Figure S1

A

| | WT p110a/p85a | WT p110a/p85b | E545K p110a/p85a | E545K p110a/p85b | H1047R p110a/p85a | H1047R p110a/p85b |
|---|---|---|---|---|---|---|
| | Ki (nM) | Ki (nM) | Ki (nM) | Ki (nM) | Ki (nM) | Ki (nM) |
| GDC-0941 | 4.13 | 3.68 | 3.84 | 3.63 | 3.99 | 3.63 |
| GNE-181 | 0.046 | 0.050 | 0.054 | 0.060 | 0.057 | 0.052 |
| GNE-102 | 0.133 | 0.130 | 0.124 | 0.107 | 0.102 | 0.083 |
| BYL-719 | 1.45 | 1.38 | 1.63 | 1.15 | 1.46 | 1.21 |
| GNE-326 | 0.145 | 0.170 | 0.180 | 0.168 | 0.166 | 0.127 |
| taselisib | 0.045 | 0.044 | 0.030 | 0.041 | 0.036 | 0.034 |
| GDC-0077 | 0.045 | 0.070 | 0.044 | 0.022 | 0.032 | 0.027 |

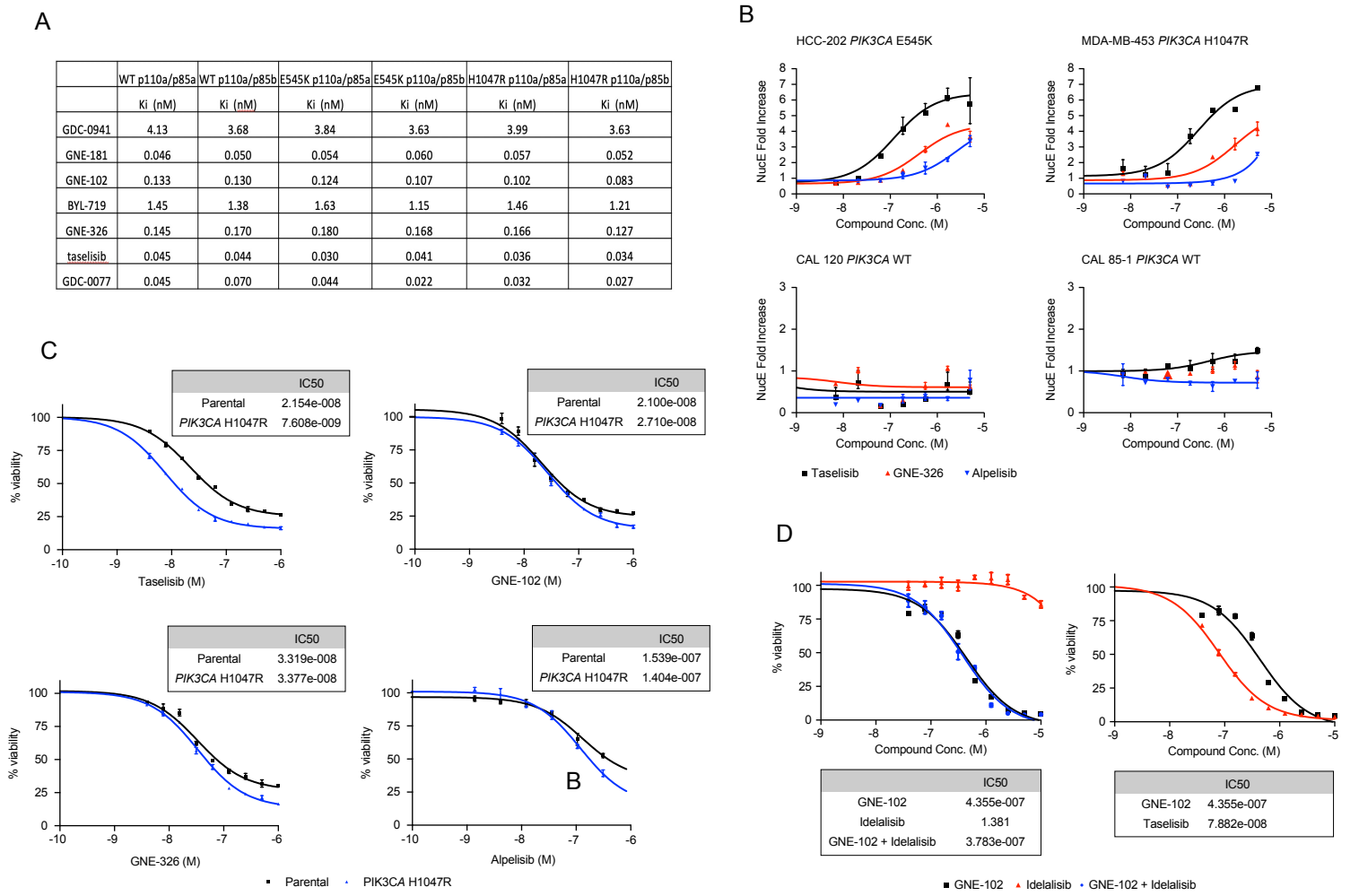

**Figure S1**

**Taselisib and GDC-0077 have increased potency in PIK3CA-mutant cancer cells**

(A) p110a WT and mutant KI. Inhibition of ATP-hydrolysis by PI3K isoforms in a biochemical assay, ADP production measured by ADP-Glo™. ᵇPlasma protein binding determined by equilibrium dialysis. Ki's were determined based on IC50 values using the Morrison equation using experimentally determined ATP Km's for each construct.

(B) PI3K inhibitors assessed for cytostasis in mutant and wild-type breast cancer cell lines in 72 hour Nucleosome ELISA. Error bars are standard deviation of triplicates.

(C) Cell potency in 4-day CellTiter-Glo® viability assay for taselisib and PI3Kα inhibitors BYL719, GNE-102, GNE-326 in SW48 isogenic H1047R and wild-type cells. Error bars are standard deviation of triplicates.

(D) Combination of PI3Kα inhibitor GNE-102 with PI3Kδ inhibitor idelalisib in 4-day viability assay in HCC1954 PIK3CA H1047R mutant cells. Error bars are standard deviation of quadruplicates.

(E) Combination of taselisib with PI3Kβ inhibitor TGX-221 in HCC1954 PIK3CA H1047R mutant cells in a 4-day viability assay. Error bars are standard deviation of quadruplicates.

(F) Intracellular drug concentrations of taselisib in cancer cell lines treated for 18 hours with 1μM taselisib. Results of LC/MS/MS for triplicate wells are shown. Error bars are standard deviation of triplicates.

(G) Individual animal data with fits of taselisib, GDC-0077, and BYL719 in HCC1954 PIK3CA H1047R breast cancer xenograft model.

(H) In vivo efficacy of GDC-0077 in PIK3CA H1047R breast cancer xenograft HCC1954 and KPL4 models, and breast cancer HCI003 PDX (patient-derived xenograft) model. GDC-0077 dosed orally and daily (QD) in MCT (0.5 % methycellulose/0.2% Tween-80) vehicle.