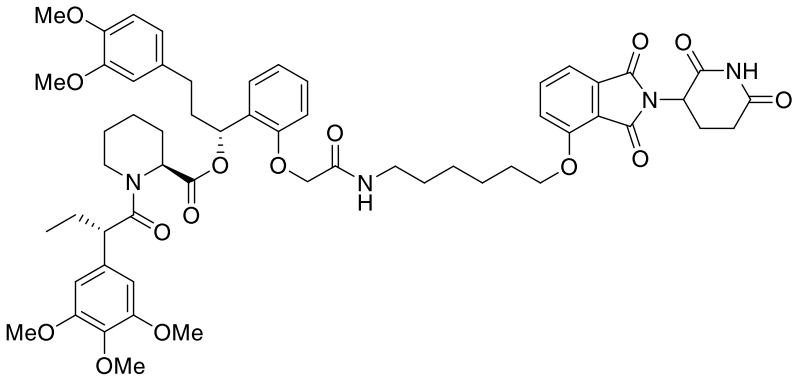
dTAG-13



Chemical Formula: $C_{57}H_{68}N_4O_{15}$
Molecular Weight: 1049.18

Category	Parameter	Description
Compound	Name	dTAG-13
	Citation	Erb et al., *Nature* 2017 (https://www.nature.com/articles/nature21688) Nabet et al., *Nature Chemical Biology* 2018 (https://www.nature.com/articles/s41589-018-0021-8)
	Chemical descriptors	Put Smile here
	Chemical name	(2*S*)-(1*R*)-3-(3,4-dimethoxyphenyl)-1-(2-(2-((6-((2-(2,6-dioxopiperidin-3-yl)-1,3-dioxoisoindolin-4-yl)oxy)hexyl)amino)-2-oxoethoxy)phenyl)propyl 1-((*S*)-2-(3,4,5-trimethoxyphenyl)butanoyl)piperidine-2-carboxylate
	Availability	dTAG-13 is not commercially available yet but can be obtained from Nathanael Gray.
In vitro profiling	Target (potency)	$FKBP12^{F36V}$ (IC_{50} of 146.80 nM in AlphaScreen)
	Target (potency)	$FKBP12^{WT}$ (IC_{50} of > 25,000 nM in AlphaScreen) CRBN (IC_{50} of 64.19 nM in AlphaScreen)
	Selectivity	dTAG-13 is extremely selective for degradation of $FKBP12^{F36V}$ fusion chimeras.
	Mechanism of degradation	dTAG-13 contains a thalidomide moiety and induces cereblon-dependent degradation of $FKBP12^{F36V}$ fusion chimeras.
Cellular profiling	Validation of cellular target	dTAG-13 treatment led to the dose-dependent degradation of multiple $FKBP12^{F36V}$ fusion chimeras including ENL (Erb et al.), $KRAS^{G12V}$ (Nabet et al.), BRD4 (Nabet et al.), HDAC1 (Nabet et al.), MYC (Nabet et al.), EZH2 (Nabet et al.), PLK1 (Nabet et al.) at 100-1000 nM in 1-4 h.
	Validation of cellular specificity	Quantitative mass spectrometry-based proteomics were performed in MV4;11 cells expressing ENL-$FKBP12^{F36V}$ (Erb et al.) and NIH/3T3 cells expressing $FKBP12^{F36V}$-$KRAS^{G12V}$ (Nabet et al.) demonstrating rapid and selective fusion protein degradation.
Pharmacodynamics		IP administration of dTAG-13 (25 mg/kg) significantly diminished bioluminescent signal in a disseminated model of leukemia (MV4;11 cells expressing luciferase-$FKBP12^{F36V}$) in 4 h (Nabet et al.).
Pharmacokinetics		$T_{1/2}$ = 0.986 h T_{max} = 1.00 h C_{max} = 220 ng/mL AUC_{last} = 431 hr*ng/mL $AUC_{0\text{-}inf}$ = 468 hr*ng/mL

Synthetic scheme