

Description of Additional Supplementary Files

Supplementary Data 1: **a** Datasets from ENCODE used in the study to construct Benchmark. **b** Common false positive pathways and corresponding FDR. Shown are minimum (min), average (mean), and median FDR values from n=100 randomization for indicated methods. Median FDR values <0.05 are highlighted with bold font. **c** Cell lines from CCLE database used in this study.

Supplementary Data 2: **a** Patient IDs from TCGA database used in this study. **b** Days to follow-up statistics from TCGA patients used in this study. Shown are mean+/-std. **c** Favorable and unfavorable top 100 significant prognostic pathways identified by PET. **d** Significant prognostic single gene and combination gene biomarkers. The pathway from which the biomarker is derived has also been indicated. **e** Leading prognostic genes identified by PET in each cancer type. **f** Top 100 DEGs identified by DESeq2 comparing tumors with unfavorable with favorable prognosis. Positive log2Foldchange values indicate higher expression of the gene in tumors with unfavorable prognosis. **g** Link to independent datasets used in this study. **h** Early combination biomarkers that remain consistent in later stages. **i** Fraction of early combination biomarkers that remain consistent in later stages in each cancer type.

Supplementary Data 3: **a** Samples with combination of favorable and unfavorable prognosis biomarkers. **b** CDKN2A methylation and copy number levels in KIRC and KIRP samples. **c** 85 unfavorable biomarkers of human bladder cancer corresponding to Fig S6a.

Supplementary Data 4: **a** List of drugs investigated in the study. **b** List of drugs predicted for each cancer type based on PET. **c** List of drugs predicted for each cancer type based on DEGs. **d** List of drugs predicted for bladder cancer based on extended set of compounds.

Supplementary Data 5: **a** CDK9 expression is associated with unfavourability scores among bladder cancer cell lines. **b** List of all expressed genes in T24 cells. DEGs after CCT treatment are indicated as those with FC>3, FDR<0.05.