Supplementary Table 1: Cell line annotation, level of genomic characterisation, CRISPR-Cas9 screening details, quality control assessment scores and final analysis set specification.

Supplementary Table 2: a, Binary scores for 7,470 fitness genes across cell lines. **b**, Overrepresentation of pathway gene sets in each cell line based on analysis of fitness genes (non-null binary scores indicate enrichments at a Benjamini-Hochberg corrected hypergeometic-test p-value < 0.05). **c**, Pathway gene sets specifications.

Supplementary Table 3: Detailed annotation of 7,470 fitness genes including membership to predefined sets of core fitness essential genes, output of the Adaptive Daisy Model (status of each gene in each cancer-type: core fitness, context specific fitness, non-fitness) and percentages of dependent cell lines (pan-cancer and for each cancer-type).

Supplementary Table 4: a, Area under ROC-curves (Mann-Whitney tested) for gene classifier (based on n.dependent cell lines) and gene-families as positives. **b**, Essential gene-enrichments within ADaM pan-cancer core-fitness genes (APCGs) and hypergeometric-test p-values. **c**, APCGs annotation. **d**, Pathways and **e**, gene-families in novel APCGs (hypergeometric-test p-values, with Benjamini-Hochberg correction).

Supplementary Table 5: a, Cancer-type specific and **b**, pan-cancer target priority scores used to compute the significance threshold for identifying priority targets.

Supplementary Table 6: Final target priority scores for each cancer-type. Includes evidence used to calculate each score and embedded formulas to recompute scores if changing the weights.

Supplementary Table 7: Final pan-cancer target priority scores. Includes evidence used to calculate each score and a template sheet with formulas to recompute scores if changing the weights.

Supplementary Table 8: Differential dependency marker classes across all cancer-types and combined across some cancer-types. In the second case, p-values refer to dedicated two-sided Student's t-tests with sample sizes for combined cancer types indicated in Supplementary Table 1. False discovery rates are calculated by correcting p-values with the Benjamini-Hochberg method.

Supplementary Table 9: Priority targets with associated markers, tractability classes and indication of targeting compounds. Genome-wide small-molecule and antibody tractability annotations with information about approved/pre-clinical drugs and their indications.

Supplementary Table 10: a, sgRNA sequences used for WRN validation experiments. **b**, Cell lines used for WRN validation experiments.