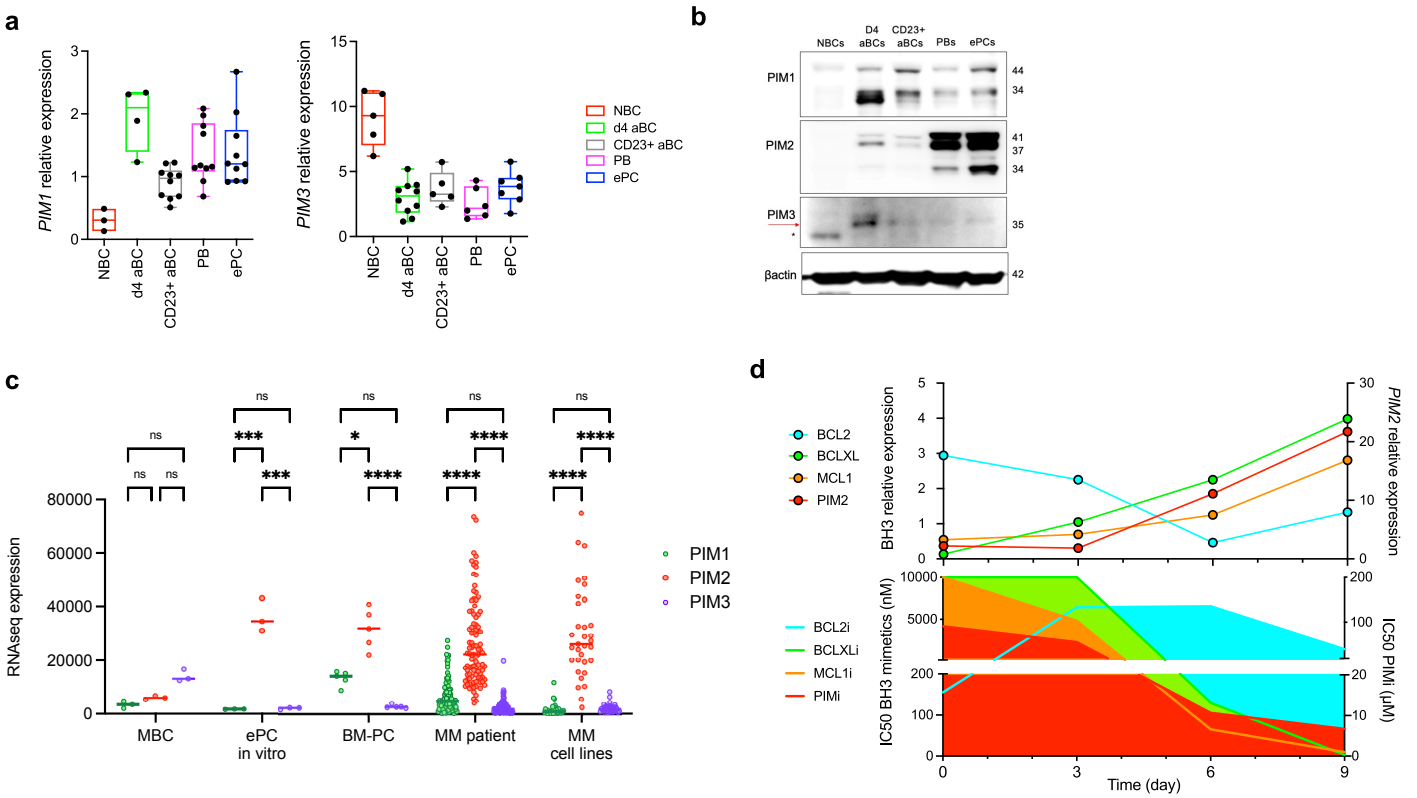


Supplementary Figure 1.

a. PIM1 and PIM3 relative expression in different B cell subsets generated in vitro at different time points. Data are shown as floating bars (min to max, mean as line) for NBC (PIM1, n = 3) and as box plots (median ± IQR, whiskers min to max) for NBCs (n = 4 for PIM3), d4 aBCs (n = 4 for PIM1, n = 9 for PIM3), CD23+ aBCs (n = 10 for PIM1; n = 5 for PIM3), PBs (n = 10 for PIM1, n = 6 for PIM3) and ePCs (n = 10 for PIM1; n = 6 for PIM3).

b. PIM1, PIM2 and PIM3 protein expression in the described cell populations. Sample derived from the same experiment with different processed gels, one for PIM1 and PIM2 (same gel as presented in Fig 1a), and another for PIM3. The blot is representative of 2 independent experiments.

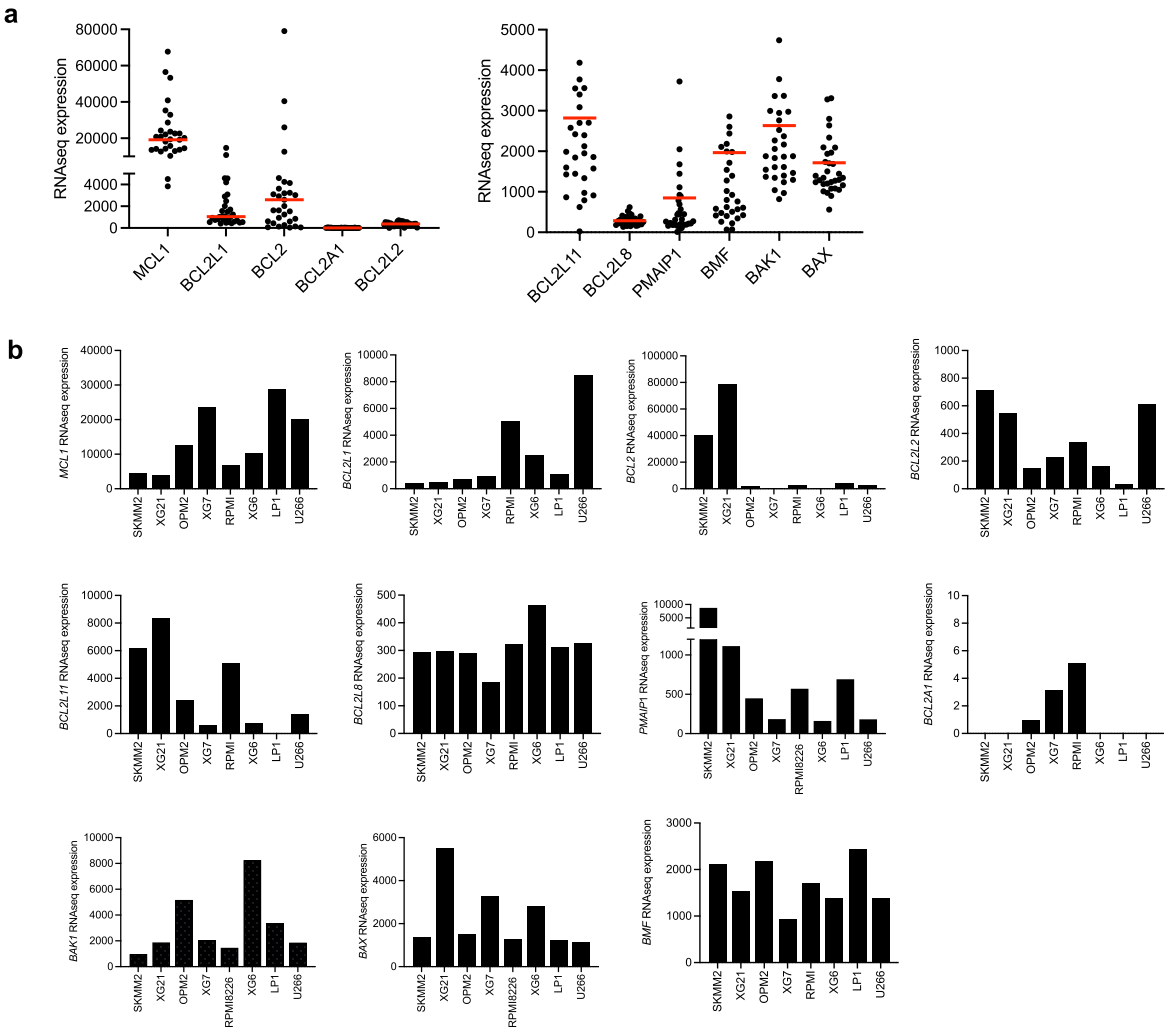
c. *PIM1*, *PIM2* and *PIM3* RNAseq expression in various cell populations: MBCs (primary memory B cells, n = 3), ePC in vitro (in vitro-produced primary plasma cells, n = 3), BM-PC (primary plasma cells from healthy volunteers, n = 5), multiple myeloma (MM) patients (a cohort of MM patients from the hospital in Montpellier, France, n = 97), and the 33 previously described MM cell lines (MMCLs).

d. Expression of the anti-apoptotic factors (MCL1, BCL-XL, BCL2, and PIM2) and the corresponding IC50 values of their inhibitors during normal B cell differentiation. The gene expression of these factors is inversely correlated with the IC50 of their respective inhibitors. Panel shows the kinetics of relative gene expression (top) and inhibitor sensitivity (bottom) during B cell differentiation.

P-values were calculated using two-way ANOVA with Sidak's multiple comparisons for panel (c). P < 0.05 is indicated as *, P < 0.01 as **, P < 0.001 as *** and P < 0.0001 as ****; 'ns' designates "not significant" on graphs. 'n' referred to the number of biological replicates. Exact p-values are provided in the Source Data fIle.

Abbreviations: NBC, naïve B cell; d4 aBC, day-4 activated B cell; CD23+ aBC, CD23-positive activated B cell; PB, plasmablast; ePC, early plasma cell; MM, multiple myeloma; BM-PC, bone marrow plasma cell; PIMi, pan-PIM inhibitor AZD1208; BCL2i, Vénétoclax; BCLXLi, BCLXL inhibitor A1155463 ; MCL1i, MCL1 inhibitor S63645.

Source data are provided as a Source Data file.

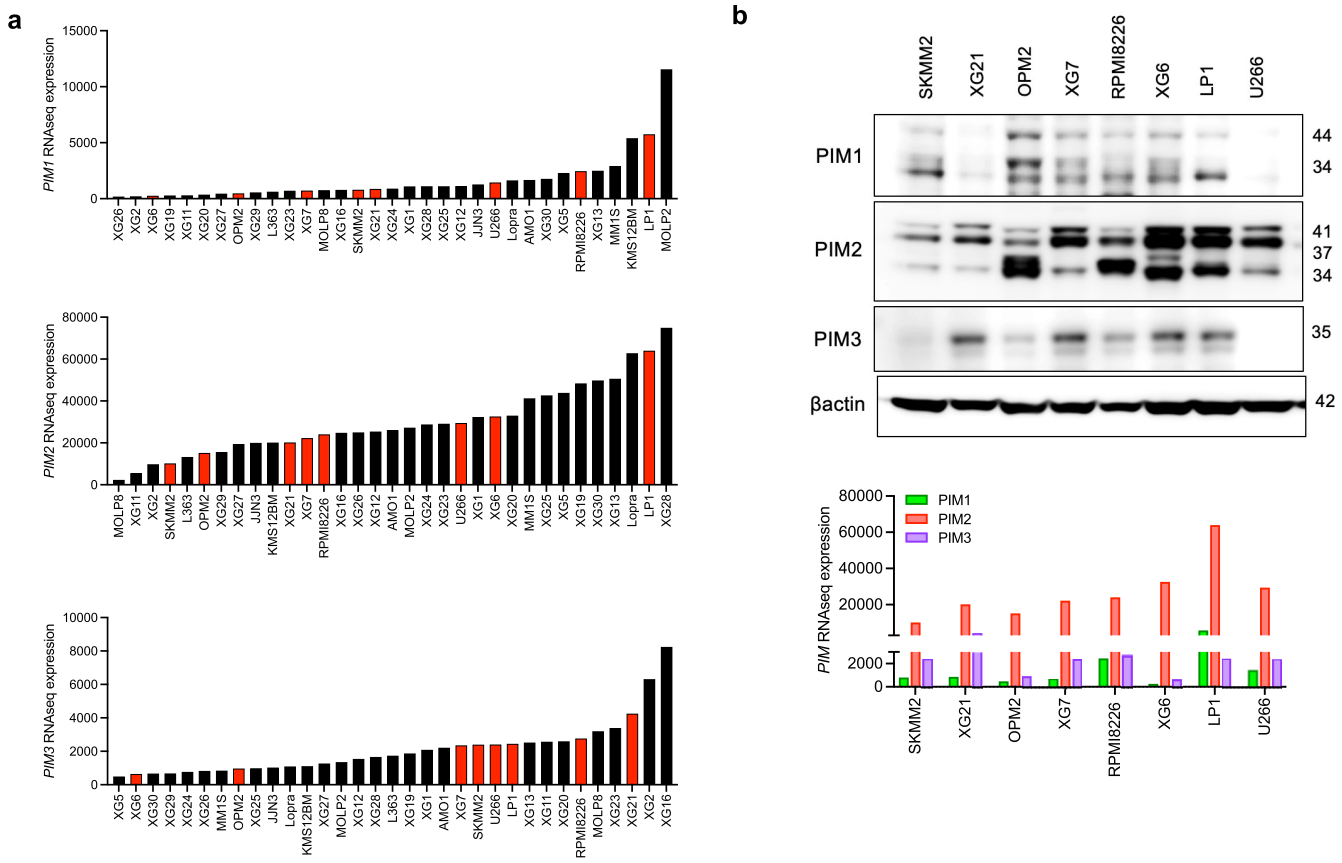


Supplementary Figure 2.

a. Anti-apoptotic factors *MCL1, BCL2L1* (encoding BCL-XL), *BCL2, BCL2A1* (encoding BFL1/A1) and BCL2L2 (encoding BCL-W),) and pro-apoptotic BH3 molecules *BCL2L11* (encoding BIM), *BCL2L8* (encoding BAD) and *PMAIP1* (encoding NOXA) RNAseq expression in 33 selected MM cell lines. Data are presented as mean values (n = 33). “n” denotes the number of distinct MMCLs.

b. Anti-apoptotic factors *MCL1, BCL2L1* (encoding BCL-XL), *BCL2, BCL2A1* (encoding BFL1/A1) and BCL2L2 (encoding BCL-W) and pro-apoptotic BH3 molecules *BCL2L11* (encoding BIM), *BCL2L8* (encoding BAD) and *PMAIP1* (encoding NOXA). Data are presented with bar.

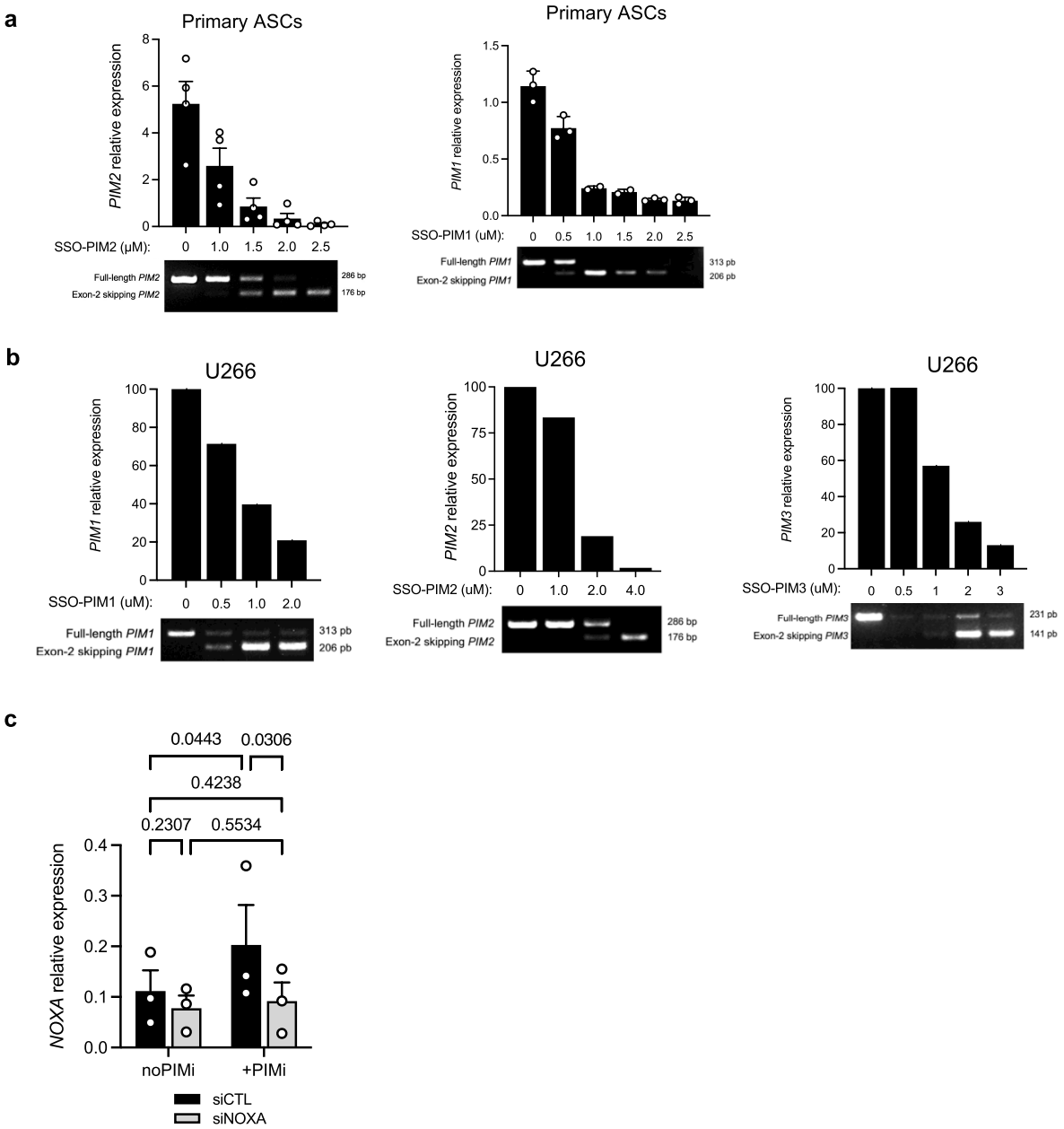
Abbreviations: MMCLs : multiple myeloma cell lines.



Supplementary Figure 3.

a. *PIM1*, *PIM2* and *PIM3* gene expression by RNAseq in 33 MMCLs; cell lines selected for subsequent experiments are shown in red. Data are presented with bar.

b. PIM1, PIM2 and PIM3 expression by RNAseq (bottom) and immunoblotting (top) in the 8 selected MMCLs. Sample derived from the same experiment with different processed gels, one for PIM1 and PIM2, and another for PIM3. Data are presented with bar. The blot is representative of 2 independent experiments.



Supplementary Figure 4.

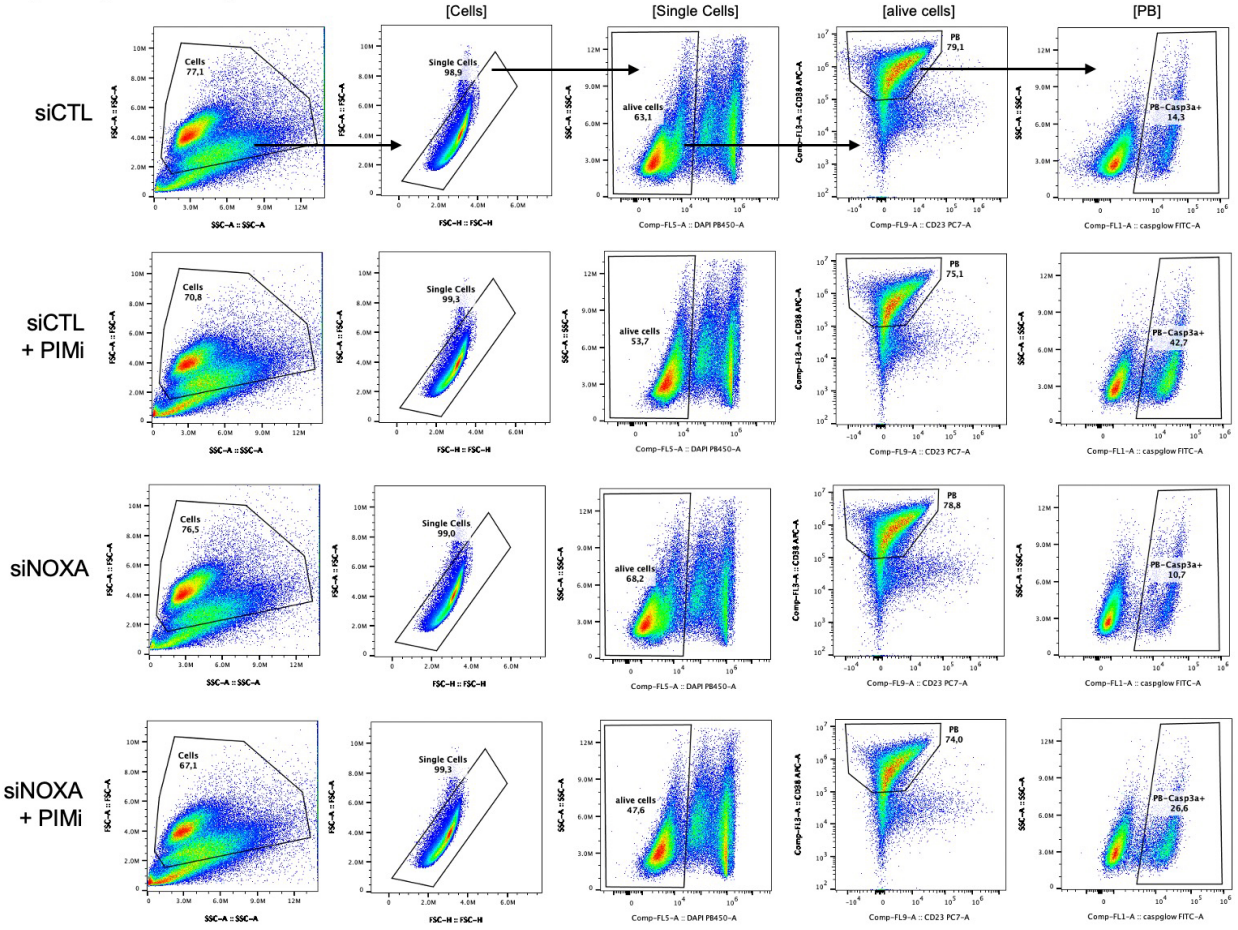
a. As described in Haas et al. (Blood, 2022), specific inhibition of PIM2 was achieved using a novel antisense RNA strategy based on splice switching oligonucleotide (SSO) morpholinos (SSO-PIM2, n = 4). The same strategy was developed for the specific inhibition of PIM1 (SSO-PIM1, n = 3). Dose escalation experiments allowed us to select a concentration of 1 μM and 2 μM for SSO-PIM1 and SSO-PIM2, respectively, for subsequent in vitro experiments.

b. U266 cells were treated with different doses of SSO-PIM1, SSO-PIM2 and SSO-PIM3 or 48 h. *PIM -1, -2 & -3* mRNA expression levels were compared with those in a control experiment. The agarose gel of the *PIM -1, -2 & -3* PCR shows the exon skipping (bottom). Dose escalation experiments allowed us to select a SSO-PIM1 concentration of 1 μM, SSO-PIM2 concentration of 4 μM and SSO-PIM3 concentration of 2 μM for subsequent experiments.

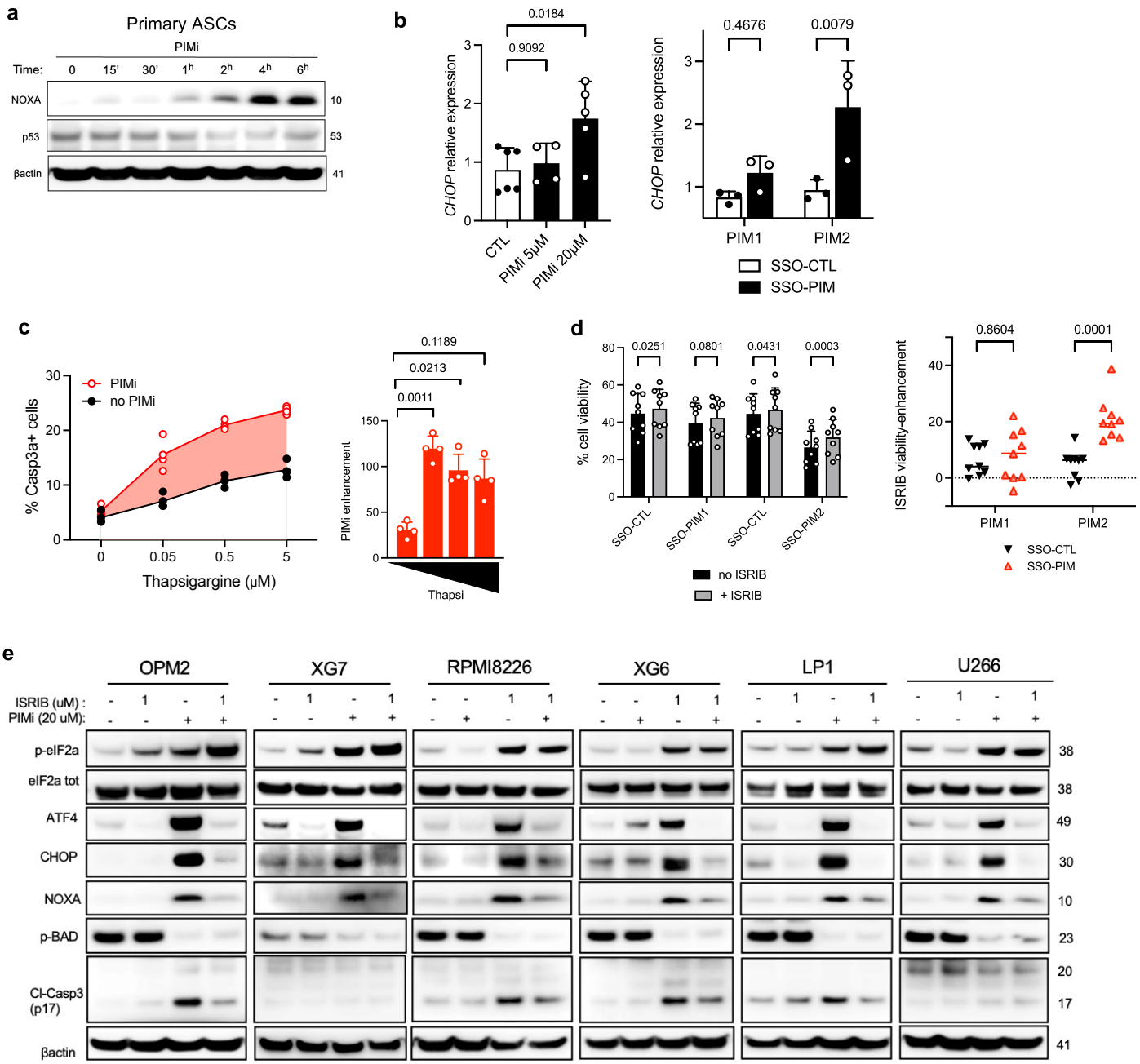
c. At day 6, primary ASCs were transfected with NOXA-specific siRNA or control siRNA. After 24 h, cells were treated with PIMi (AZD1208, 20 μM) for 6 h. NOXA mRNA expression was determined by qPCR. Data are presented as mean +/- SD (n = 3).

P-values were calculated using two-way ANOVA (Fisher's LSD test) for panel (c). 'n' referred to the number of biological replicates.

in primary cells at day8



Supplementary Figure 5. Gating strategy of the Fig. 2f.



Supplemental Figure 6.

a. At day 6, ASCs were treated with PIMi (AZD1208, 20 μM) and cells were harvested at the indicated time points. Immunoblotting was used to assess protein expression of NOXA and p53. The blot is representative of 2 independent experiments.

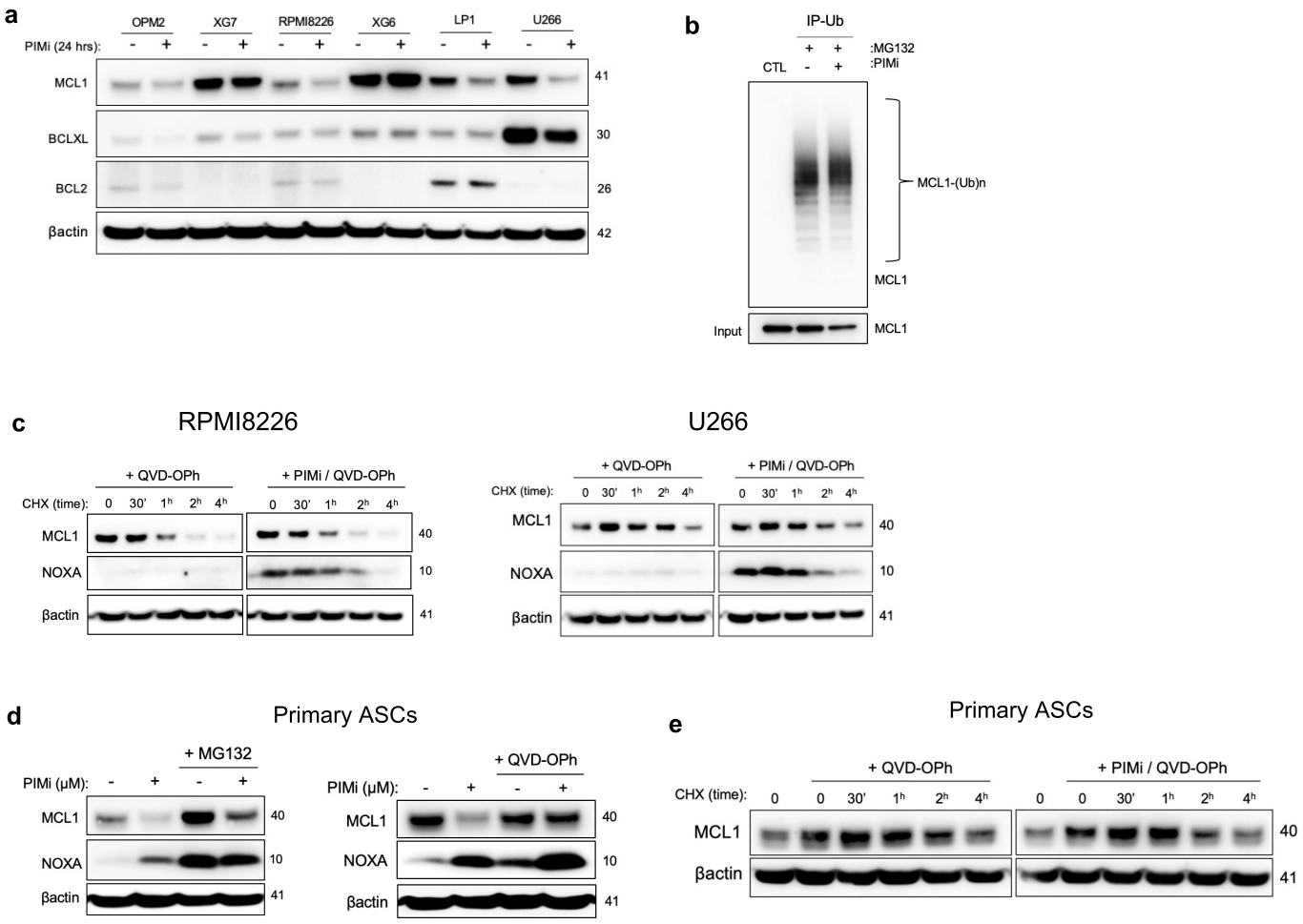
b. At day 6, ASCs were treated with PIMi (AZD1208, 5 and 20 μM) for 6 h or with SSO-PIM for 24 h. mRNA expression of *DDIT3*/CHOP. Data are presented as mean values +/- SD (CTL, n = 6; PIMi 5 μM, n = 4; PIMi 20 μM, n = 5; SSO-CTL and SSO-PIM, n = 3).

c. U266 cells were treated with PIMi (AZD1208, 20 μM) followed by increasing doses of thapsigargin (from 50 nM to 5 μM) for 16 h. Flow cytometry (CaspGlow staining) was used to assess Caspase 3 activation. Data are presented as mean values +/- SEM (n = 4).

d. Left, on day 6, ASCs were treated or not with ISRIB 2 h prior to the addition of SSO-PIM for overnight exposure. The viability of ASCs (ASCs DAPI negative and caspase 3 active negative) was evaluated by flow cytometry. Analysis of cell viability enhancement by ISRIB for SSO-PIM treated cells compared to SSO-CTL. Since ISRIB treatment improved the cell viability in SSO-CTL treated cells, this condition was used as a control and for comparison with SSO-PIM conditions. Right, the enhancement of cell viability by the addition of ISRIB to SSO-CTL or SSO-PIM was determined by normalizing the viability after the ISRIB condition to SSO alone (0 = no effect; 100% = complete cell killing). Data are presented as mean values +/- SEM (n = 9).

e. The six selected MM cell lines were treated with or without ISRIB 2 h before the addition of PIMi (AZD1208, 20 μM) for 6 h. Immunoblotting was used to assess protein expression of p-eIF2α, eIF2α total, ATF4, CHOP, NOXA, pBAD, and Caspase 3. The blot is representative of 1 independent experiment.

P-values were calculated using ordinary on-way ANOVA with Dunnett multiple comparisons in panel (b, right), or ordinary two-way ANOVA with Sidak's multiple comparisons in panel (b, left), Kruskal-Wallis test with Dunn's multiples comparison for panel (c) and two-way ANOVA with Sidak's multiple comparisons for panel (d) were used. 'n' referred to the number of biological replicates.



Supplemental Figure 7.

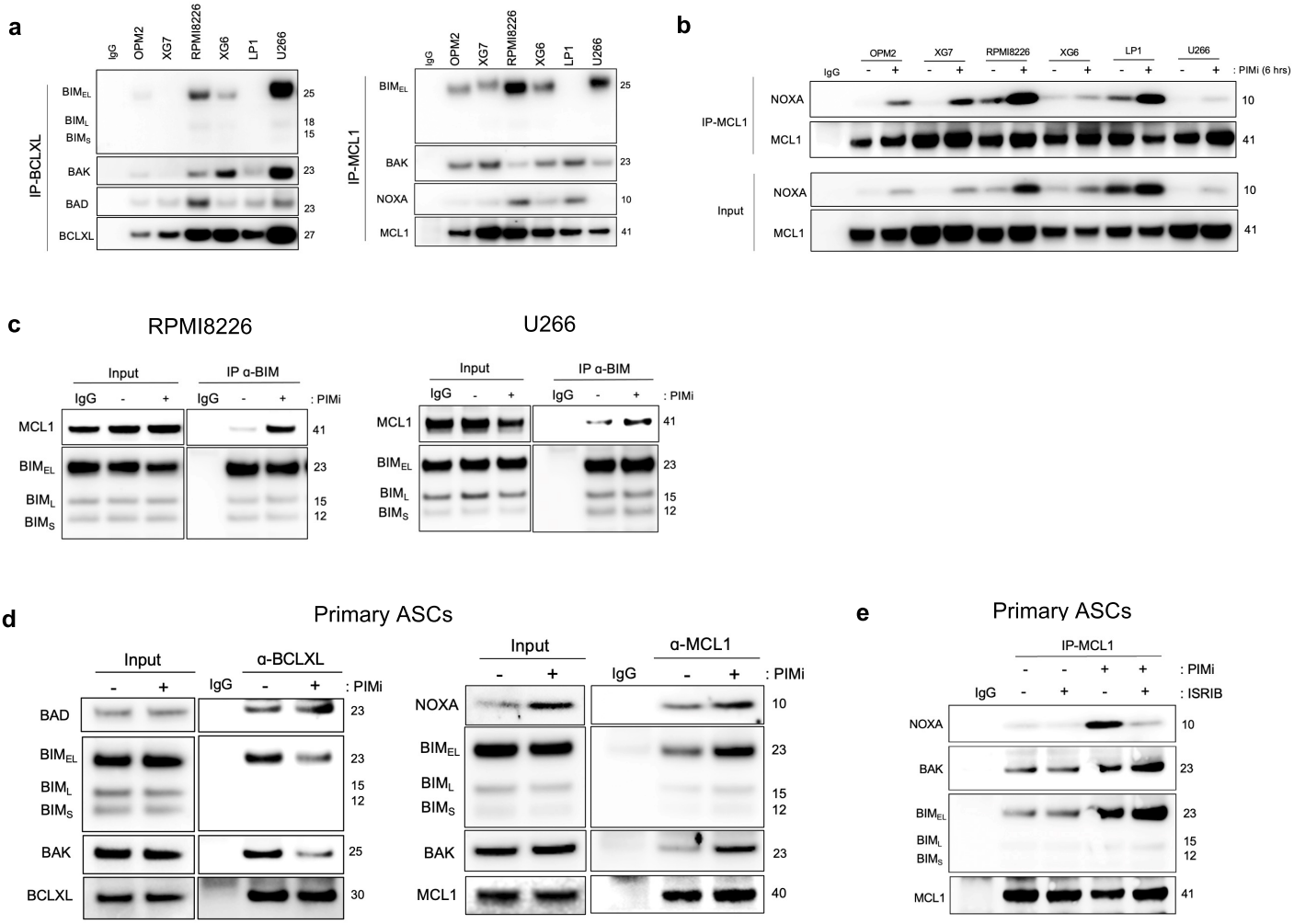
a. The 8 selected multiple myeloma cell lines were treated with PIMi (AZD1208, 20 μM). MCL1, BCLXL and BCL2 protein expression was evaluated by immunoblotting. The blot is representative of 2 independent experiments.

b. U266 cells were treated with PIMi (AZD1208, 20 μM) for 16 h and then MG132 was added for 3 h. Total ubiquitinated proteins were immunoprecipitated. Total MCL1 and ubiquitinated MCL1 were assessed by immunoblotting. The blot is representative of 1 independent experiment.

c. RPMI8226 (left) and U266 (right) cells were treated with PIMi for 24 h in the presence of the pan-Caspase inhibitor QVD-OPH, followed by the addition of cycloheximide. Cells were harvested at the indicated time points. Immunoblotting was used to assess MCL1 and NOXA protein expression. The blot is representative of 1 independent experiment.

d. Right, at day 6, ASCs were treated for 6 h with PIMi (AZD1208, 20 μM), and then MG132 was added for 3 h. MCL1 and NOXA were assessed by immunoblotting. Left, At day 6, ASCs were treated with PIMi (AZD1208, 20 μM) for 6 h in the presence of QVD-OPH. MCL1 and NOXA were evaluated by immunoblotting. The blot is representative of 1 independent experiment.

e. At day 6, primary ASCs, incubated or not in the presence of QVD-OPh, were treated with PIMi (AZD1208, 20 μM) for 6 h. Cycloheximid was then added and cells were harvested at each time point. MCL1 was analyzed by immunoblotting. The blot is representative of 1 independent experiment.



Supplemental Figure 8.

a. BCL-XL (left) and MCL1 (right) were immunoprecipitated in MMCLs (OPM2, XG7, RPMI8226, XG6, LP1 and U266) and protein expressions were assessed by immunoblotting. BIM, BAK, BAD and BCL-XL were evaluated on IP-BCL-XL and BIM, BAK, NOXA and MCL1 on IP-MCL1.

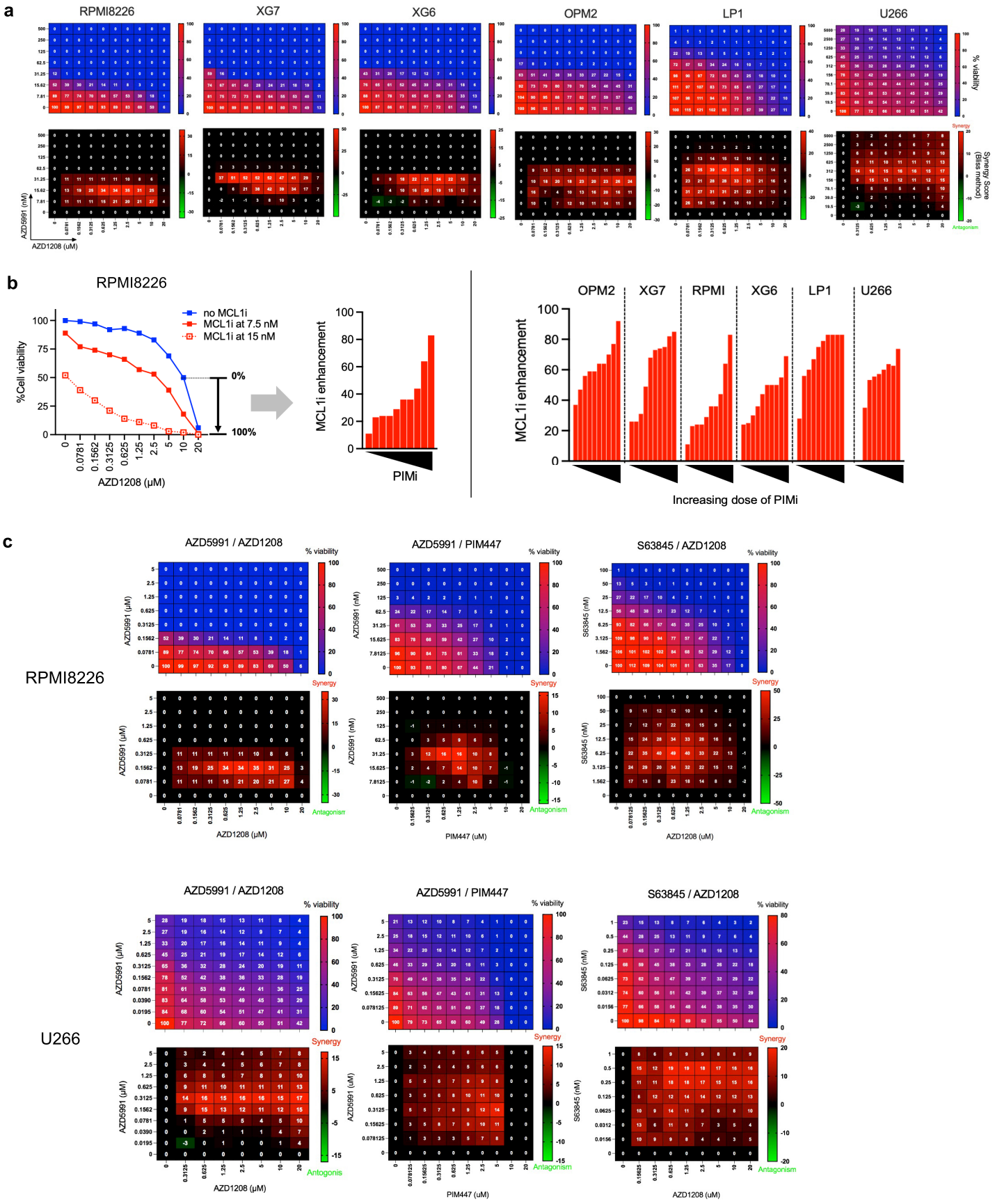
b. MCL1-positive MMCLs (OPM2, XG7, RPMI8226, XG6, LP1 and U266) were treated with PIMi (AZD1208, 20 μM) for 6 h. MCL1 was immunoprecipitated. MCL1 and NOXA were detected by immunoblotting.

c. RPMI8226 and U266 were treated with PIMi (AZD1208, 20 μM) for 24 h. BIM was immunoprecipitated. MCL1 and BIM were detected by immunoblotting.

d. At day 6, primary ASCs were treated with PIMi for 6 h. BCL-XL and MCL1 were immunoprecipitated, and interaction with BAK, BIM, pBAD, BAD, and MCL1 was assessed by immunoblotting.

e. At day 6, primary ASCs were treated with ISRIB for 2 h and then with PIMi (AZD1208, 20 μM) for 6 h. MCL1 was immunoprecipitated. NOXA, BAK, BIM and MCL1 were detected by immunoblotting.

All blots are representative of 1 independent experiment.

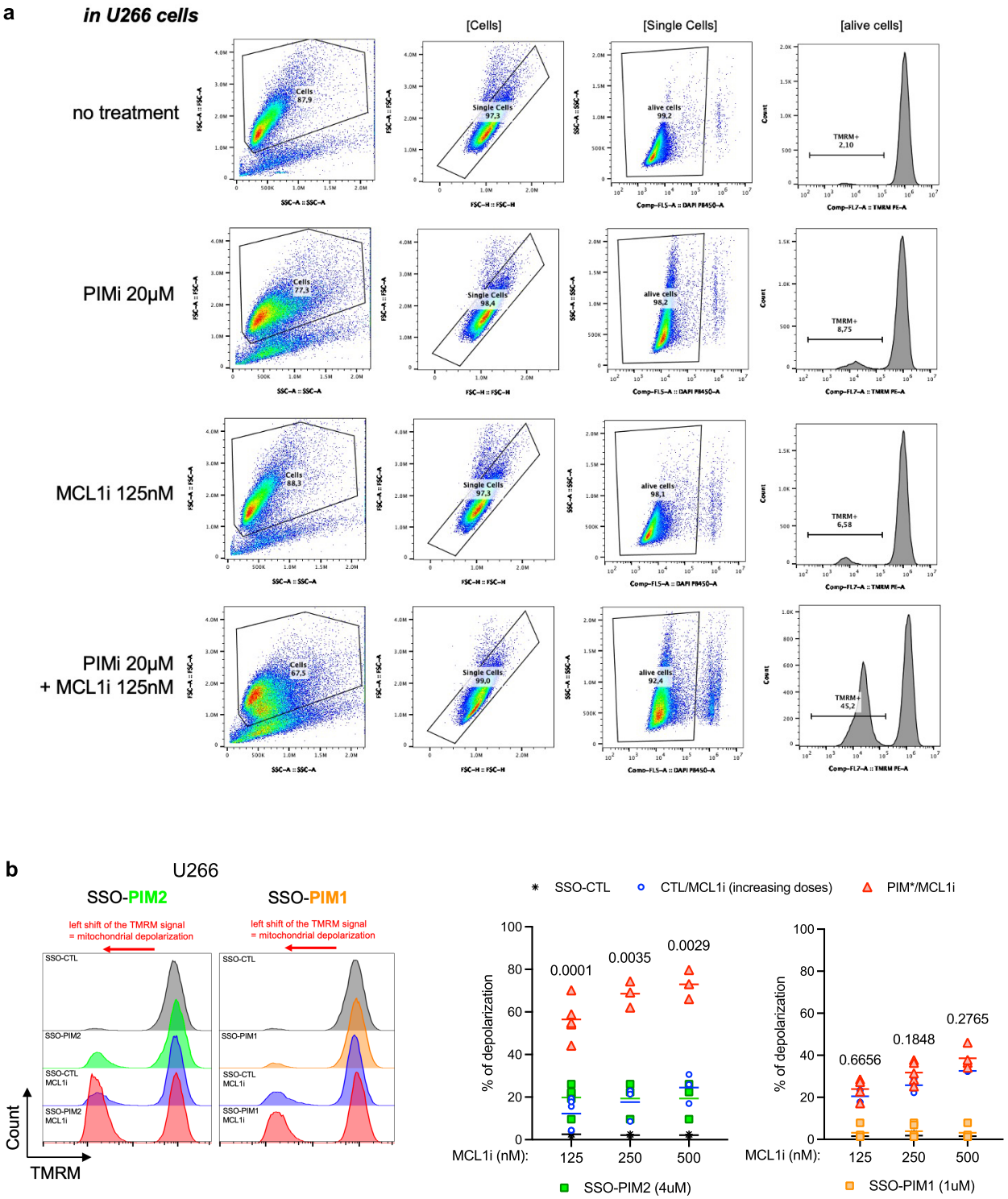


Supplementary Figure 9.

a. Results of a cell viability assay and synergy analysis following treatment with increasing concentrations of AZD1208 (PIMi) and AZD5991 (MCL1i) in MCL1-dependent Multiple Myeloma cell lines (RPMI8226, XG7, XG6, OPM2, LP1 and U266).

b. The enhancement of growth inhibition by the addition of increasing doses of PIMi to a selected dose of MCL1 inhibitor was determined by normalizing viability after combination treatment to MCL1i alone for each dose point (0 = no effect; 100% = complete cell killing). Data are presented with bar.

c. The results of cell viability assays and synergy analysis after treatment with increasing concentrations of different combinations of PIM inhibitor (AZD1208 or PIM447) and MCL1 inhibitor (AZD5991 or S63845) in RPMI8226 and U266 cells.

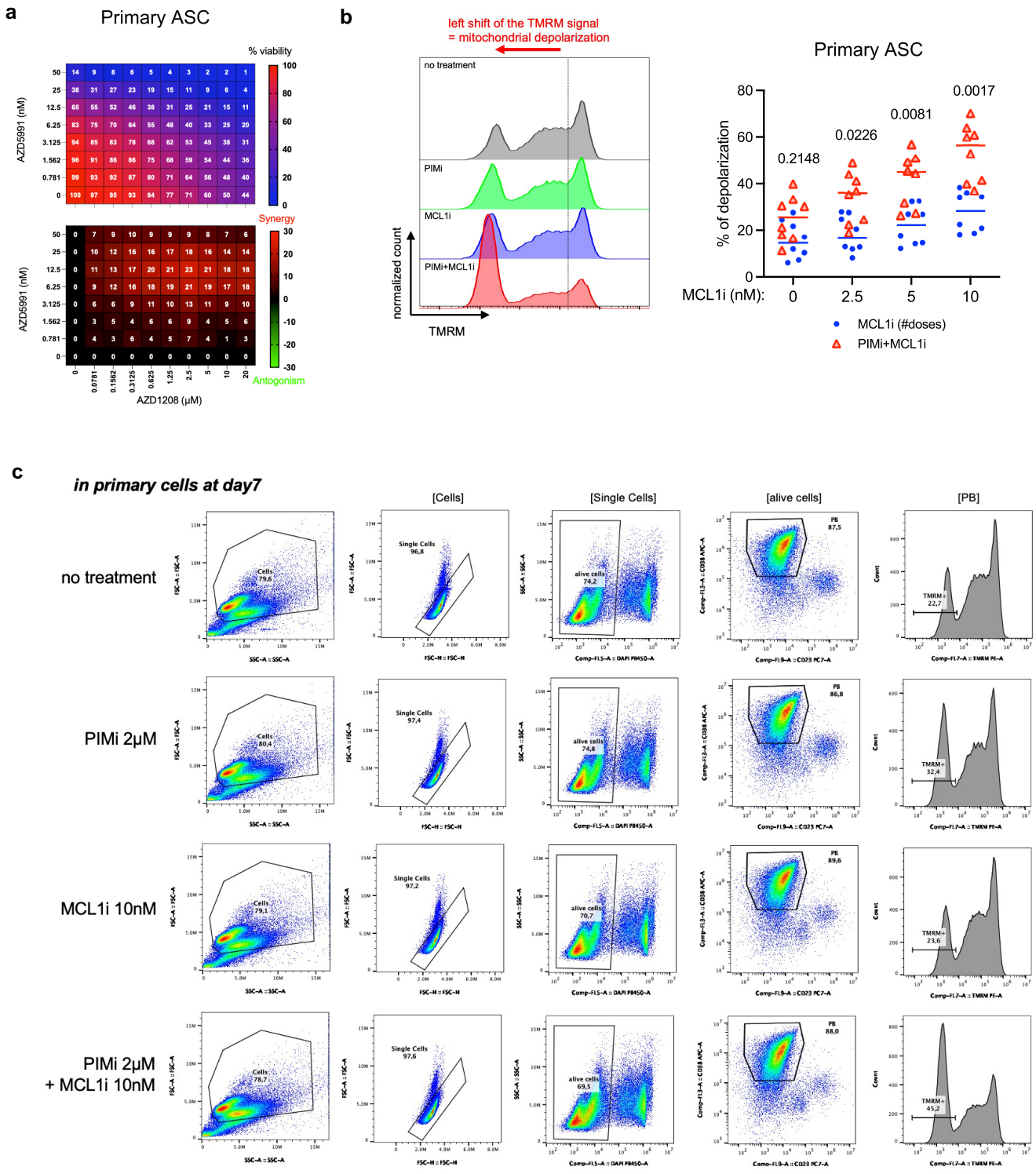


Supplementary Figure 10.

a. Gating strategy for all analysis of TMRM signals in U266 cells.

b. U266 cells were treated with SSO-PIM1 and -PIM2 for 24 h before adding increasing doses of MCL1i for 16 h. Bottom; a representative result of the TMRM signal (analyzed by flow cytometry) after treatment with MCL1i (AZD5991, 125 nM) in SSO-PIM-specific pretreated cells (SSO-PIM1, right in orange; SSO-PIM2, left in green). Right; assessment of the percentage of depolarized cells after exposure to increasing doses of MCL1i in SSO-PIM-specific pretreated U266 cells. Data are presented as mean values (n = 3).

P-values were calculated using two-way ANOVA (Mixed-effects analysis) with Sidak's multiples comparison for panel (b). 'n' referred to the number of biological replicates.



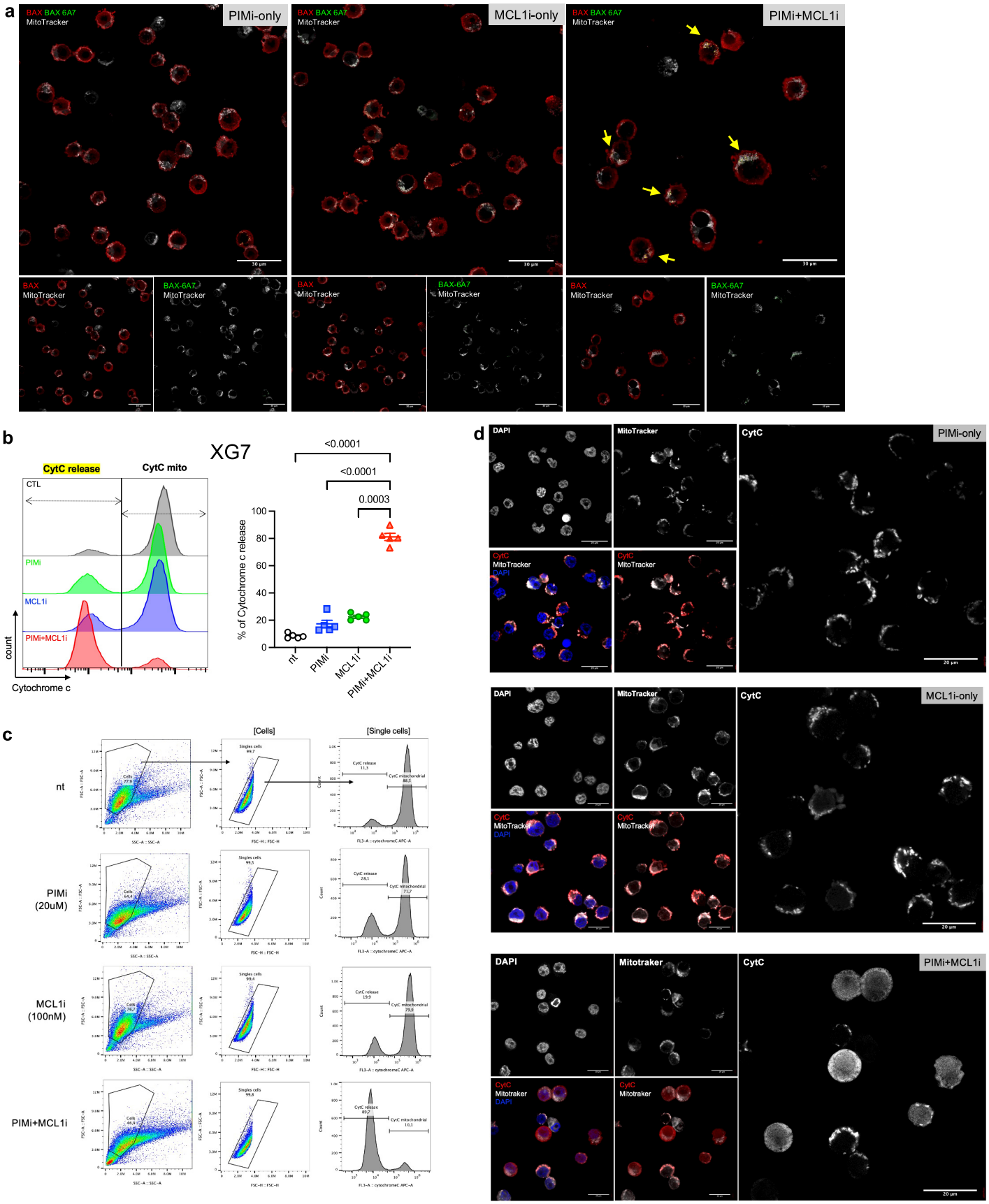
Supplementary Figure 11.

a. Results of a cell viability assay and synergy analysis after treatment with increasing concentrations of AZD1208 (PIMi) and AZD5991 (MCL1i) on primary ASCs at day 7.

b. At day 7, primary ASCs were treated with PIMi (AZD1208, 5 µM) 6 h before the addition of increasing doses of MCL1i. Left, a representative TMRM signal after treatment with MCL1i (AZD5991, 10 nM) in PIMi-pretreated cells. Right, Assessment of the percentage of depolarized cells after exposure to MCL1i in PIMi pretreatment ASCs. Data are presented as mean values (n = 8).

c. Gating strategy for all analysis of TMRM signals in primary ASCs.

P-values were calculated using two-way ANOVA (Mixed-effects analysis) with Sidak's multiples comparison for panel (b). 'n' referred to the number of biological replicates.



Supplementary Figure 12.

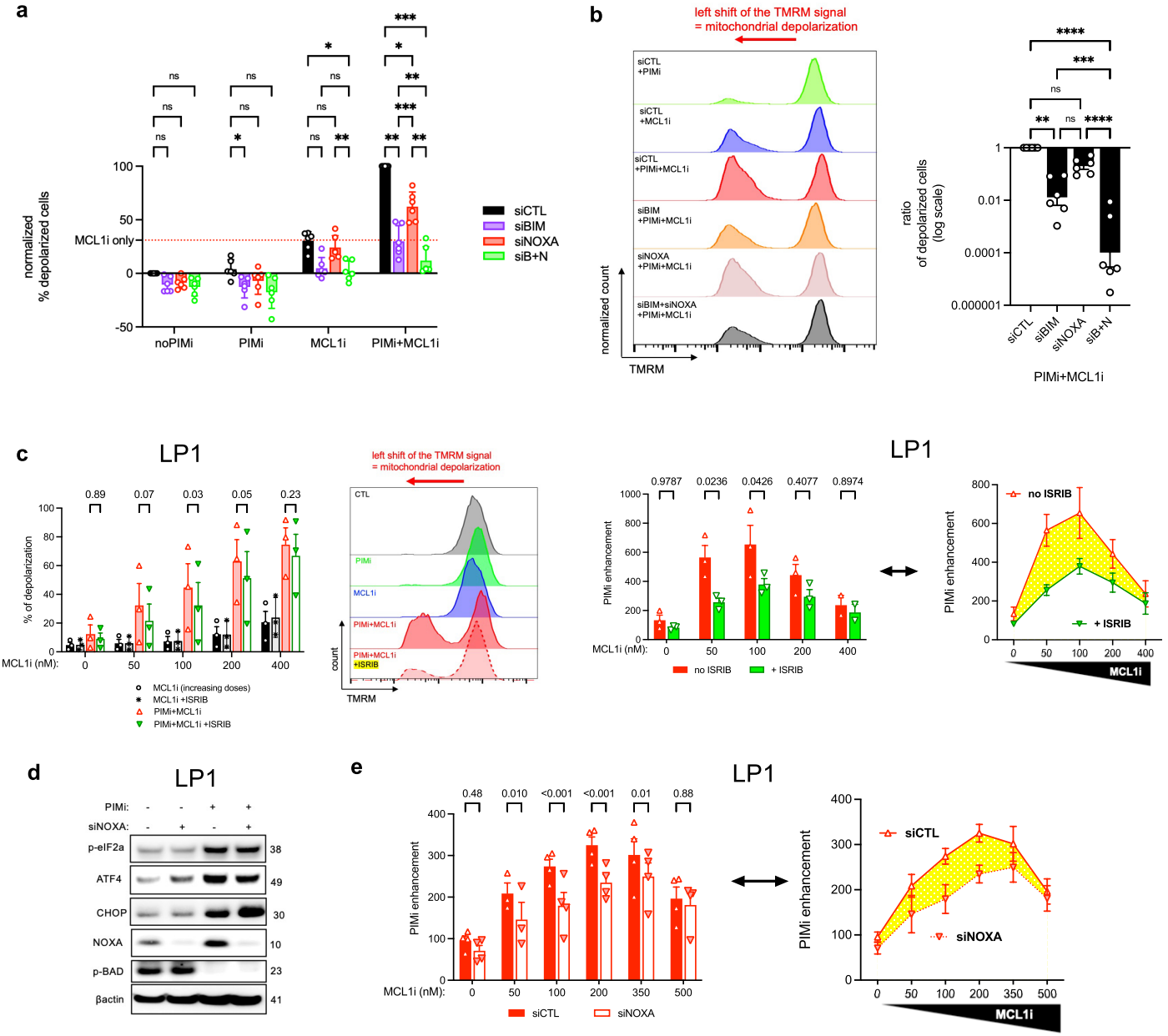
a. XG7 cells were treated with PIMi (AZD1208, 20 μM) for 16 h before adding increasing doses of MCL1i for 4 h. Immunofluorescence staining of BAX total (red), BAX active (BAX 6A7; green) and mitochondria (MitoTraker dye; white). Provided mages are representative of 3 images.

b. XG7 cells were treated with PIMi (AZD1208, 20 μM) for 16 h before adding increasing doses of MCL1i for 5 h. Cytochrome c release was assessed by flow cytometry.

c. Gating strategy for all analyses of Cytochrome c release in MMCLs.

d. XG7 cells were treated with PIMi (AZD1208, 20 μM) for 16 h before adding increasing doses of MCL1i for 4 h. Immunofluorescence staining of Cytochrome c (red) and mitochondria (MitoTracker dye; white). Provided mages are representative of 3 images.

P-values were calculated using RM tow-way ANOVA with Tukey's multiple comparisons for panel (b). 'n' referred to the number of biological replicates.



Supplementary Figure 13.

a. RPMI8226 cells were transfected with NOXA BIM and BIM+NOXA siRNA or control siRNA. After 24 h, cells were pretreated with PIM inhibitor before adding increasing doses of MCL1 inhibitor. TMRM signal and percentage of depolarized cells were evaluated. Data were normalized to the control condition and ratio are presented as mean values +/- SEM (n = 6).

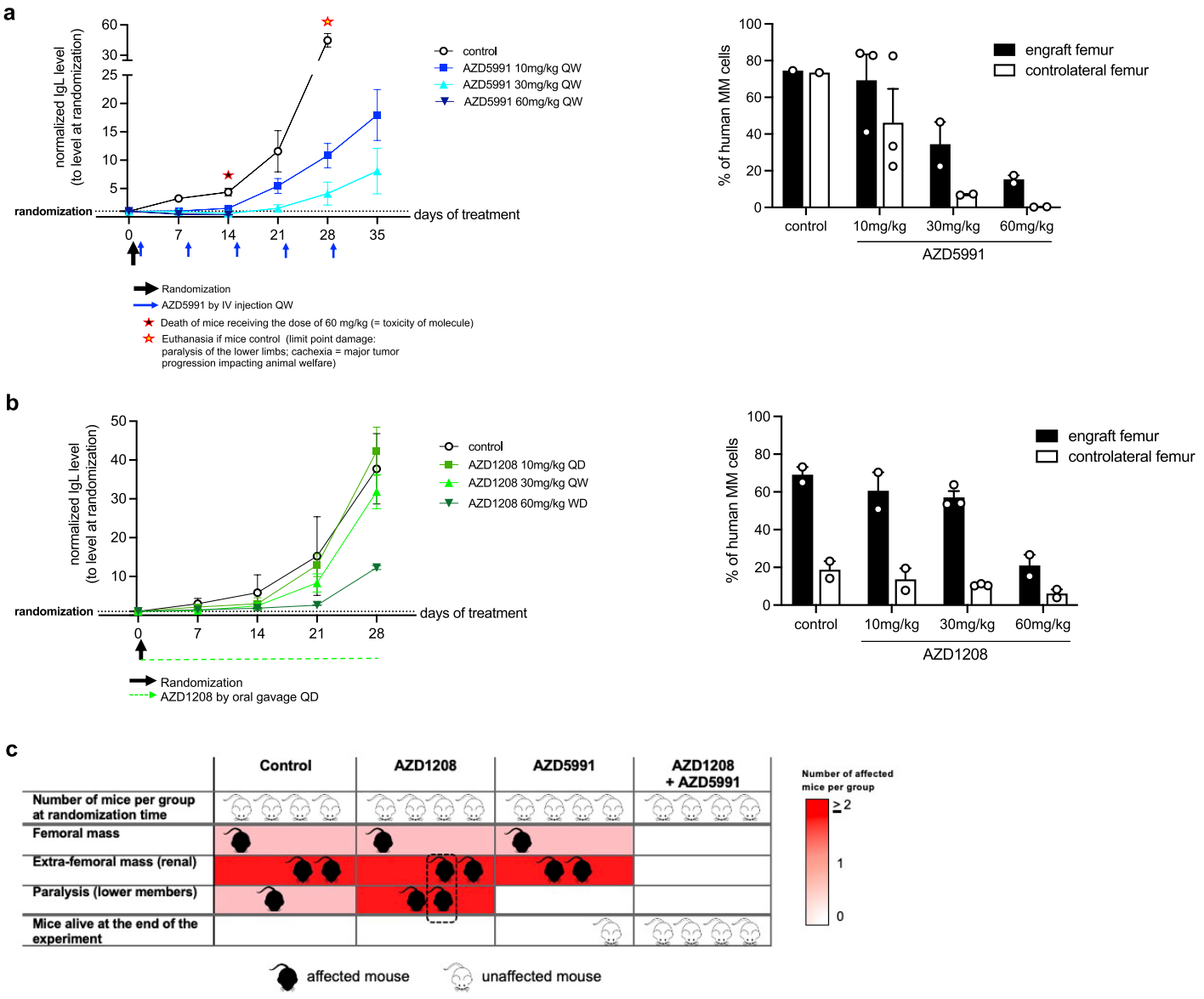
b. RPMI8226 cells were transfected with NOXA, BIM and BIM+NOXA siRNA or control siRNA. After 24 h, cells were pretreated with PIM inhibitor before adding increasing doses of MCL1 inhibitor. TMRM signal and percentage of depolarized cells were evaluated. In PIMi+MCL1i condition, data were normalized to siCTL condition and presented in log scale as mean values +/- SEM (n = 6).

c. Left, LP1 cells incubated with or without ISRIB were treated with PIMi (AZD1208, 20 µM) for 16 h before adding increasing doses of MCL1i for 5 h. Left, Evaluation of the percentage of depolarized cells after exposure to increasing doses of MCL1i in PIMi-pretreated LP1 cells in the presence or absence of ISRIB. Right, a representative result of the TMRM signal (analyzed by flow cytometry) after treatment. Data are presented as mean values +/- SEM (n = 3). Right, The enhancement of cell depolarization by the addition of increasing doses of MCL1i to PIMi at 20 µM was determined by normalizing the depolarization after combination treatment to MCL1i alone for each dose point (0 = no effect; 100% = complete cell depolarization) and in the presence or absence of ISRIB in LP1 cells. Data are presented as mean values +/- SEM (n = 3).

d. LP1 cells were transfected with siRNA specific for *PMAIP1* (encoding NOXA; siNOXA) or siRNA control. After 24 h, cells were treated or not with PIMi (AZD1208, 20 µM) for 6 h. p-eIF2α, ATF4, NOXA and p-BAD were assessed by immunoblotting. The blot is representative of 2 independent experiments.

e. The enhancement of LP1 depolarization by the addition of increasing doses of MCL1i to SSO was determined by normalizing the depolarization after combination treatment to MCL1i alone for each dose point (0 = no effect; 100% = complete cell depolarization) and in the presence or absence of ISRIB (top, in green). Data are presented as mean values +/- SEM (n = 4).

P-values were calculated using two-way ANOVA with Sidak's multiples comparison for panels (a), (c), (e) and RM two-way ANOVA with Tukey's multiple comparisons for panel (b). P < 0.05 is indicated as *, P < 0.01 as **, P < 0.001 as *** and P < 0.0001 as ****; 'ns' designates "not significant" on graphs. Exact p-vales are indicated in the Source Data File. 'n' referred to the number of biological replicates.



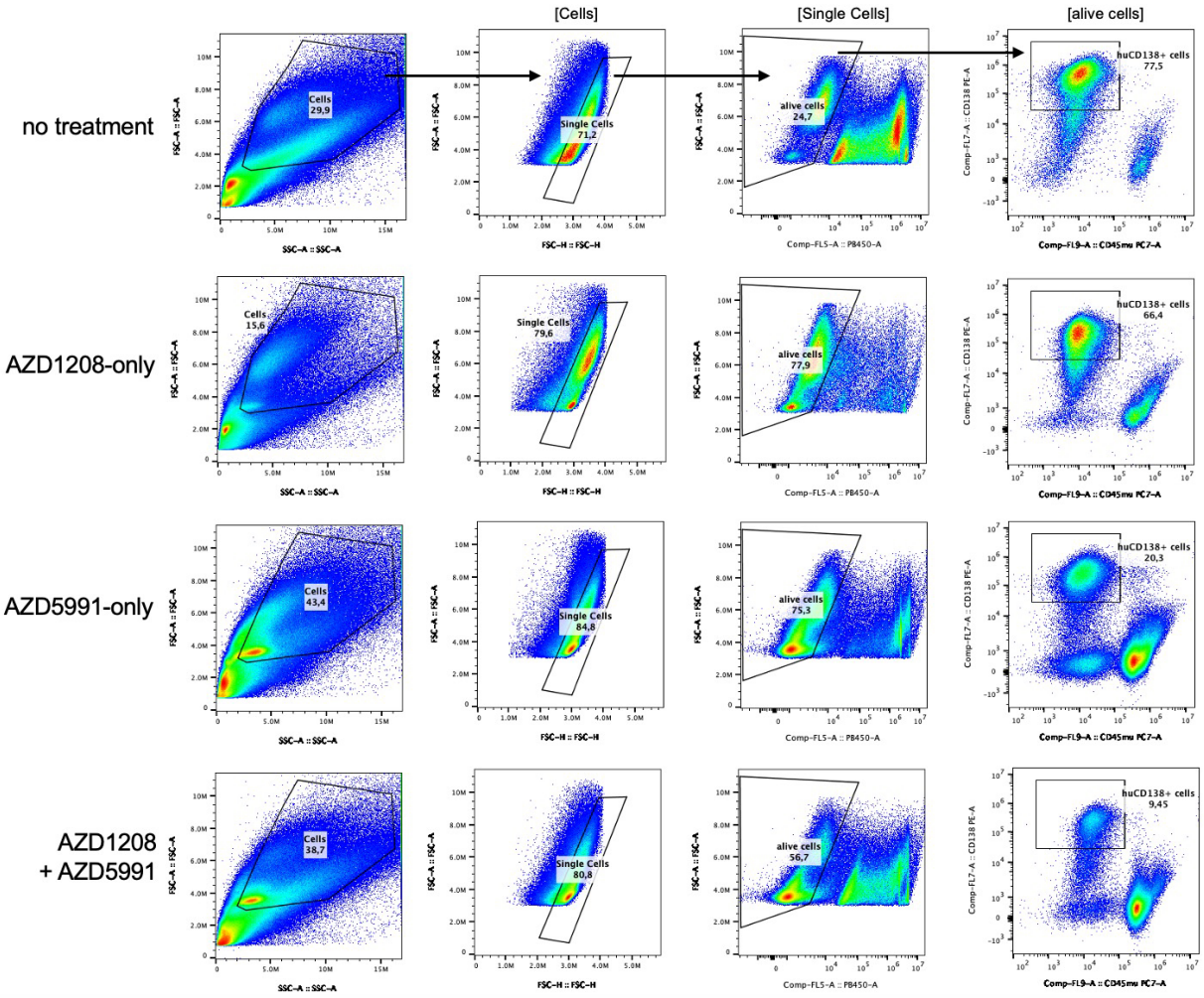
Supplementary Figure 14.

a. Evaluation of single agent AZD5991 (MCL1i) efficacy in the MM cell line (RPMI8226) xenograft model. Left; serum IgL levels were followed weekly from treatment initiation (at the time the mice were randomized) to the endpoint experiment after 5 weeks of treatment (day 35). Serum IgL levels were normalized to the level at the time of randomization (equals 1). Data are represented as mean +/- SEM (vehicle and 30mg/kg, n = 2; 30mg/kg and 60mg/kg, n = 3). Right; at the endpoint (or at the time of mouse euthanasia), mice were euthanized and cells from the right (engrafted femur) and left (contralateral femur) femurs were harvested and analyzed by flow cytometry. The bar graph shows the percentage of viable CD138+ human cells among all collected cells (mouse and human cells) from the femoral flush. Data are presented as mean +/- SEM (vehicle, n = 1; 10mg/kg, n = 3; 30 and 60 mg/kg, n = 2).

b. Evaluation of single agent AZD1208 (PIMi) efficacy in the RPMI8226 cell line xenograft model. Left; follow-up of serum IgL levels from treatment initiation (at the time mice were randomized) to the endpoint experiment after 4 weeks of treatment (day 28). Serum IgL levels were normalized to the level at the time of randomization (equals 1). Data are represented as mean +/- SEM (vehicle, 10mg/kg, and 30mg/kg, n = 2, and 60mg/kg, n = 3). Right, at the endpoint, mice were euthanized and cells from the right (engrafted femur) and left (contralateral femur) femurs were harvested and analyzed by flow cytometry. The bar graph shows the percentage of viable CD138+ human MM cells among all cells collected (mouse and human cells) from femoral flush. Data are presented as mean +/- SEM (vehicle, 10mg/kg, and 60mg/kg, n = 2, and 30mg/kg, n = 3).

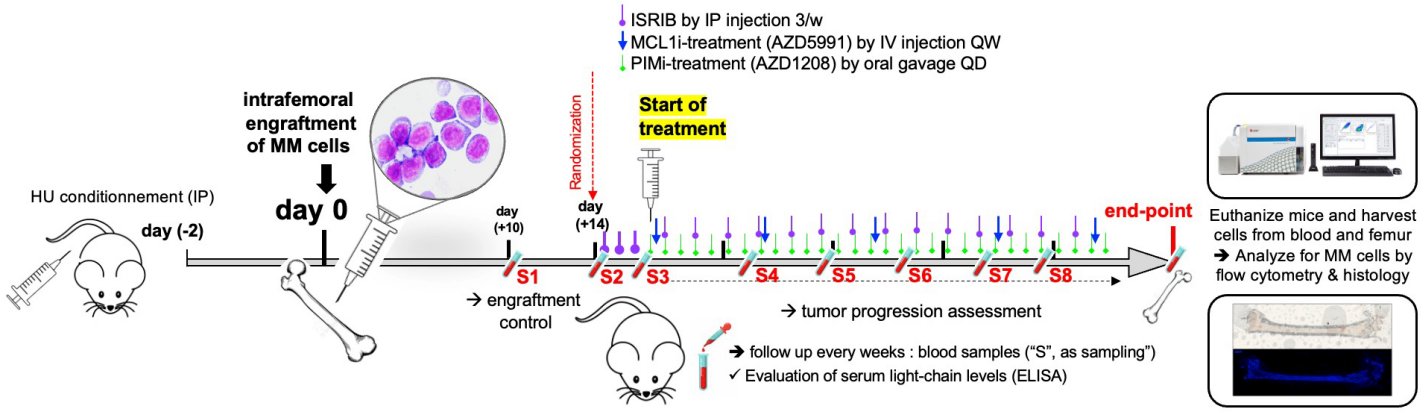
c. Schematic representation of mice showing clinical signs during (requiring early euthanasia of the animal) or at the end of the experiment. Each of the 4 experimental groups consisted of 4 mice. The clinical signs evaluated were classified into 3 categories according to 1) the presence of extrafemoral tumors, i.e. in other organs, especially in the kidney (evaluated only at the time of animal sacrifice), 2) the presence of a visible mass in the femur, which can severely impair the mobility of the mouse, 3) progressive paralysis of the lower limbs, which leads to a deterioration in the health status of the mouse, usually associated with weight loss, and justifies animal euthanasia. Lower limb paralysis is a prominent sign of tumor progression involving nerve compression by the tumor. Mice affected by any of these clinical signs are colored black and unaffected mice are colored white. Each group is qualitatively scored using 3 colors: white if no mice in the group show any signs, light red if 1 mouse shows signs, and bright red if 2 or more mice show signs.

in cells harvested from engrafted femur of mice

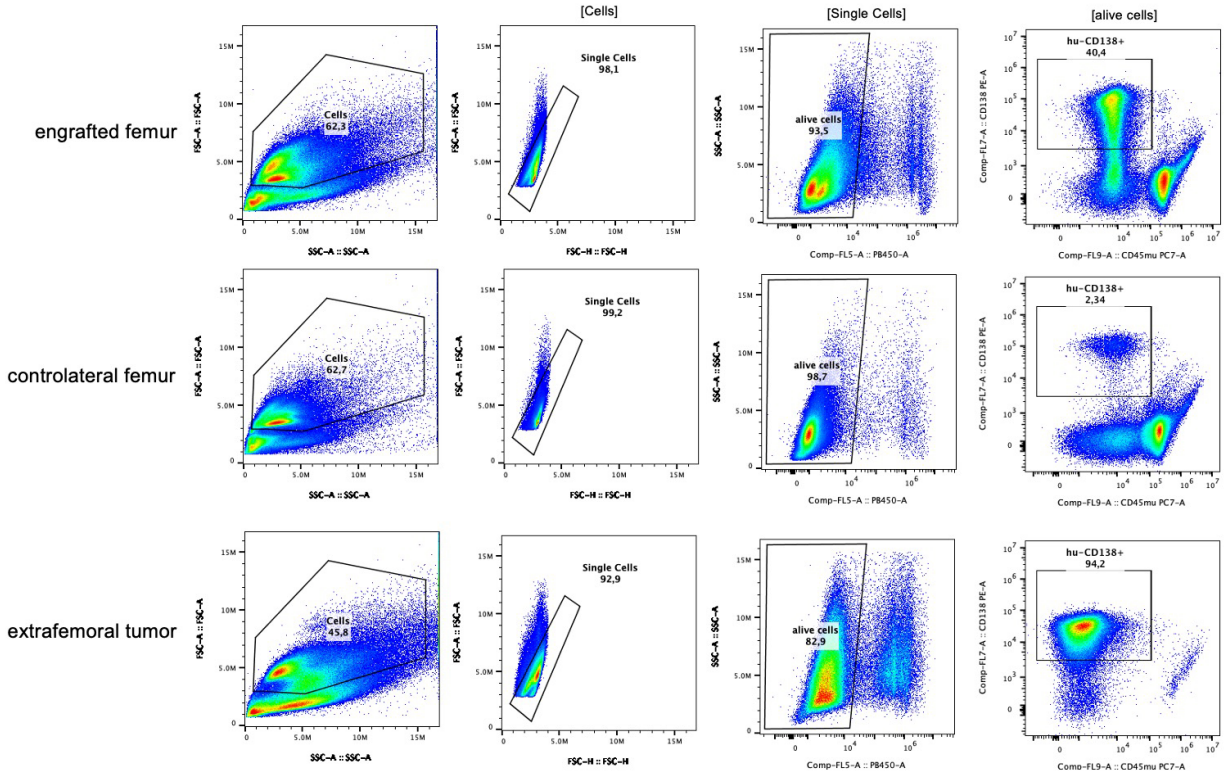


Supplementary Figure 15. Gating strategy of Fig. 6e.

a



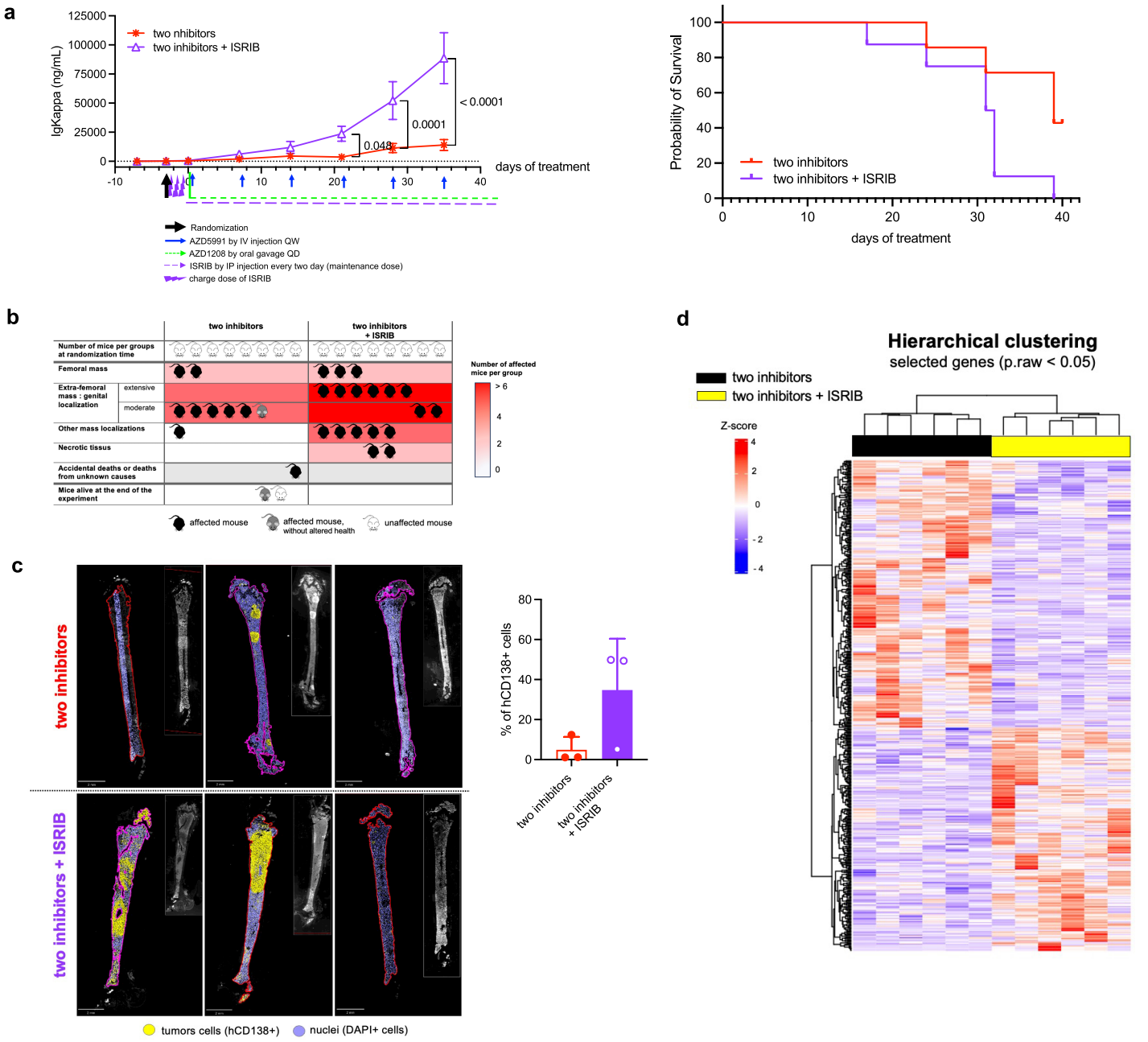
b ***in cells harvested from femurs and extrafemoral tumor of a mouse***



Supplemental Figure 16.

a. For the XG7 xenograft model, procedures described in the Fig. 6c were applied. The ISRIB treatment was added in one group of animals under combined inhibitor treatment. Tumor progression was monitored periodically by evaluating serum Ig light chain kappa (IgK) levels by ELISA. When the mean of IgK level reached 200 ng/mL, groups of 5 mice were randomized to receive either vehicle, PIMi alone (by oral gavage, once daily), MCL1i alone (by intravenous injection, once weekly), or both molecules together, in the presence or absence of ISRIB. Each sample is written in red with the letter "S" followed by a number corresponding to the sample number. Randomization was performed at S2. S3 was performed just before the start of inhibitor treatment and is considered as the pretreatment baseline sample. At day 14, after randomization, mice in this group received loading doses of ISRIB for 3 consecutive days. At day 18, inhibitor treatment was initiated in all groups. Maintenance doses of ISRIB were then injected every two days. Created with BioRender.com

b. Gating Strategy for Fig. 7d.



Supplemental Figure 17.

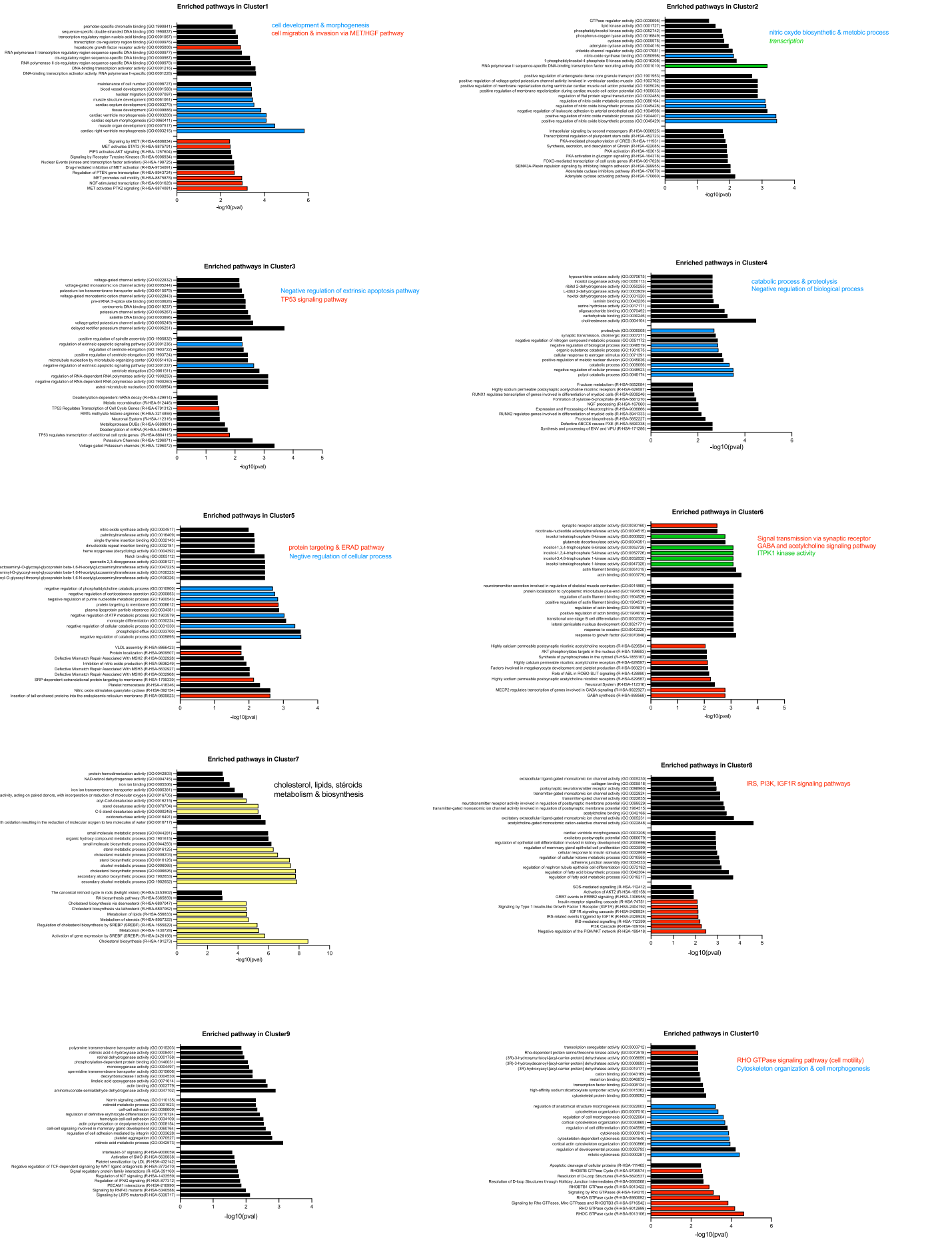
a. A second experiment tested the combination of AZD1208 and AZD5991 in the presence or absence of ISRIB after engraftment of XG7 cells was monitoring. Left, serum IgK levels were followed from baseline to the endpoint experiment after 4 weeks of treatment. Data are presented as mean values +/- SEM (n = 8). Right, survival curve of animals during the second experiment testing the combination of AZD1208+AZD5991 in the presence or absence of ISRIB after engraftment of XG7 cells. Animals were considered "dead" when euthanasia was required to limit animal suffering. Causes of early euthanasia include paralysis of the lower limbs, severe generalized weakness, weight loss, and incapacitating femoral tumors.

b. Schematic representation of mice showing clinical signs during (requiring early euthanasia of the animal) or at the end of the experiment. The 2 experimental groups consisted of 8 mice each. The clinical signs evaluation were classified into 4 categories according to: 1) the presence of a mass at the femoral site (evaluated only at mouse sacrifice); 2) the presence of extrafemoral tumors at the genital site (main location found) for which the masses were assessed qualitatively (moderate or extensive); 3) the presence of extrafemoral tumors in other locations, and 4) the development of visible necrotic tissue. Mice affected by any of these clinical signs are colored black. Unaffected mice are colored in white. Each group is qualitatively scored using 5 colors: white if no mice in the group show signs, beige if 1 mouse shows signs, light pink if 2 or 3 mice show signs, light red if 4, 5 or 6 mice show signs, and bright red if more than 6 mice show signs. Mice colored gray are considered "affected" but whose disease did not require early sacrifice of the animal.

c. Quantification of CD138 human tumor cells after immunostaining of femurs. Above, hCD138 immunostaining on femur sections was quantified using QuPath software. The number of total cells (mouse and human) was assessed by total nuclei, in purple, using DAPI staining, and the number of human tumor cells, in yellow, was quantified using hCD138 staining. Bottom, the bar graph represents the proportion of human tumor cells quantified on sections from 3 contralateral femurs (nongrafted femurs) in each treatment group. Data are presented as mean +/- SD (n = 3)

d. DEG analysis (pval < 0.05) of the RNAseq dataset between samples of two inhibitor-only group and two inhibitors + ISRIB combination. Heatmap of the 547 genes significantly differentially expressed (pval < 0.05) between the 2 conditions. Unsupervised analysis of the data revealed significantly enriched pathways between the two groups.

P-values were calculated using two-way ANOVA (Mixed-effects analysis) with uncorrected Fisher's LSD test for panel (a). P < 0.05 is indicated as *, and P < 0.0001 as ****. 'n' referred to the number of biological replicates.



Supplementary Figure 18.
GSEA analysis for DGE modules identified from Gene Ontology (biological pathway (BP) and molecular function (MF)) and Reactome databases. The 10 best significant pathways (pval < 0.05) from each database (GO-BP, GO-MF and Reactome) are shown. The data are presented in the graph as -log10 (pval). The most interesting pathways are highlighted with colors, which are qualified by terms next to the graphs for each module.

Supplementary Table 1. List of peptides used for BH3-profiling analysis.

Peptides used for BH3-profiling			
Peptide	**Sequence**	**Binding partners**	**Class**
BIM	Acetyl-MRPEIWIAQELRRIGDEFNA-Amide	All	Activator
PUMA	Acetyl-EQWAREIGAQLRRMADDLNA-Amide	All	Sensitizer
PUMA2A	Acetyl-EQWAREIGAQARRMAADLNA -Amide	Mutant control	Negative control
BAD	Acetyl-LWAAQRYGRELRRMSDEFEGSFKGL-Amide	BCL2/W/XL	Sensitizer
NOXAA	Acetyl-AELPPEFAAQLRKIGDKVYC-Amide	MCL1, BFL1	Sensitizer
MS1	Acetyl-RPEIWMTQGLRRLGDEINAYYAR-Amide	MCL1	Sensitizer
HRK-Y	Acetyl-SSAAQLTAARLKALGDELHQY-Amide	BCLXL	Sensitizer

Supplementary Table 2. List of primers used for quantitative RT-PCR analysis.

Gene	*Forward primer*	*Reverse primer*
ABL1	5'-GGTCATCAGGGAGGGTTAGG-3'	5'-GCTCTGTCAAGGTCCAGGAG-3'
PIM2	5'-CCTCATCAGGGAGGGTTAGG-3'	5'-GCCCTCCTGTGTCTCAAACC-3'
PIM1	5'-CGCGACATCAAGGACGAAAA-3'	5'-GAGGGCTATACACTCGGGTC-3'
PIM3	5'-GATGCTGCTCTCCAAGTTCG -3'	5'-GCTCTCCTTGTCCGCCTT-3'
PMAIP1	5'-GTTGGAGGCTGAGGTTCCC-3'	5'-TAGCACACTCGACTTCCAGC-3'
CHOP	5'-TGTTAAAGATGAGCGGGTGG-3'	5'-CAGGTGTGGTGATGTATGAAGA-3'
MCL1	5'-AGGAGTTGTACCGGCAGTC-3'	5'-GAACTCCACAAACCCATCCTTG-3'
BCL2L1	5'-TGCAGGTATTGGTGAGTCGG-3'	5'-CCACAGTCATGCCCGTCAG-3'
BCL2	5'-GACTGAGTAGAACCGGC-3'	5'-GGCCAAACTGAGCAGAGTCT-3'
TP53	5'-GCCCCTCCTGAGCATCTTAT-3'	5'-AGTTGTAGTGGATGGTGGTACA-3'
BCL2L11	5'-AGTGCAATGGCTTCCATGAGG-3'	5'-CCTCCTTGCATAGTAAGCGTT-3'

Supplementary Table 3. List of all antibodies used for immunoblots, flow cytometry, cell sorting and immunofluorescence analysis.

Antibodies for immunoblots		
β actin (AC-15)	Sigma-Aldrich	A1978
BAD (D24A9)	Cell Signaling	#9239
BAD	Cell Signaling	9292
phospho-BAD (Ser112) (40A9)	Cell Signaling	#5284
Caspase 3	Cell Signaling	#9662
PIM2 (D1D2)	Cell Signaling	#4730
PIM1 (D8D7Y)	Cell Signaling	#54523
PIM3 (D17C9)	Cell Signaling	#4165
phospho-eIF2a (Ser51) (D9G8)	Cell Signaling	#3398
eIF2a (D7D3)	Cell Signaling	#5324
ATF4 (W16016A)	Biolegend	#693902
CHOP	Cell Signaling	#2895
NOXA (D8L7U)	Cell Signaling	#14766
BCLXL	Cell Signaling	#2762
MCL1 (D5V5L)	Cell Signaling	#39224
BCL2 (4D7)	BD Biosciences	#551098
BAX	Cell Signaling	#2772
BAX 6A7	Biolegend	#633802
BAK (D4E4)	Cell Signaling	#12105
BIM (C34C5)	Cell Signaling	#2933
Ubiquitine-HRP antibody (P4D1)	Cytoskeleton	AUB01
Isotype Rabbit IgG (DA1E)	Cell Signaling	#3900
Clean blot	Thermo Fisher	21230
HRP-Donkey anti-Rat IgG (Poly4054)	BioLegend	405405
HRP-Donkey anti-Rabbit IgG (Poly4064)	BioLegend	406401
HRP-Donkey anti-Mouse IgG (Poly4053)	BioLegend	405306

Antibodies for Flow Cytometry and cell sorting		
CD38-APC	BD Biosciences	555462
CD38-APC	Miltenyi Biotech	130-113-429
CD38-PE	BD Biosciences	555460
CD23-PE	BD Biosciences	555711
CD23-PC.7	BD Biosciences	561167
CD20-FITC	BioLegend	302304
CD20-FITC	Miltenyi Biotech	130-113-429
CD138-PE	Miltenyi Biotech	130-119-840
CD44-APC	BD Biosciences	559942
CD27-PE	BD Biosciences	566944
CD19-FITC	BD Biosciences	555412

Antibodies for immunofluorescence		
CD138	R&D Systems	NB100-64980
BAX	R&D Systems	NBP2-67285
BAX (6A7)	Biolegend	633802
Cytochrome c (6H2.B4)	BD Pharrmigen	556432