Supplementary Figure Legends For:

Molecular profiling of the residual disease in triple-negative breast cancers after neoadjuvant chemotherapy identifies actionable therapeutic targets

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Supplementary Figure 1: Association of high Ki67 with basal-like status. A) Bar chart of the molecular subtype of post-NAC TNBC samples as determined by PAM50[7] analysis using NanoString gene expression data. B) Kaplan-Meier analysis of RFS (left) and OS (right) in BLBCs vs. non-BLBC. C) Association of post-NAC Ki67 score with underlying molecular subtype. D) Kaplan-Meier analysis of RFS (left) and OS (right) in TNBCs with high vs. low Ki67 in the RD after NAC. E) Change in Ki67 score in the pre- to the

post-NAC tumor. p-value represents result of a two-tailed paired student's t-test, n=43. F) Association of change in Ki67 score during NAC with molecular subtype.

Supplementary Figure 2: Association of node status with RFS and OS, stratified by menopausal status.

Supplementary Figure 3: Association of gene alterations with gene expression. Gene expression quantified by NanoString was compared to gene status as determined by NGS (* $p<0.05$, one-tailed students t-test).

Supplementary Figure 4: Gains, enrichments, reductions and losses of gene alterations post-NAC in TNBCs. Alterations in copy number or allele frequency in genes identified by NGS are depicted (n=20 paired specimens); G: gain, not detected in pre, detected in post; E: enrichment, detected in pre and post but higher in the post; R: reduction, detected in pre and post but higher in the pre; L: loss, detected in pre but not in post. Of 20 pairs, 11 were core needle biopsies (in gold), and 9 were excisional biopsies. Data in this figure were not adjusted for tumor purity estimations.

Supplementary Figure 5: MCL1 overexpression enhances docetaxel resistance in non-amplified TNBC cell lines. A) Western blot of cells lentivirally-transduced with GFP or MCL1. B) Cell viability after 48 h of treatment with the indicated doses of docetaxel. C) Cell viability of MCF10A cells after 48 h of treatment with the indicated doses of docetaxel or doxorubicin.

Supplementary Figure 6: MEK activity is required for MYC-induced soft agar colony formation. A) Representative images of agar-embedded MCF10A colonies from Figure 4D. B) P-AKT and P-ERK western blot analysis of lysates of MCF10A 5XMYC and

vector control cells treated for 4 h with the MEK inhibitors selumetinib (SEL) and GSK1120212 or the PI3K inhibitor BKM120. C) Immunofluorescence of ZO-1 and DAPI in MCF10A 5XMYC and vector control cells treated with 100 nM GSK1120212/trametinib. Scale bars represent 50 μm. D) Immunofluorescence of cytokeratin 8, cytokeratin 5 and DAPI in MCF10A 5XMYC and vector control cells treated with 100 nM GSK1120212/trametinib. Scale bars represent 50 μm.

Supplementary Figure 7: *TSC1* truncation in the RD of a TNBC after NAC. A) Integrated genomics Viewer [37] image of reads spanning the 25KB deleted region between intron 8 and the 3'UTR. B) Schema of deleted region. C) PCR detection of the truncation product using primers spanning introns 8-23 (~170 bp product). Control primers for amplification were used, spanning the breakpoint in intron 23 (~100bp product). The truncated product was identified only in tumor 1(A-B), and not in a second control tumor, or either matched normal breast control sample. D) Sanger sequencing confirmation of TSC1 Q516X mutation in RD. Tumor cellularity estimation in the sample was 20-40%.

Supplemental Table Titles:

Supplemental Table 1: Patient demographics

Supplemental Table 2: Genes included in targeted NGS panel

Supplemental Table 3: Complete NGS data from 81 post-NAC cancers and 21 pre-treatment biopsies.

Supplemental Table 4: Comparison of frequency of alterations between post-NAC TNBCs and primary BLBCs (TCGA).

Supplemental Table 5: NanoString gene expression data, normalized and median centered.

Supplemental Table 6: Genes upregulated in Clusters I-III

Supplemental Table 7: Gene sets enriched in Clusters I-III

Supplemental Table 8: Actionability table with references