Supplemental Methods

Treatment of AML cell lines with ABT-263 and ABT-737 in Fig 1A
AML cells were incubated for appropriate time in RPMI 1640 medium supplemented with 10% FCS and titrated concentrations of ABT-199, ABT-737. Viable AML cells were enumerated by flow cytometry using counting beads with concurrent Annexin-V and propidium iodide (PI) staining. Briefly, AML cells were washed twice with Annexin-V binding buffer (ABB) and resuspended in 100 μL ABB buffer containing Annexin-V FITC (Roche Diagnostics, Indianapolis, IN). Cells were then incubated in dark at room temperature for 15 min, washed again and resuspended in 300 μL ABB buffer. To determine cell number, 10,000 CountBright™ counting beads (Invitrogen, CarlsBAD, CA) were added per sample. PI (Sigma-Aldrich) was added immediately before analysis by Gallios flow cytometer (Beckman Coulter, Indianapolis, IN). Kaluza software (Beckman Coulter) was used for data analysis. EC50 values were calculated using CalcuSyn software (Biosoft, Cambridge, MA) based on the number of live cells (Annexin-V-/PI-).

Short-term treatment of primary AML cells with ABT-737 and ABT-199 in Figure 4A
Fresh AML cells were resuspended in mixture of 10 mL of MEM, Alpha 1X containing 20% FBS, 0.1 mg/ml heparine, 10 units/mL DNase (Thermo Scientific), and 10mM MgSO4 (Sigma). Cells were incubated for 15 minutes in 37°C incubator in the above mixture and centrifuged at 1500 rpm for 5 minutes prior to resuspension of cell pellet for experiments. AML mononuclear cells were cultured at 1 million cells/ml in minimum essential medium (MEM) alpha (Cat. 15-012-CV, Mediatech, Inc. Manassas, VA) containing 5% fetal bovine serum (FBS), 5% horse serum (HS) and supplemented with IL-3, TPO and SCF at 10 ng/ml. Cells were treated with ABT-199 or ABT-737 at 125 nM for 24 h, after which cells were washed twice in PBS and resuspended in annexin binding buffer containing a 1:50 dilution of Annexin V-Cy5 (BD Biosciences) and 1:100 dilution of 7-Aminoactinomycin (7-AAD, Sigma-Aldrich). Cell numbers were determined by adding 20,000 CountBright counting beads.
(Invitrogen) per sample, within AnnexinV/7-AAD-negative cell population. Cells were then analyzed by the BD FACSArray bioanalyzer using green (532 nm) and red (635 nm) excitation lasers. If >50% spontaneous cell death was observed, the sample was excluded from analysis.

**Short-term treatment of primary AML cells with ABT-263 and ABT-199 in Fig 4B**

Primary AML cells were obtained by informed consent from the Dana-Farber Cancer Institute, Leukemia Group, the Pasquarello Tissue Bank at the Dana-Farber Cancer Institute, the University of Texas MD Anderson Cancer Center, Leukemia Tissue Bank Shared Resource from the Ohio State University Comprehensive Cancer Center and the Germany-Austrian Study Group according to protocols approved by the Institute’s Institutional Review Board. Samples were Ficoll purified, and viably frozen in 90% FBS/10%DMSO. Thawed mononuclear cells were washed 1x in PBS, pelleted at 400 xg for 5 min at RT and resuspended at a density of 4 x 10^5 cells/mL in IMDM with L-glutamine and HEPES (Invitrogen), 100 U/mL penicillin and 100 mg/mL streptomycin, 100 ng/mL FLT3 ligand and 100 ng/mL stem cell factor, 20 ng/mL IL-3 and 20 ng/mL IL-6 (all supplements obtained from Peprotech). Cells were treated with varying concentrations of ABT-263 and ABT-199 (1-1000nm) for 8 h in a humidified atmosphere of 5% CO2 at 37°C. Cells were pelleted at 400 xg for 5 min at 4C and stained with CD45-V450 in FACS buffer for 20 min on ice. Cells were washed, pelleted and resuspended in Annexin Buffer (10mM Tris-HCl pH 7.4, 140 mM NaCl, 2.5 mM CaCl2) and stained with Annexin-V-FITC and PI. Viability was assessed by Annexin-V/PI negativity. Viability is expressed as a percent of the untreated control cells. Measurements were performed by FACS on a LSR Fortessa flow cytometer (BD Bioscience). AML blasts were identified by low-mid CD45/low SSC-A. EC50 values were determined as described above. If >55% spontaneous cell death was observed following 8h culture, the sample was excluded from analysis.