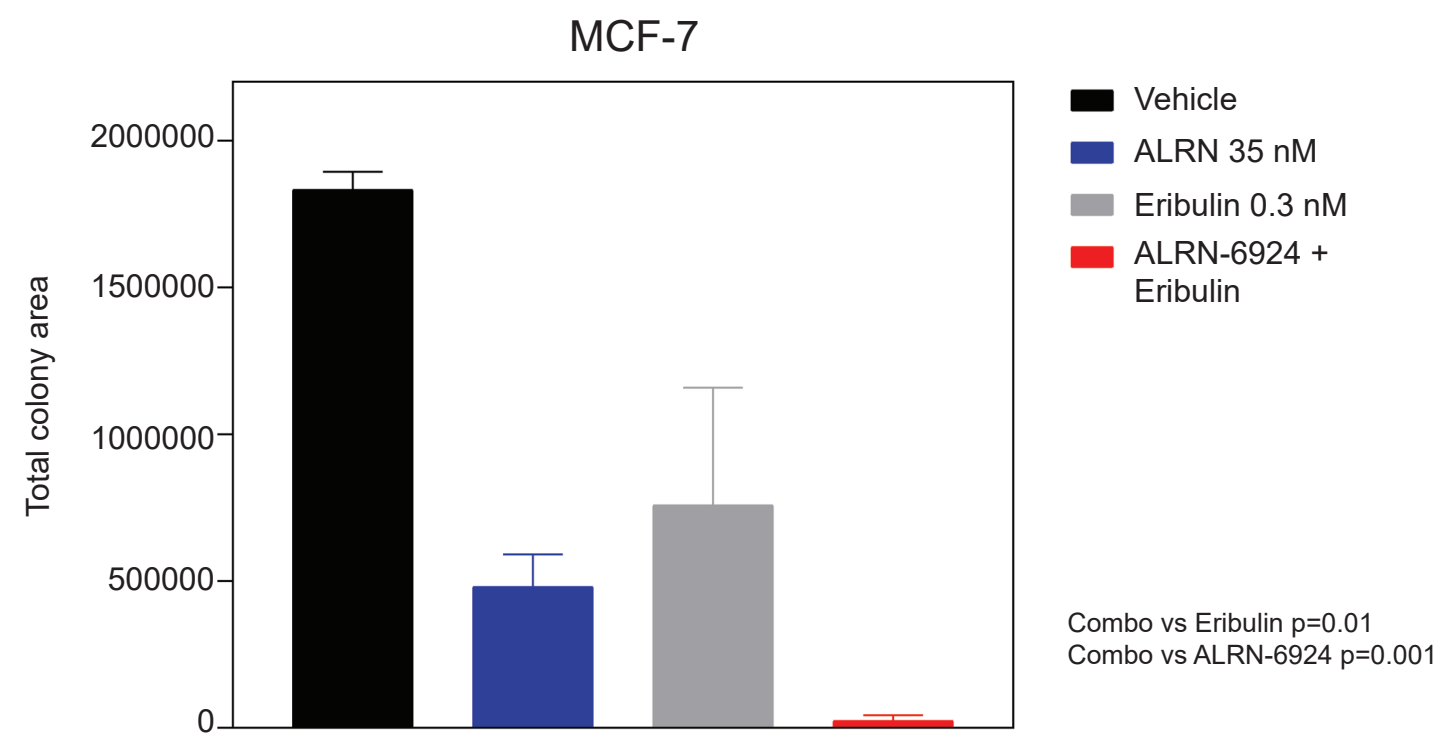
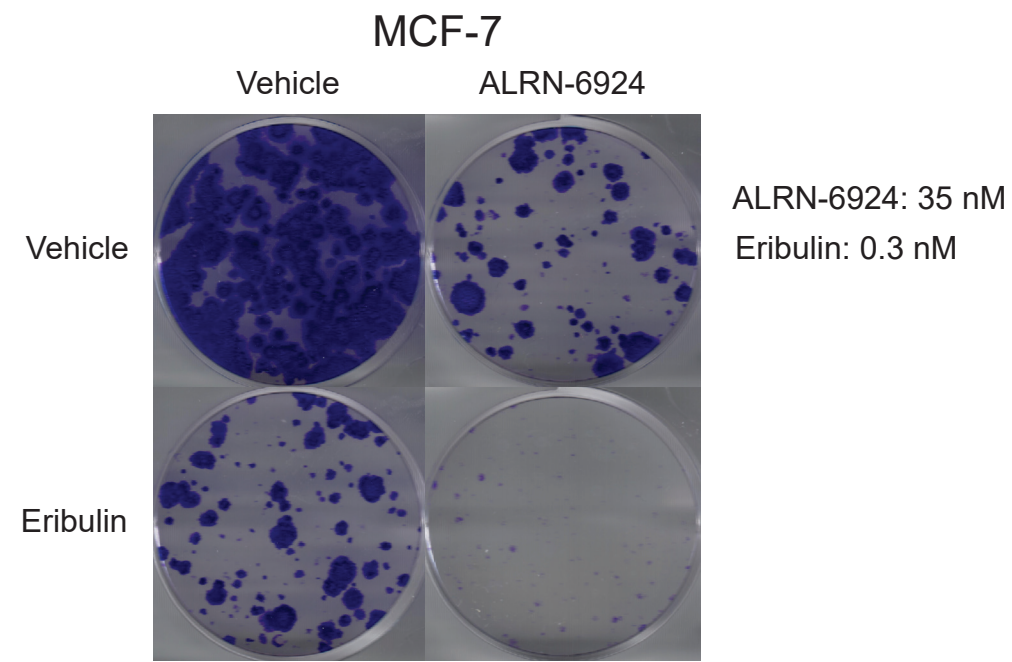
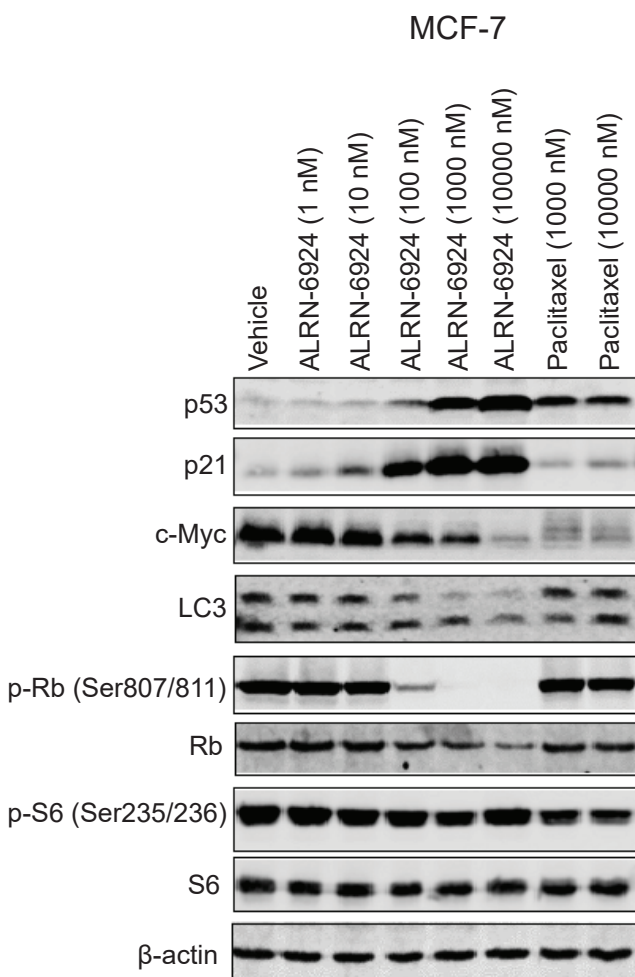


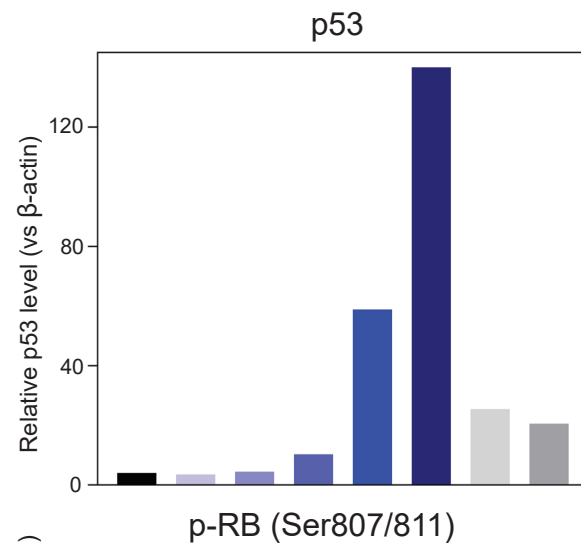
Figure S1



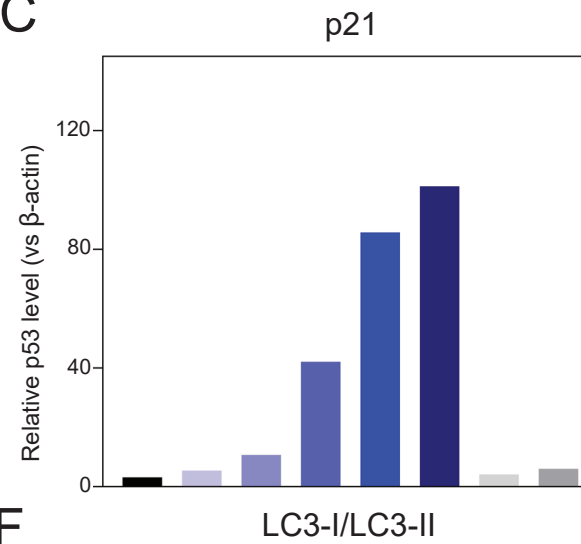
A



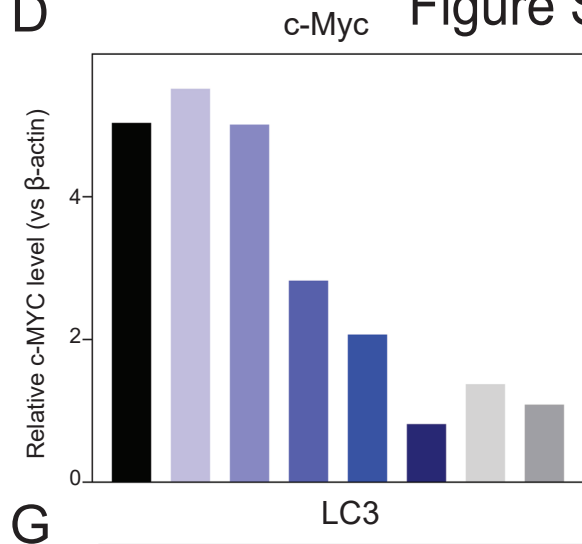
B



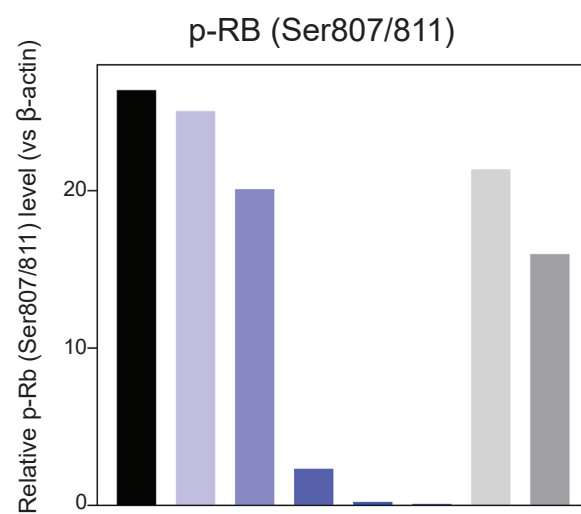
C



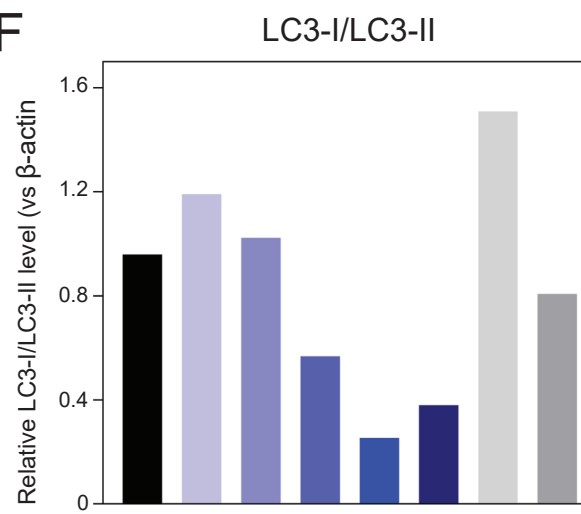
D



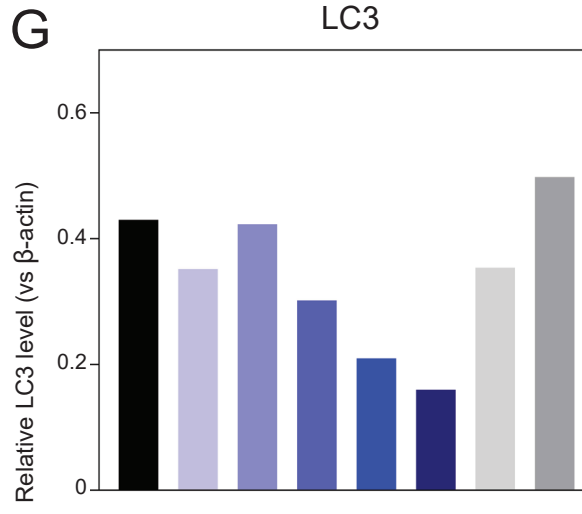
E



F



G



H

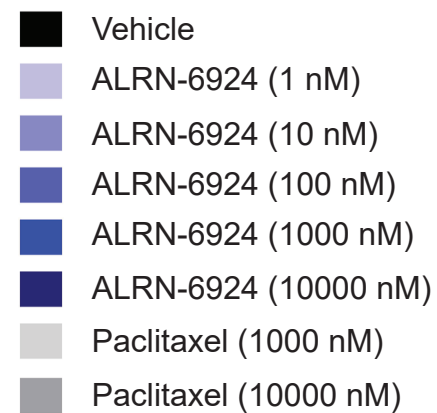
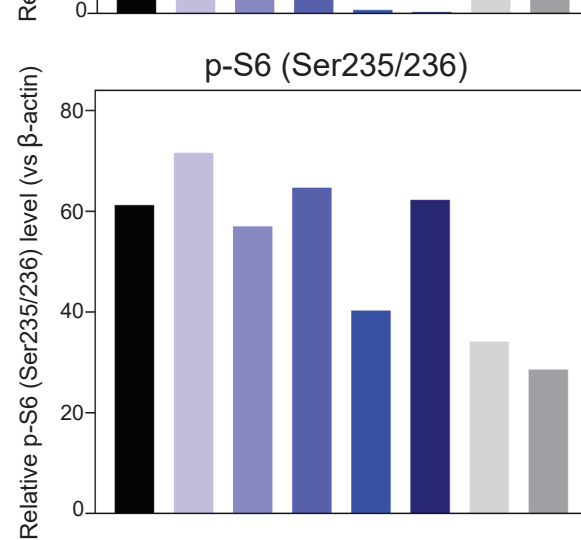
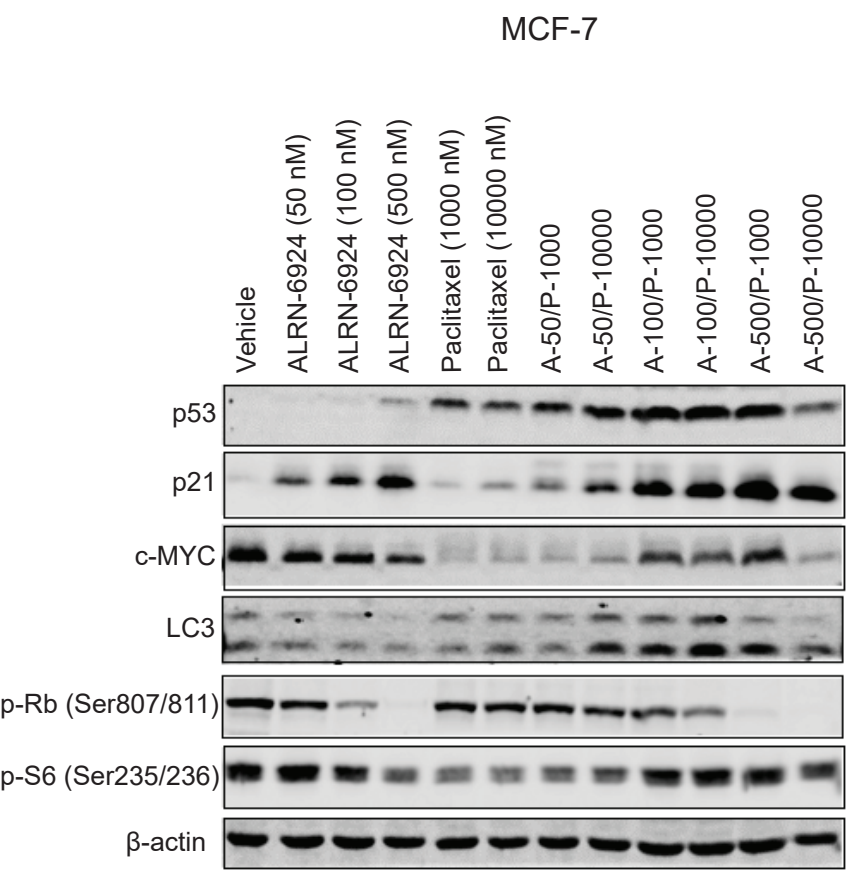
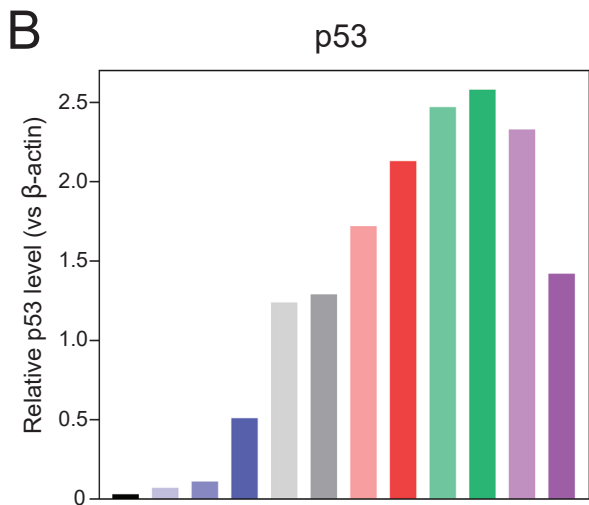


Figure S3

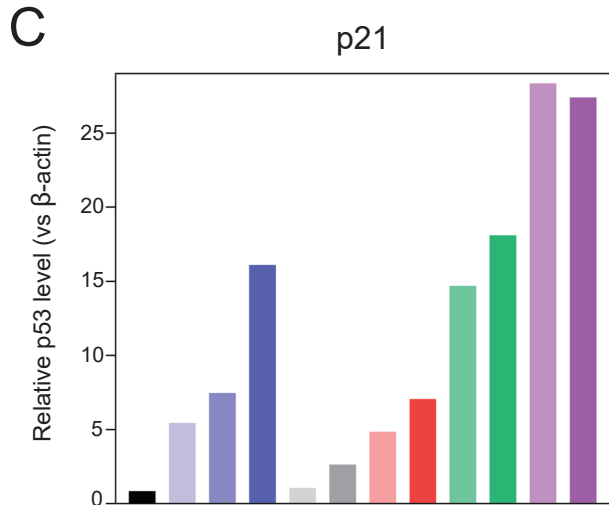
A



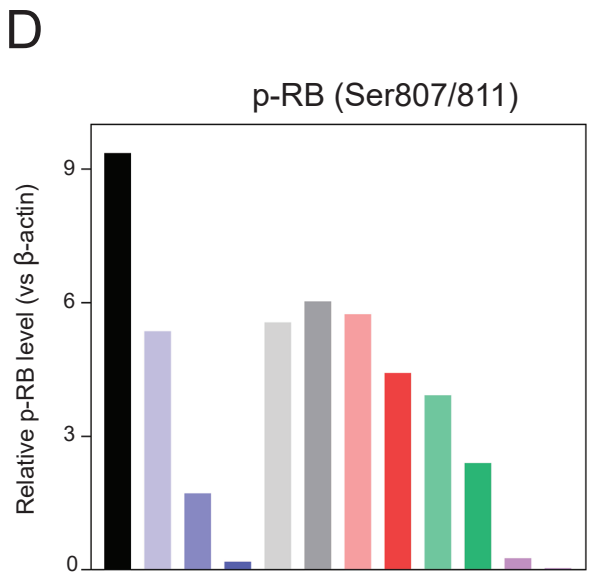
B



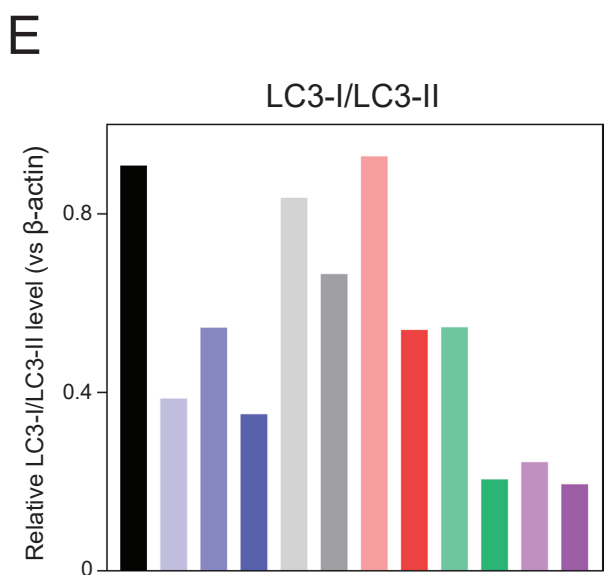
C



D



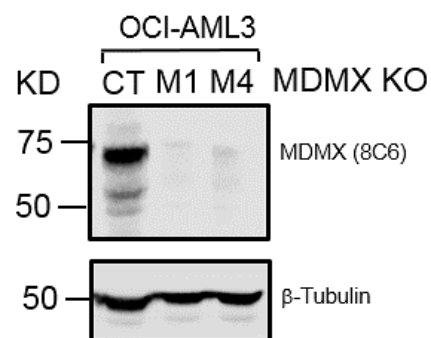
E



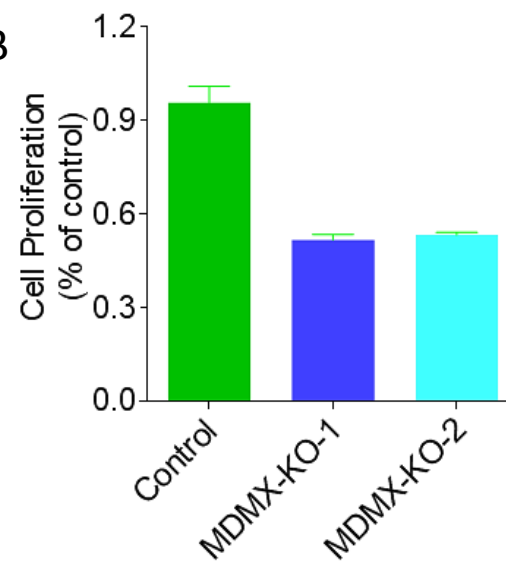
- Vehicle
- ALRN-6924 (1 nM)
- ALRN-6924 (10 nM)
- ALRN-6924 (100 nM)
- Paclitaxel (1000 nM)
- Paclitaxel (10000 nM)
- ALRN-50/Paclitaxel-1000
- ALRN-50/Paclitaxel-10000
- ALRN-100/Paclitaxel-1000
- ALRN-100/Paclitaxel-10000
- ALRN-500/Paclitaxel-1000
- ALRN-500/Paclitaxel-10000

Figure S4

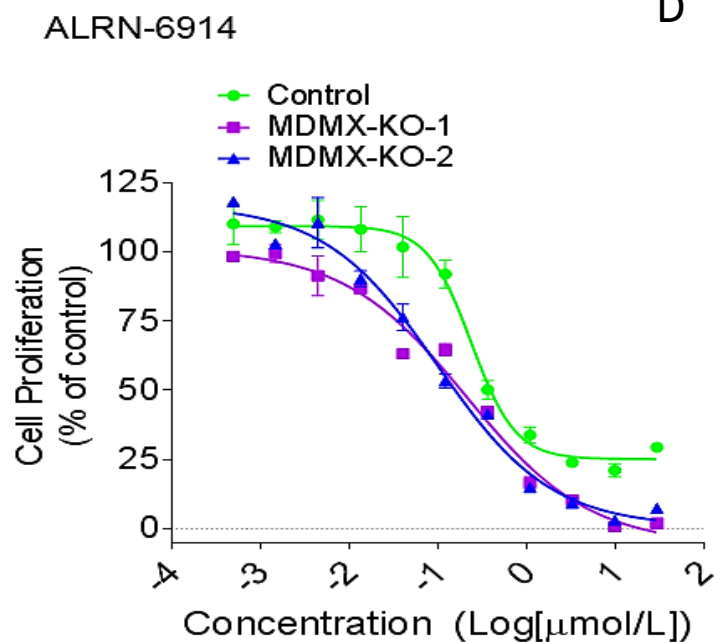
A



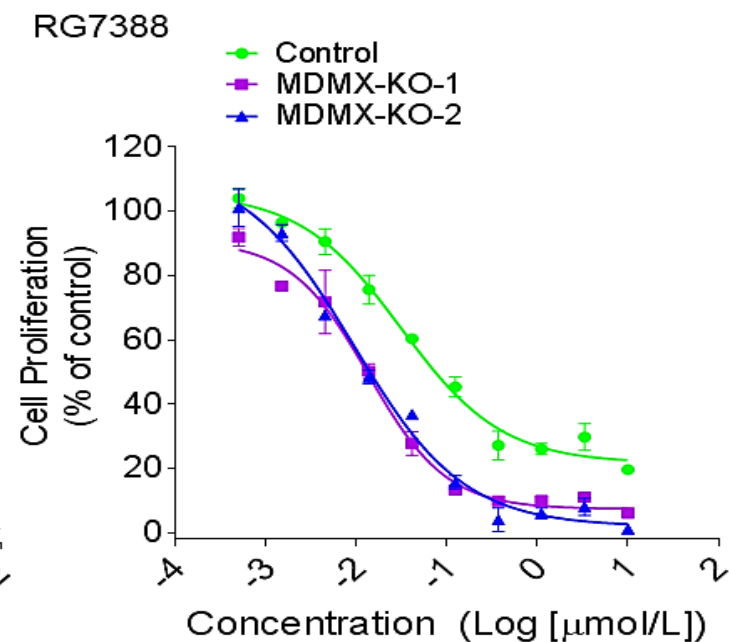
B



C



D



Supplementary Table 1

Cell Line	Cancer Type	TP53 Status	Source	HPV or SV40 infected	ALRN-6924 EC ₅₀ (μM)	RG7112 EC ₅₀ (μM)	RG7338 EC ₅₀ (μM)
DU-4475	Breast cancer	WT	Horizons		0.305	0.471	0.0711
MEL-JUSO	Melanoma	WT	Horizons		0.279	0.539	0.0424
MEL-HO	Melanoma	WT	Horizons		0.552	0.983	0.0546
GRANTA-519	Lymphoma	WT	Horizons		0.409	0.35	0.0371
MDA-MB134-VI	Breast cancer	WT	Horizons		2.29	4.51	0.123
NH-6	Neuroblastoma	WT	Horizons		0.299	0.551	0.0601
SK-MEL-31	Melanoma	WT	Horizons		1.94	1.03	0.133
SK-N-SH	Neuroblastoma	WT	Horizons		0.084	0.154	0.0071
UACC-62	Melanoma	WT	Horizons		1.01	0.516	0.00754
OAW-42	Ovarian cancer	WT	Horizons		0.546	0.567	0.164
RMG-I	Ovarian cancer	WT	Horizons		0.308	0.573	0.0034
HCT-116	Colon cancer	WT	Horizons		0.103	0.14	0.0202
HEC-151	endometrial cancer	WT	Horizons		0.239	1.64	0.522
HEC-265	endometrial cancer	WT	Horizons		0.544	1.6	0.243
HUH-6 Clone 5	Liver cancer	WT	Horizons		0.194	0.293	0.0188
IST-MES1	Lung cancer	WT	Horizons		0.814	0.974	>30
KP-N-RT-BM-1	Neuroblastoma	WT	Horizons		0.202	0.118	0.0224
KP-N-S19s	Neuroblastoma	WT	Horizons		0.031	0.22	0.00921
LoVo	Colon cancer	WT	Horizons		0.258	0.516	0.0245
LS-174T	Colon cancer	WT	Horizons		0.135	0.656	0.0157
MSTO-211H	Lung cancer	WT	Horizons		0.048	0.0753	0.00496
MV-4-11	AML	WT	Horizons		0.169	0.123	0.0226
NCI-H929	multiple myeloma	WT	Horizons		0.618	0.383	0.0351
PA-1	Ovarian cancer	WT	Horizons		0.135	0.526	0.0682
WM-115	Melanoma	WT	Horizons		0.369	0.661	0.108
COLO-205	Colon cancer	WT	Horizons		0.275	0.362	0.0142
COLO-849	Melanoma	WT	Horizons		0.619	1.21	0.0364
NCI-H28	Lung cancer	WT	Horizons		2.22	0.885	>30
Colo-678	Colon cancer	WT	Horizons		0.179	1.44	3.15
SK-MEL-5	Melanoma	WT	Horizons		0.585	1.88	>30
COLO-792	Melanoma	WT	Horizons		0.605	1.76	0.0372
SK-MEL-24	Melanoma	WT	Horizons		2.37	2.31	0.0165
KP-4	Pancreatic cancer	WT	Horizons		>30	13.2	>30
C3A	Liver cancer	WT	Horizons		0.069	0.389	0.00449
A101D	Melanoma	WT	Horizons		1.3	1.54	>30
C32	Melanoma	WT	Horizons		0.683	>30	>30
HCC1395	Breast cancer	Mutant	Horizons		11	11.4	11.9
MDA-MB-361	Breast cancer	Mutant	Horizons		>30	12.6	12.8
HCC2218	Breast cancer	Mutant	Horizons		>30	8.945334	30
HCC1937	Breast cancer	Mutant	Horizons		>30	7.57	7.09
IGR-37	Melanoma	Mutant	Horizons		>30	>30	>30
Au565	Breast cancer	Mutant	Horizons		>30	4.61	3.09
BT-474	Breast cancer	Mutant	Horizons		>30	11.2	7.15

OCI-Ly7	Lymphoma	Mutant	Horizons	>30	10.1	>30
SK-BR-3	Breast cancer	Mutant	Horizons	>30	11.1	6.65
SK-MEL-2	Melanoma	Mutant	Horizons	>30	>30	>30
SK-MEL-30	Melanoma	Mutant	Horizons	>30	13.4	>30
SNU-387	Liver cancer	Mutant	Horizons	19.3	>30	>30
SNU-398	Liver cancer	Mutant	Horizons	10.9	3.44	3.13
SNU-423	Liver cancer	Mutant	Horizons	15.7	6.94	30
SNU-449	Liver cancer	Mutant	Horizons	>30	>30	>30
ECC12	Gastric cancer	Mutant	Horizons	>30	11.4	>30
EVSA-T	Breast cancer	Mutant	Horizons	9.49	6.46	>30
Hs 766T	Pancreatic cancer	Mutant	Horizons	>30	12.9	>30
MDA-MB-436	Breast cancer	Mutant	Horizons	14.6	>30	>30
OCI-Ly1	Lymphoma	Mutant	Horizons	30	10.5	>30
OE33	esophageal cancer	Mutant	Horizons	16.7	4.27	>30
Panc 02.03	Pancreatic cancer	Mutant	Horizons	>30	7.34	>30
Panc 04.03	Pancreatic cancer	Mutant	Horizons	>30	8.2	>30
PANC-1	Pancreatic cancer	Mutant	Horizons	>30	9.21	15.4
IA-LM	NSC lung cancer	Mutant	Horizons	>30	12.2	15.5
Karpas-422	Lymphoma	Mutant	Horizons	>30	12.5	>30
Mino	Lymphoma	Mutant	Horizons	12.4	6.03	>30
REC-1	Lymphoma	Mutant	Horizons	20.2	2.65	>30
A2058	Melanoma	Mutant	Horizons	>30	16.1	>30
AsPC-1	Pancreatic cancer	Mutant	Horizons	>30	9.74	11.9
Caov-3	Ovarian cancer	Mutant	Horizons	>30	8.35	>30
Caov-4	Ovarian cancer	Mutant	Horizons	>30	14.7	>30
COLO-679	Melanoma	Mutant	Horizons	>30	7.65	8.97
COLO-684	endometrial cancer	Mutant	Horizons	9.71	12.6	>30
COLO-741	Melanoma	Mutant	Horizons	>30	12.2	>30
EBC-1	NSC lung cancer	Mutant	Horizons	>30	6.39	>30
ECC10	Gastric cancer	Mutant	Horizons	>30	7.48	14.6
KG-1	erythroleukemia	Mutant	Horizons	>30	16.2	>30
KM12	Colon cancer	Mutant	Horizons	>30	6.73	10.8
LS-123	Colon cancer	Mutant	Horizons	>30	>30	>30
Mia PaCa-2	Pancreatic cancer	Mutant	Horizons	>30	>30	>30
NCI-H508	Colon cancer	Mutant	Horizons	>30	6.6	11.4
OVCAR-3	Ovarian cancer	Mutant	Horizons	>30	13.4	>30
RPMI-7951	Melanoma	Mutant	Horizons	>30	12.2	>30
SF126	Brain cancer	Mutant	Horizons	>30	13.9	>30
SK-OV-3	Ovarian cancer	Mutant	Horizons	>30	15	>30
SW480	Colon cancer	Mutant	Horizons	>30	11.2	>30
MPP-89	Lung cancer	Mutant	Horizons	>30	>30	>30
NCI-H2452	Lung cancer	Mutant	Horizons	>30	13.7	>30
HEC-6	endometrial cancer	Mutant	Horizons	>30	10.7	13.2
PANC-08-13	Pancreatic cancer	Mutant	Horizons	>30	3.47	>30
NCI-H838	NSC lung cancer	Mutant	Horizons	>30	>30	>30
HEC-108	endometrial cancer	WT	Horizons	0.291	2.94	>30
Daudi	Lymphoma	Mutant	Eurofins	0.1		
SW1353	Bone	Mutant	Eurofins	0.179		

MOLT-16	Leukemia	Mutant	Eurofins	0.35
U266B1	Myeloma	Mutant	Eurofins	8.8
SW-13	Adrenal gland	Mutant	Eurofins	9.13
SK-NEP-1	Kidney	Mutant	Eurofins	9.47
AN3 CA	Endometrium	Mutant	Eurofins	10.1
HLE	Liver	Mutant	Eurofins	10.5
DMS114	Lung	Mutant	Eurofins	10.6
Cal 27	Mouth	Mutant	Eurofins	11
MHH-PREB-1	Lymphoma	Mutant	Eurofins	11
HMCB	Skin	Mutant	Eurofins	11.7
HS 746T	Stomach	Mutant	Eurofins	11.7
DMS273	Lung	Mutant	Eurofins	11.8
RL95-2	Uterus	Mutant	Eurofins	11.9
RD	Soft tissue	Mutant	Eurofins	12.1
RKOE6	Colon	Mutant	Eurofins	12.1
SJRH30	Sarcoma	Mutant	Eurofins	12.2
CHL-1	Skin	Mutant	Eurofins	12.5
SK-N-AS	CNS	Mutant	Eurofins	12.5
Detroit 562	Pharynx	Mutant	Eurofins	12.8
SW1783	Brain	Mutant	Eurofins	21.1
Hs 578T	Breast	Mutant	Eurofins	23.9
5637	Bladder	Mutant	Eurofins	>30
639-V	Ureter	Mutant	Eurofins	>30
647-V	Bladder	Mutant	Eurofins	>30
786-O	Kidney	Mutant	Eurofins	>30
A431	Vulva	Mutant	Eurofins	>30
A-673	Bone	Mutant	Eurofins	>30
ARH-77	Myeloma	Mutant	Eurofins	>30
BE(2)C	CNS	Mutant	Eurofins	>30
BFTC-905	Bladder	Mutant	Eurofins	>30
BHT-101	Thyroid	Mutant	Eurofins	>30
BM-1604	Prostrate	Mutant	Eurofins	>30
BT20	Breast	Mutant	Eurofins	>30
BT-549	Breast	Mutant	Eurofins	>30
BxPC-3	Pancreas	Mutant	Eurofins	>30
C-33A	Cervix	Mutant	Eurofins	>30
CAL-62	Thyroid	Mutant	Eurofins	>30
Calu1	Lung	Mutant	Eurofins	>30
Calu6	Lung	Mutant	Eurofins	>30
CAMA-1	Breast	Mutant	Eurofins	>30
Capan-1	Pancreas	Mutant	Eurofins	>30
Capan-2	Pancreas	Mutant	Eurofins	>30
CCRFCM	Leukemia	Mutant	Eurofins	>30
CEM-C1	Leukemia	Mutant	Eurofins	>30
CFPAC-1	Pancreas	Mutant	Eurofins	>30
CGTH-W-1	Thyroid	Mutant	Eurofins	>30
ChaGoK1	Lung	Mutant	Eurofins	>30
Colo 201	Colon	Mutant	Eurofins	>30

Colo 205	Colon	Mutant	Eurofins	>30
Colo 320 HSR	Colon	Mutant	Eurofins	>30
Colo 320DM	Colon	Mutant	Eurofins	>30
COR-L23	Lung	Mutant	Eurofins	>30
Daoy	CNS	Mutant	Eurofins	>30
DB	Lymphoma	Mutant	Eurofins	>30
DLD-1	Colon	Mutant	Eurofins	>30
DMS53	Lung	Mutant	Eurofins	>30
DU145	Prostrate	Mutant	Eurofins	>30
EB-3	Lymphoma	Mutant	Eurofins	>30
EFM-19	Breast	Mutant	Eurofins	>30
EM-2	Leukemia	Mutant	Eurofins	>30
ES-2	Ovary	Mutant	Eurofins	>30
FaDu	Pharynx	Mutant	Eurofins	>30
HCT-15	Colon	Mutant	Eurofins	>30
HEC-1-A	Endometrium	Mutant	Eurofins	>30
HEL-92-1-7	Leukemia	Mutant	Eurofins	>30
HLF	Liver	Mutant	Eurofins	>30
HOS	Bone	Mutant	Eurofins	>30
HPAF-II	Pancreas	Mutant	Eurofins	>30
HT	Lymphoma	Mutant	Eurofins	>30
HT1376	Bladder	Mutant	Eurofins	>30
HT-29	Colon	Mutant	Eurofins	>30
HT-3	Cervix	Mutant	Eurofins	>30
HuCCT1	Biliary duct	Mutant	Eurofins	>30
HuP-T4	Pancreas	Mutant	Eurofins	>30
J82	Bladder	Mutant	Eurofins	>30
J-RT3-T3-5	Leukemia	Mutant	Eurofins	>30
Jurkat	Leukemia	Mutant	Eurofins	>30
K562	Leukemia	Mutant	Eurofins	>30
KATO III	Stomach	Mutant	Eurofins	>30
KHOS-240S	Bone	Mutant	Eurofins	>30
KLE	Uterus	Mutant	Eurofins	>30
L-428	Lymphoma	Mutant	Eurofins	>30
LS1034	Large intestine	Mutant	Eurofins	>30
MC-IXC	CNS	Mutant	Eurofins	>30
MDA MB 231	Breast	Mutant	Eurofins	>30
MDA MB 453	Breast	Mutant	Eurofins	>30
MDA MB 468	Breast	Mutant	Eurofins	>30
MEG01	Leukemia	Mutant	Eurofins	>30
MeWo	Skin	Mutant	Eurofins	>30
MG-63	Bone	Mutant	Eurofins	>30
NCI-H295R	Adrenal gland	Mutant	Eurofins	>30
NCIH441	Lung	Mutant	Eurofins	>30
NCIH446	Lung	Mutant	Eurofins	>30
NCI-H520	Lung	Mutant	Eurofins	>30
NCI-H596	Lung	Mutant	Eurofins	>30
NCI-H661	Lung	Mutant	Eurofins	>30

NCI-H69	Lung	Mutant	Eurofins	>30
NCI-H747	caecum	Mutant	Eurofins	>30
OE19	Esophagus	Mutant	Eurofins	>30
OE21	oesophagus	Mutant	Eurofins	>30
PC-3	Prostrate	Mutant	Eurofins	>30
Raji	Lymphoma	Mutant	Eurofins	>30
Ramos (RA 1)	Lymphoma	Mutant	Eurofins	>30
RPMI 8226	Myeloma	Mutant	Eurofins	>30
SaOS2	Bone	Mutant	Eurofins	>30
SCaBER	Urinary Tract	Mutant	Eurofins	>30
SCC-25	Mouth	Mutant	Eurofins	>30
SCC-4	mouth	Mutant	Eurofins	>30
SCC-9	mouth	Mutant	Eurofins	>30
SHP-77	Lung	Mutant	Eurofins	>30
SK-LMS-1	Soft tissue	Mutant	Eurofins	>30
SK-MEL-1	Skin	Mutant	Eurofins	>30
SK-MEL-28	Skin	Mutant	Eurofins	>30
SK-MEL-3	Skin	Mutant	Eurofins	>30
SKMES1	Lung	Mutant	Eurofins	>30
SK-N-DZ	CNS	Mutant	Eurofins	>30
SK-N-FI	CNS	Mutant	Eurofins	>30
SKOV3	Ovary	Mutant	Eurofins	>30
SK-UT-1	Soft tissue	Mutant	Eurofins	>30
SNB-19	CNS	Mutant	Eurofins	>30
SNU-16	Stomach	Mutant	Eurofins	>30
SNU-5	Stomach	Mutant	Eurofins	>30
ST486	Lymphoma	Mutant	Eurofins	>30
SU.86.86	Pancreas	Mutant	Eurofins	>30
SW1088	CNS	Mutant	Eurofins	>30
SW1417	Colon	Mutant	Eurofins	>30
SW1463	Rectum	Mutant	Eurofins	>30
SW403	Colon	Mutant	Eurofins	>30
SW579	Thyroid	Mutant	Eurofins	>30
SW620	Colon	Mutant	Eurofins	>30
SW684	Soft tissue	Mutant	Eurofins	>30
SW837	Rectum	Mutant	Eurofins	>30
SW872	Soft tissue	Mutant	Eurofins	>30
SW900	Lung	Mutant	Eurofins	>30
SW948	Colon	Mutant	Eurofins	>30
SW954	Vulva	Mutant	Eurofins	>30
SW962	Vulva	Mutant	Eurofins	>30
T24	Urinary Tract	Mutant	Eurofins	>30
T47D	Breast	Mutant	Eurofins	>30
T98G	CNS	Mutant	Eurofins	>30
TCCSUP	Urinary Tract	Mutant	Eurofins	>30
Thp1	Leukemia	Mutant	Eurofins	>30
U-138MG	Brain	Mutant	Eurofins	>30
UM-UC-3	Bladder	Mutant	Eurofins	>30

WiDr	Colon	Mutant	Eurofins	>30
YAPC	Pancreas	Mutant	Eurofins	>30
AGS	Stomach	WT	Eurofins	0.03
D283 Med	CNS	WT	Eurofins	0.04
U-87 MG	CNS	WT	Eurofins	0.04
DBTRG-05MG	CNS	WT	Eurofins	0.05
SNU-1	Stomach	WT	Eurofins	0.05
G-402	Kidney	WT	Eurofins	0.05
G-401	Kidney	WT	Eurofins	0.06
DOHH-2	Lymphoma	WT	Eurofins	0.06
A172	CNS	WT	Eurofins	0.07
A375	Skin	WT	Eurofins	0.07
H4	CNS	WT	Eurofins	0.08
SW982	Sarcoma	WT	Eurofins	0.0783
HCT-8	Colon	WT	Eurofins	0.09
CRO-AP2	Lymphoma	WT	Eurofins	0.09
Caki-1	Kidney	WT	Eurofins	0.1
KPL-1	Breast	WT	Eurofins	0.106
CHP-212	CNS	WT	Eurofins	0.12
SR	Lymphoma	WT	Eurofins	0.12
Hs 294T	Skin	WT	Eurofins	0.125
U2OS	Bone	WT	Eurofins	0.13
HT-1080	Soft tissue	WT	Eurofins	0.13
NCI-H292	Lung	WT	Eurofins	0.13
BV-173	Leukemia	WT	Eurofins	0.14
RKO-AS45-1	Colon	WT	Eurofins	0.15
MALME3M	Skin	WT	Eurofins	0.16
A204	Soft tissue	WT	Eurofins	0.19
A498	Kidney	WT	Eurofins	0.2
RKO	Colon	WT	Eurofins	0.21
JEG-3	Placenta	WT	Eurofins	0.21
MOLT-3	Leukemia	WT	Eurofins	0.21
COR-L105	Lung	WT	Eurofins	0.21
COLO 829	Skin	WT	Eurofins	0.22
C32TG	Skin	WT	Eurofins	0.23
Caki-2	Kidney	WT	Eurofins	0.25
SH-4	Skin	WT	Eurofins	0.26
22Rv1	Prostrate	WT	Eurofins	0.27
HepG2	Liver	WT	Eurofins	0.27
NALM-6	Leukemia	WT	Eurofins	0.28
MES-SA	Soft tissue	WT	Eurofins	0.31
MT-3	Breast	WT	Eurofins	0.31
SJSA1	Bone	WT	Eurofins	0.33
DK-MG	CNS	WT	Eurofins	0.33
A549	Lung	WT	Eurofins	0.38
CML-T1	Leukemia	WT	Eurofins	0.39
MCF7	Breast	WT	Eurofins	0.41
HT-1197	Bladder	WT	Eurofins	0.411

Hs 695T	Skin	WT	Eurofins		0.44
RPMI 6666	Lymphoma	WT	Eurofins		0.45
ACHN	Kidney	WT	Eurofins		0.47
A427	Lung	WT	Eurofins		0.55
BC-1	Lymphoma	WT	Eurofins		0.55
SW48	Colon	WT	Eurofins		0.552
JAR	Placenta	WT	Eurofins		0.66
LNCaP	Prostrate	WT	Eurofins		0.77
769-P	Kidney	WT	Eurofins		0.77
NCI-H460	Lung	WT	Eurofins		1.09
BeWo	Placenta	WT	Eurofins		1.66
Y79	Eye	WT	Eurofins		2.15
CCF-STTG1	CNS	WT	Eurofins		3.6
BPH1	Prostrate	WT	Eurofins	Yes	>30
C-4 I	Cervix	WT	Eurofins	Yes	>30
C-4 II	Cervix	WT	Eurofins	Yes	>30
DoTc2 4510	Cervix	WT	Eurofins	Yes	>30
HeLa	Cervix	WT	Eurofins	Yes	>30
SiHa	Cervix	WT	Eurofins	Yes	>30

Supplementary Table 2.

MCF-7 ALRN-6924 + Paclitaxel vs Control IPA analysis – Top Canonical Pathways

Name	p-value
p53 Signaling	9.59E-06
Estrogen-mediated S-phase Entry	5.82E-05
Cell-cycle: G1/S Checkpoint Regulation	3.92E-04
Small Cell Lung Cancer Signaling	4.40E-04
Cyclins and Cell cycle Regulation	5.73E-04