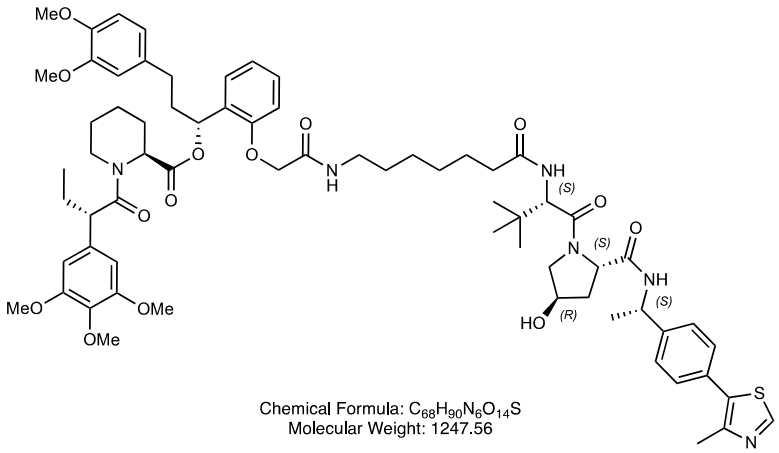
dTAGv-1



Chemical Formula: $C_{68}H_{90}N_6O_{14}S$
Molecular Weight: 1247.56

Category	Parameter	Description
Compound	Name	dTAGv-1
	Citation	Nat Commun, 2020, 11(1), 4687.
	Chemical descriptors	O=C([C@@H]1CCCCN1C([C@@H](CC)C2=CC(OC)=C(OC)C(OC)=C2)=O)O[C@H](CCC3=CC=C(OC)C(OC)=C3)C4=C(OCC(NCCCCCCC(N[C@@H](C(C)(C)C)C(N5C[C@H](O)C[C@H]5C(N[C@@H](C)C6=CC=C(C7=C(C)N=CS7)C=C6)=O)=O)=O)=O)C=CC=C4
	Chemical name	(*R*)-3-(3,4-dimethoxyphenyl)-1-(2-(2-((7-(((*S*)-1-((2*S*,4*R*)-4-hydroxy-2-(((*S*)-1-(4-(4-methylthiazol-5-yl)phenyl)ethyl)carbamoyl)pyrrolidin-1-yl)-3,3-dimethyl-1-oxobutan-2-yl)amino)-7-oxoheptyl)amino)-2-oxoethoxy)phenyl)propyl (*S*)-1-((*S*)-2-(3,4,5-trimethoxyphenyl)butanoyl)piperidine-2-carboxylate
	Entries in chemical databases	
	Availability	Tocris BioTech (pending publication)
	Papers that use the compounds	Nat Genet. 2020 Jul;52(7):719-727. doi: 10.1038/s41588-020-0635-0. Epub 2020 Jun 1. PMID: 32483291
	Additional comments	Negative control dTAGv-NEG is also available
In vitro profiling	Target (potency)	$FKBP^{F36V}$-tagged fusion chimeras. Sub 1 µM, context-dependent
	Target (potency)	n/a, selective
	Selectivity	No off-targets detected
	Potential reactivity	n/a
	SAR	Carbon linkers favourable over PEG
	Mechanism of inhibition	Targeted proteins degradation
	Structure of target-probe complex	n/a
	Additional comments	
Cellular profiling	Validation of cellular target	Western blot
	Validation of cellular specificity	Mass-spectrometry based global proteomics analysis
	Additional comments	
Pharmacodynamics		n/a

Pharmacokinetics

C57BL/6J male mice

		dTAG-13		dTAG^V-1		
Parameter	**Unit**	**IV**	**IP**	**IV**	**IP**	**IP**
Dose	mg kg^{-1}	2	10	2	2	10
T_{max}	hr	0.08	2.00	0.08	1.67	2.00
$T_{1/2}$	hr	1.46	2.41	3.02	3.64	4.43
C_{max}	ng mL^{-1}	2373	1263	7780	595	2123
AUC_{last}	hr*ng mL^{-1}	1242	5619	3245	2245	18088
AUC_{inf}	hr*ng mL^{-1}	1253	6140	3329	3136	18517
CL	ml min^{-1} kg^{-1}	32.5	28	10.1	10.7	9.05
V_{ss}	L kg^{-1}	1.8	-	0.56	-	-
F[b]	%	-	-	-	-	-

Synthetic scheme