Web: www.taiclone.com
Tel: +886-2-2735-9682
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UNC1999

Catalog No: tcsc1658

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg

Specifications

CAS No:
1431612-23-5

Formula:
$C_{33}H_{43}N_7O_2$

Pathway:
Epigenetics;Epigenetics;Autophagy

Target:
Histone Methyltransferase;Epigenetic Reader Domain;Autophagy

Purity / Grade:
>98%

Solubility:
DMSO : 135 mg/mL (236.95 mM; Need ultrasonic); H2O :

Observed Molecular Weight:
569.74

Product Description

UNC1999 is a SAM-competitive, potent and selective inhibitor of **EZH2** (**IC_{50}**EZH1 (**IC_{50}**=45±3 nM).

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IC50 & Target: IC50: [1]

In Vitro: UNC1999, the first orally bioavailable inhibitor that has high in vitro potency for wild-type and mutant EZH2 as well as EZH1, a closely related H3K27 methyltransferase that shares 96% sequence identity with EZH2 in their respective catalytic domains. UNC1999 is highly selective for EZH2 and EZH1 over a broad range of epigenetic and non-epigenetic targets, competitive with the cofactor SAM, and non-competitive with the peptide substrate. UNC1999 has K_i values of 4,700 nM, 65 nM, 300 nM, and 1,500 nM for sigma1, sigma2, histamine H_3, and NET (norepinephrine transporter), respectively. NC1999 selectively kills DB cells, a DLBCL cell line with the EZH2 Y641N mutation. UNC1999 displays a concentration- and time-dependent inhibition of DB cell proliferation (EC_{50} =633±101 nM (n=3))[1].

In Vivo: A single intraperitoneal (IP) injection of UNC1999 at 15, 50, or 150 mg/kg achieved high C_{max} (9,700-11,800 nM) and exhibited dose linearity in male Swiss albino mice. Both the 150 and 50 mg/kg IP doses resulted in the plasma concentrations of UNC1999 above its cellular IC_{50} over the entire 24 h period while the 15 mg/kg IP dose led to the plasma concentrations of UNC1999 above its cellular IC_{50} for approximately 12 h. We next examined whether UNC1999 is orally bioavailable and are pleased to find that a single 50 mg/kg oral dose of UNC1999 achieved high C_{max} (4,700 nM) and good exposure levels in male Swiss albino mice. The plasma concentrations of UNC1999 are maintained above its cellular IC_{50} for approximately 20 h following this single oral dose. It is worth noting that all doses including the 150 mg/kg IP dose are well tolerated by all test mice, and no adverse effects are observed[1].