µm. **D.** Preclinical organoid screening platform with FDA-approved chemotherapeutics for PDAC and novel agents including TFIIH/XPB/CDK transcriptional kinase inhibitors; scatter plot of calculated IC₅₀s from fitted dose response curves on 5 KRAS mutant PDAC PDTOs (left); scatter plot of potency fold change vs. normal pancreas organoid (NPO) IC₅₀s from fitted dose response curves (right).