Supplementary Table 1: Gene Alterations in AML Cell Lines used in This Study

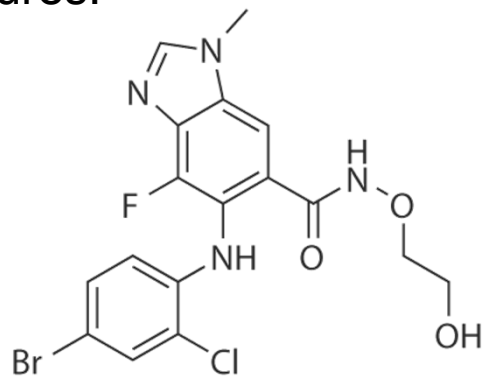
Cell Line	Type	Gene Alterations
OCI/AML3	Myeloid Leukemia	N-Ras(Q61), NPM mutation, TP53-wt
MOLM13	AML	FLT3/ITD, NPM1-wt, TP53-wt
U937	Myeloid Leukemia	TP53 mutation, PTEN mutations
KG-1	AML	Ras-wt, FLT3-wt, p53 truncation, PTEN (+)
MV4-11	Biphenotypic Leukemia	FLT3/ITD, NPM1-wt, TP53-wt

Supplementary table S2: Gene alterations and cytogenetic information on 10 periphoral blood or bone marrow samples obtained from AML patients

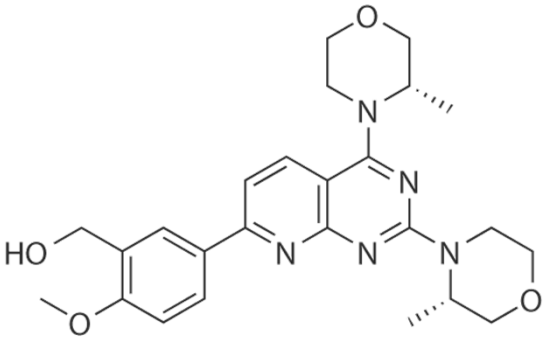
Case no.	Sample type	Blasts (%)	Disease status	RAS	FLT3	NPM1	CEBPA	cytogenetic information
1	PB	65	newly diagnosed	NRAS (G12S & G12C)	–	–	–	Diploid
2	PB	96	refractory	NRAS (Q61R)	–	–	–	46,XY,t(11;17)(q23;q25)[13]; 46,idem,del(20)(q11.2q13.1)[2]; 46,XY, der(11)t(11;17)(q23;q25),der(12)t(11;12)(q23;p13),der(17)t(11;17)t(11;12)[5]
3	PB	87	refractory	NRAS (G12D)	–	–	–	46,XY,add(3)(q27)[16]
4	PB	76	relapsed/refractory	NRAS (G12D)	–	–	–	46,XY,del(6)(q13q27)[7], 46,XY[13]
5	PB	95	refractory	NRAS (G12D)	–	–	–	46,XY,del(3)(q12q25)[1]
6	BM	62	newly diagnosed	NRAS (Q61K)	–	+	–	46,XY,t(8;21)(q22;q22)[20]
7	PB	89	refractory	NRAS (G13R)	–	–	–	46,XY,inv(3)(q21q26.2)[1]
8	BM	96	refractory	–	–	–	+	46,XY,del(6)(q24).ish del(6)(MYB+)[1]
9	PB	67	relapsed/refractory	–	–	–	–	Diploid
10	PB	75	relapsed	–	–	+	–	46,XY,del(9)(q13q22)[18]; 46,XY[2]
11	BM	84	newly diagnosed	–	ITD	+	–	Diploid
12	PB	48	relapsed/refractory	–	ITD	–	–	Diploid
13	BM	80	newly diagnosed	–	D835	+	–	47,XX,+mar[1]; 46,XX[1]
14	BM	90	newly diagnosed	–	D835	–	–	45,XX,1p-,-3,5q+,-7,+mar[9]

Abbreviations: NPM1, Nucleophosmin 1; CEBPA, CCAAT/enhancer-binding protein alpha; PB, peripheral blood; BM, bone marrow.

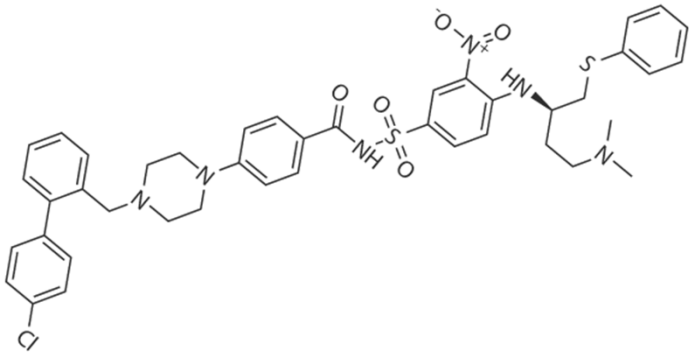
Supplementary Figures:



Selumetinib (AZD6244) Chemical Structure.
Molecular Weight: 457.68



AZD8055 Chemical Structure
Molecular Weight: 465.54



ABT737 Chemical Structure
Molecular Weight: 813.43

Fig. S1. Molecular structures of drugs used in this study.

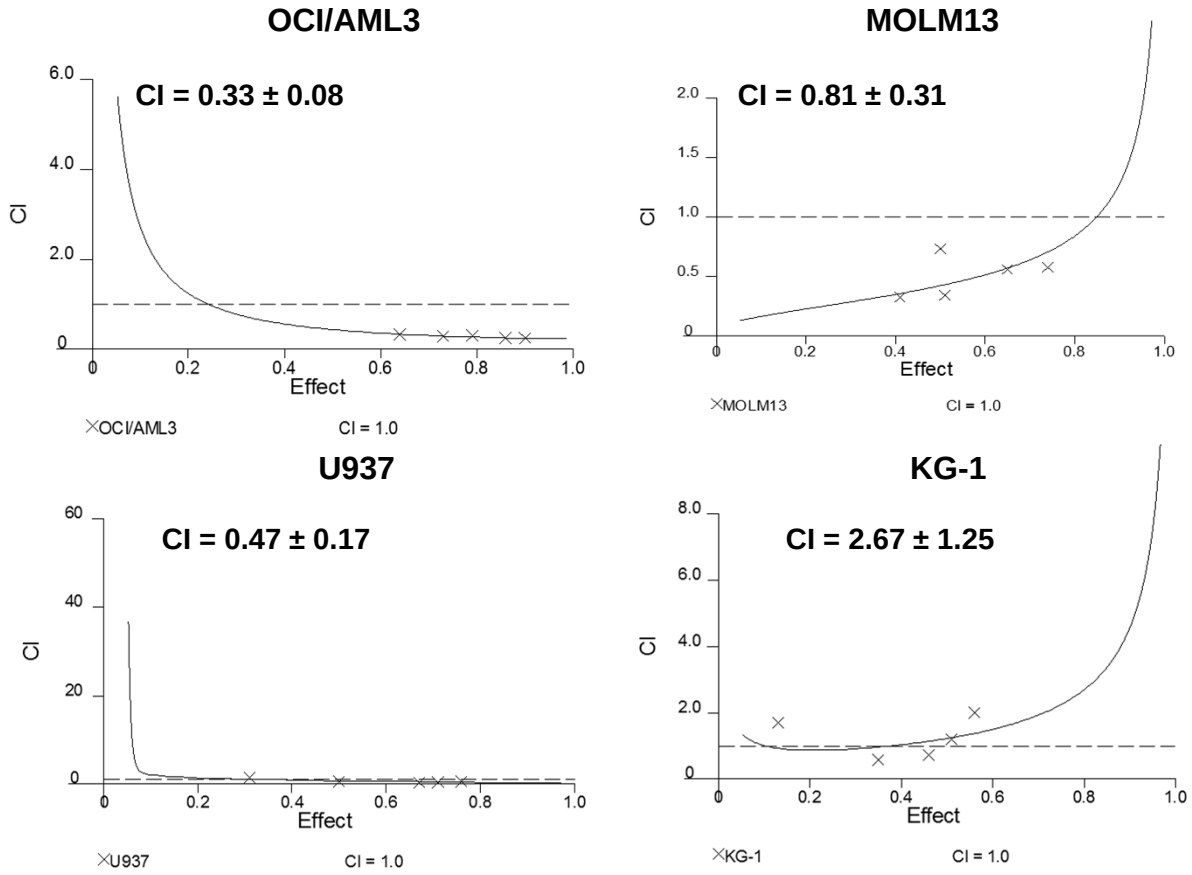


Fig. S2. The Chou-Talalay method [Chou et al. Cancer Res. 2010; *70:* 440-446] was used to determine combination indices (CIs) in AML cell lines treated with combination of AZD8055 and selumetinib for 48 hours.

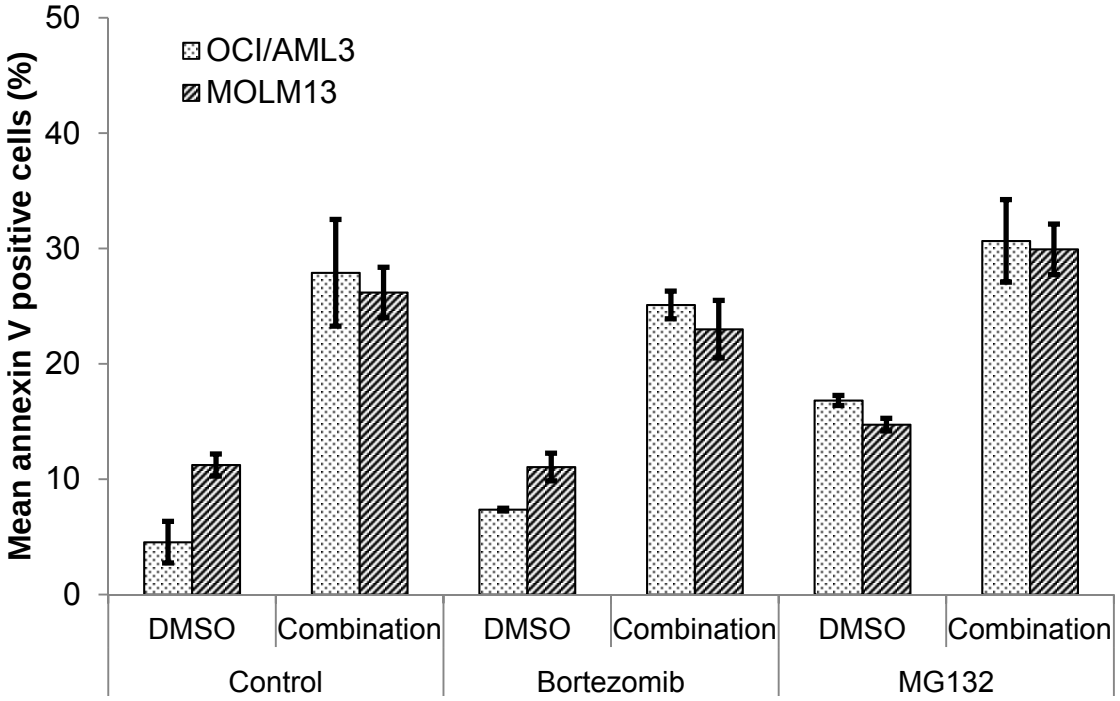


Fig. S3. OCI/AML3 cells were pretreated with proteasome inhibitors bortezemib (0.01 μmol/L) or MG132 (0.5 μmol/L) for 2 hours following by combination of AZD8055 (0.4 μmol/L) and selumetinib (0.2 μmol/L) for additional 48 hours. The apoptosis induction was measured using flow cytometry.

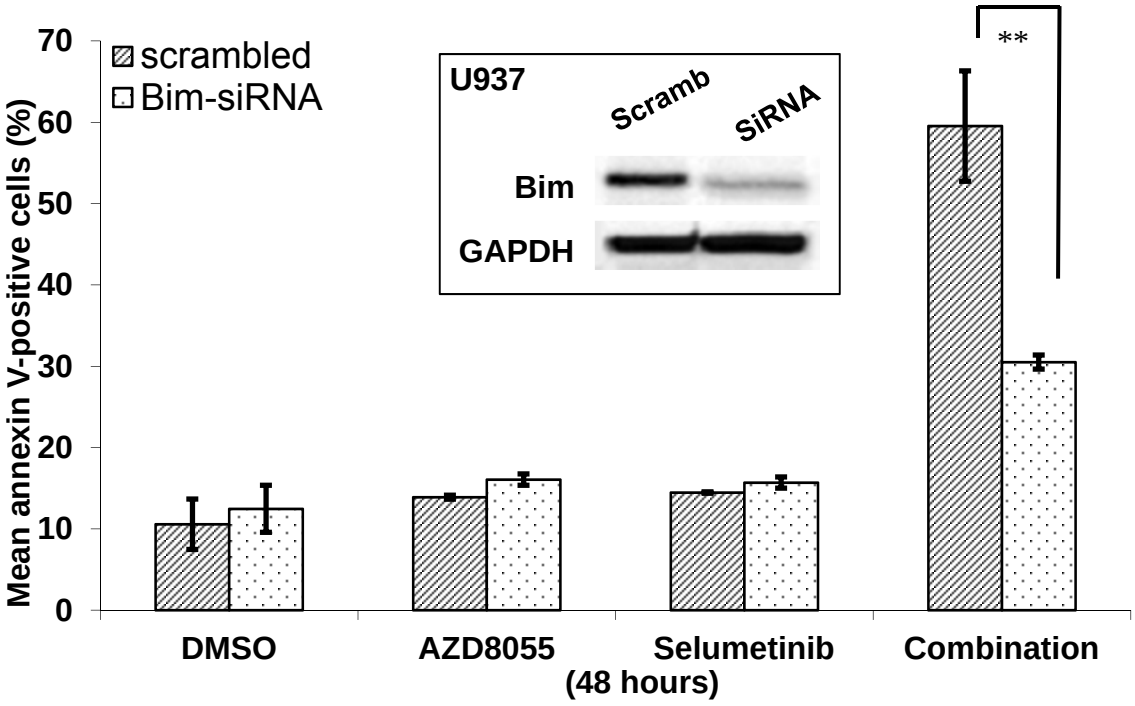


Fig. S4. U937 cells were electroporated with Bim siRNA or scrambled siRNA for 24 hours, treated with AZD8055 (0.4 μmol/L) and/or selumetinib (0.2 μmol/L) for 48 hours, and examined for apoptosis induction. Inset: knockdown of basal level of Bim protein expression.

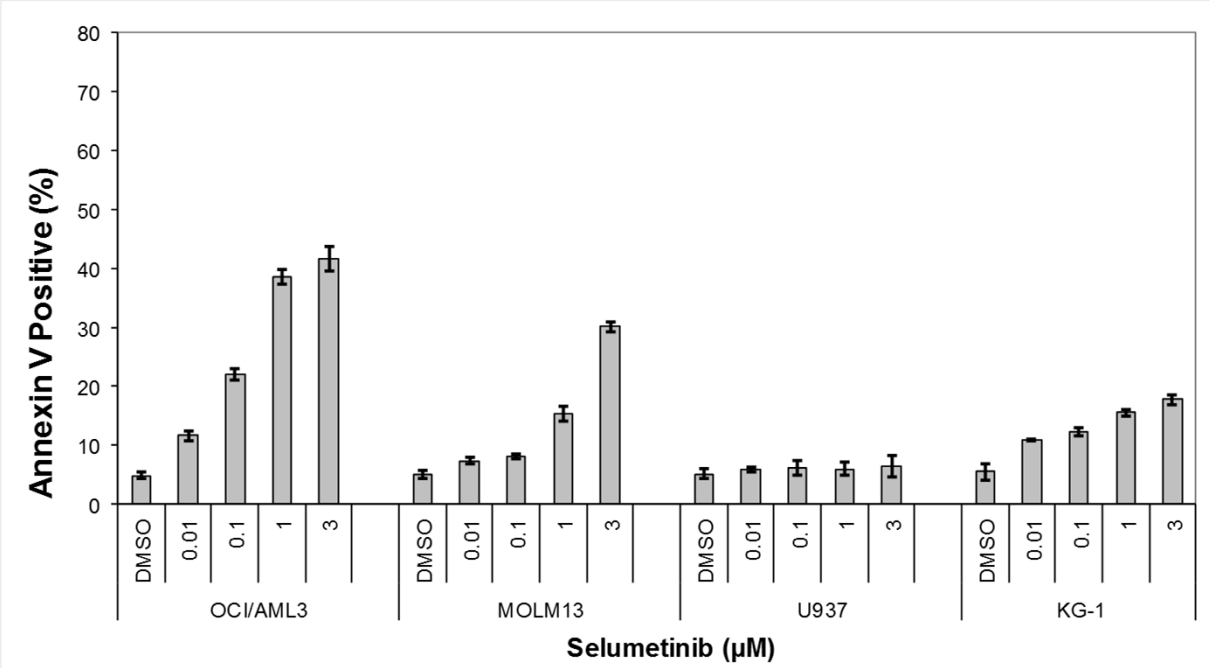


Fig. S5. AML cells were treated with indicated doses of selumetinib for 48 hours and apoptosis induction was determined using flow cytometry by measuring percentage of Annexin V positivity.

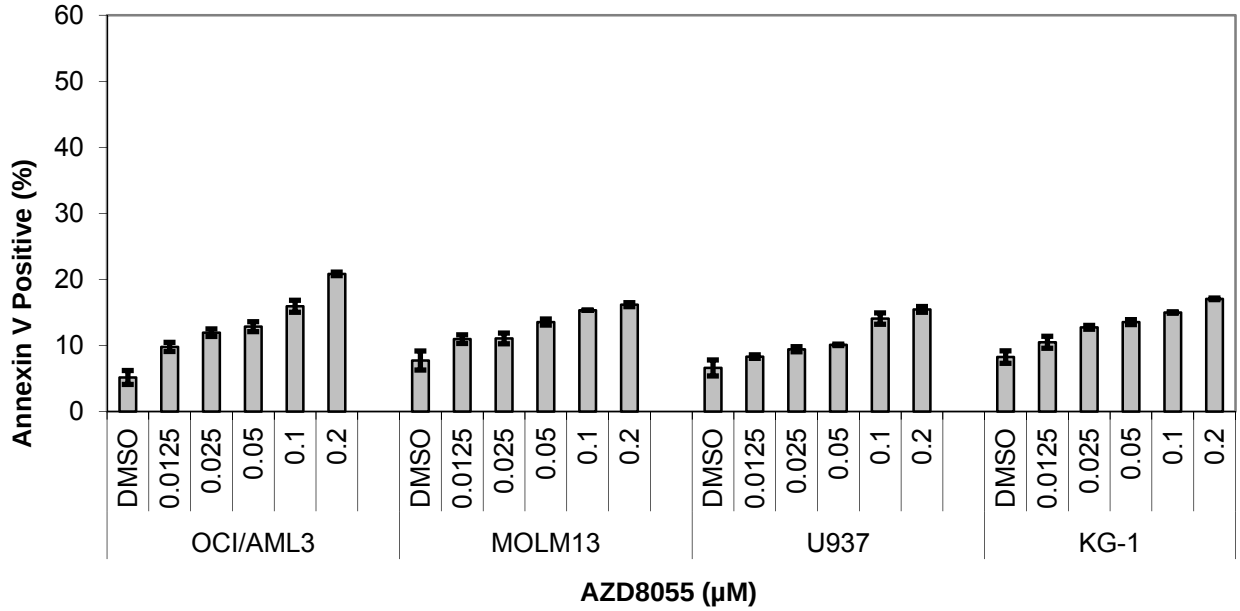


Fig. S6. AML cells were treated with indicated doses of AZD8055 for 48 hours and apoptosis induction was determined using flow cytometry by measuring percentage of Annexin V positivity.

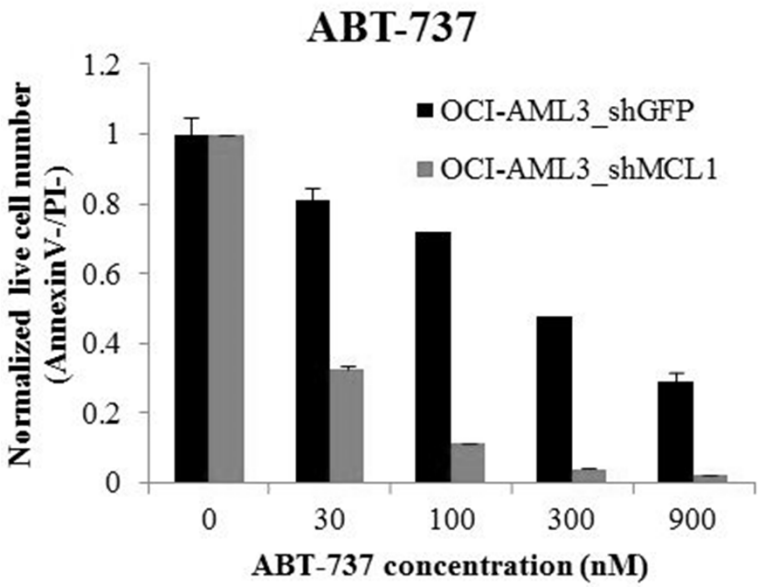


Fig. S7. OCI/AMl3_shGFP and OCI/AMl3_shMcl-1 AML cells were treated with indicated doses of ABT-737 for 48 hours and apoptosis induction was determined using flow cytometry by measuring Annexin V^-/PI^- population.