## **SUPPLEMENTARY INFO**

**Supplemental Table 1.** Demographic and clinical characteristics of the 65 HNSCC patients from whom this PDX collection was derived. Includes site of primary tumor, American Joint Committee on Cancer (AJCC) staging, age, sex, and HPV status.

Supplemental Table 2. Full PDX characteristics table.

**Supplemental Table 3.** Median centered RPPA data from PDX samples, biomarker groups, and statistical comparison between PDX clusters.

**Supplemental Table 4.** Temporal PDX tumor volume measurements.

Supplemental Table 5. Median centered RNA sequencing data from PDX samples.

Supplemental Table 6. Quantification from patient tumor sample histology.

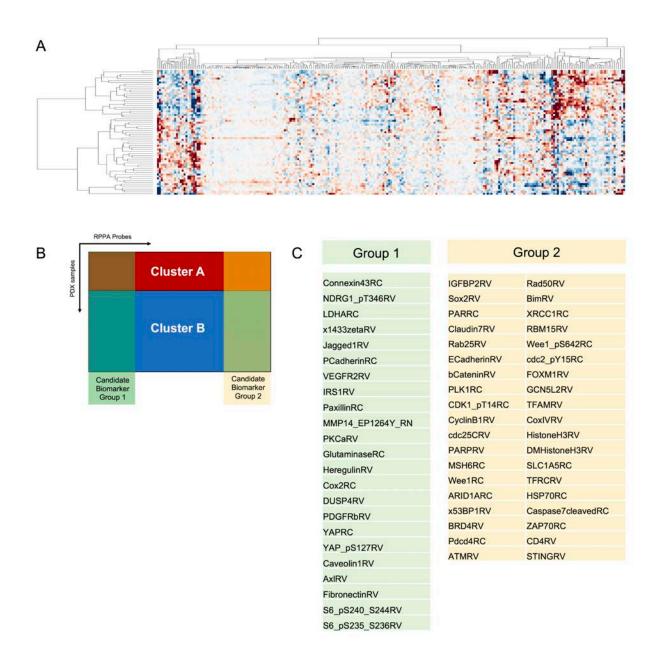
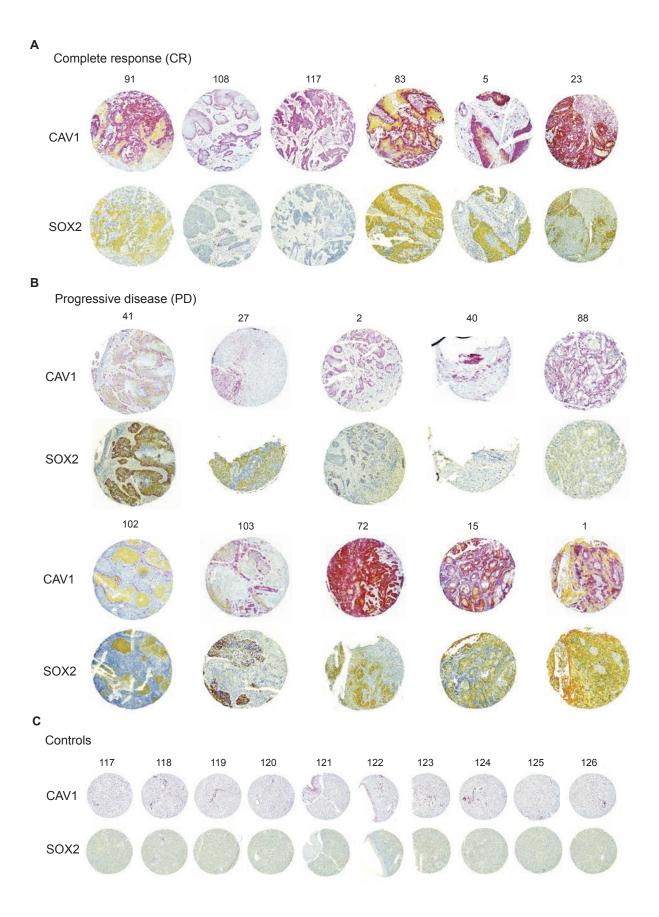


Figure S1. Full hierarchical clustering results and biomarker group definitions.

(A) Complete clustergram for unbiased hierarchical clustering using the "ward" algorithm (evaluated in MATLAB) for all 247 probes measured across the 65 PDXs. Rows indicate PDX samples and columns indicate RPPA probes. (B) Schematic representation of PDX division into two cluster subtypes, defined by differential expression of Biomarker Groups 1 and 2. (C) Full list of proteins belonging to Biomarker Group 1 and Group 2.



## Figure S2. Images of stained patient tumor samples.

(A) Tumor sections from patients who experienced a complete response (CR) to cetuximab treatment. CAV1 (purple) is stained on the top and SOX2 (purple) is stained on the bottom. Cytokeratin 5,6 is in yellow on both. (B) Tumor sections from patients who experienced progressive disease (PD) (i.e. resistance) to cetuximab treatment. CAV1 (purple) is stained on the top and SOX2 (purple) is stained on the bottom. Cytokeratin 5,6 is in yellow and nucleic acid (nuclei) is stained using DAPI (blue) on both. (C) CAV1 (top) and SOX2 (bottom) stained non-tumor hepatocyte controls. Numbering corresponds to core number (see Table S6 for relationship between core number and patient number).