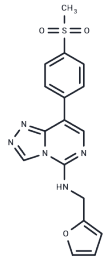
Data Sheet (Cat.No.T3458)

TargetMol

EED226

Chemical Properties



CAS No. : 2083627-02-3

Formula: C17H15N5O3S

Molecular Weight: 369.4

Appearance: no data available

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

Biological Description

Description	EED226 is a potent, selective, and orally bioavailable embryonic ectoderm development (EED) inhibitor with an IC50 of 22 nM.
Targets(IC50)	Histone Methyltransferase
In vitro	EED226 induces a conformational change upon binding EED, leading to loss of PRC2 activity. EED226 also effectively inhibits PRC2 containing a mutant EZH2 protein resistant to SAM-competitive inhibitors. It regulates histone H3K27 methylation and PRC2 target gene expression in cells. In the in vitro enzymatic assays, EED226 inhibits PRC2 with an IC50 (half-maximal inhibitory concentration) of 23.4 nM when the H3K27me0 peptide is used as substrate and an IC50 of 53.5 nM when the mononucleosome is used as the substrate, with the stimulatory H3K27me3 added at 1 × Kact (1.0 μM). EED226 is noncompetitive with both SAM and peptide substrate. EED226 bound to EED and PRC2 complex with a 1:1 stoichiometry and Kd of 82 nM and 114 nM, respectively. EED226 does not disrupt the PRC2 complex and could still occupy its binding pocket with a SAM-competitive EZH2 inhibitor bound to PRC2. EED226 shows remarkable selectivity for PRC2 complex over 21 other protein methyltransferases, kinases and other protein classes, The only other histone methyltransferase that can be inhibited by EED226 is the EZH1-PRC2 complex. EED226 with moderate permeability leads to a dose-dependent decrease of both global H3K27me3 and H3K27me2 markers in G401 cell[1].
In vivo	EED226 effectively induces tumor regression in a mouse xenograft model. EED226 in a solid dispersion formulation are well tolerated in animals. EED226 clearly demonstrates a dose-dependent efficacy in the mouse xenograph study[1]. EED226 inhibits the growth of diffuse large B-cell lymphoma (DLBCL) xenografts and reduces H3K27me3 levels to a similar extent as an EZH2 inhibitor[2]. EED226 has very low in vivo and in vitro clearance and approximately 100% oral bioavailability, low volume of distribution (0.8 L/kg), reasonable terminal t1/2 (2.2 h), and moderate plasma protein binding (PPB)(14.4%). Its solubility is relatively low and with little dependency on the pH of the medium[3].
Cell Research	G401 cells are treated with EED226 for 3 d at the indicated concentrations. Total histone H3 is shown as a loading control. WB analysis for protein expression of H3K27me3, H3K27me2, H3K27me1. (Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 55 mg/mL (148.89 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.7071 mL	13.5355 mL	27.0709 mL
5 mM	0.5414 mL	2.7071 mL	5.4142 mL
10 mM	0.2707 mL	1.3535 mL	2.7071 mL
50 mM	0.0541 mL	0.2707 mL	0.5414 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

Qi W, et al. Nat Chem Biol. 2017, 13(4):381-388.
Cancer Discov. 2017, 7(4):OF8. doi: 10.1158/2159-8290.CD-RW2017-030.
Y Huang, et al. J Med Chem. 60 (6):2215-2226.