Therapeutic horizons in the development of PROTAC-based EZH2 inhibitors: Recent achievements, comparative analysis, and future perspectives

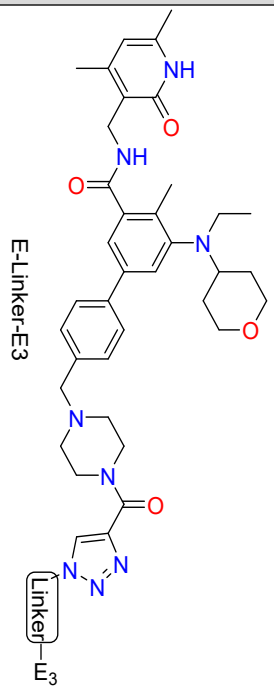
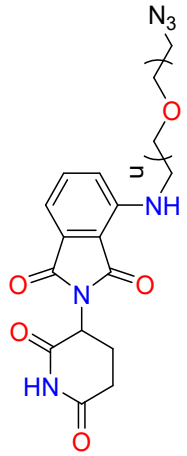
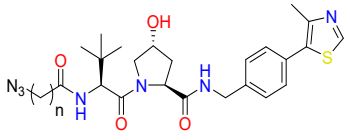
Supplementary file

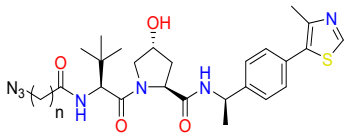
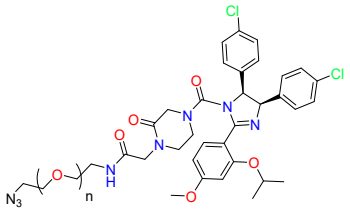
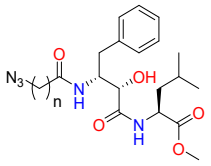
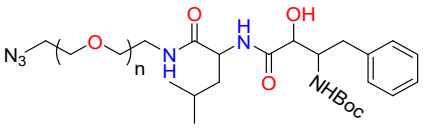
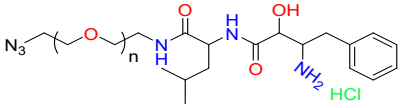
Table S1: Biochemical and cellular activities of PROTAC-based EZH2 inhibitors 19-25

ID	IC_{50} (μM) EZH2	IC_{50} for Cancer cells (μM)									
		NCI-BL209	Raji	Daudi	Namalwa	JVM-2	Jeko-1	MINO	SU-DHL-2	SU-DHL-4	SU-DHL-6
19	> 3.00	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
V2 (YM281 (20))	0.734	8.043	7.53	5.752	7.091	6.196	7.214	4.53	1.49	3.462	0.95
V3 (YM181 (21)	0.502	ND	ND	ND	ND	ND	ND	ND	3.991	5.098	2.006
23	> 3.00	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
22	> 3.00	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
25	> 5.00	ND	ND	ND	ND	ND	ND	ND	>10.00	>10.00	ND
YM620	> 5.00	ND	ND	ND	ND	ND	ND	ND	>5.00	ND	>5.00
Tazemetostat	*ND	>10.00	>10.00	>10.00	>10.00	>10.00	>10.00	11.70	2.37	4.286	0.4377

*ND = Not Determined

Table S2: The structures of PROTAC-based EZH2 inhibitors 46-69

Structure	Core structure	n	N_3-Linker-E3
	E-2P-T	2	
	E-3P-T	3	
	E-4P-T	4	
	E-5P-T	5	
	E-CH2-V1	1	

Structure	Core structure	n	N_3-Linker-E3
	E-5CH2-V1	5	
	E-CH2-V2	1	
	E-3CH2-V2	3	
	E-5CH2-V2	5	
	E-7CH2-V2	7	
	E-P-MDM2	1	
	E-2P-MDM2	2	
	E-3P-MDM2	3	
	E-4P-MDM2	4	
	E-CH2-B4	1	
	E-4W-CH2-B4	1	
	E-4W-3CH2-B4	3	
	E-4W-2P-B5	2	
	E-4W-3P-B5	3	
	E-4W-4P-B5	4	
	E-4W-2P-B5T	2	
	E-4W-3P-B5T (57)	3	
	E-4W-4P-B5T	4	

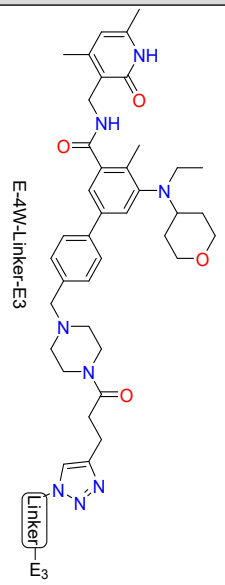
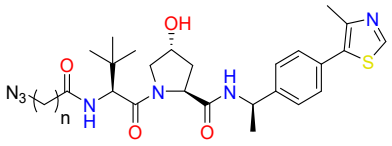
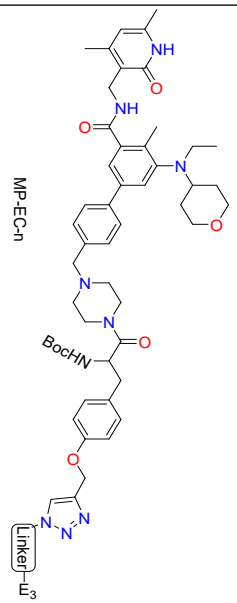
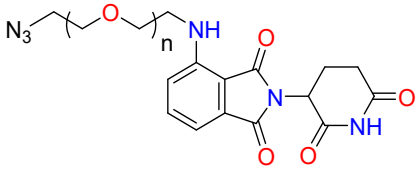
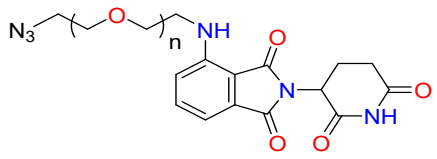
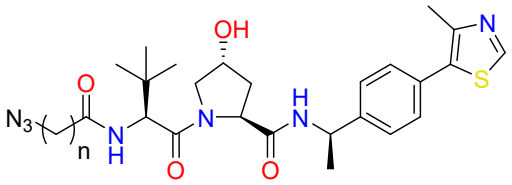
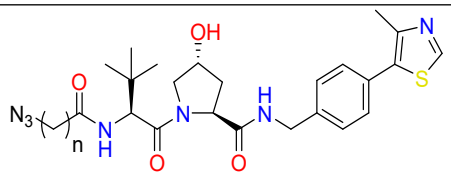
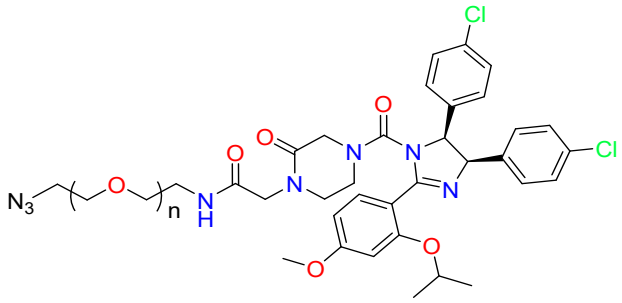
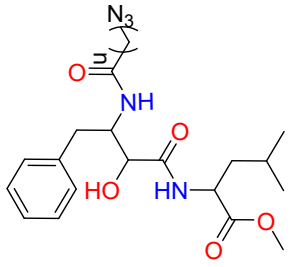
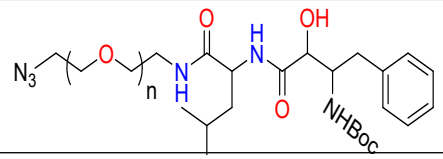
Structure	Core structure	n	N_3-Linker-E3
	E-4W-7CH2-V2	7	
	MP-EC-2	2	
	MP-EC-3	3	
	MP-EC-4	4	

Table S3: The structures of compounds N3-Linker-E3 for PROTAC-based EZH2 inhibitors 46-69

Compound	n	N_3-Linker-E3
N3-2P-T	2	
N3-3P-T	3	
N3-4P-T	4	
N3-5P-T	5	
N3-CH2-V2	1	
N3-3CH2-V2	3	
N3-5CH2-V2	5	
N3-7CH2-V2	7	
N3-CH2-V1	1	
N3-5CH2-V1	5	
N3-P-MDM2	1	
N3-2P-MDM2	2	
N3-3P-MDM2	3	
N3-4P-MDM2	4	
N3-CH2-B4	1	
N3-3CH2-B4	3	
N3-2P-B5	2	
N3-3P-B5	3	

Compound	n	N_3-Linker-E3
N3-4P-B5	4	