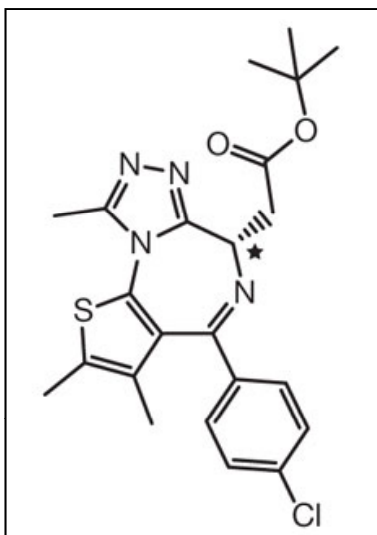


Supplemental Figure 1

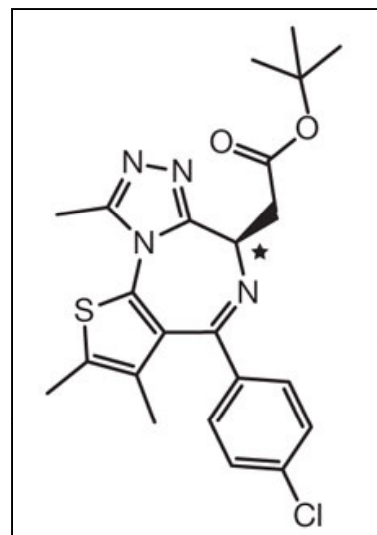
A

(S)-JQ1



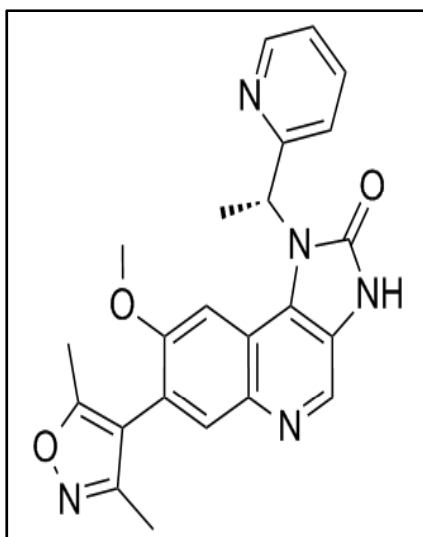
B

(R)-JQ1



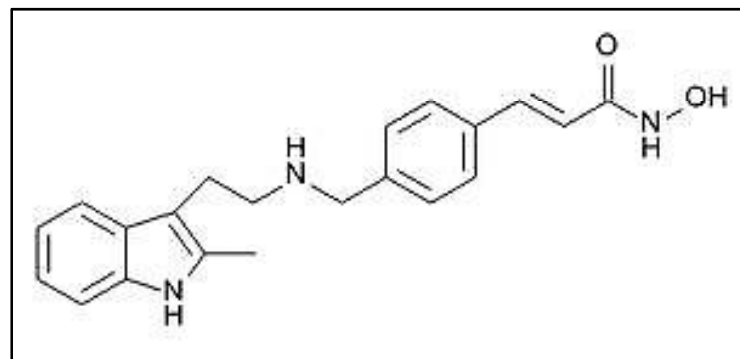
C

I-BET151

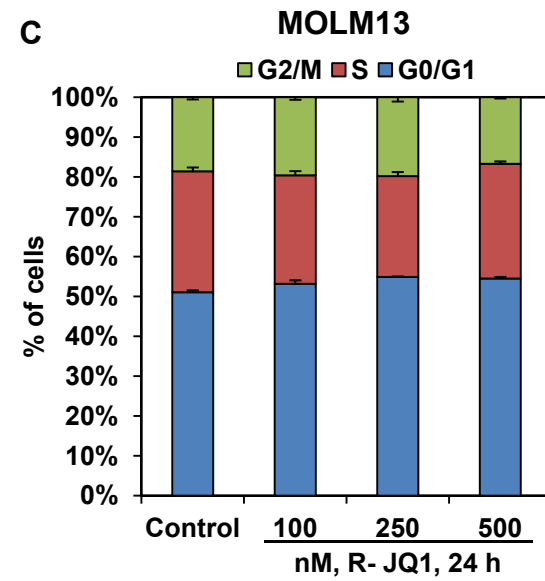
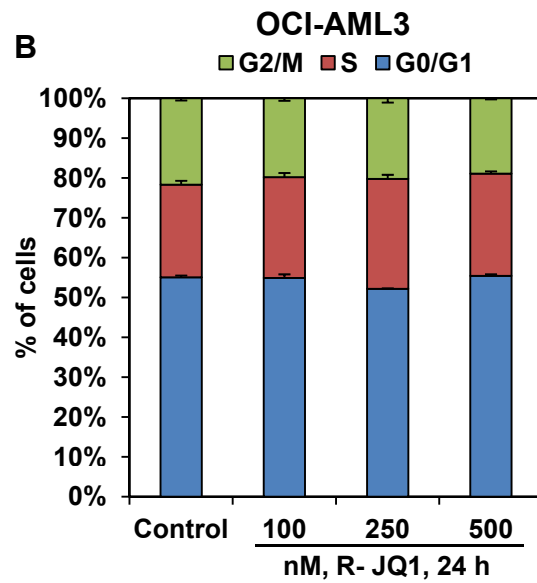
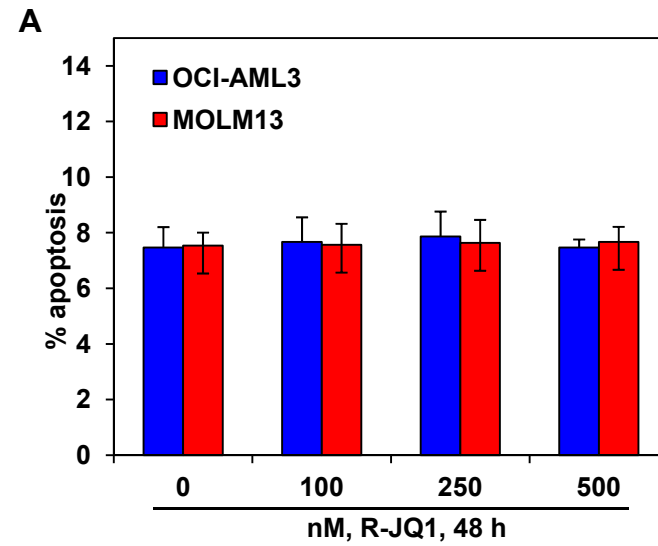


D

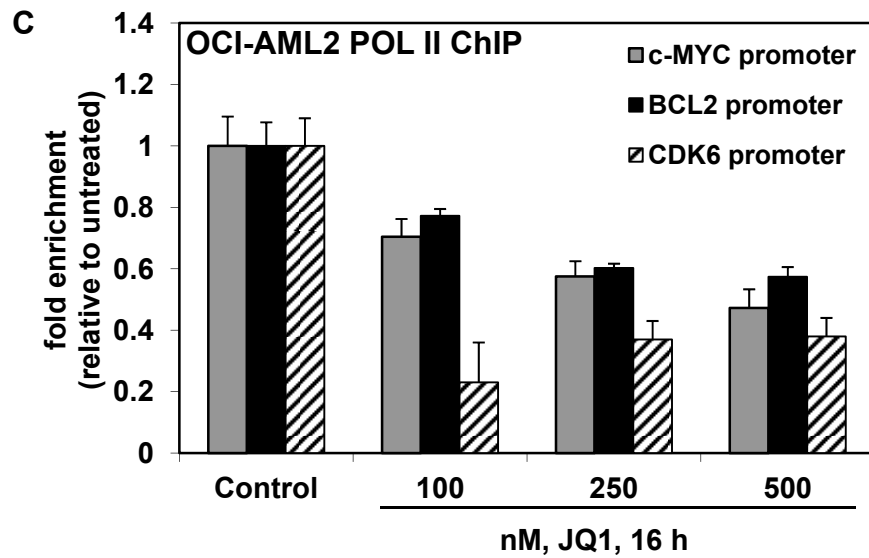
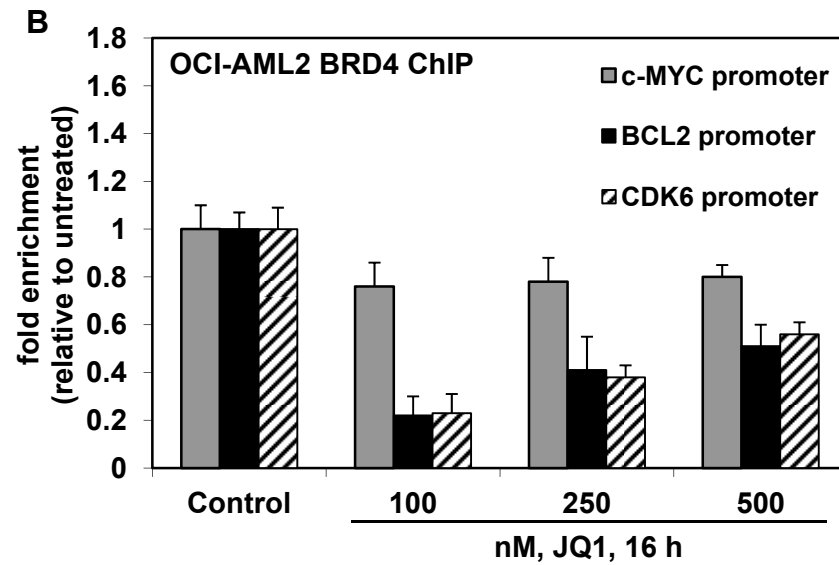
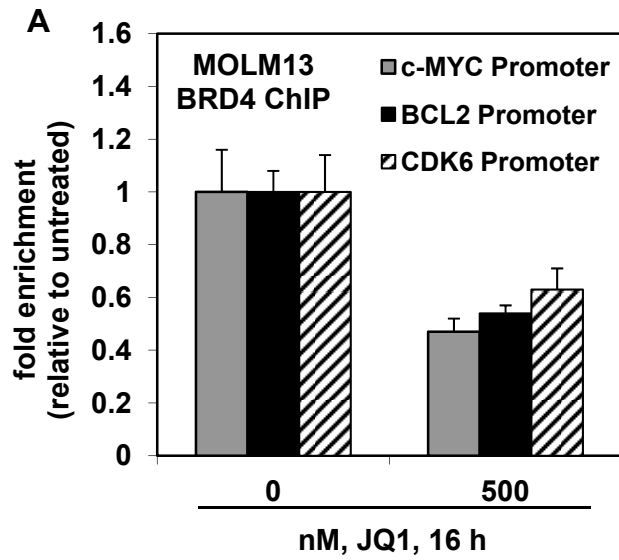
panobinostat



Supplemental Figure 2

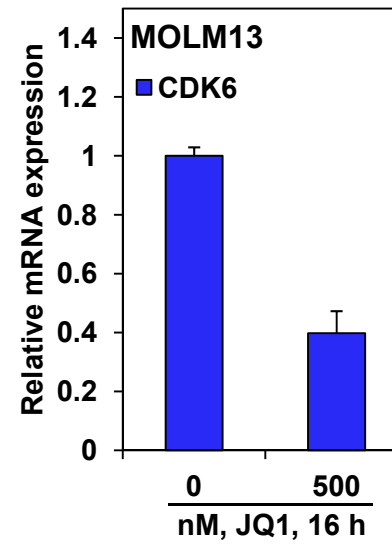
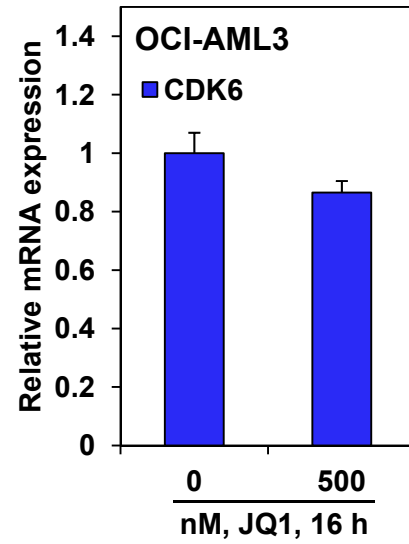


Supplemental Figure 3

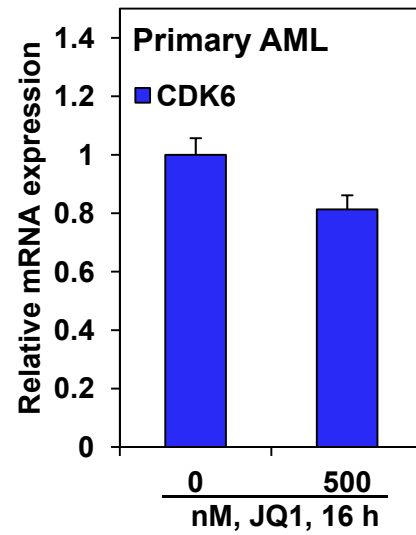


Supplemental Figure 4

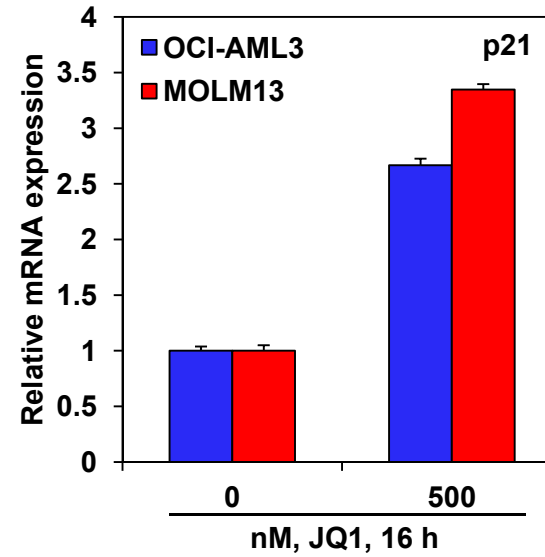
A



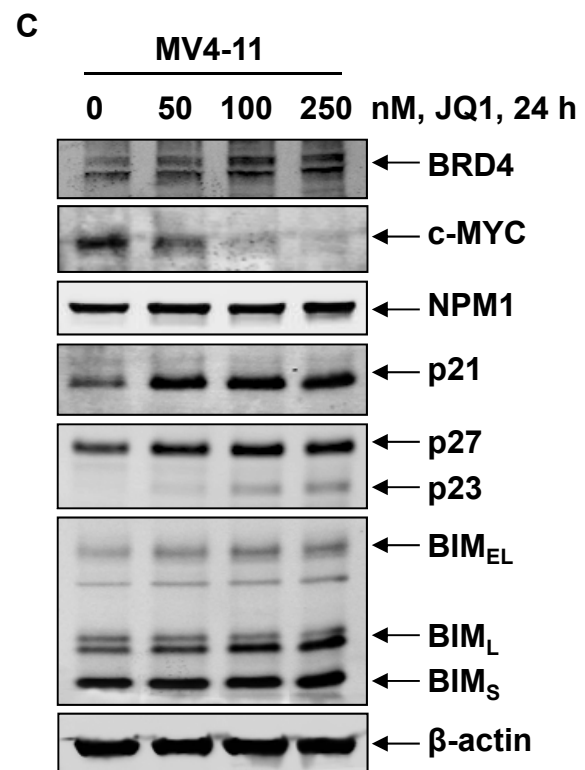
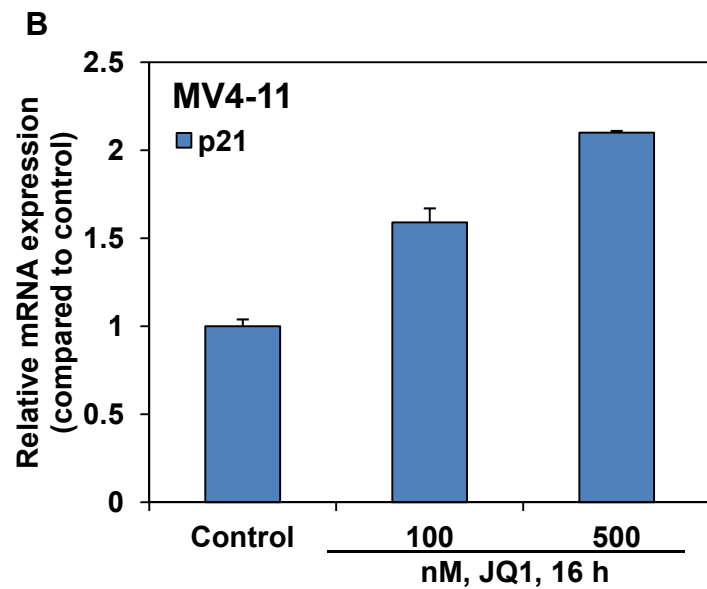
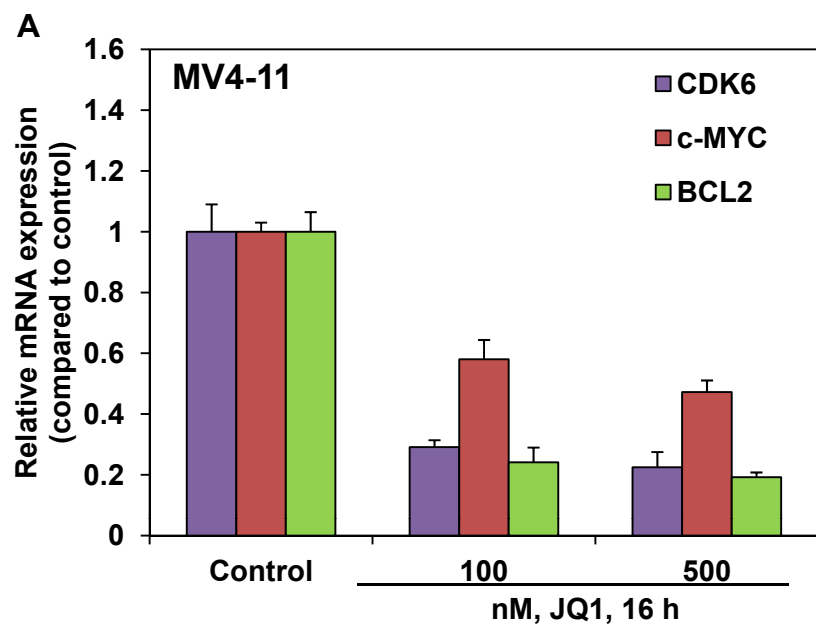
B



C



Supplemental Figure 5

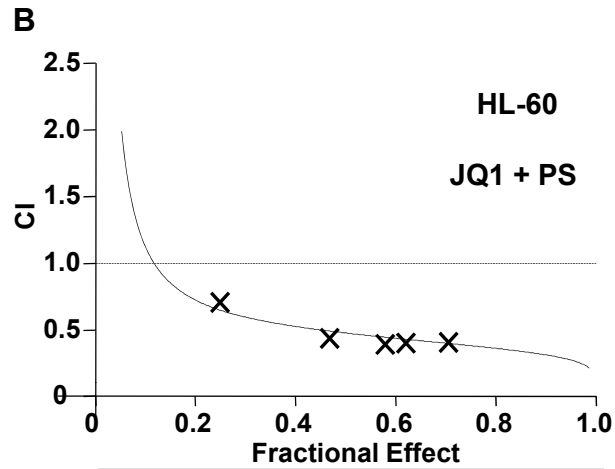


Supplemental Figure 6

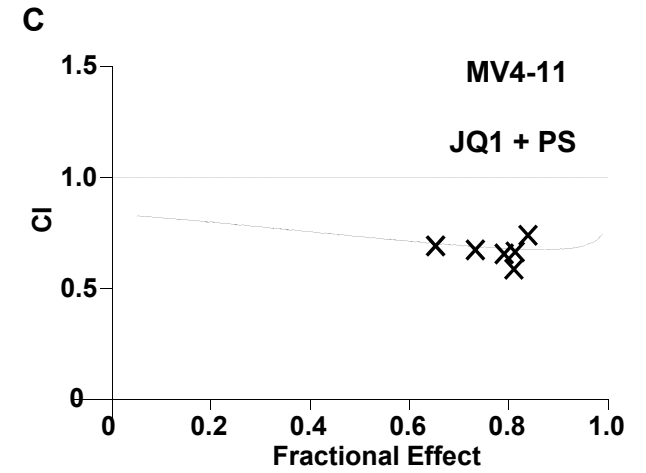
A

OCI-AML3 cells			
JQ1 (nM)	PS (nM)	Fraction Affected	CI
50	5	0.465	0.831
60	6	0.526	0.880
75	7.5	0.658	0.832
80	8	0.743	0.723
90	9	0.798	0.696
100	10	0.86	0.621

MOLM13 cells			
JQ1 (nM)	PS (nM)	Fraction Affected	CI
300	6	0.734	0.786
350	7	0.813	0.729
375	7.5	0.818	0.768
400	8	0.878	0.654
450	9	0.867	0.771
500	10	0.906	0.715

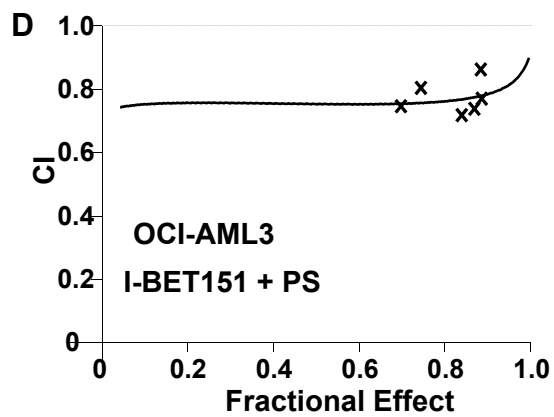


HL-60			
JQ1 (nM)	PS (nM)	Fraction Affected	CI
250	5	0.244	0.727
300	6	0.463	0.458
350	7	0.574	0.411
400	8	0.615	0.426
500	10	0.700	0.430

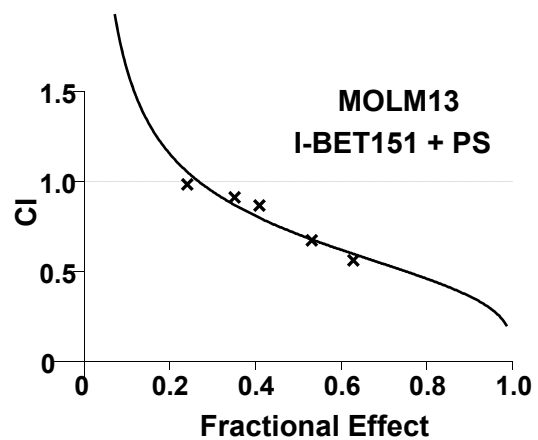
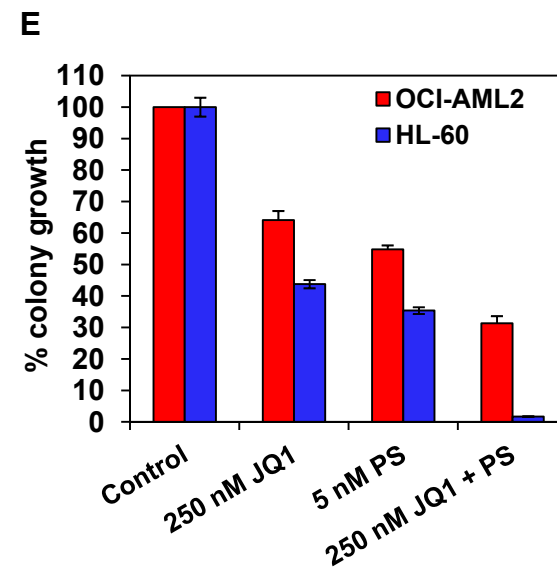


MV4-11			
JQ1 (nM)	PS (nM)	Fraction Affected	CI
120	2.4	0.647	0.709
150	3	0.728	0.688
175	3.5	0.805	0.602
180	3.6	0.785	0.672
200	4	0.808	0.679
250	5	0.834	0.755

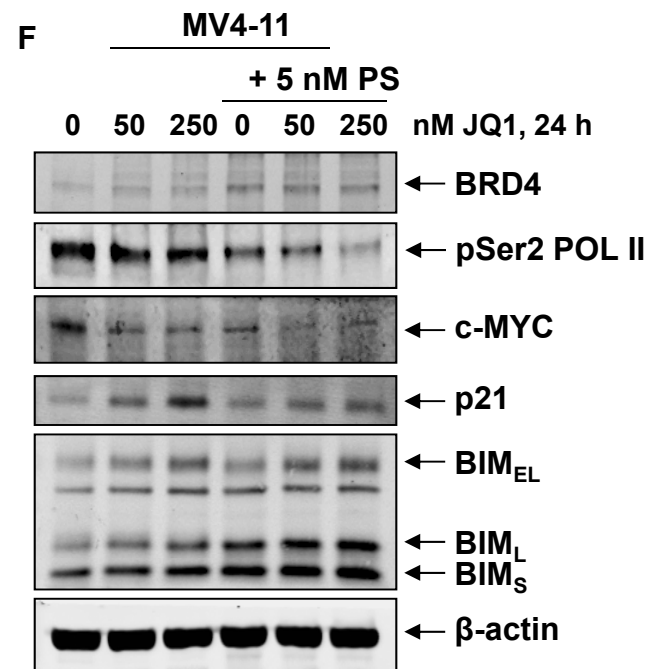
Supplemental Figure 6



OCI-AML3			
I-BET151 (nM)	PS (nM)	Fraction Affected	CI
250	5	0.698	0.747
300	6	0.745	0.805
350	7	0.84	0.719
400	8	0.869	0.739
450	9	0.887	0.770
500	10	0.885	0.864



MOLM13			
I-BET151 (nM)	PS (nM)	Fraction Affected	CI
250	5	0.242	0.984
350	7	0.352	0.913
400	8	0.41	0.866
450	9	0.532	0.676
500	10	0.628	0.563



Supplemental Table 1: Clinical presentation and mutation status of the primary AML samples

AML Sample #	Mutation Status	Clinical Presentation
1	NPM1c+	Newly Diagnosed
2	FLT3-ITD	Relapsed
3	FLT3-ITD	Relapsed
4	NPM1c+	Newly Diagnosed
5	NPM1c+/FLT3-ITD	Relapsed
6	FLT3-ITD	Relapsed
7	NPM1c+	Newly Diagnosed
8	NPM1c+/FLT3-ITD	Relapsed
9	NPM1c+	Newly Diagnosed
10	NPM1c+/FLT3-ITD	Relapsed

Note: The NPM1 status was determined by quantitative PCR utilizing primers for exon 12 of the NPM1 cDNA. The setup for this PCR utilizes a common forward primer and two separate reverse primers, one that anneals and amplifies wild type NPM1 cDNA and the other which anneals to and amplifies the mutant NPM1 cDNA. The positive control for this qPCR is cDNA amplified from OCI-AML3, an AML cell line known to express mutant NPM1. The negative control is cDNA from HL-60 cells which only express wild type NPM1. For detection of FLT-ITD, total RNA was isolated and converted to cDNA. Exon 14 of FLT3, the location in which internal tandem duplications are known to occur, was amplified by PCR utilizing primers designed to specifically amplify exon 14 of FLT3. Amplified PCR products were resolved on a 2% agarose gel and documented with a UV transilluminator. Primary AML cells exhibiting amplicons that migrate at greater than 366 base pairs (the size of the wild type FLT3 exon 14) are considered to be positive for FLT3-ITD.

Supplemental Table 2: Fold expression change of the 40 most up (I) and downregulated (II) mRNAs in OCI-AML3 cells following treatment with 500 nM of JQ1 for 8 hours.

I.

Affy ID	Gene Name	Fold Change
214455_at	HIST1H2BC	39.7739
236193_at	LOC100506979	26.8164
203455_s_at	SAT1	20.3079
210592_s_at	SAT1	20.0623
202708_s_at	HIST2H2BE	19.0892
206110_at	HIST1H3H	18.2425
214472_at	HIST1H2AD /// HIST1H3D	17.9147
210387_at	HIST1H2BG	16.8808
215779_s_at	HIST1H2BG	15.4988
232035_at	LOC100507025	14.196
239146_at	CLDND1	13.7459
205352_at	SERPINI1	13.0939
215071_s_at	HIST1H2AC	12.7731
225842_at	PHLDA1	12.701
214657_s_at	NEAT1	11.6615
204720_s_at	DNAJC6	10.8363
224566_at	NEAT1	10.807
224797_at	ARRDC3	10.7285
207156_at	HIST1H2AG	10.2182
210959_s_at	SRD5A1	10.0011
234192_s_at	GKAP1	9.83419
234040_at	HELLS	9.74844
201631_s_at	IER3	9.66125
212724_at	RND3	9.60692
214290_s_at	HIST2H2AA3	9.34777
209911_x_at	HIST1H2BD	9.20341
218280_x_at	HIST2H2AA3	9.05897
219371_s_at	KLF2	8.59847
204748_at	PTGS2	8.57626
207046_at	HIST2H4A	8.27043
217996_at	PHLDA1	8.15897
214522_x_at	HIST1H2AD /// HIST1H3D	7.83386
231817_at	USP53	7.74812
214469_at	HIST1H2AE	7.7153
202814_s_at	HEXIM1	7.69271
221986_s_at	KLHL24	7.68113
205308_at	FAM164A	7.62144
225571_at	LIFR	7.59786
203158_s_at	GLS	7.53654
201242_s_at	ATP1B1	7.39546

II.

Affy ID	Gene Name	Fold Change
206978_at	CCR2	-63.058
219714_s_at	CACNA2D3	-44.324
203887_s_at	THBD	-30.521
207725_at	POU4F2	-24.837
223204_at	FAM198B	-23.918
203477_at	COL15A1	-21.253
1553849_at	CCDC26	-20.941
203888_at	THBD	-18.922
214920_at	THSD7A	-17.291
210147_at	ART3	-16.552
227265_at	FGL2	-16.531
204470_at	CXCL1	-16.206
202664_at	WIPF1	-14.686
206067_s_at	WT1	-13.054
204430_s_at	SLC2A5	-12.709
226517_at	BCAT1	-12.685
229159_at	THSD7A	-12.643
206304_at	MYBPH	-12.499
224356_x_at	MS4A6A	-12.371
221648_s_at	LOC100507192	-12.367
209960_at	HGF	-12.229
1557411_s_at	SLC25A43	-11.977
221748_s_at	TNS1	-11.73
223343_at	MS4A7	-11.464
243601_at	LOC285957	-11.374
230550_at	MS4A6A	-11.062
225021_at	ZNF532	-11.02
210279_at	GPR18	-10.9
213894_at	THSD7A	-10.89
216950_s_at	FCGR1A /// FCGR1C	-10.864
223344_s_at	MS4A7	-10.564
216598_s_at	CCL2	-10.266
214511_x_at	FCGR1B	-10.246
223828_s_at	LGALS12	-10.191
239529_at	C5orf20	-10.175
230008_at	THSD7A	-10.136
225285_at	BCAT1	-9.5322
212224_at	ALDH1A1	-9.4788
202431_s_at	MYC	-9.4328
219666_at	MS4A6A	-9.2174

Supplemental Table 3: Ingenuity Pathway Analysis of the 5 most perturbed networks in OCI-AML3 following treatment with 500 nM of JQ1 for 8 hours.

Top 5 most perturbed networks in OCI-AML3	Score
Infectious Disease, Respiratory Disease, Neurological Disease	36
Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking	31
Cellular Development, Cellular Growth and Proliferation, Reproductive System Development and Function	29
Drug Metabolism, Molecular Transport, Small Molecule Biochemistry	24
Nervous System Development and Function, Cell-To-Cell Signaling and Interaction, Tissue Development	17

Note: Ingenuity Pathway Analysis (IPA) was performed utilizing gene expression changes from 80 mRNA targets (40 most up regulated and 40 most down regulated mRNAs) identified by microarray expression analysis. A Score was assigned by IPA for each network. The score assigned by IPA for the associated network functions (i.e. a score of 36) indicates that there is a 1 in 10^{36} chance that the focus genes in the dataset are together in a network due to random chance alone.