

Supplementary Materials

Synthesis and biological activity of a VHL-based PROTAC specific for p38 α

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Figure S1. ^1H and ^{13}C NMR spectra and HPLC chromatograms of **NR-11a**.

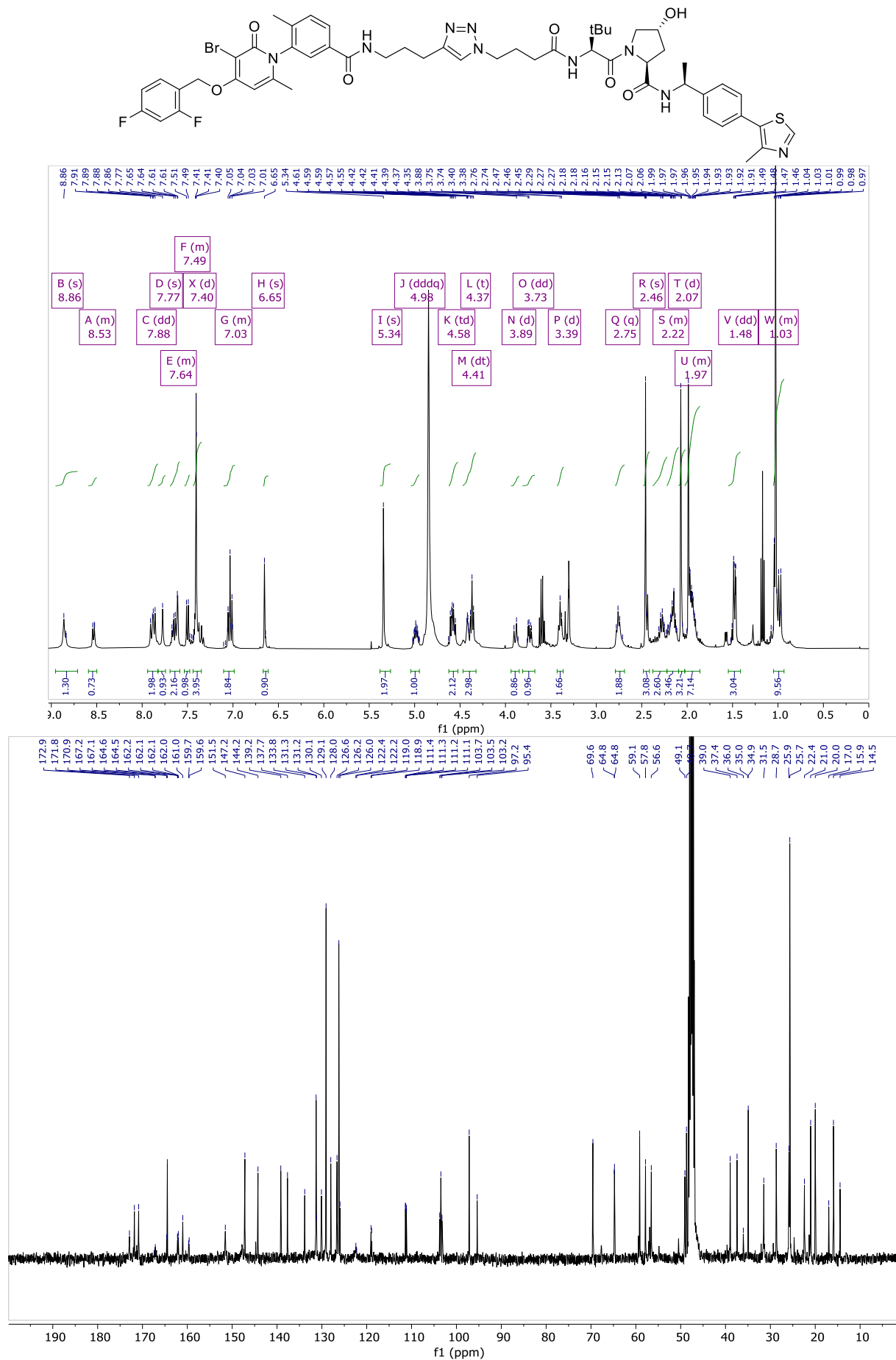
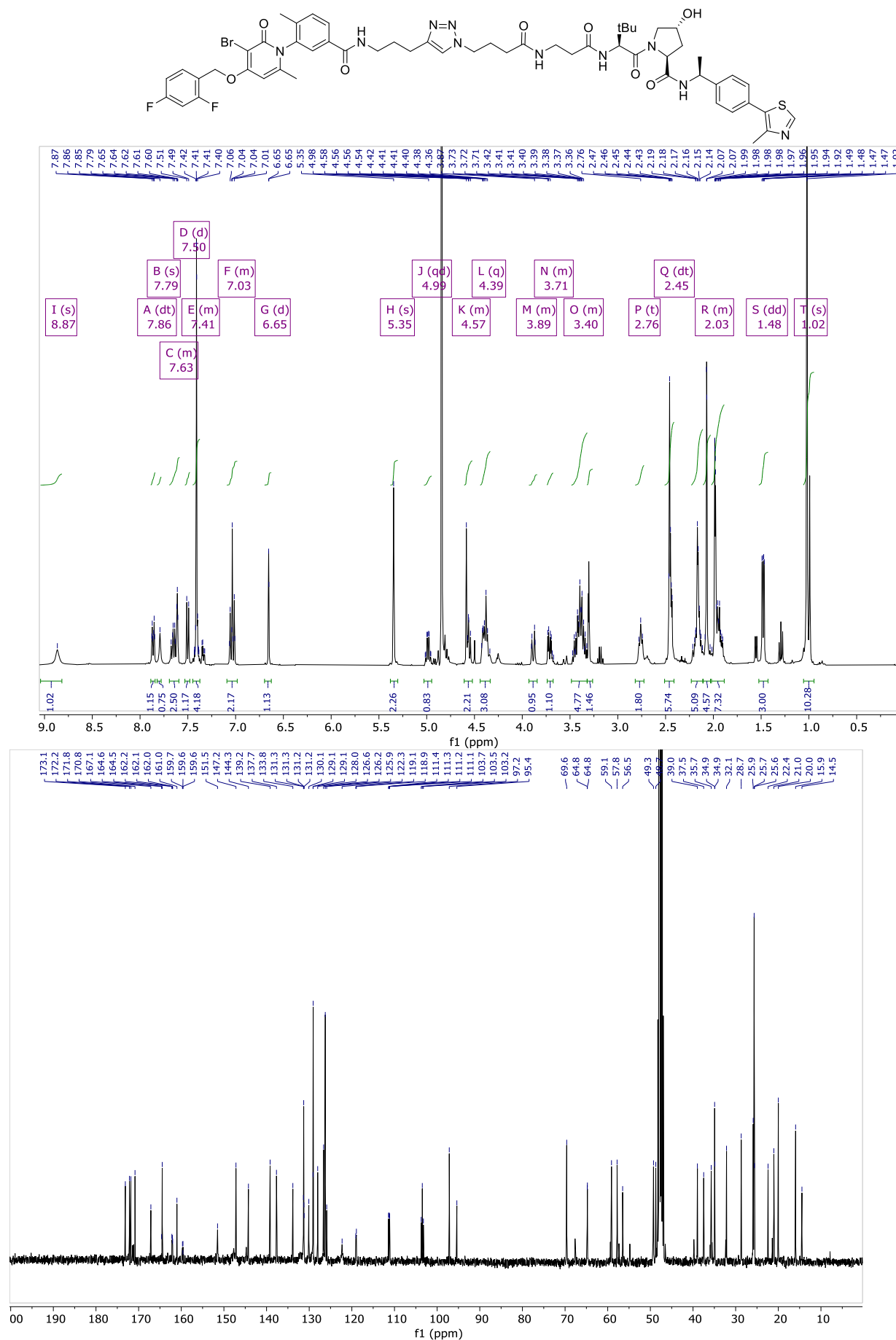
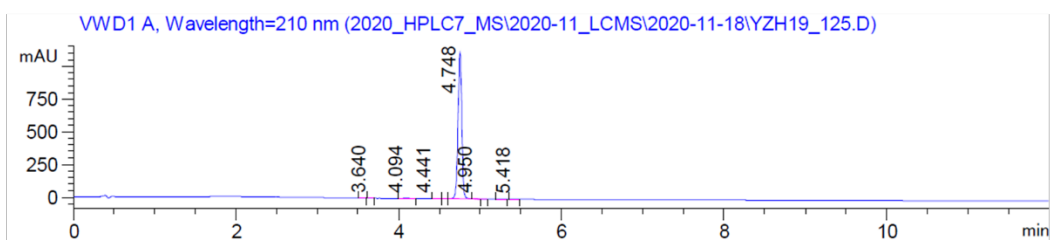


Figure S2. ^1H and ^{13}C NMR spectra and HPLC chromatograms of NR-11b.

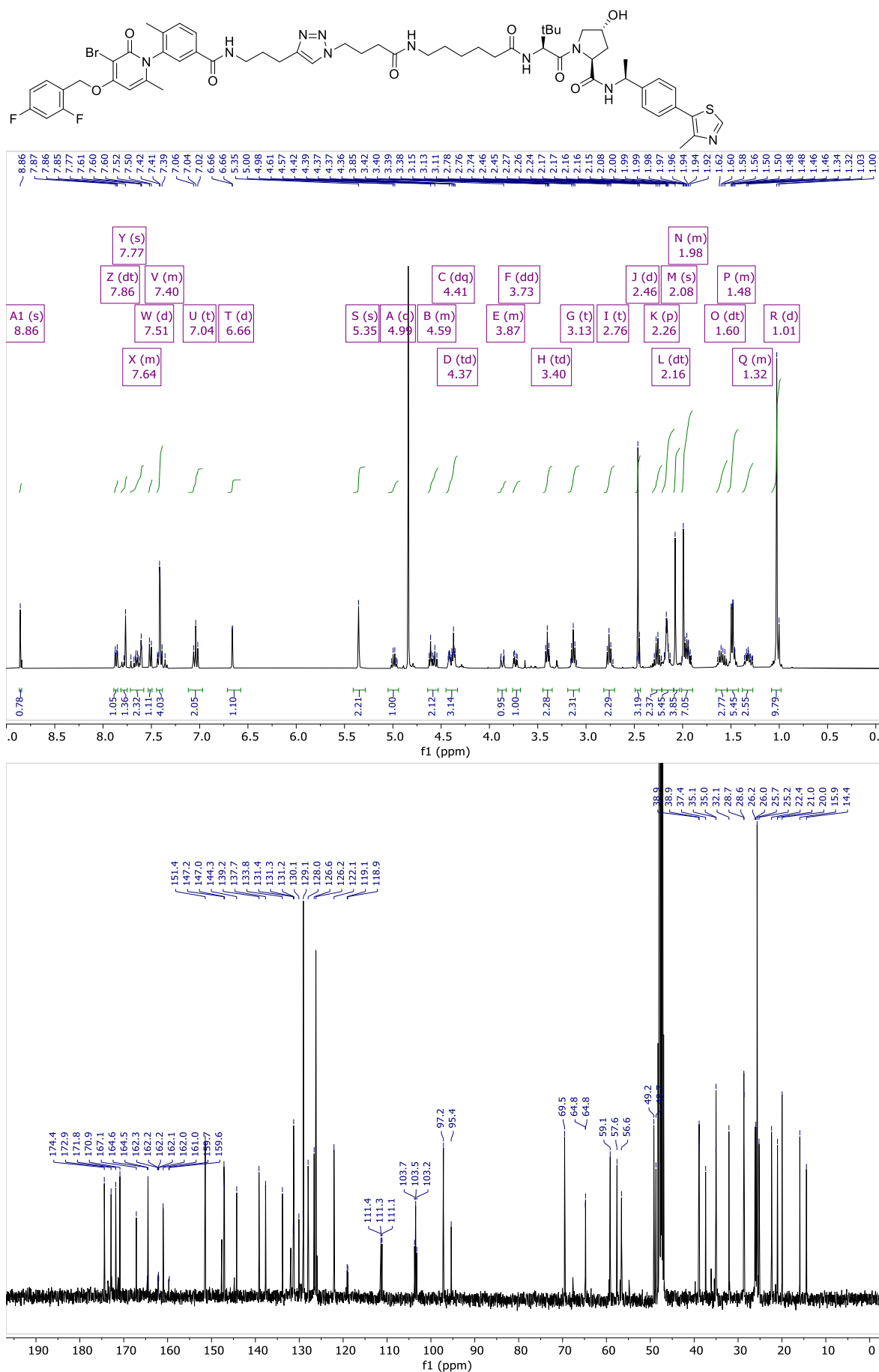
Injection date: 11/18/2020 9:10:44 PM 1.5 ml/min
 Sample Name: YZH19 1.0uL
 Acq Operator: Analyst 57
 Analysis method: C:\Chem32\1\Methods\1W_4_KN50_01_GD95B10F1-5S11_T40P.M 281bar

Method Info Kinetex EVO C18 50x 4.6mm, 2.6um; Mobile phase: 10mM
 NH4HCO3 pH8 / ACN (95:5)--0.5min---(95:5)---6.5min----(0:
 100)---2min----(0:100) post run 1.5 min

Sample Info: Aprox. 1 mg/mL ACN
 Walkup method: 'M1_Positive_Standard'
 Target:



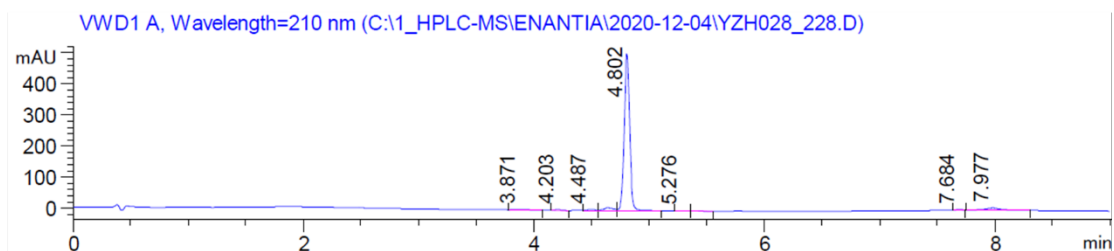
#	Meas.	Ret	Peak	Width	Area	Response
1		3.543	MM	0.056	2.147	0.059
2		3.640	MM	0.044	2.193	0.061
3		4.094	BB	0.057	24.734	0.683
4		4.441	MF	0.073	1.724	0.048
5		4.572	MF	0.056	5.836	0.161
6		4.748	FM R	0.053	3.570e3	98.567
7		4.950	MM T	0.064	2.101	0.058
8		5.243	BB	0.047	5.987	0.165
9		5.418	BV	0.053	7.190	0.198

Figure S3. ^1H and ^{13}C NMR spectra and HPLC chromatograms of **NR-11c**.

Injection date:	12/4/2020	7:51:21 PM	1.0uL
Sample Name:	YZH028		81
Acq Operator:	Analyst		225bar
Analysis method:	C:\Chem32\1\Methods\1W 4 KN50 01 GD95B10F1-5S11 T40P.M		

Method Info Kinetex EVO C18 50x 4.6mm, 2.6um; Mobile phase: 10mM
NH4HCO3 pH8 / ACN (95:5)--0.5min---(95:5)---6.5min---(0:
100)---2min---(0:100) post run 1.5 min

Sample Info: Aprox. 1 mg/mL MeOH
Walkup method: 'M1_Positive_Standard'
Target:



#	Meas.	Ret	Peak	Width	Area	Response
1	3.871	BB	0.095	17.074	0.925	
2	4.203	VB	0.052	9.677	0.524	
3	4.487	BV	0.064	15.761	0.854	
4	4.635	VV	0.082	54.632	2.961	
5	4.802	VB	0.050	1.663e3	90.121	
6	5.276	BV	0.054	3.558	0.193	
7	5.415	VB	0.055	7.088	0.384	
8	7.684	MM	0.052	4.341	0.235	
9	7.977	MF	0.162	70.140	3.802	

Figure S4. HPLC chromatograms of NR-11c*.

Datafile: C:\1\DATA\2021_HPLC7-MS\2111_HPLC7-MS\2021-11-03\GL796_27.D

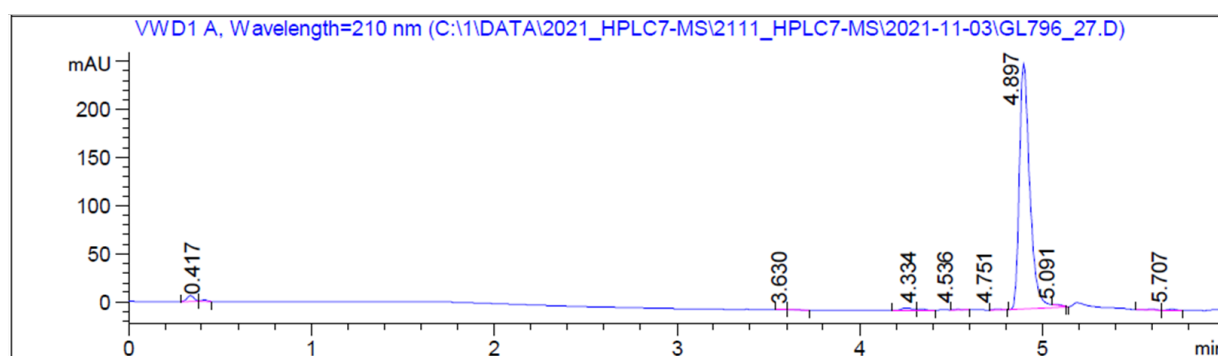
Injection date: 03-Nov-21 11:31:45 Flow: 1.5ml/min 1.0uL
 Sample Name: GL796 Pos: 27 351bar
 Analysis method: C:\1\Methods\1W_4_KN50_01_GD95B_L210F1-5S11_T40P.M

Kinetex EVO C18 50x 4.6mm, 2.6um; Mobile phase: 10mM NH₄HCO₃ pH8 / ACN (95:5)--0.5min---(95:5)---6.5min----(0:100)---2min----(0:100) post run 1.5 min; T^a40°C

Aprox. 1 mg/mL MeOH

Walkup method: 'M1_Positive_Standard_9min'

Target:



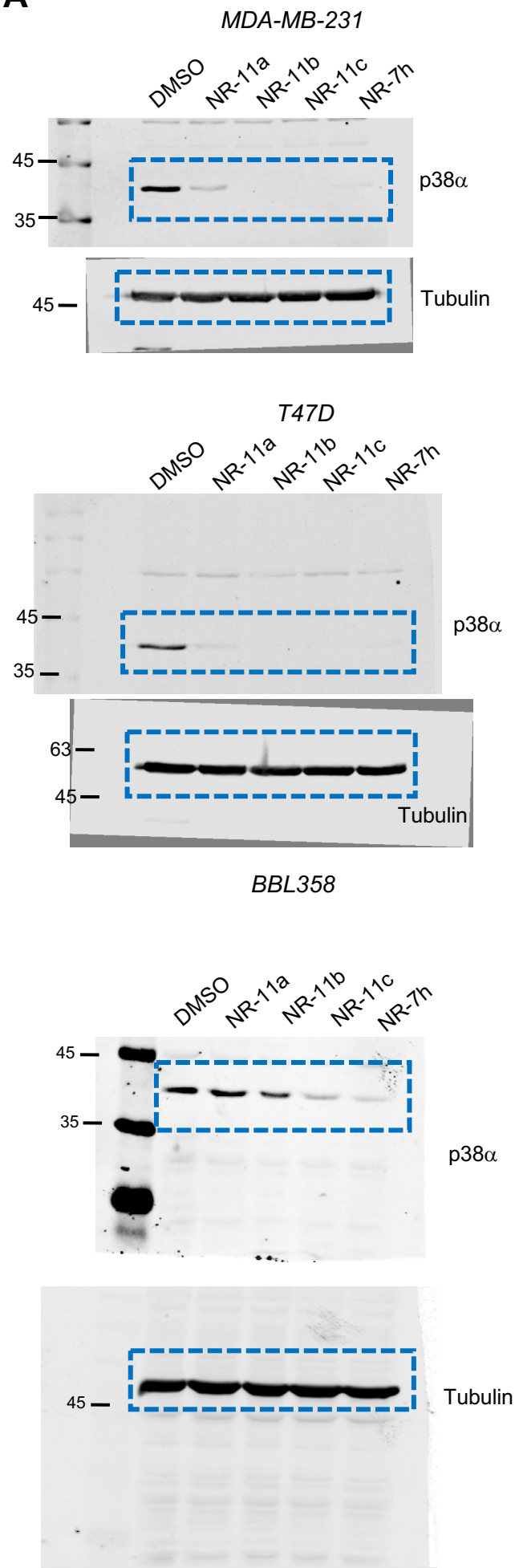
Signal: 2-> : VWD1 A, Wavelength=210 nm

#	Meas. Ret. Time	Area	Area %

1	0.338	15.26	1.44
2	0.417	3.14	0.30
3	3.572	1.17	0.11
4	3.630	1.26	0.12
5	4.254	10.62	1.00
6	4.334	4.83	0.46
7	4.536	2.30	0.22
8	4.751	2.56	0.24
9	4.897	1009.97	95.14
10	5.091	2.71	0.26
11	5.601	4.34	0.41
12	5.707	3.36	0.32

Figure 2

A



B

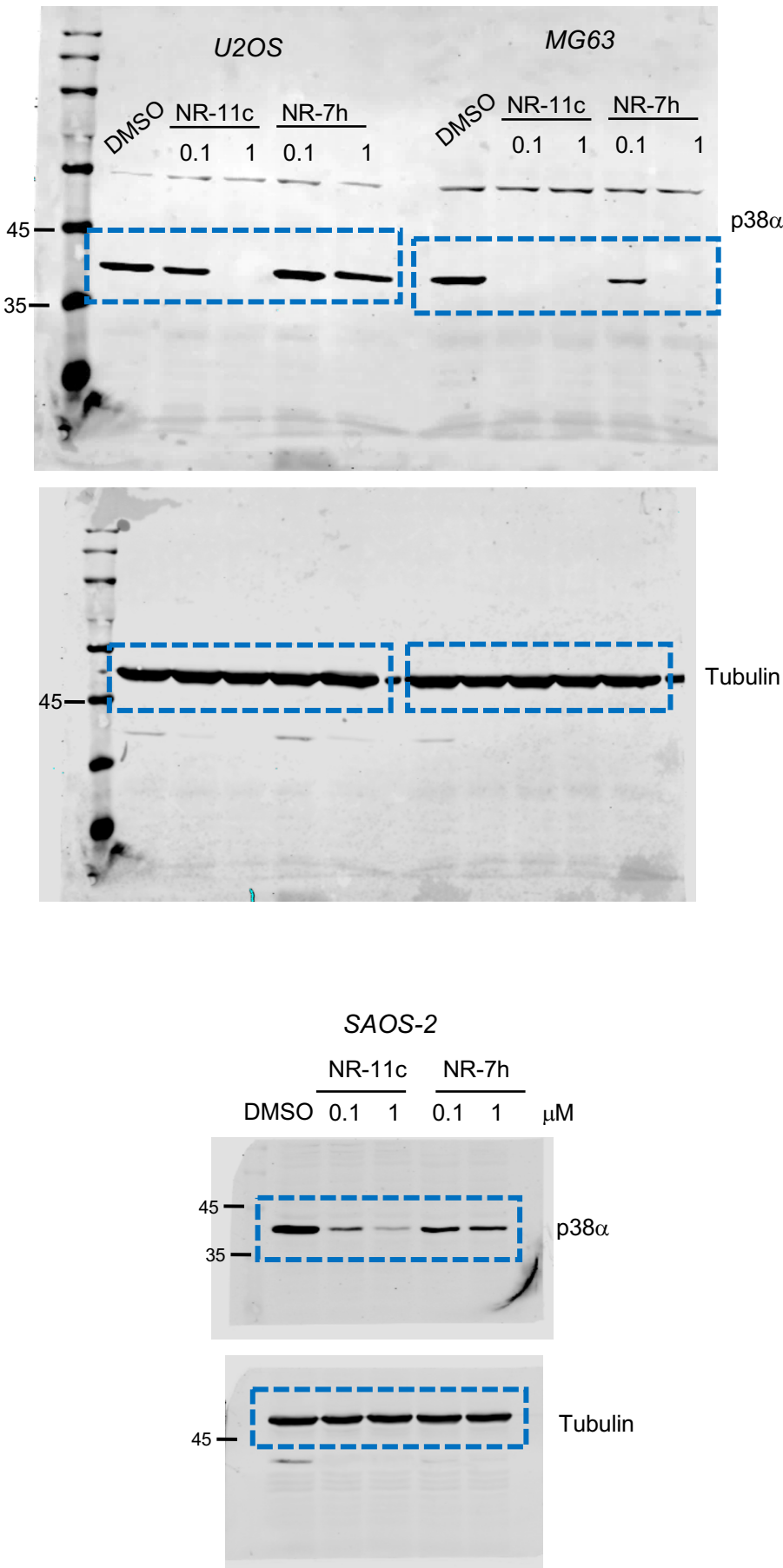


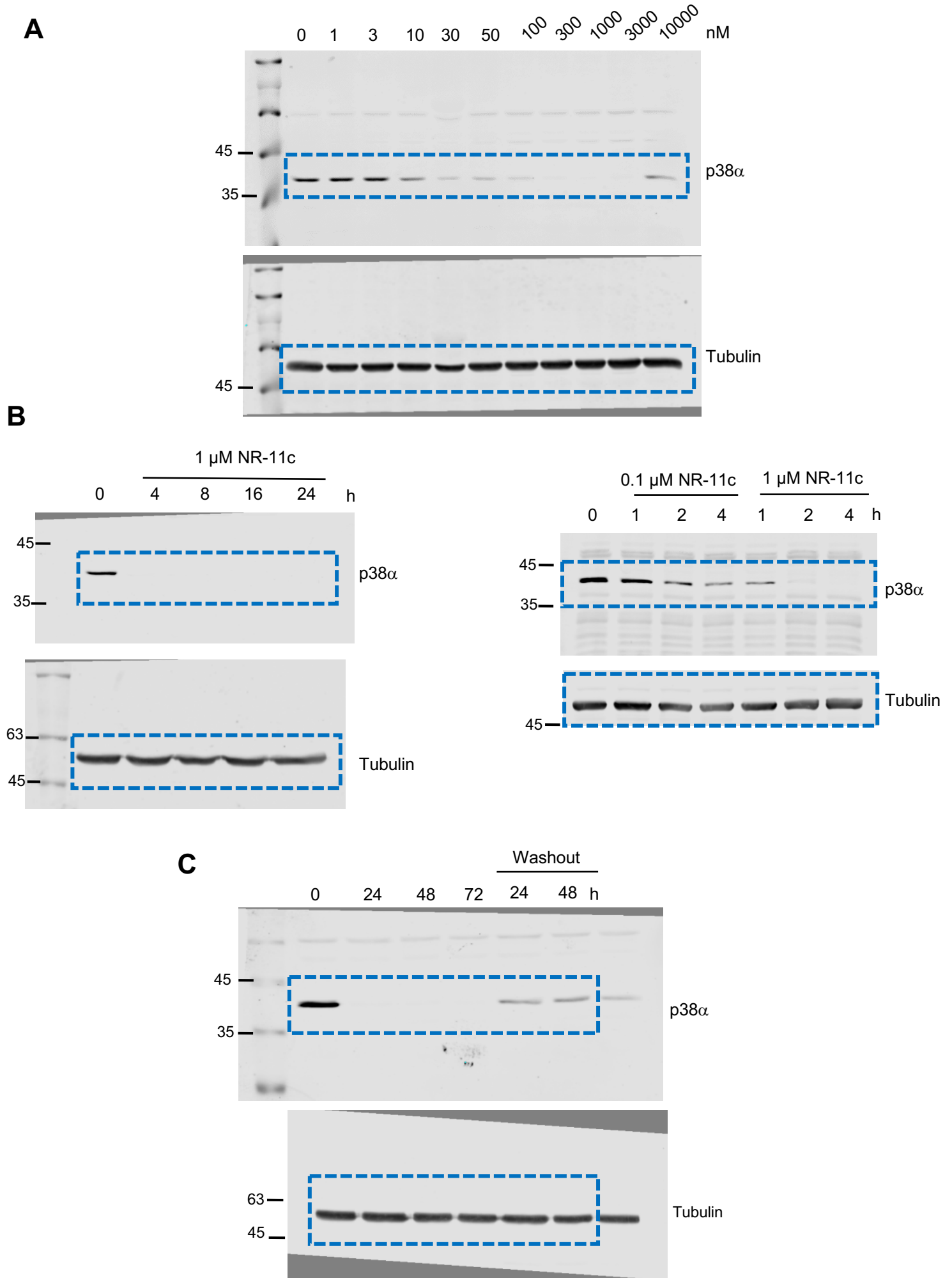
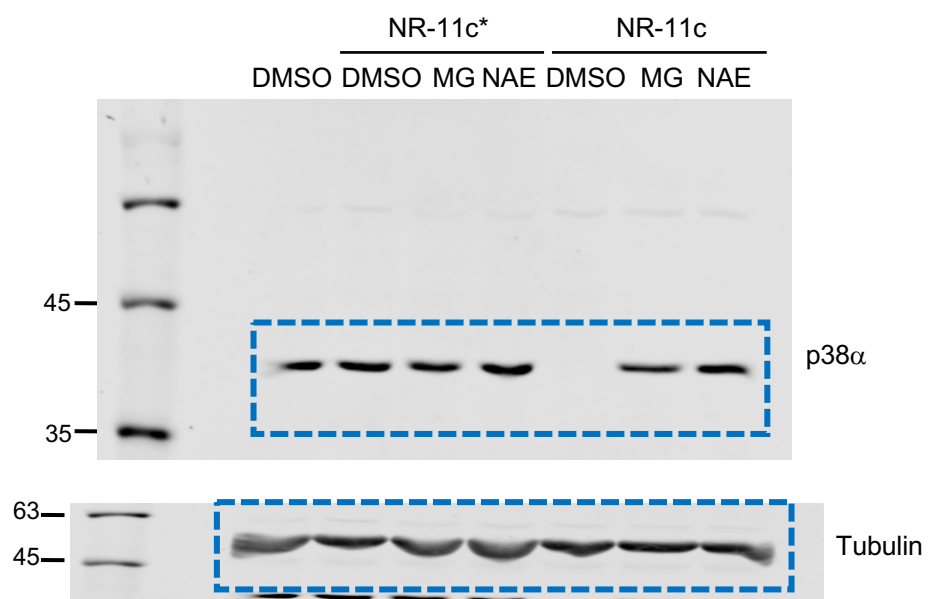
Figure 3

Figure 4**A****C**

DMSO NR-11c* NR-11c siRNA

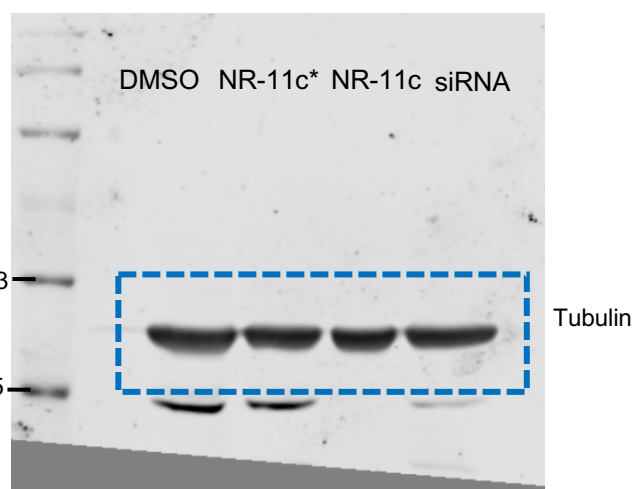
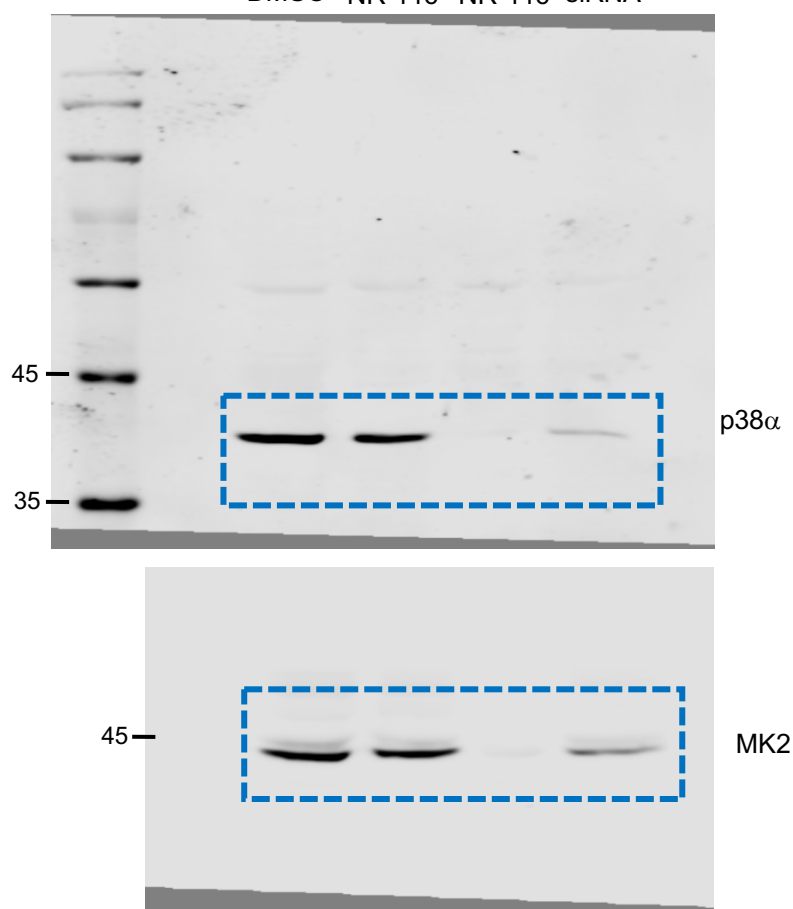


Figure 5

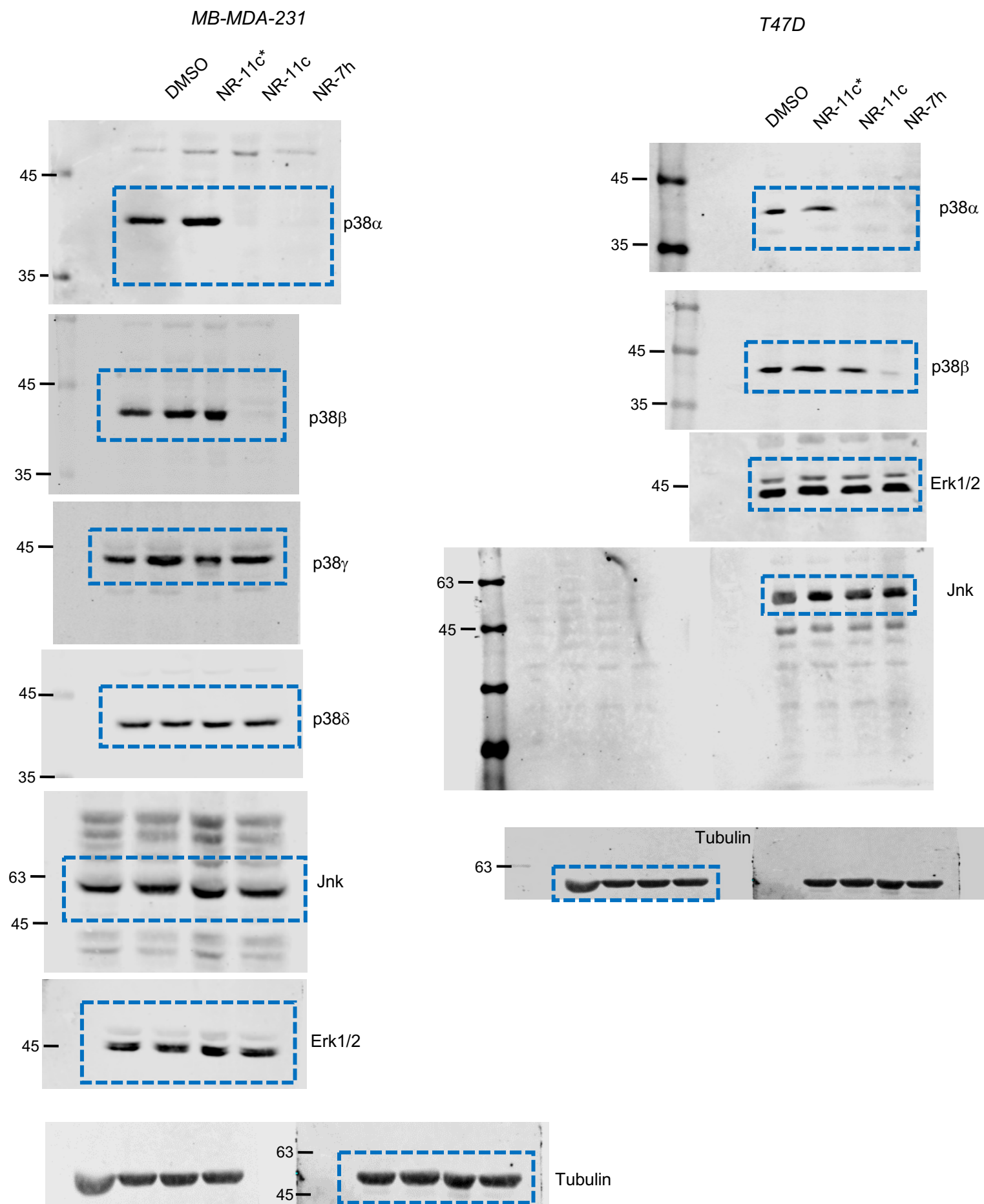
A

Figure 6

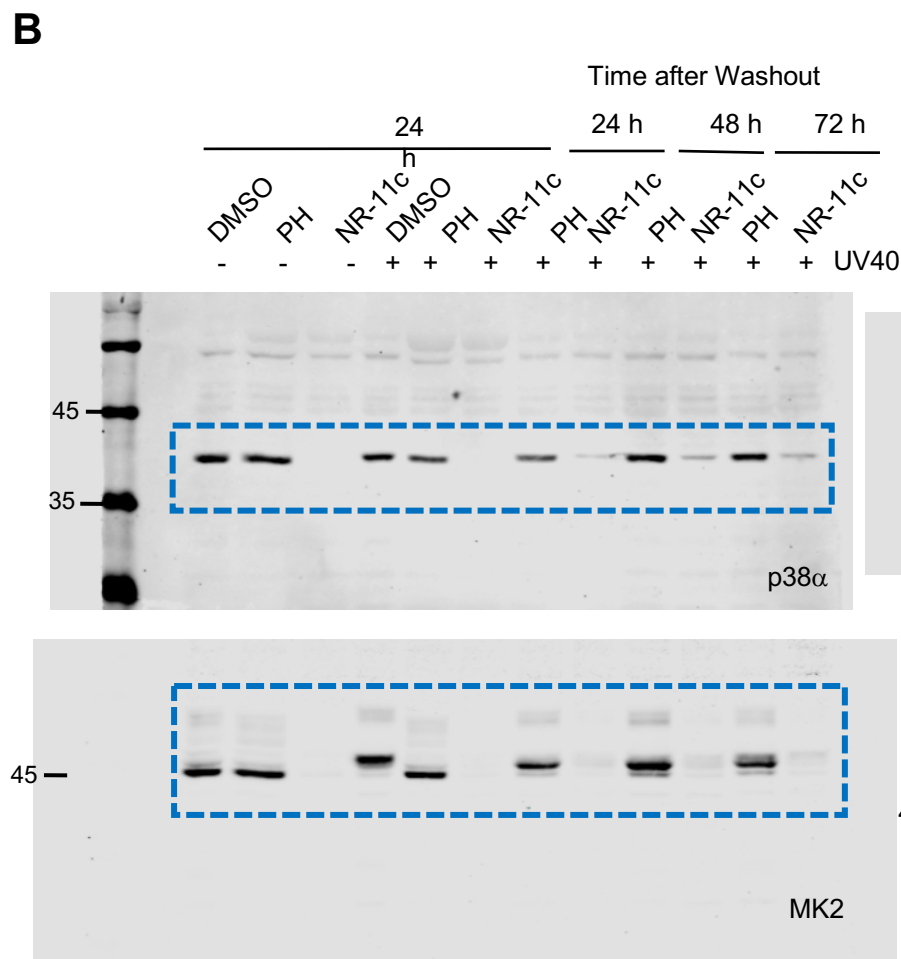
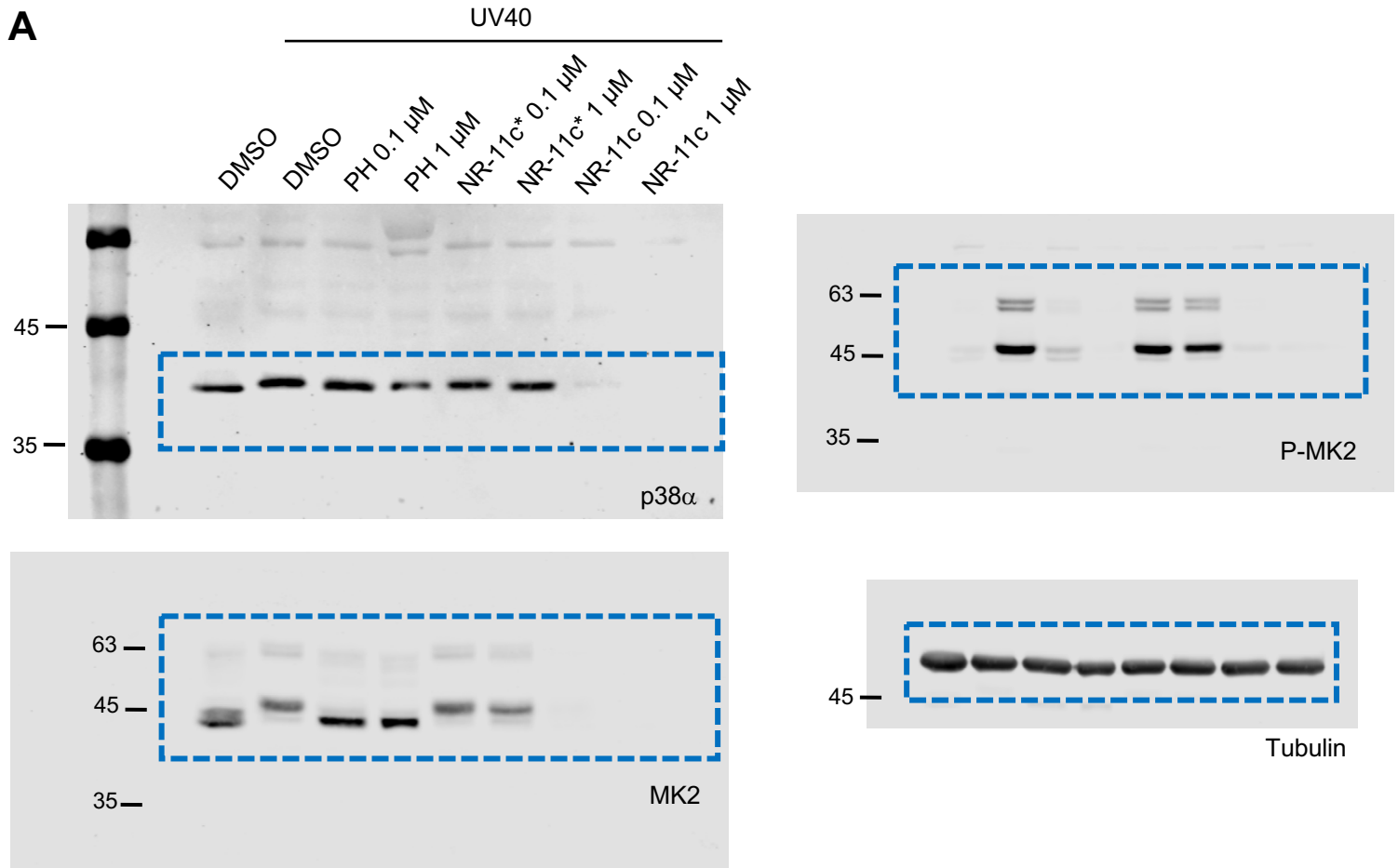


Figure 7