

## Supplemental Figures

Fig. S1 Target inhibition after treatments with NVP-BKM120 *in vivo*. Tumor-bearing MMTV-CreBRCA1<sup>f/f</sup>p53<sup>+/-</sup> mice were biopsied before treatment, and tumor tissues harvested within 3 hours after the last treatment. Tissues were fixed and processed for immunohistochemistry with anti-phospho AKT (S473) antibodies. 400 x magnification.

Fig. S2 FDG-uptake and CT-PET scanning of mice before and after 2 weeks of treatment with NVP-BKM120. Tumor-bearing female MMTV-CreBRCA1<sup>f/f</sup>p53<sup>+/-</sup> mice were imaged with PET-CT scans before and after treatments with NVP-BKM120 at 50 mg/kg/day. Yellow arrows in the upper panel point to the dominant mass in each mouse before treatment. Synchronous additional tumors are indicated with green arrows. The lower panel displays the same mice imaged within 3 hours of treatment with a two-week course of NVP-BKM120 at 50 mg/kg/day. Percent decrease of FDG-uptake in the dominant mass was determined as described in Materials and Methods.

Fig. S3 Effects of the combination of NVP-BKM120 and Olaparib (left pair, treated with NVP-BKM120 at 30 mg/kg/day and Olaparib at 50 mg/kg/day) and of Olaparib alone (right pair, 50 mg/kg/day). Mice were imaged before and after 3 daily treatments, the repeat scan was obtained within 3 hours after the third treatment. The mouse on the right had multiple synchronous primary tumors, labeled in the before and after images with blue, orange and yellow arrows. Percent FDG-uptake was 65% (tumor with orange arrow), 55% (tumor with blue arrow) and 64% (tumor with yellow arrow). The mouse in the image pair on the right that was treated with Olaparib carried only one

macroscopically detectable tumor (red arrow). Olaparib treatments increased FDG-uptake by 75% in this tumor. Note that in the after-Olaparib-treatment image (far right) several hotspots in the upper thorax are visible which upon necroscopy were found to be tumors of less than 2 mm in diameter.

Fig. S4 In vitro responses of BRCA1-mutant breast cancer cell lines to treatments with NVP-BKM120 (1  $\mu$ M), Olaparib (10  $\mu$ M) or their combination. Cells were seeded in quadruplicate in 96-well plates and treated for 7 days as indicated. A. HCC1937 parental cells, B. SUM149 cells, C. HCC1937 cells stably transfected with vector control or a PTEN expression construct (D).

Fig. S5 Standard Curve for the quantitation of NVP-BKM120 in tumor cell lysates. Counts were measured from the peaks of the total ion current for NVP-BKM-120, integrated using MultiQuant v2.0 software (AB/SCIEX). For the concentration curve data, BKM-120 was prepared at concentrations of 1 nM, 10 nM, 100 nM, 500 nM, 1  $\mu$ M and 10  $\mu$ M in 40% methanol.

Fig. S6 Erk phosphorylation after treatments with NVP-BKM120 *in vivo*. Tumor tissues were harvested from MMTV-CreBRCA1<sup>fl/fl</sup>p53<sup>+/-</sup> mice within 3 hours after the last treatment with NVP-BKM120. Tissues were fixed and processed for immunohistochemistry with anti-phospho ERK (Thr202/Tyr204) antibodies. 400 x magnification.