

**Supplementary information, Figure S3** Syngeneic tumor transplantation model recapitulates the both molecular and biological features of the original PTEN-/-/NIC mice.

(A) Scheme demonstrating how syngeneic tumor transplantation was done. Details of the model are given in Methods section. (B) Western blots demonstrating similar alterations of the signaling pathway components in donor and transplant PTEN-//NIC mice compared to PTEN+/+/NIC. Actin was used as a loading control. (C) Tumor volume fold change (FC) of the transplant mice treated with PBS (ctrl) or Ab7.16.4. *ns*: not significant (*P*>0.05) by two-tailed t-test. (D) Tumor volume fold change (FC) of the transplant mice treated with vehicle (ctrl) or Ab7.16.4 and lapatinib combination. Volume fold change was calculated by the ratio of volume at day 15 to volume at day 10 from the treatment start. \*\*\*\*P<0.001, by two-tailed t-test. (E) Ki-67 staining of the sensitive and resistant tumors treated with Ab7.16.4 and lapatinib combination. \*\*P<0.01, \*\*\*P<0.001 by two-tailed t-test. (F) TUNEL staining of the tumor tissue obtained from transplant mice treated with Ab+Lapatinib and classified as sensitive and resistant according to tumor volume fold change. *ns*: not significant (*P*>0.05) by two-tailed t-test. (G) MTT viability assay showing resistance of BT474.LapR cells to trastuzumab compared to BT474.Par cells. \*\*P<0.01 by two-tailed t-test.