

## **Supplemental Information**

### **Chemically Induced Degradation of Epigenetic Targets**

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## Summary Table 1: Heterobifunctional degraders for epigenetic targets

Epigenetic Effector	Target (POI)	Compound	E3 Ligase	Disease	DC <sub>50</sub> <sup>a</sup>	Time <sup>b</sup>	In-vivo study	Ref <sup>c</sup>
<b>Writers</b>	EZH2	MS1943	-	TNBC	~2.5 $\mu$ M	24h	Yes	35
		E7	CRBN	DLBCL	~1 $\mu$ M	48h	No	37
		YM181	VHL	DLBCL	~1 $\mu$ M	48h	No	39
		YM281	VHL	DLBCL	~1 $\mu$ M	48h	Yes	39
		MS177	CRBN	AML	0.2 $\mu$ M	16h	Yes	15

		U3i	CRBN	TNBC	~1 $\mu$ M	48h	No	40
		MS8815	VHL	TNBC	0.14 $\mu$ M	48h	No	41
	WDR5	8g	VHL	AML	0.056 $\mu$ M	24h	No	50
		17b	VHL	AML	1.24 $\mu$ M	24h	No	50
		MS33	VHL	AML	0.26 $\mu$ M	18h	No	51
		MS67	VHL	AML	0.0037 $\mu$ M	18h	Yes	51
		MS40	CRBN	AML	0.05 $\mu$ M	18h	Yes	52
	NSD3	MS9715	VHL	AML	4.9 $\mu$ M	48h	No	62

		Compound 8	VHL	NSCLC	1.43 $\mu$ M	72h	Yes	63
	NSD2	MS159	CRBN	MM	5.2 $\mu$ M	48h	No	65
	PRMT5	MS4322	VHL	Multiple cancer	1.1 $\mu$ M	6 days	No	72
	PCAF/GCN5	GSK983	CRBN	Inflammation	PCAF – 0.0015 $\mu$ M GCN5 – 0.003 $\mu$ M	5 days	No	81
	P300/CBP	dCBP-1	CRBN	MM	~ 0.001 $\mu$ M	6h	No	82
		JQAD1	CRBN	NB	~ 3 $\mu$ M	24h	Yes	85

Readers	BRD4	MZ1	VHL	-	0.1 $\mu$ M	24h	No	99
		AT1	VHL	-	$\sim$ 1 $\mu$ M	24h	No	19
		ARV-771	VHL	CRPC	0.005 $\mu$ M	16h	Yes	100
		MZP-54	VHL	AML	< 0.05 $\mu$ M	24h	No	101
		dBET1	CRBN	AML	<0.1 $\mu$ M	18h	Yes	103
		dBET6	CRBN	AML	<0.1 $\mu$ M	3h	Yes	105
		ARV-825	CRBN	CCA	<0.001 $\mu$ M	24h	No	104
		BETd-260	CRBN	AML	<0.001 $\mu$ M	3h	Yes	106

		QCA570	CRBN	AML	<0.001 $\mu$ M	3h	Yes	108
		Compound 15	CRBN	AML	<0.001 $\mu$ M	3h	No	109
	EED	UNC6852	VHL	DLBCL	0.247 $\mu$ M	24h	No	117
		PROTAC 1/2	VHL	NHL	~0.12 $\mu$ M	48h	No	119
	BMI1/RING1B	MS147	VHL	Multiple cancers	~5 $\mu$ M	24h	No	126
	TRIM24	dTRIM24	VHL	AML	~5 $\mu$ M	24h	No	133
	BRD9	dBRD9	CRBN	AML	0.05 $\mu$ M	4h	No	143
	BRD7/9	VZ185	VHL	DLBCL	BRD7 – 0.0045 $\mu$ M  GCN5 – 0.00176 $\mu$ M	4h	No	145

	SMARCA2/4	ACBI1	VHL	AML	SMARCA2 - 0.006 $\mu$ M SMARCA4 - 0.011 $\mu$ M	18h	No	151
		AU-15330	VHL	CRPC	~1 $\mu$ M	8h	Yes	152
		ACBI2	VHL	NSCLC	SMARCA2 - 0.001 $\mu$ M SMARCA4 - 0.032 $\mu$ M	18h	Yes	154
		A947	VHL	NSCLC	SMARCA2 <0.001 $\mu$ M SMARCA4 - 0.0011 $\mu$ M	18h	Yes	155
	ENL	SR-1114	CRBN	AML	10 $\mu$ M	16h	No	167
		Compound 1	CRBN	AML	0.037 $\mu$ M	24h	Yes	168

Erasers	HDAC1/2/3	Compound 4	VHL	CC	<0.1 $\mu\text{M}$	24h	No	176
	HDAC3	XZ9002	VHL	TNBC	0.063 $\mu\text{M}$	14h	No	178
	HDAC6	dHDAC6	CRBN	Breast Cancer	0.034 $\mu\text{M}$	12h	No	179
		Compound 12d	CRBN	MM	0.0016 $\mu\text{M}$	6h	No	181
		NP8	CRBN	MM	0.0038 $\mu\text{M}$	24h	No	182
		Compound 3j	VHL	MM	0.0071 $\mu\text{M}$	6h	No	183
	SIRT2	Protac 12	CRBN	-	0.2 $\mu\text{M}$	4h	No	186

<sup>a</sup>DC<sub>50</sub> values were taken from the primary references when explicitly reported and DC50 values, when they were not reported by the primary references, were estimated based on the reported data such as Western Blots and shown in the table with “~” or “<” symbols.



<sup>b</sup> Time listed is the treatment time used to calculate DC50 when reported or it is the treatment time of the dose response data used for the DC50 estimation.

<sup>c</sup> References listed here refers to the citation in the main manuscript text.