SUPPLEMENTARY TABLE AND FIGURE LEGEND

Supplementary Table 1. Kinase Inhibitor Gene Targets. The gene target tiers for each of the 66 small-molecule kinase inhibitor targets for 322 gene targets (including mutant versions of genes) is shown. Gene targets are represented in tiers 1-5 with 1 being the best gene targets for each drug. The tiers are defined by identification of the gene with lowest Kd or IC50 for a given drug. Any genes with Kd or IC50 that fall within a range from that lowest value to 10-fold higher than that lowest value are defined as tier 1. Each successive tier represents an additional log10 range for Kd or IC50 values. Wherever a drug exhibits no activity against a gene target (or no data exists), a 0 is used.

Supplementary Table 2. Patient Clinical Information. Available and relevant clinical and demographic information on all 151 de-identified patients from which these specimens were derived is presented.

Supplementary Table 3. 151 Patient IC_{50}s. The IC_{50}s for all 151 patients for all 66 small-molecule kinase inhibitors are shown as well as the median IC_{50} used to compute percentage of median for evaluation of effectiveness or ineffectiveness of each drug for each patient. All values are expressed in nM.

Supplementary Table 4. 151 Patient Drug Curve Raw Data Points. The raw data points for all 151 patients for all 66 small-molecule kinase inhibitors are shown. All values are normalized to wells where cells were cultured in the absence of drug and are expressed as a decimal fraction of these no drug values where 0 represents lowest viability and 1 represents viability of no drug wells.

Supplementary Table 5. 151 Patient Gene Target Scores. The algorithm gene target scores for 290 genes (mutant version of genes removed) for all 151 patients is shown.

Supplementary Table 6. Cumulative Gene Target Scores. The cumulative gene target scores for ALL, AML, CLL, CML, CMML, and other MPN are shown. Values range from 0 to 1 with 0 being no evidence of pathogenic involvement and 1 being most frequent prediction of pathogenic involvement.

Supplementary Table 7. Sources of Small-Molecule Kinase Inhibitors.

Supplementary Figure 1: Scheme for profiling leukemia patient samples with a panel of kinase inhibitors. Primary cells were isolated from blood or bone marrow obtained from patients with a diversity of hematologic malignancies. Mononuclear cells were purified on Ficoll gradients and distributed across three 96-well plates (50,000 cells per well) containing graded concentrations of 66 small-molecule kinase inhibitors (four concentrations per drug listed in **Supplementary Table 6**). After three days, cell viability was assessed by subjecting cells to the tetrazoliumbased MTS assay. The mean absorbance value of seven wells with cells but without any drug was tabulated, and this value was defined as 100% viability. The rest of the plate was normalized to this 100% value. IC_{50} values for each drug were then calculated using a second-order polynomial curve fit. The IC_{50} of every patient for each drug was compiled and median IC_{50} values for the entire 151 patient cohort for each drug were computed. An individual patient response was determined by comparison of the IC_{50} for that individual patient

sample versus the median IC_{50} for all 151 patients. A cut-off of 20% of median IC_{50} was used to define hypersensitivity of any individual sample to any drug.

Supplementary Figure 2: Rank ordering of 151 sample IC_{50} values for each small-molecule kinase inhibitor. Individual patient sample IC_{50}s were determined for 151 patients for 66 small-molecule kinase inhibitors as described in Figure 1. The IC_{50}s for each drug are ranked from lowest to highest. When a sample did not reach IC_{50}, the highest plated concentration of that drug is shown.

Supplementary Figure 3: One-way clustering of leukemia patient sample response to small-molecule kinase inhibitors. Individual patient sample IC_{50}s were determined for 151 patients for 66 small-molecule kinase inhibitors as described in Figures 1 and 2. These data are subjected to a one-way Pearson correlation for unsupervised hierarchical clustering of patient sample responses. As in Figure 2, the darkest red indicates most sensitive and white indicates completely insensitive. Patient samples are color-coded by diagnosis (ALL – red; AML – green; CLL – yellow; MPN – blue). Kinase inhibitors are arranged based on family of primary gene targets for each drug.

Supplementary Figure 4: Two-way clustering of leukemia patient sample response to small-molecule kinase inhibitors. Individual patient sample IC_{50}s were determined for 151 patients for 66 small-molecule kinase inhibitors as described in Figures 1 and 2. These data are subjected to a two-way Pearson correlation for unsupervised hierarchical clustering of both patient sample responses and drug activity profiles. As in Figure 2, the darkest red indicates most sensitive and white indicates completely insensitive. Patient samples are color-coded by diagnosis (ALL – red; AML – green; CLL – yellow; MPN – blue).