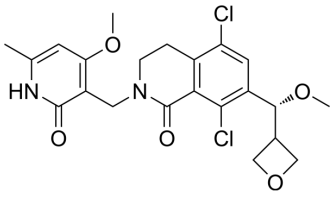
PF-06821497

Cat. No.:	HY-101571A
CAS No.:	1844849-10-0
Molecular Formula:	$C_{22}H_{24}Cl_2N_2O_5$
Molecular Weight:	467.34
Target:	Epigenetic Reader Domain; Histone Methyltransferase
Pathway:	Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (213.98 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1398 mL	10.6988 mL	21.3977 mL
5 mM	0.4280 mL	2.1398 mL	4.2795 mL
10 mM	0.2140 mL	1.0699 mL	2.1398 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.35 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.35 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.35 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-06821497 (compound 23a) is a potent, selective and orally active Enhancer of Zeste Homolog 2 (EZH2) inhibitor, with a K_i value <0.1 nM against mutant Y641N EZH2. Exhibits robust tumor growth inhibition[1].

IC_{50} & Target

Ki: <0.1 nM (Y641N EZH2)[1].

In Vivo

PF-06821497 (compound 23a: 100 mg/kg, PO twice daily for 31 days) treatment results in significant inhibition of tumor growth, and the the tumor regression effect can be sustained for another 40 days after the terminal administration[1].

PF-06821497 with the dose of 300 mg/kg has minimal impact on animal body weights[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Mice bearing Karpas-422 DLBCL tumor xenografts (which contain the Y641N EZH2 mutation)[1].
Dosage:	100 mg/kg and 300 mg/kg.
Administration:	PO twice daily for 31 days.
Result:	100 mg/kg dose resulted in significant inhibition of tumor growth and 300 mg/kg dose minimal effected animal body weights.

REFERENCES

[1]. Kung PP, et al. Optimization of Orally Bioavailable Enhancer of Zeste Homolog 2 (EZH2) Inhibitors Using Ligand and Property-Based Design Strategies: Identification of Development Candidate (R)-5,8-Dichloro-7-(methoxy(oxetan-3-yl)methyl)-2-((4-methoxy-6-methyl-2-oxo-1,2-dihydropyridin-3-yl)methyl)-3,4-dihydroisoquinolin-1(2H)-one (PF-06821497). J Med Chem. 2018 Feb 8;61(3):650-665.

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