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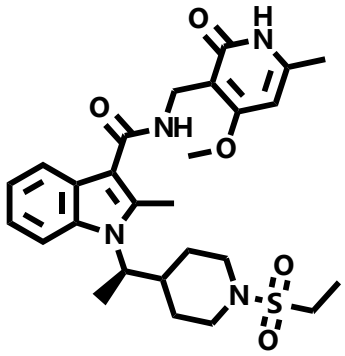
EZH2 Methyltransferase Inhibitor – CPI-169

Chemical Name: (R)-1-(1-(1-(ethylsulfonyl)piperidin-4-yl)ethyl)-N-((4-methoxy-6-methyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-2-methyl-1H-indole-3-carboxamide



Molecular Weight:	528.66
Formula:	$C_{27}H_{36}N_4O_5S$
Purity:	≥98%
CAS#:	1450655-76-1
Solubility:	DMSO up to 100 mM EtOH up to 100 mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

Biological Activity:

CPI-169 is a highly potent and selective small molecule inhibitor of histone methyltransferase EZH2. It potently inhibits wild-type EZH2, mutant EZH2 Y641N and EZH1 with IC_{50} of 0.24 nM, 0.51 nM and 6.1 nM, respectively. It decreases cellular levels of H3K27me3 with an EC_{50} of 70 nM, and triggers cell cycle arrest and apoptosis across a large cell panel representing various non-Hodgkin's lymphoma (NHL) subtypes. a variety of cell lines. Administered subcutaneously at 200 mpk twice daily (BID), CPI-169 is well tolerated in mice with no observed toxic effect or body weight loss. The drug treatment led to tumor growth inhibition (TGI) of an EZH2 mutant KARPAS-422 DLBCL xenograft. CPI-169 selectively affects the turnover of trimethylated, but not monomethylated histone H3 lysine 27 at pharmacologically relevant doses.

How to Use:

In vitro: CPI-169 was used at 10 μM final concentration in vitro and in cellular assays.

In vivo: CPI-169 was subcutaneously (SC) dosed to mice bearing KARPAS-422 subcutaneous xenografts at 200 mg/kg twice per day.

Reference:

1. Bradley WD., et al. EZH2 inhibitor efficacy in non-Hodgkin's lymphoma does not require suppression of H3K27 monomethylation. (2014) Chem Biol. 21(11):1463-75.