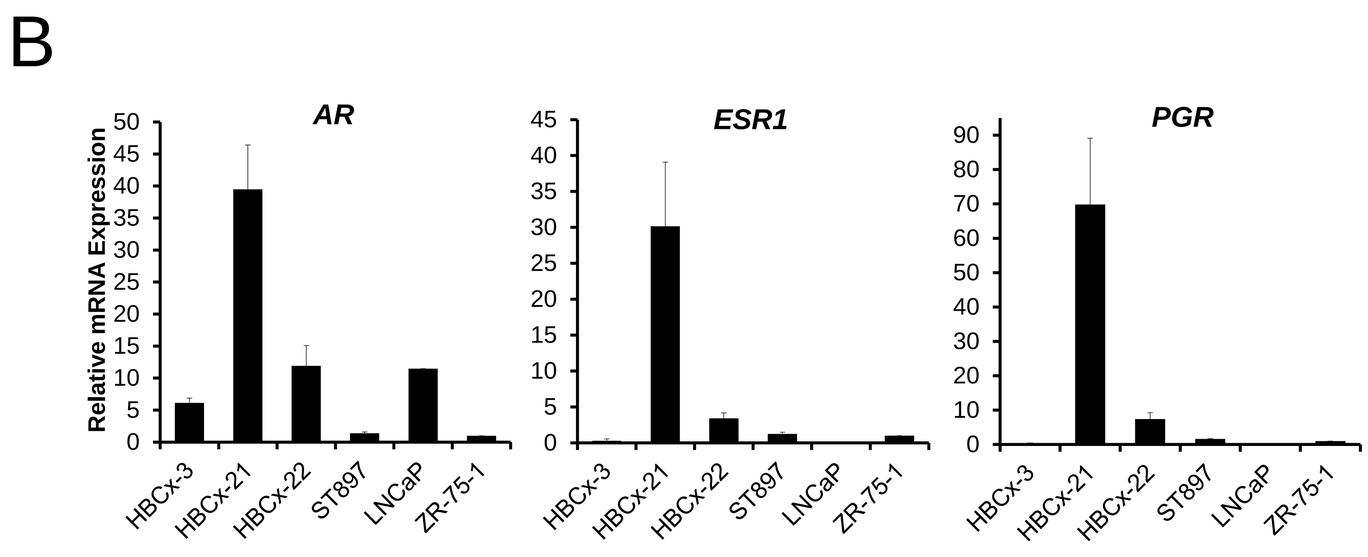
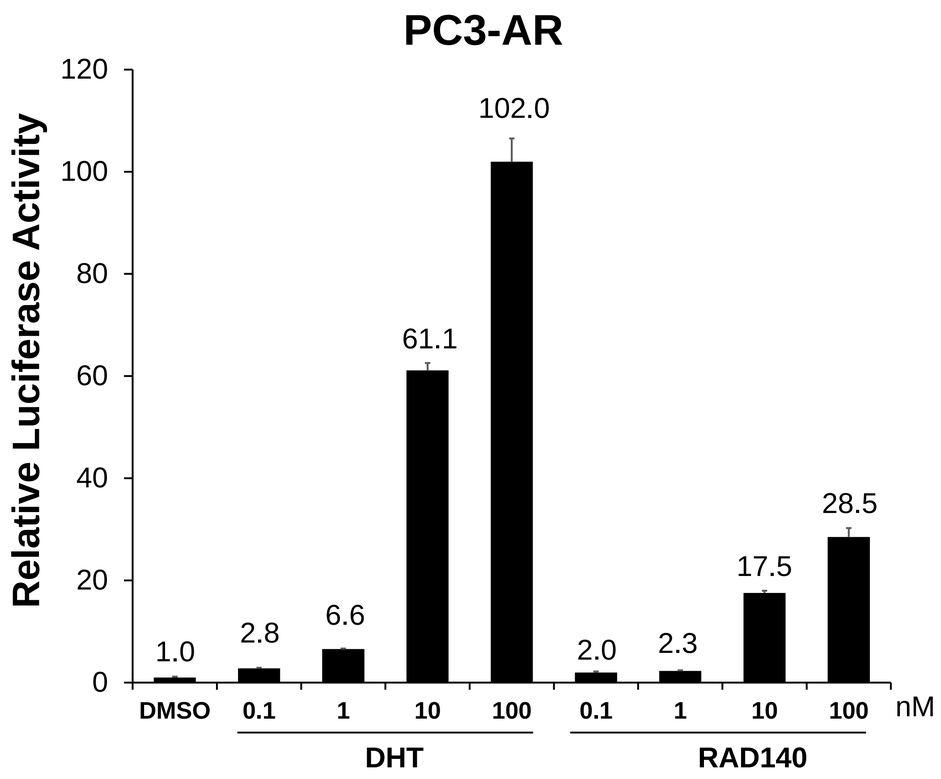


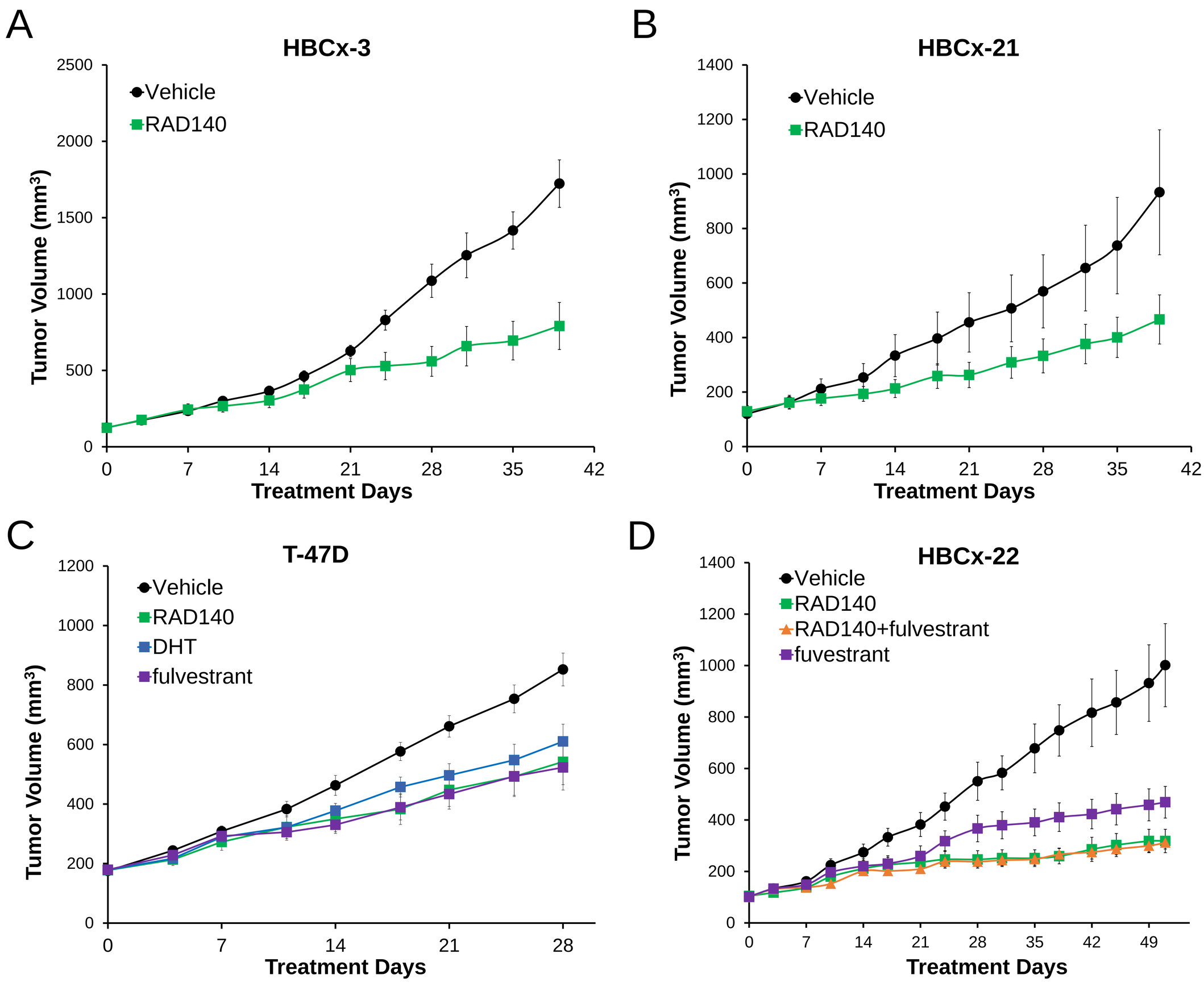

# Supplementary Figure S1

**Supplementary Figure S1.** AR, ER, and PR status of the PDX models used in the present study. **A,** WB analysis of three vehicle-treated tumors from HBCx-3, HBCx-21, HBCx-22, and ST897 PDX models, and the HCC1428 LTED cells. Lysate of LNCaP cells were used for positive control for AR and negative control for ERα. Lysate of ZR-75-1 cells were included as positive control for AR and ERα. **B,** RNA isolated from the same tumors as mentioned in A, and LNCaP and ZR-75-1 cells were subjected to qPCR analysis for the expression of *ESR1*, *AR,* and *PGR*. The mRNA expression levels of AR, ERα, and PR in the indicated PDX tumors and LNCaP cells were presented as relative values to those in the ZR-75-1 cells.



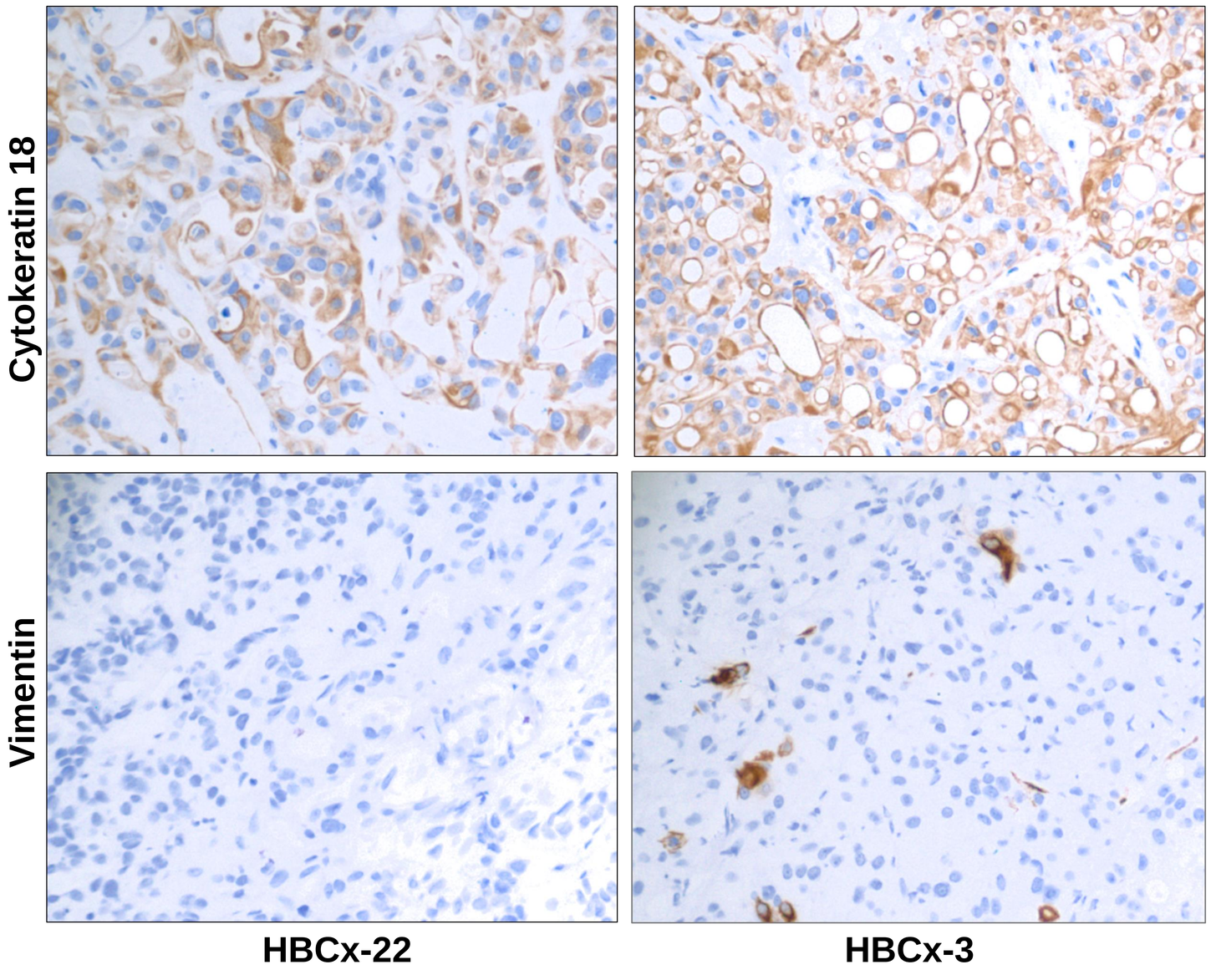

# Supplementary Figure S2

**Supplementary Figure S2.** PC3-AR prostate cancer cells were transfected with ARE-luc and Renilla luciferase constructs in medium containing 5% CSS. Twenty-four hours after the transfection, cells were treated with RAD140 or DHT at the indicated final concentrations. ARE-driven luciferase activity was measured and normalized to that of Renilla luciferase. Data presented are mean±SD of biological triplicates.



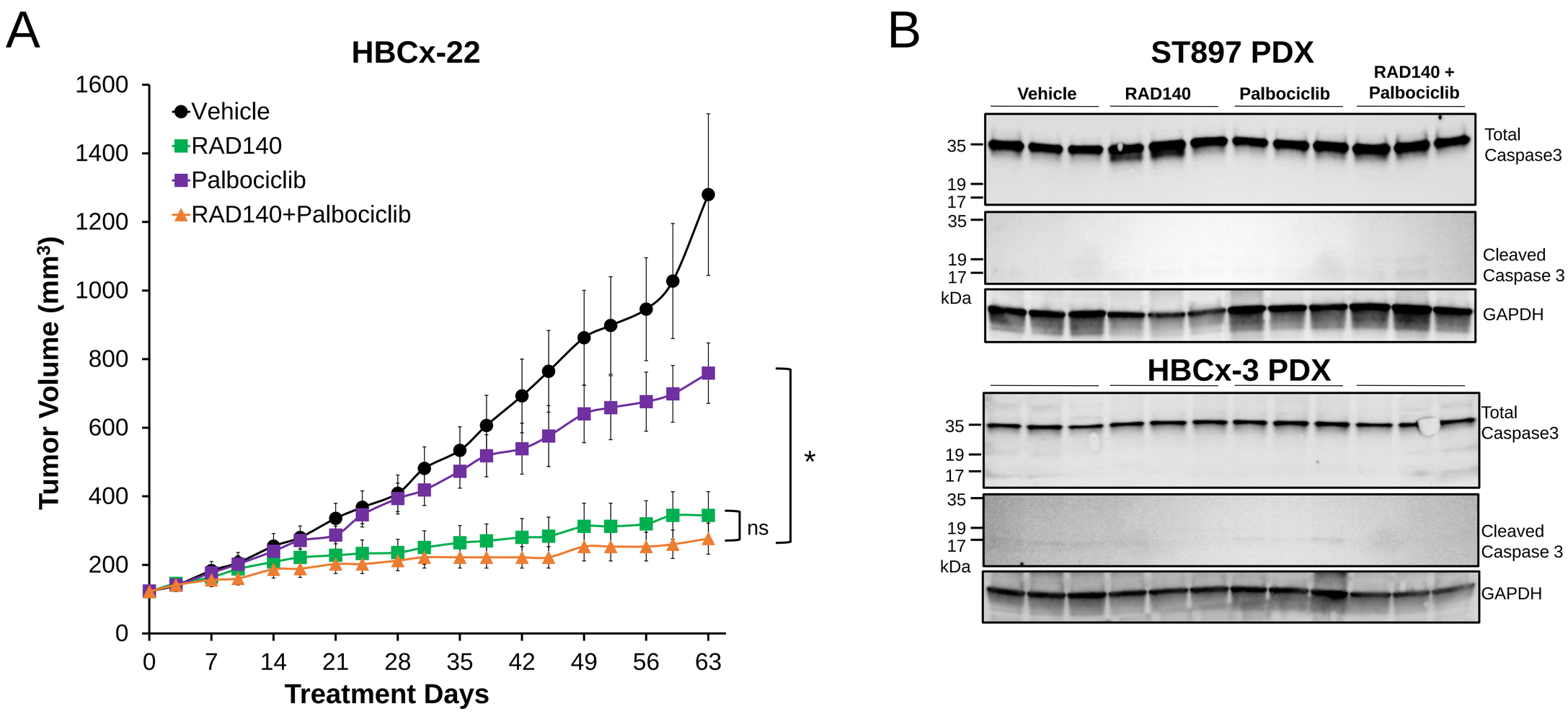

# Supplementary Figure S3

**Supplementary Figure S3.** Efficacy of RAD140 in additional breast cancer xenograft models. **A,** Mean tumor volumes ± SEM of HBCx-3 PDX treated with vehicle or RAD140 (100 mg/kg twice daily) for the indicated period of time (N=7/group). For the comparison between the ΔTV of vehicle and RAD140 groups, $p<0.01$; **B,** Mean tumor volumes ± SEM of HBCx-21 PDX treated with vehicle or RAD140 (100 mg/kg once daily) for the indicated period of time (N=10/group). For the comparison between the ΔTV of vehicle and RAD140 groups, $p<0.01$; **C,** Mean tumor volumes ± SEM of T-47D cell line-derived xenografts treated with vehicle, RAD140 (100 mg/kg twice daily), fulvestrant (3 mg once a week) or DHT (12.5 mg 60-day release pellet) for the indicated period of time (N=8-9/group). The tumor growth inhibition seen with RAD140, fulvestrant or DHT were all statistically significant ($p < 0.05$); No statistically significant difference was seen between the RAD140, fulvestrant or DHT group; **D,** Mean tumor volumes ± SEM of HBCx-22 as shown in Figure 2A, with the addition of the growth curve of the RAD140 (100 mg/kg once daily) and fulvestrant (1 mg once per week) co-administration group. Comparisons of TGI between the RAD140-fulvestrant group and either of the agents alone did not reach statistical significance.



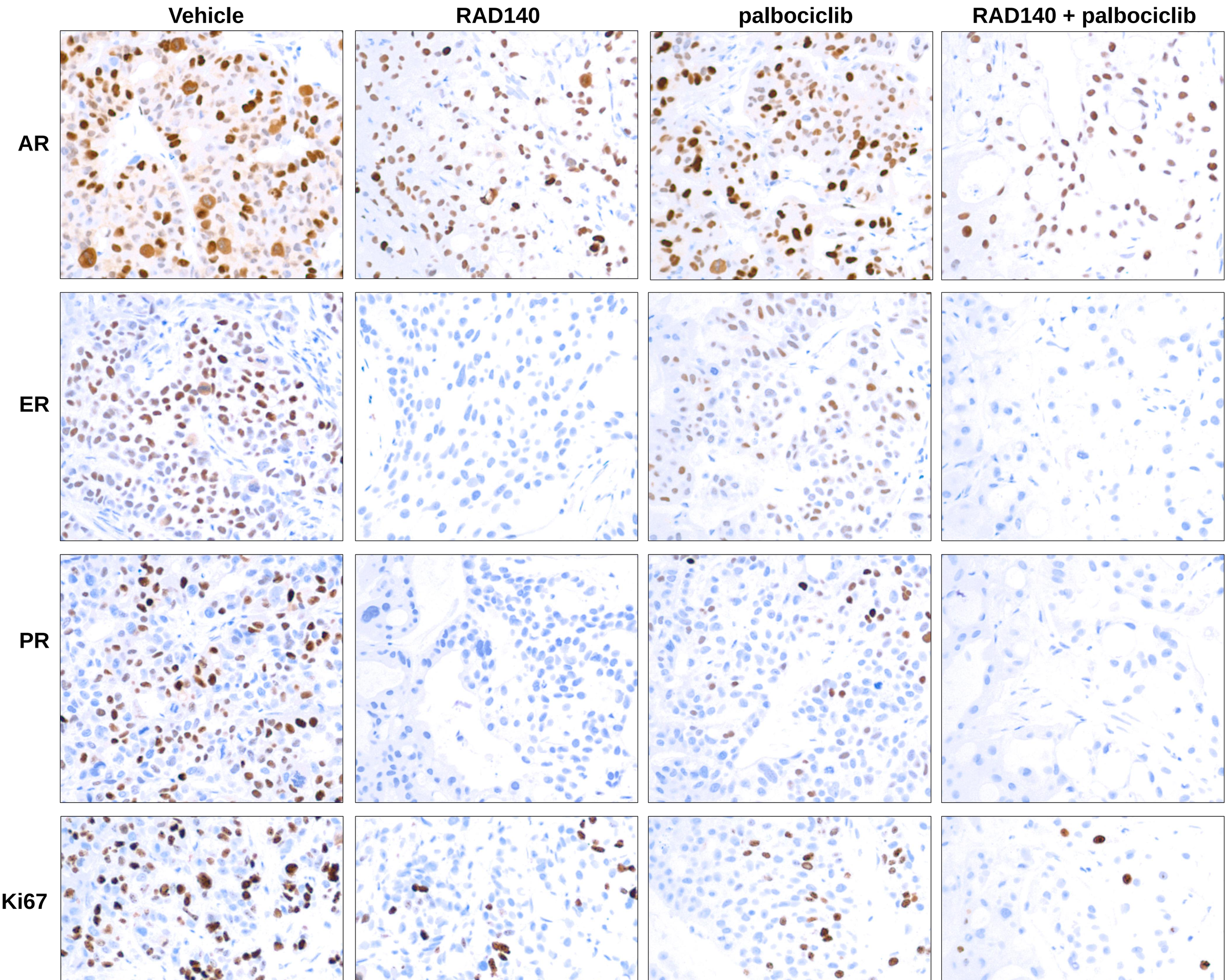

# Supplementary Figure S4

**Supplementary Figure S7.** Characterization of terminal tumors treated with RAD140. Samples of HBCx-22 and HBCx-3 PDX treated with RAD140 exhibit predominantly epithelial phenotype. Three individual tumors of each model were subjected to IHC staining with Cytokeratin 18 (EPR1626, Abcam) and Vimentin (SP20, Cell Marque) antibodies. One representative image is shown.




# Supplementary Figure S5

**Supplementary Figure S5. A,** The efficacy of RAD140 in combination with palbociclib in additional AR/ER+ breast cancer PDX models. Plotted are the mean tumor volumes ± SEM of HBCx-22 breast cancer xenografts treated with vehicle, RAD140 (10 mg/kg twice daily), palbociclib (75 mg/kg once daily) or a combination of RAD140 and palbociclib for the indicated period of time. N=9/group. Inter-group comparisons were carried out using student's t-test for the changes in tumor volume (ΔTV) from the beginning to the end of the study. *, $p=3.4\times10^{-5}$; ns, not significant (p=0.28); **B,** WB analysis of total and cleaved Caspase 3 (both antibodies from Cell Signaling) for samples of ST897 and HBCx-3 PDX tumors treated with RAD140, palbociclib or a combination of the two agents. Three samples from each treatment group were analyzed.




Supplementary Figure S6

**Supplementary Figure S6.** IHC staining of HBCx-3 PDX treated with RAD140 and palbociclib as single agents or in combination. Three individual tumors of each treatment group were subjected to IHC staining using AR, ER, PR, Ki67, and phospho-Rb (p-Rb) antibodies. One representative image is shown.