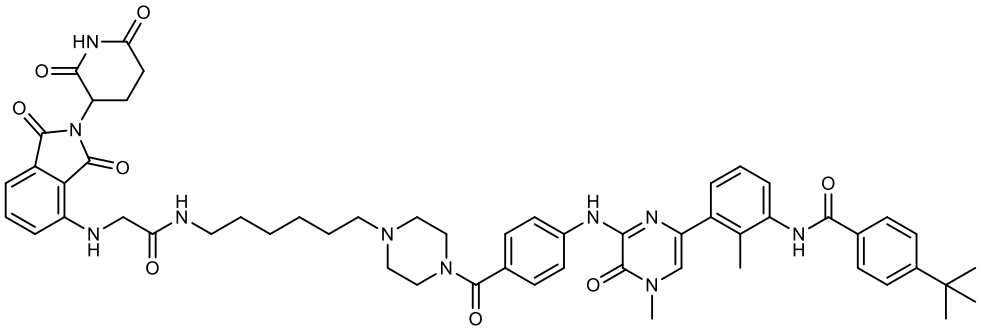
DD-03-171



Chemical Formula: $C_{55}H_{62}N_{10}O_8$
Molecular Weight: 991.16

Category	Parameter	Description
Compound	Name	DD-03-171
	Citation	*Blood*. 133(9):952-961 (2019) https://www.ncbi.nlm.nih.gov/pubmed/30545835
	Chemical descriptors	CN1C=C(N=C(NC2=CC=C(C=C2)C(=O)N2CCN(CCCCCCNC(=O)CNC3=C4C(=O)N(C5CCC(=O)NC5=O)C(=O)C4=CC=C3)CC2)C1=O)C1=C(C)C(NC(=O)C2=CC=C(C=C2)C(C)(C)C)=CC=C1
	Chemical name	4-(tert-butyl)-N-(3-(6-((4-(4-(6-(2-((2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)amino)acetamido)hexyl)piperazine-1-carbonyl)phenyl)amino)-4-methyl-5-oxo-4,5-dihydropyrazin-2-yl)-2-methylphenyl)benzamide
	Entries in chemical databases	**CID** 138059681
	Availability	
	Papers that use the compounds	
	Additional comments	
In vitro profiling	Target (potency)	BTK (IC50 = 5.1 nM in biochemical assay)
	Target (potency)	
	Selectivity	Selective for BTK by Kinomescan
	Potential reactivity	
	SAR	
	Mechanism of inhibition	Targeted BTK degradation by recruitment of Cereblon
	Structure of target-probe complex	
	Additional comments	
Cellular profiling	Validation of cellular target	Dose-dependent degradation of BTK with maximal degradation at 100 nM Dose-dependent inhibition of proliferation of TMD8 (EC50 = 29.2 nM) and Mino (EC50 = 12 nM) cells
	Validation of cellular specificity	Degrades IKZF1/3 (immunoblot and proteomics)
	Additional comments	

Pharmacodynamics	DD-03-171 induced BTK degradation significantly slowed tumor growth in PDX model of mantle cell lymphoma
Pharmacokinetics	$T_{1/2}$ = 2.28 h; CL = 307 ml/min/Kg (10 mg/kg IP)
Synthetic scheme