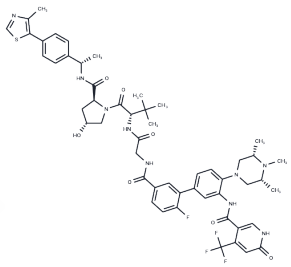
Data Sheet (Cat.No.T39976)

TargetMol

MS67

Chemical Properties



CAS No. : 2407452-77-9

Formula: C52H59F4N9O7S

Molecular Weight: 1030.14

Storage: Keep away from direct sunlight
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	MS67 is a potent and selective degrader of WD40 repeat domain protein 5 (WDR5) with a dissociation constant (Kd) of 63 nM, exhibiting no activity against protein methyltransferases, kinases, G-protein-coupled receptors (GPCRs), ion channels, and transporters, and notably demonstrating significant anticancer properties.
Targets(IC50)	Histone Methyltransferase,PROTACs
In vitro	MS67, at concentrations ranging from 0.001 to 1 μM, effectively induces the degradation of WDR5, with noticeable activity initiating at concentrations as low as 1 nM. This compound demonstrates a pronounced ability to deplete WDR5 across various cell lines, including six mixed lineage leukemia (MLL)-rearranged (MLL-r) acute myeloid leukemia (AML) and four pancreatic ductal adenocarcinoma (PDAC) cell lines, without exhibiting a hook effect and displaying a concentration-dependent efficacy in PDAC cells. Furthermore, MS67 reduces H3K4me2/3 levels in both MV4;11 and MIA PaCa-2 cells, while not affecting other histone methylation markers such as H3K9me3, H3K27me3, and H3K36me3. It suppresses WDR5-related gene expression and WDR5/MLL-induced H3K4 methylations on chromatin. The GI50 values for the most sensitive AML cell lines, MV4;11 and EOL-1, are 15 nM and 38 nM, respectively, highlighting its potency. The sensitivity to MS67 is distinct in MLL-r acute leukemia cell lines (MV4;11, EOL-1, MOLM13, KOPN8, RS4;11, and THP-1), in contrast to leukemia cell lines lacking MLL-r arrangements, such as K562, HL60, and a murine AML line transformed by Hoxa9 plus Meis1, which show insensitivity to MS67. Additionally, MS67 exhibits binding affinity to the VCB (VHL-Elongin C-Elongin B ternary complex) with a Kd of 140 nM. Western Blot Analysis further confirms MS67-induced WDR5 degradation in MV4;11 cells across various concentrations after 18 hours of incubation, showcasing significant activity at a DC50 of 3.7 nM.
In vivo	MS67, administered intraperitoneally (i.p.) at a dose of 75 mg/kg twice daily for five days a week over a period of 20 days, significantly inhibits tumor growth in vivo and extends the survival of treated mice[1]. A single i.p. injection of MS67 at 75 mg/kg yields a peak concentration (Cmax) of approximately 4.2 μM, maintaining a concentration above 0.5 μM for over 12 hours[1]. This was observed in an MV4;11 MLL-r AML xenograft mouse model, demonstrating MS67's efficacy in inhibiting tumor growth in vivo under the specified conditions[1].

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	0.9707 mL	4.8537 mL	9.7074 mL
5 mM	0.1941 mL	0.9707 mL	1.9415 mL
10 mM	0.0971 mL	0.4854 mL	0.9707 mL
50 mM	0.0194 mL	0.0971 mL	0.1941 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Xufen Yu, et al. A selective WDR5 degrader inhibits acute myeloid leukemia in patient-derived mouse models. Sci Transl Med. 2021 Sep 29;13(613):eabj1578.