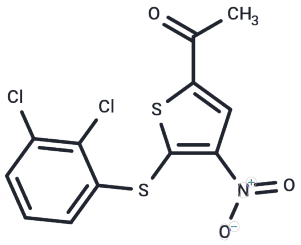
Data Sheet (Cat.No.T6925)

P005091

Chemical Properties



CAS No. : 882257-11-6

Formula: C12H7Cl2NO3S2

Molecular Weight: 348.22

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	P005091 (P5091) is a selective and potent inhibitor of ubiquitin-specific protease 7 (USP7) with EC50 of 4.2 μM.
Targets(IC50)	DUB
In vitro	P5091 demonstrates synergistic anti-multiple myeloma (anti-MM) activity when used in combination with Lenalidomide, the HDAC inhibitor SAHA, or Dexamethasone. In animal tumor models, P5091 is well-tolerated, inhibits tumor growth, and prolongs survival.
In vivo	P5091 exhibits potent, specific, and selective deubiquitinating (deubiquitinase) activity against USP7. Conversely, P5091 does not inhibit other tested DUBs or proteases from different families (EC50 >100 mM). It decreases HDM2 and HDMX levels while upregulating p53 and p21. P5091-induced cytotoxicity is partly mediated via the HDM2-p21 signaling axis, and despite the upregulation of p53 following P5091 treatment, its cytotoxic effects do not depend on p53. P5091 concentration-dependently inhibits USP7 tagged with HA-UbVME and dose-dependently inhibits USP7-mediated disassembly of ultra-high molecular weight ubiquitin chains. Moreover, P5091 inhibits the breakdown of polyK48-linked ubiquitin chains specifically by USP7 rather than USP2 or USP8. It suppresses USP7 deubiquitinase activity in MM cells without inhibiting protease activities and overcomes bone marrow stromal cell-induced MM cell growth.
Kinase Assay	Recombinant enzymes in 20 mM Tris-HCl (pH 8.0), 2 mM CaCl2, and 2 mM β-mercaptoethanol are incubated with dose ranges of P005091 for 30 min in a 96-well plate before the addition of Ub-PLA2 and NBD C6-HPC or Ub-EKL and EKL substrate. The liberation of a fluorescent product within the linear range of the assay is monitored using a Perkin Elmer Envision fluorescence plate reader. Vehicle (2% [v/v] DMSO) and 10 mM N-ethylmaleimide (NEM) are included as controls.
Animal Research	Animal Models: CB-17 SCID-mice are subcutaneously inoculated with MM.1S, ARP-1, or RPMI-8226 cells in 100 μL of serum free RPMI-1640 medium. Formulation: P005091 is dissolved in 4% NMP(N-methyl-2-Pyrrolidone), 4% Tween-80, and 92% Milli-Q water at a final concentration of 2 mg/mL.

Solubility Information

Solubility	DMSO: 68 mg/mL (195.28 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.8717 mL	14.3587 mL	28.7175 mL
5 mM	0.5743 mL	2.8717 mL	5.7435 mL
10 mM	0.2872 mL	1.4359 mL	2.8717 mL
50 mM	0.0574 mL	0.2872 mL	0.5743 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.

Reference

Chauhan D, et al. Cancer Cell, 2012, 22(3), 345-358.
Park, Su H., et al. Posttranslational regulation of FOXA1 by Polycomb and BUB3/USP7 deubiquitin complex in prostate cancer.. Science Advances. 2021 Apr 7;7(15):eabe2261. doi: 10.1126/sciadv.abe2261. Print 2021 Apr.
Wu W, Xu H, Liao C, et al. Blockade of USP14 potentiates type I interferon signaling and radiation-induced antitumor immunity via preventing IRF3 deubiquitination. Cellular Oncology. 2022: 1-15
Weinstock J, et al. ACS Med Chem Lett. 2012, 3(10):789-92.
Park, Su H., et al. Posttranslational regulation of FOXA1 by Polycomb and BUB3/USP7 deubiquitin complex in prostate cancer. Science Advances. 7.15 (2021): eabe2261.
Yue X, Liu T, Wang X, et al.Pharmacological inhibition of BAP1 recruits HERC2 to competitively dissociate BRCA1-BARD1, suppresses DNA repair and sensitizes CRC to radiotherapy.Acta Pharmaceutica Sinica B.2023