Supplementary Tables

Abbreviation	Full form (Cell type)
HSC	Hematopoietic stem cell
MPP	Multipotential progenitors
CMP	Common myeloid progenitor cell
GMP	Granulocyte monocyte progenitors
MEP	Megakaryocyte-erythroid progenitor cell
early_PM	Early Promyelocyte
Late_PM	Late Promyelocyte
MM	Metamyelocytes
MY	Myelocyte
Mono	Monocytes
Normal	AML[a] with Normal karyotype
Complex	AML with Complex karyotype
inv(16)	AML with inv[b](16)
t(15;17)	AML with t[c](15;17)
t(8;21)	AML with t[c] (8;21)
t(11q23)/MLL	AML with t[c] (11q23)/MLL
MDS	Myelodysplastic Syndrome
nan	AML with no karyotype information
Trisomy 8	AML with Trisomy 8
del(5q)	AML with deld(5q)
del(7q)/7q-	AML with deld (7q)/7q-
t(9;11)	AML with t[c](9;11)
Other	AML with Other abnormalities
7	AML with +7
Complex_del(5q)	AML with Complex del[d] (5q)
Complex_untypical	AML with Complex untypical karyotype
inv(3)	AML with inv[b](3)
trisomy 11	AML with trisomy 11
trisomy 13	AML with trisomy 13
t(6;9)	AML with t[c](6;9)
t(8;16)	AML with t[c](8;16)
del(9q)	AML with del[d](9q)
t(1;3)	AML with t[c](1;3)
-5/7(q)	AML with -5/7(q)
-9q	AML with -9q
8	AML with +8
t(9;22)	AML with t[c](9;22)
abn(3q)	AML with abn[e] (3q)

Abbreviations: [a] Acute Myelogenous Leukemia; [b] inversion; [c] translocation; [d] deletion; [e] abnormal.

6 Supplementary Table S2. Comparative analysis of significance based on survival curves generated
7 using GraphPad.

Log-rank (Mantel-Cox) test	
Chi square	14.81
df[a]	1
P value	0.0001
P value summary	***
Are the survival curves significantly different?	Yes
Gehan-Breslow-Wilcoxon test	
Chi square	12.35
df[a]	1
P value	0.0004
P value summary	***
Are the survival curves significantly different?	Yes
Median survival	
WT	38
ULK1-KO	69
Ratio (and its reciprocal)	0.5507
95% CI of ratio	0.1997 to 1.519

8 **Abbreviations:** [a] Degrees of freedom.

9

Supplementary Table S3. Mutational profiles of AML cell lines and their sensitivity to SBI-0206965.

Cell Line	Mutations	IC_{50}[a]	ED_{50}[b]
OCI-AML3	*NPM1*[type A] *DNMT3A*[R882C] *NRAS*	3.1 uM	7.9 uM
HL-60	*TP53 NRAS CDKN2A*	3.2 uM	10.1 uM
MOLM13	*FLT3*[ITD] *MLL-AF9* CD34+ CD13- CD14- CD15+ CD33+	400 nM	958.8 nM
MOLM14	*FLT3*[ITD] *MLL-AF9* CD34- CD13+ CD14- CD15+ CD33+	806.4 nM	2.5 uM
MV4;11	*FLT3*[ITD] *MLL-AF4*	253 nM	4.5 uM

Abbreviations: [a] Concentration of drug at which the cell number is reduced to 50%; [b] Concentration of drug at which 50% apoptosis is induced.

14   Supplementary Table S4. Mutational profiles of AML patient derived primary samples.

Sample	Mutations
AML#1	*CEBPA+*
AML#2	*SRFS2*[P95L] *TET2*[R1465] *TP53*[Y236S]
AML#3	*KMT2A* rearrangement with deletion of 3' locus
AML#4	*ASXL1*[S577] *PHF6*[R129; G10fs[a]] *BCORL1*[Q1133] *FLT3*[ITD[b]]
AML#5	*NPM1*[W288fs[a]] *TET2*[T1047fs[a]; R1216] *NOTCH1*[P2340L]
AML#6	*FLT3*[D835] *KIT*[D816V] *KRAS*[G12D] *NRAS*[Q61K] *DNMT3A*[G298R] *CBFB* rearrangement
AML#7	*TP53*[994-1G>A] *DNMT3A*[Y874]
AML#8	*FLT3*[D835; ITD[b]] *DNMT3A*[R882C] *IDH1*[R132H] *KIT*[D816V] *NPM1*[W288fs[a]] *NRAS*[G13D] *BRAF*[V600E] *HNRNPK*[E85K]
AML#9	*FLT3*[ITD] *WT1*[1133_1142dup[c]TTGTACGGTC p.A382fs[a]] *KMT2A*[D2817N] *GATA2*[989_993delins[d] CATTCAT p.R330fs[a]]
AML#10	*FLT3*[ITD] *DNMT3A*[R598] *DNMT3A*[F827L] *IDH2*[R140Q] *PIGA*[Y468C] *RUNX1*[G170R] *ZRSR2*[399+1G>A]
AML#11	Unknown
AML#12	*FLT3*[ITD] *IDH2*[R140Q] *RUNX1*[D326fs[a]] *SRSF2*[P95L]
PDX#1	*FLT3*[ITD] *DNMT3A*mut[e] *NPM1*mut[e] [by CMS53 panel]
PDX#2	*FLT3*[ITD] *DNMT3A*mut[e] *IDH1*mut[e] *NPM1*mut[e] [by CMS28 panel]
PDX#3	*IDH1*[R132H] *NPM1*[W288fs[a]] *SRSF2*[P95H] *FLT3*[Y572C] *PRPF40B*[P766L]
PDX#4	*EZH2*mut[e] *NRAS*mut[e] *TET3*mut[e] [by CMS28 panel]

15 **Abbreviations:** [a] frameshift; [b] internal tandem duplication; [c] duplication; [d] deletion-insertion; [e]
16 mutations detected by high-throughput gene panels identifying specific mutations.

17   Supplementary Table S5. IC_{50} values of drug resistant cells.

Cell Line	IC_{50}[a]
AraC sensitivity	
OCI-AML3	75 nM
OCI-AML3-r	10 uM
ABT-199 sensitivity	
MOLM13	7.8 nM
MOLM13-r	2.1 uM
OCI-AML2	93.7 nM
OCI-AML2-r	2.5 uM

18   **Abbreviations:** [a] Concentration of drug at which the cell number is reduced to 50%.

19

20 Supplementary Table S6. Combinatorial Index (CI-value) of combination treatments.

Treatment➡	AraC		Idarubicin		ABT-199	
Cell type ⬇	Cell No.	Apoptosis	Cell No.	Apoptosis	Cell No.	Apoptosis
OCI-AML3	0.7	0.6	0.7	0.4	0.3	0.2
MOLM13	0.8	0.5	0.6	0.5	0.3	0.2
Primary (Bulk)	-	0.5	-	-	-	0.1
Primary (Stem/Prog)	-	0.5	-	-	-	0.1

21

22 Supplementary Table S7. Comparative analysis of significance based on survival curves generated
23 using GraphPad (Ex vivo model).

	Vehicle vs SBI	Vehicle vs ABT-199	SBI vs Combo	ABT vs Combo
Log-rank (Mantel-Cox) test				
Chi square	9.039	2.213	1.907	4.332
df[a]	1	1	1	1
P value	0.0026	0.1368	0.1673	0.0374
P value summary	**	ns	ns	*
Are the survival curves significantly different?	Yes	No	No	Yes
Median survival				
Group A	40	40	47	43
Group B	47	43	52	52
Ratio (and its reciprocal)	0.8511 (1.175)	0.8696 (1.15)	0.9038 (1.106)	0.8269 (1.209)
95% CI of ratio	0.2464 to 2.94	0.2517 to 3.004	0.2617 to 3.122	0.2394 to 2.856

24 **Abbreviations:** [a] Degrees of freedom.

25 Supplementary Table S8. List of Antibodies.

Antibody	Source	Catalog Number
Antibodies for Western Blotting		
ULK1 (A705) antibody	Cell Signaling Technology (CST)	4776
ULK1 (D8H5) Rabbit mAb	CST	8054
Phospho-ULK1 (Ser555) (D1H4) Rabbit mAb	CST	5869
LC3B antibody	CST	2775
Phospho-Stat3 (Tyr705) antibody	CST	9131
Phospho-p44/42 MAPK (Erk1/2) (Thr202/Tyr204) antibody	CST	9101
Phospho-ATM (Ser1981) (D25E5) Rabbit mAb	CST	13050
Anti phospho-p53 (Ser15) antibody	CST	9284
Cleaved PARP (Asp 214) (D64E10) XP	CST	5625
Cleaved Caspase-3 antibody (Asp175)	CST	9661
BclXL antibody	CST	2762
CD44 antibody	CST	3578
xCT/SLC7A11 (D2M7A) Rabbit mAb	CST	12691
Atg13 (D4P1K) Rabbit mAb	CST	13273
p53 (DO-1) antibody	Santa Cruz Biotechnology (SCBT)	sc-126
Mcl1 antibody	SCBT	sc-819
Bcl2 antibody	SCBT	sc-7302
PARP-1 antibody (F-2)	SCBT	sc-8007
Anti-beta Actin clone AC-74	Sigma	A5316
Atg13 phospho S318 antibody	Rockland antibodies & assays	600-401-C49S
Anti-gamma H2A.X (phospho S139) antibody	Abcam	ab11174

IRDye 680 Donkey Anti-mouse IgG (H+L)	LI-COR Biosciences (LI-COR)	926-32222
IRDye 800CW Donkey Anti-mouse IgG(H+L)	LI-COR	926-32212
IRDye 680RD Donkey Anti-rabbit IgG (H+L)	LI-COR	926-68073
IRDye 800CW Donkey Anti-rabbit IgG(H+L)	LI-COR	926-32213
Antibodies for Immunofluorescence		
Anti-gamma H2A.X (phospho S139) antibody	Abcam	ab11174
Donkey anti-Rabbit IgG (H+L) Secondary Antibody, Alexa Fluor 594 conjugate	Thermo Fisher Scientific	A21207
Antibodies for Flow Cytometry		
LC3B (D11) XP Rabbit mAb (PE Conjugate)	CST	8899
Annexin V-FLUOS	Sigma	11828681001
Annexin V-APC antibody	BD Bioscience (BD)	550474
Anti-human CD45-APC antibody	BD	555485
Anti-human CD34-PE antibody	BD	348057
Anti-human CD38-PC5.5	Beckman Coulter	A70205
Anti-human CD45 (HI30) PE/Cy7 antibody	BioLegend (BL)	304016
Anti-human CD44-PE antibody	BL	338807
Anti-SLC7A11/xCT-DY488 antibody	LSBio	LS-C142125
Anti-human CD98-APC antibody	Miltenyl Biotec (MB)	130-105-662
Anti-mouse CD45-APC antibody	MB	130-110-798
Anti-mouse CD45-PE antibody	MB	130-110-797
Antibodies for CyTOF		
Phospho-PI3K(p85/p55)	CST	4228BF
Phospho-MEK1/2	CST	9154BF
p21	CST	2947BF
cMyc	CST	5605BF

Phospho-AKT	BD	560397
Mcl1	BD	559027
CD123	BD	554527
Bcl-2	BL	658702
CD38	BL	303502
CD90	BL	328102
Phospho-ERK1/2	DVS-Fluidigm (DVS-F)	3167005A
Phospho-p38(180/182)	DVS-F	3156002A
CD44	DVS-F	3166001B
PARP (cleaved)[Asp214]	DVS-F	3143011A
Caspase 3, cleaved	DVS-F	3142004A
CD45	DVS-F	3154001B
CD34	DVS-F	3148001B
HIF-1α	Novus	NB100-479
Survivin	R&D	AF6471

26

27 Supplementary Table S9. List of Primers.

Name	Source	Identifier/ Sequence (5'-3')
Taqman Probes		
MCL1	Thermo Fisher Scientific (Thermo)	Cat# Hs01050896_m1
ABL1	Thermo	Cat# Hs01104728_m1
SYBR Green Primers		
CD44 Forward	Integrated DNA Technologies (IDT)	GCAGTCAACAGTCGAAGAAGG
CD44 Reverse	IDT	TGTCCTCCACAGCTCCATT
CD44v8-10 Forward	IDT	TCCCAGACGAAGACAGTCCCTGGAT
CD44v8-10 Reverse	IDT	CACTGGGGTGGAATGTGTCTTGGTC
mtND1 Forward	IDT	CCCATTCGCGTTATTCTT
mtND1 Reverse	IDT	AAGTTGATCGTAACGGAAGC
mtND6 Forward	IDT	CAAACAATGTTCAACCAGTAACCACTAC
mtND6 Reverse	IDT	ATATACTACAGCGATGGCTATTGAGGA
PPARGC1A Forward	IDT	CGGAAATCATATCCAACCAG
PPARGC1A Reverse	IDT	TGAGAACCGCTAGCAAGTTTG
18S rRNA Forward	IDT	GTAACCCGTTGAACCCCATT
18S rRNA Reverse	IDT	CCATCCAATCGGTAGTAGCG

28