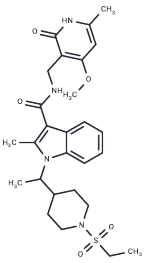
Data Sheet (Cat.No.T6809)

TargetMol

CPI-169 racemate

Chemical Properties



CAS No. : 1450655-76-1

Formula: C27H36N4O5S

Molecular Weight: 528.66

Storage: 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	CPI-169 racemate (CPI 169) is a potent, and selective EZH2 inhibitor with IC50 of 0.24 nM, 0.51 nM, and 6.1 nM for EZH2 WT, EZH2 Y641N, and EZH1, respectively.
Targets(IC50)	Epigenetic Reader Domain,Histone Methyltransferase
In vitro	In KARPAS-422 cells, CPI-169 shows a dose-dependent inhibitory effect on cell viability, and produces synergy anti-proliferative activity when used in combination with ABT-199. In 16 out of 25 NHL cell lines, CPI-169 also suppresses cell growth with GI50 of <5 μM. [1]
In vivo	In mice bearing KARPAS-422 xenografts, CPI-169 (200 mg/kg, s.c.) effectively suppresses H3K27me3 levels and results in lymphoma tumor regression without affecting body weight or causing any overt adverse effects. [1]
Kinase Assay	Biochemical Assays: Compound potency is also assessed through incorporation of 3H-SAM into a biotinylated H3 peptide. Specifically, PRC2 containing either EZH1 (160 pM), wt EZH2 (40 pM), or Y641N mutant EZH2 (80 pM, both EZH2 prepared in-house) is pre-incubated with 3H-SAM (0.9 μM), 2 μM H3K27me3 activating peptide (H2N-RKQLATKAAR (Kme3)SAPATGGVKKP-amide) and compounds (as 10 point duplicate dose response titrations) for 120 min in a buffer consisting of 50 mM Tris (pH 8.5), 1 mM DTT, 0.07 mM Brij-35, 0.1% BSA, and 0.8% DMSO in a total volume of 12.5 μl in a black 384 well plate. Reaction is initiated with biotinylated H3 substrate peptides (H3K27me1 for wt EZH2, H3K27me2 for Y641N mutant EZH2; H2N-RKQLATKAAR(Kmen)SAPATGGVKKP-NTPEGBiot) as a 2 μM stock in 12.5 μL and allowed to react at room temperature for 5 h. Quenching is accomplished by addition of 20 μl of STOP solution (50 mM Tris (pH 8.5), 200 mM EDTA, 2 mM SAH). 35 μL of the quenched solution is transferred to Streptavidin Flashplates, incubated overnight, washed, and read in a TopCount Reader. For titrations all compound dilutions are in DMSO, final DMSO concentrations are 0.8% (v/v), and turnover is kept to less than < 5%. IC50s are calculated using non-linear least square four parameter fits (GraphPad 6.0).
Cell Research	Relative cell numbers are assessed by Cell Titer-Glo (CTG) luminescent cell viability assay using an Envision instrument. GraphPad Prism 6.0 is used for curve fitting, IC50/GI50 and Hill coefficient (H) calculations. The GI90 is calculated using the formula: EC90 = (90 /100-90)1/H * EC50.(Only for Reference)

Animal Research	Animal Models: Mice bearing KARPAS-422 subcutaneous xenograftsFormulation: 10% DMSO + 60% polytheylene glycol 400 + 30% ddH2ODosages: 200 mg/kg, BIDAdministration: s.c.

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 93 mg/mL (175.92 mM),Sonication is recommended. DMSO: 93 mg/mL (175.92 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8916 mL	9.4579 mL	18.9157 mL
5 mM	0.3783 mL	1.8916 mL	3.7831 mL
10 mM	0.1892 mL	0.9458 mL	1.8916 mL
50 mM	0.0378 mL	0.1892 mL	0.3783 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

Bradley WD, et al. Chem Biol. 2014, 21(11), 1463-1475.