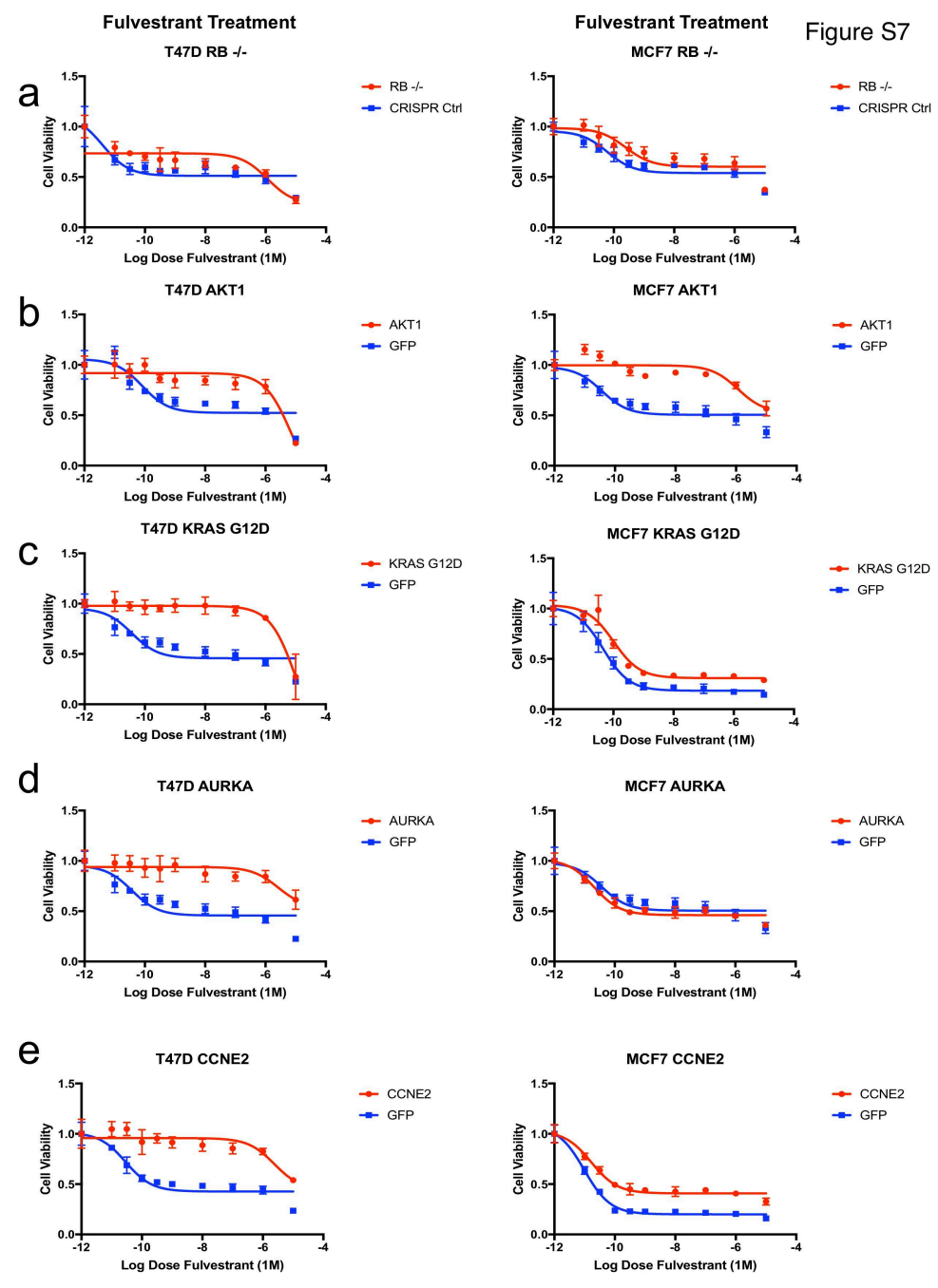
Figure S7


Fulvestrant Treatment
T47D RB -/-
MCF7 RB -/-
RB -/-
CRISPR Ctrl
a
T47D AKT1
MCF7 AKT1
AKT1
GFP
b
T47D KRAS G12D
MCF7 KRAS G12D
KRAS G12D
GFP
c
T47D AURKA
MCF7 AURKA
AURKA
GFP
d
T47D CCNE2
MCF7 CCNE2
CCNE2
GFP
e
Cell Viability
Log Dose Fulvestrant (1M)

Supplemental Figure 7. Candidate alterations provoke variable anti-estrogen resistance *in vitro*.

Cell lines modified to reflect potential resistance drivers (per Figure 4 and Supplemental Figure 6; T47D – left, MCF7 - right) were exposed to escalating doses of fulvestrant (a – e). Drug response was assessed via cell-titer-glo (CTG) assay. Control (CRISPR non-targeting guide, GFP) cells are plotted along with the resistance driver of interest (RB1 – a, AKT1 – b, KRAS G12D – c, AURKA – d, CCNE2 – e). Parental and variant cell lines are normalized to vehicle control and viability is plotted as a function of increasing CDK4/6i (graphed as triplicate average +/- standard deviation). AKT1 and CCNE2 provoke fulvestrant resistance *in vitro* in both T47D and MCF7 cells. RB1 provokes minimal fulvestrant resistance in both T47D and MCF7. KRAS G12D and AURKA provoke significant fulvestrant resistance in T47D; KRAS G12D provokes minimal resistance in MCF7, while AURKA does not convey any resistance in MCF7. Corresponding IC50 values are included in Supplemental Table 7.