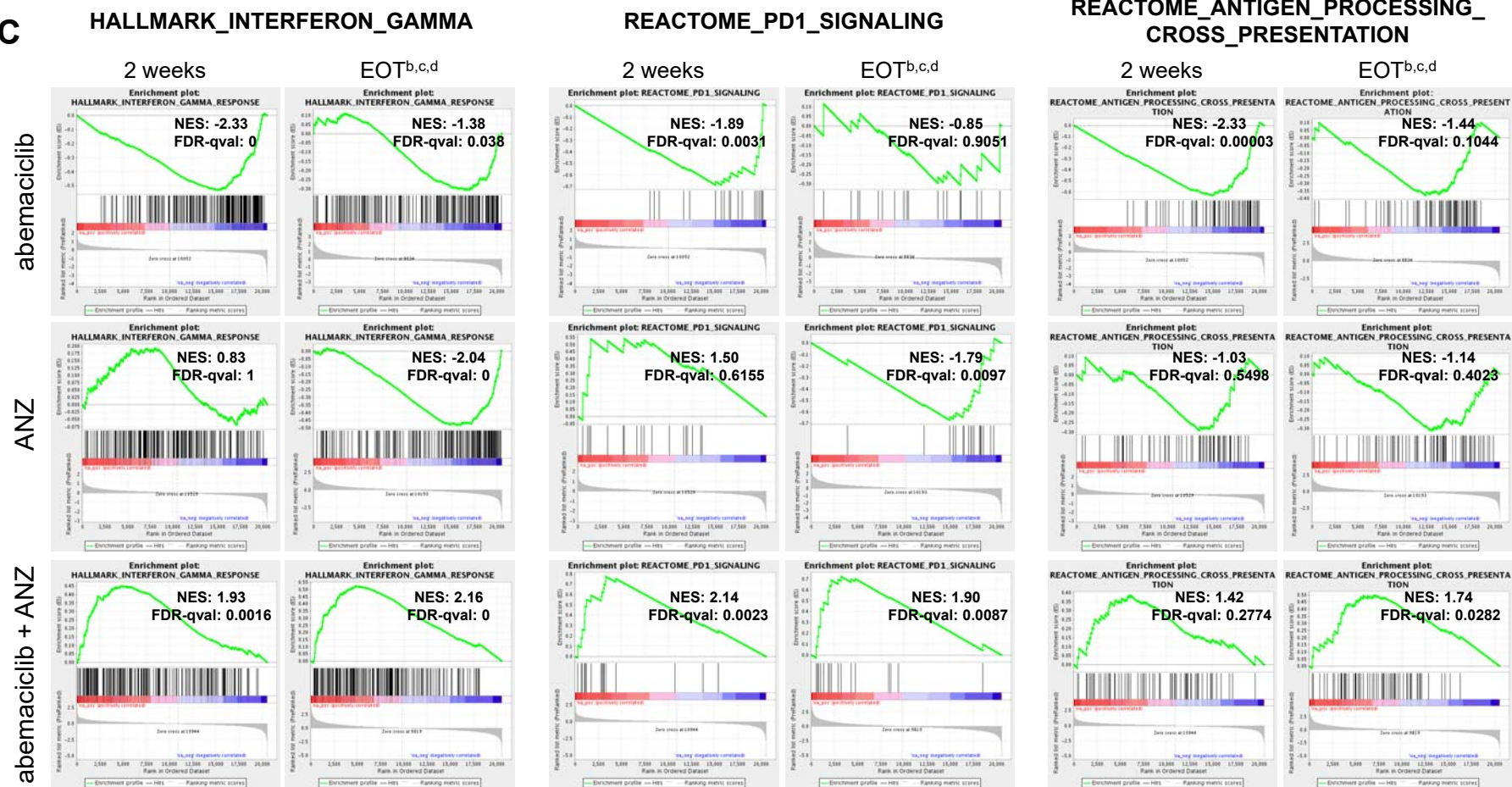


**C**

**Supplementary Figure S5. A.** Analysis of the RNAseq samples. Serial biopsies were collected at three timepoints: Baseline (prior to treatment), Early (after 2 weeks of therapy with abemaciclib, ANZ, or abemaciclib plus ANZ), and Late (after 2 weeks of initial therapy followed by 14 weeks of abemaciclib plus ANZ). Extracted RNAs were subjected to RNAseq analysis. Tumors from patients who went off the drug before biopsy at late stage were excluded from that time point. Patients with biopsy date issues (i.e., biopsy not performed exactly after 2 weeks of initial therapy and/or at EOT) were removed from the analyses. <sup>a</sup>Prior to switching over to the combination, abemaciclib+ANZ. **B.** Top downregulated GSEA gene sets across treatment arms. **C.** Top upregulated GSEA gene sets in combination treatment arm. <sup>b</sup>2 weeks of initial therapy with abemaciclib followed by 14 weeks with combination therapy. <sup>c</sup>2 weeks of initial therapy with ANZ followed by 14 weeks with combination therapy. <sup>d</sup>2 weeks of initial therapy with abemaciclib+ANZ followed by 14 weeks with combination therapy. Abbreviations: ANZ, anastrozole; EOT, end of treatment; GSEA, gene set enrichment analysis; NES, normalized enrichment score; FDR-qval, false discovery rate q-values.