Product Data Sheet

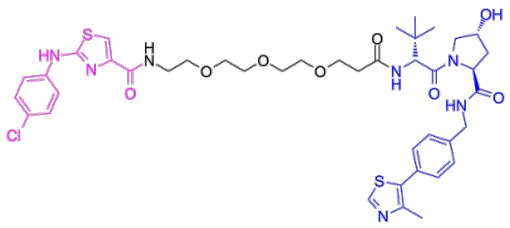
Product Name: PROTAC USP39 Degrader-1
Cat. No.: GC80895

Chemical Properties

Cas. No.

Formula	$C_{41}H_{52}ClN_7O_8S_2$	M.Wt	870.48
Solubility	DMSO: 100 mg/mL (114.88 mM; Need ultrasonic)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Background

PROTAC USP39 Degrader-1 is a USP39 PROTAC degrader with K d values of 136 nM and 232 nM,

and a DC_{50} value of 1.06 nM (24 h). PROTAC USP39 Degrader-1 binds to the VHL E3 ubiquitin ligase, forms a ternary complex with USP39, mediates USP39 ubiquitination and proteasomal degradation dependent on VHL recruitment, modulates splicing activity and induces 5' splice site-specific splicing patterns. PROTAC USP39 Degrader-1 can be used in the research of cervical cancer [1]. (Pink: USP39 ligand; Blue: VHL ligand; Black: linker).

In Vitro, PROTAC USP39 Degrader-1 (compound USP39_PROTAC_V1) reduces the thermal stability of purified full-length USP39 protein, decreasing its melting temperature by 1.5 °C[1]. PROTAC USP39 Degrader-1 (0.5 nM-5 μM; 24 h) induces dose-dependent degradation of USP39 protein in HEK293T, LNCap and Kelly cells[1]. PROTAC USP39 Degrader-1 (10 nM-1 μM; 24 h) alters splicing activity in HEK293T cells[1]. PROTAC USP39 Degrader-1 (1 nM-1 μM; 6-24 h) exerts significant target protein degradation activity in HeLa cells transiently overexpressing USP39-OFP, with the optimal treatment condition being 16 h of serum starvation followed by 24 h of compound treatment[1]. PROTAC USP39 Degrader-1 (0.5 nM-5 μM; 6 h-24 h) exerts potent activity in degrading endogenous USP39 protein in HeLa-WT cells (with a 24 h DC_{50} of approximately 1.06 nM). It degrades its target with high specificity across the whole proteome, resulting in significant downregulation of USP39 and stress-related proteins without affecting homologous proteins[1]. The USP39-degrading effect of PROTAC USP39 Degrader-1 (0.1 nM-0.1 μM; 24 h) is significantly inhibited by the proteasome inhibitor MG132 in co-treated HeLa-WT cells[1]. The degradation effect of PROTAC USP39 Degrader-1 (10 nM; 24 h) is blocked by the Neddylation inhibitor MLN4924 in HeLa-USP39-OFP cells co-treated with 1 μM MLN4924[1]. When PROTAC USP39 Degrader-1 is co-treated with 5 μM MLN4924 in HeLa-USP39-OFP cells, its DC_{50} increases from 13 nM to 204 nM, and its degradation activity is significantly attenuated[1]. PROTAC USP39 Degrader-1 (0.5 nM-0.5 μM) shows significantly attenuated USP39-degrading activity in VHL-knockout HeLa cells, and exhibits potent degrading activity only in the presence of wild-type VHL in HEK293T cells co-expressing USP39-OFP and different VHL plasmids (VHL_WT or truncated VHL_m)[1]. PROTAC USP39 Degrader-1 (0.5 nM-0.5 μM) promotes the formation of a ternary complex between the target protein and VHL_WT in HEK293T cells transfected with different types of plasmids (KD = 12 nM), whereas the complex formation is extremely weak in the presence of VHL_m[1]. PROTAC USP39 Degrader-1 (100 nM; 6 h) significantly enriches USP39 and polyubiquitination, and promotes the binding of USP39 to VHL in HeLa cells co-treated with 10 μM MLN4924[1]. PROTAC USP39

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Degrader-1 (10 nM; 24 h) induces aberrant usage of non-canonical 5'-splice sites in HEK293T cells, recapitulating the splicing defects associated with USP39 depletion[1].

References:

[1]. Schäfer D, et al. Targeting the Spliceosomal Protein USP39 Through Allosteric Ligands and PROTAC-Induced Degradation. Angewandte Chemie (International ed. in English). 2026 Jan 28;65(5):e16809.

Caution: Product has not been fully validated for medical applications. For research use only.
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