

Product Name: PROTAC mHTT Degrader-1
Cat. No.: GC81038

Cas. No. 2919475-43-5

Formula $C_{33}H_{35}N_5O_7$

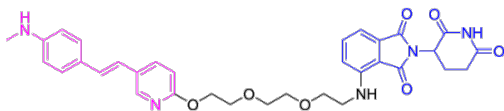
M.Wt 613.66

Solubility	Storage	Store at -20°C
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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.
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Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.
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Structure



PROTAC mHTT Degrader-1 is a blood-brain barrier-penetrant mutant huntingtin (mHTT) PROTAC degrader. PROTAC mHTT Degrader-1 specifically recognizes pathogenic mHTT aggregates and recruits Cereblon (CRBN), thereby inducing ubiquitination and proteasomal degradation of mHTT. PROTAC mHTT Degrader-1 alleviates mHTT-induced cytotoxicity and neuroinflammation. In the R6/2 Huntington's disease mouse model, PROTAC mHTT Degrader-1 reduces cerebral protein aggregation levels and improves body weight, motor coordination and survival rate of animals. PROTAC mHTT Degrader-1 can be used for research on PROTAC therapies for Huntington's disease and other neurodegenerative diseases ^[1]. (Pink: Huntingtin ligand; Blue: Cereblon ligand;

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Product Data Sheet

Black: linker).

In Vivo, In wild-type B6CBA mouse models treated with PROTAC mHTT Degrader-1 (PROTAC 2') (3 mg/kg; subcutaneous injection; single dose; observation for 6 h post-administration), PROTAC 2' can cross the blood-brain barrier, remains detectable in mouse brain tissue within 6 h post-administration, and maintains an average concentration of approximately 1.96 ppb^[1]. Following long-term administration of PROTAC mHTT Degrader-1 (3 mg/kg/week; subcutaneous injection; once weekly for 5 consecutive weeks) in wild-type B6CBA mouse models, no significant differences are observed in mouse body weight, cerebral cortex thickness, or striatal volume compared with the control group. No abnormalities are detected in serum liver and kidney function indices, and no obvious toxicity is found in the liver, kidney, or brain tissues^[1]. PROTAC mHTT Degrader-1 (3 mg/kg/week; continuous administration via subcutaneously implanted osmotic pump; continuous infusion; 4 weeks of treatment) significantly retards body weight loss, improves motor coordination and spontaneous exploratory behavior, and prolongs survival in B6CBA-R6/2 Huntington's disease mouse models. Meanwhile, it reduces the level of mHTT aggregates and neuroinflammation in the mouse brain, alleviates cortex and striatum atrophy, and partially restores neuronal function^[1].

In Vitro, PROTAC mHTT Degrader-1 (PROTAC 2') (1 μ M; 22 h) significantly reduces the proportion of mHTT aggregate-positive cells and the level of insoluble mHTT aggregates in N2a cells expressing HTT (Q)109-eYFP, while exerting no significant effect on the level of soluble mHTT. It decreases the level of the intracellular DNA damage marker p-H2A.X (Ser139) and inhibits the activation of mHTT-induced apoptotic pathways^[1]. PROTAC mHTT Degrader-1 (1 μ M; 22 h) reduces the proportion of intracellular mHTT oligomers, achieving simultaneous targeted degradation of soluble oligomers and insoluble aggregates; its degradation effect is significantly reversed by the proteasome inhibitor MG132, confirming that it functions via the ubiquitin-proteasome system^[1]. PROTAC 2' (0.01-10 μ M; 22 h) dose-dependently and selectively degrades mHTT aggregates in N2a cells expressing HTT (Q)109-eYFP, with no significant effect on the levels of non-pathogenic HTT (Q)25-eYFP^[1]. PROTAC 2' (1 μ M; 48 h) significantly increases the viability of N2a cells expressing HTT (Q)109-eYFP, and effectively alleviates mHTT-induced neurotoxicity^[1].

References:

[1]. Lu PC, et al. PROTAC-Mediated Degradation of mHTT Aggregates Attenuates Neurotoxicity in

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Cellular and R6/2 Mouse Models of Huntington's Disease. J Am Chem Soc. 2026;148(8):8107-8121.

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