Supplementary Tables

Supplementary Table 1

Indication	Cell line	Number of cells/well	Culture conditions
Multiple myeloma	KMS-11	20,000	RPMI 1640 medium with 300 mg/L (2 mM) L-glutamine adjusted to contain 2.0 g/L sodium bicarbonate; fetal bovine serum, 10%; P/S 1% (referred as 10% FBS RPMI 1640 complete medium)
	RPMI-8226	20,000	10% FBS RPMI 1640 complete medium)
	MOLP-8	20,000	RPMI 1640 medium with 300 mg/L (2 mM) L-glutamine adjusted to contain 2.0 g/L sodium bicarbonate; fetal bovine serum, 20%; P/S 1%
	NCI-H929	20,000	RPMI 1640 medium with 300 mg/L (2 mM) L-glutamine adjusted to contain 2.0 g/L sodium bicarbonate, 2-mercaptoethanol to a final concentration of 0.05 mM; fetal bovine serum, 10%; P/S 1%
	OPM-2	20,000	10% FBS RPMI 1640 complete medium
Myelogenous leukemia	THP-1	20,000	RPMI 1640 medium with 300 mg/L (2 mM) L-glutamine adjusted to contain 1.5 g/L sodium bicarbonate, 4.5 g/L glucose, 10 mM HEPES, and 1.0 mM sodium pyruvate; fetal bovine serum, 10%; P/S 1% (referred as 10% FBS 10 mM HEPES RPMI 1640 complete medium)
	MV-4-11	25,000	ATCC complete growth medium: Iscove's modified Dulbecco's medium with 4 mM L-glutamine adjusted to contain 1.5 g/L sodium bicarbonate; fetal bovine serum, 10%; P/S 1% (referred as 10% IMDM complete medium)
	HEL	15,000	10% FBS RPMI 1640 complete medium
	TF-1a	15,000	10% FBS 10mM HEPES RPMI 1640 complete medium
	KG-1	20,000	10% FBS IMDM complete medium
	ML-2	25,000	10% FBS RPMI 1640 complete medium
	MOLM-13	20,000	10% FBS RPMI 1640 complete medium
	HL-60	25,000	10% FBS RPMI 1640 complete medium
	K-562	12,000	10% FBS RPMI 1640 complete medium
T-lymphoblastic leukemia	KARPAS-299	20,000	10% FBS RPMI 1640 complete medium
	Jurkat, Clone E6-1	20,000	10% FBS 10 mM HEPES RPMI 1640 complete medium
	MOLT-4	20,000	10% FBS RPMI 1640 complete medium
	RS4;11	25,000	
Burkitt's lymphoma	Daudi	20,000	10% FBS 10 mM HEPES RPMI 1640 complete medium
	Raji	20,000	10% FBS RPMI 1640 complete medium
	Ramos	20,000	10% FBS RPMI 1640 complete medium
B-cell lymphoma	ARH-77	20,000	10% FBS RPMI 1640 complete medium
	BC-3	20,000	10% FBS RPMI 1640 complete medium
	Z-138	25,000	10% FBS IMDM complete medium
	OCI-LY1	20,000	ATCC complete growth medium: Iscove's modified Dulbecco's medium with 4 mM L-glutamine adjusted to contain 1.5 g/L sodium bicarbonate; fetal bovine serum, 20%; P/S 1%
	OCI-LY3	20,000	ATCC complete growth medium: Iscove's modified Dulbecco's medium with 4 mM L-glutamine adjusted to contain 1.5 g/L sodium bicarbonate, 2-mercaptoethanol to a final concentration of 0.05 mM; fetal bovine serum, 20%; P/S 1%
	OCI-LY8	20,000	10% FBS RPMI 1640 complete medium
	OCI-LY19	20,000	α-MEM; fetal bovine serum, 20%; P/S 1%
	SU-DHL-4	20,000	RPMI 1640 medium with 300 mg/L (2 mM) L-glutamine adjusted to contain 2.0 g/L sodium bicarbonate; fetal bovine serum, 20%; P/S 1%
	Toledo	20,000	10% FBS RPMI 1640 complete medium
	DOHH-2	20,000	

Supplementary Table 2

A

CLL patient (P)	IC_{50} (nM)	
	APG-2575	**ABT-199**
P2	25.89	47.63
P4	20.63	53.42
P6	16.28	15.15
P7	8.48	51.87

B

	IC_{50} (nM)	
	APG-2575	**ABT-199**
CLL PB301	38.25	55.28
CLL PB302	42.98	62.17
CLL PB303	44.15	51.25
CLL PB304	34.15	42.98
CLL PB305	47.51	256.54
CLL PB306	50.24	195.48
CLL PB307	39.77	75.59
CLL PB308	48.54	98.17
CLL PB309	95.54	302.15
CLL PB310	75.15	305.28

Supplementary Table 3

Cells/patients	APG-2575 (IC_{50}, mean ± SD, μM)	ABT-199 (IC_{50}, mean ± SD, μM)
KMS11	2.26 ± 0.66	4.9 ± 0.88
KMS12BM	3.89 ± 0.11	4.1 ± 0.24
KMS12PE	3.92 ± 0.22	4.77 ± 0.33
MM pt #1	1.92 ± 0.17	2.98 ± 0.42
MM pt #2	1.11 ± 0.54	3.01 ± 0.14
MM pt #3	1.33 ± 0.39	3.5 ± 0.37
BCWM.1	2.58 ± 0.33	5.33 ± 0.17
MWCL.1	3.77 ± 0.25	9.36 ± 0.42
RPCL-WM.1	2.98 ± 0.27	6.45 ± 0.29
WM pt #1	2.21 ± 0.65	2.57 ± 1.09
WM pt #2	1.97 ± 0.25	2.14 ± 1.54
WM pt #3	2.49 ± 0.48	2.22 ± 1.69

Supplementary Table 4

A

Cell line	IC_{50} (μM), Mean ± SD, n = 2	
	APG-2575	ABT-199
Raji	14.85±5.713	16.28±7.396
BC-3	12.007±4.884	16.735±3.401
Z-138	11.24±0.679	6.484±0.805
MOLP-8	10.945±0.134	18.49±1.287
ARH-77	10.715±2.228	13.03±3.267
KARPAS-299	10.385±0.163	12.63±3.041
Ramos	9.993±3.517	10.051±4.949
HEL	9.491±0.946	10.129±2.250
Daudi	8.176±0.867	4.75±0.194
Jurkat, Clone E6-1	7.991±2.330	9.999±7.483
NCI-H929	5.323±0.971	6.213±1.240
K-562	4.76±1.093	0.299±0.0007
OCI-LY3	4.374±0.626	6.848±2.815
TF-1a	3.549±1.082	5.707±1.820
OPM-2	3.221±0.099	2.410±0.634
MOLT-4	3.082±0.579	4.105±0.904
KMS-11	2.253±1.146	1.406±0.238
SU-DHL-4	1.446±0.476	1.489±0.628
THP-1	0.405±0.198	0.722±0.319
ML-2	0.123±0.088	0.096±0.120
KG-1	0.059±0.044	0.050±0.029
Toledo	0.049±0.005	0.075±0.011
HL-60	0.027±0.015	0.025±0.004
OCI-LY1	0.023±0.009	0.036±0.008
OCI-LY19	0.011±0.001	0.0006±0.0006
RS4;11	0.009±0.00071	0.012±0.006
OCI-LY8	0.006±0.002	0.011±0.005
DOHH-2	0.004±0.001	0.005±0.002
MV-4-11	0.003±0	0.004±0.001
MOLM-13	0.002±0	0.003±0.001

B

Cancer type	Cell line	IC_{50}(μM), Mean±SD, n=2	
		APG-2575	ABT-199
Myeloma	KMS-11	2.253±1.146	1.406±0.238
	MOLP-8	10.945±0.134	18.49±1.287
	NCI-H929	5.323±0.971	6.213±1.240
	OPM-2	3.221±0.099	2.410±0.634
Acute monocytic leukemia	THP-1	0.405±0.198	0.722±0.319
Biphenotypic B myelomonocytic leukemia	MV-4-11	0.003±0	0.004±0.001
Erythroleukemia	HEL	9.491±0.946	10.129±2.250
	TF-1a	3.549±1.082	5.707±1.820
Acute myelogenous leukemia(AML)	KG-1	0.059±0.044	0.050±0.029
	ML-2	0.123±0.088	0.096±0.120
	MOLM-13	0.002±0	0.003±0.001
Acute promyelocytic B-cell leukemia	HL-60	0.027±0.015	0.025±0.004
Chronic myelogenous leukemia(CML)	K-562	4.76±1.093	0.299±0.0007
T lymphoblastic leukemia	KARPAS-299	10.385±0.163	12.63±3.041
T cell acute lymphoblastic leukemia(ALL)	Jurkat, Clone E6-1	7.991±2.330	9.999±7.483
	MOLT-4	3.082±0.579	4.105±0.904
	RS4;11	0.009±0.00071	0.012±0.006
Burkitt's lymphoma	Daudi	8.176±0.867	4.75±0.194
	Raji	14.85±5.713	16.28±7.396
	Ramos	9.993±3.517	10.051±4.949
B lymphoma	ARH-77	10.715±2.228	13.03±3.267
	BC-3	12.007±4.884	16.735±3.401
Human mantle cell lymphoma (MCL) cell line	Z-138	11.24±0.679	6.484±0.805
Diffuse large B cell lymphoma, DLBCL, NHL	OCI-LY1	0.023±0.009	0.036±0.008
	OCI-LY3	4.374±0.626	6.848±2.815
	OCI-LY8	0.006±0.002	0.011±0.005
	OCI-LY19	0.011±0.001	0.0006±0.0006
	SU-DHL-4	1.446±0.476	1.489±0.628
	Toledo	0.049±0.005	0.075±0.011
Follicular lymphoma, NHL	DOHH-2	0.004±0.001	0.005±0.002

Supplementary Table 5

PK-dose correlation in RS4;11 mouse xenografts

Plasma	Units	APG-2575			ABT-199
		6.25 mg/kg	25 mg/kg	100 mg/kg	25 mg/kg
C_{max}	ng/mL	1,060.7	3,353.3	7,803.3	2,506.7
T_{max}	hr	2.0	1.0	4.0	2.0
$T_{1/2}$	hr	5.2	5.8	6.0	6.3
$AUC_{0\text{-last}}$	hr•ng/mL	9,825.4	3,6615.6	12,3401.2	30,006.3
$AUC_{0\text{-inf}}$	hr•ng/mL	9,849.3	3,6727.0	12,3437.4	30,029.1

Tumor	Units	APG-2575			ABT-199
		6.25 mg/kg	25 mg/kg	100 mg/kg	25 mg/kg
C_{max}	ng/g	134.7	534.0	1,175.5	368.0
T_{max}	hr	4.0	8.0	4.0	4.0
$T_{1/2}$	hr	48.1	29.8	13.2	18.1
$AUC_{0\text{-last}}$	hr•ng/g	7,224.6	18,392.0	50,633.2	12,279.0
$AUC_{0\text{-inf}}$	hr•ng/g	7,974.7	18,752.6	50,999.5	13,352.3

Supplementary Table 6

A

Changes in hematology parameters in APG-2575-treated mice

Dose (mg /kg)	Gender	RBC (E6/μL)	HGB (g/dL)	HCT (%)	MCH (pg)	MCHC (g/dL)	WBC (E3/μL)	LYM (E3/μL)
0	M	8.51±0.377	13.7±0.22	46.5±1.78	16.1±0.55	29.5±0.81	2.89±0.908	2.19±0.757
	F	8.64±0.121	14.2±0.34	48.1±1.09	16.5±0.33	29.6±0.68	4.35±0.908	3.43±0.798
100	M	8.44±0.827	13.2±1.05	44.3±3.18	15.6±0.34	29.7±0.33	1.52±0.63	1.04±0.499
	F	8.86±0.673	13.6±0.83	48.5±3.25	15.4±0.48*	28.1±0.61*	1.89±0.751*	1.10±0.569*
300	M	8.34±0.527	12.6±0.64	45.0±1.93	15.1±0.36*	27.9±0.54*	1.76±1.754	0.58±0.143*
	F	8.55±0.427	13.1±0.44*	46.0±1.41	15.4±0.49*	28.6±0.28*	1.59±0.768*	0.89±0.527*
1,000	M	8.00±0.93	11.2±1.00*	40.2±2.38*	14.1±0.61*	27.8±0.98*	1.29±0.239	0.56±0.178*
	F	7.67±0.528*	11.2±0.73*	40.7±2.38*	14.6±0.31*	27.5±0.23*	1.15±0.393*	0.53±0.157*

B

Changes in bone marrow differential in APG-2575-treated mice

Dose	Gender	Metarubricyte	Erythroid	Lymphocyte
0	M	68.0±16.9	107±24.9	103±27.4
	F	97.0±10.4	130±16.6	103±15.4
100	M	87.0±17.8	132±28.7	99.0±18.0
	F	100±14.6	139±16.5	96.0±21.8
300	M	91.0±13.9*	138±28.7	93.0±22.1
	F	106±19.5	147±24.5	112±20.3
1,000	M	106±27.8*	150±34.8*	74.0±22.8*
	F	118±17.9*	148±22.6	97.0±11.4