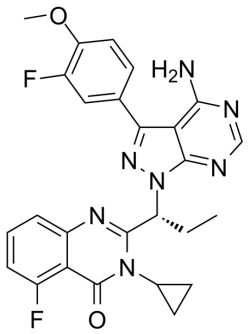
IHMT-PI3Kδ-372

Cat. No.:	HY-131910
CAS No.:	2429889-62-1
Molecular Formula:	$C_{26}H_{23}F_2N_7O_2$
Molecular Weight:	503.5
Target:	PI3K; Cytochrome P450
Pathway:	PI3K/Akt/mTOR; Metabolic Enzyme/Protease
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 : 41.67 mg/mL (82.76 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9861 mL	9.9305 mL	19.8610 mL
	5 mM	0.3972 mL	1.9861 mL	3.9722 mL
	10 mM	0.1986 mL	0.9930 mL	1.9861 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: ≥ 2.08 mg/mL (4.13 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.13 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

IHMT-PI3Kδ-372 is a potent and selective PI3Kδ inhibitor with an IC_{50} of 14 nM. IHMT-PI3Kδ-372 shows high selectivity over other class I PI3Ks (56-83 fold) and other protein kinases. IHMT-PI3Kδ-372 can be uesd for chronic obstructive pulmonary disease (COPD) research[1].

IC_{50} & Target

PI3Kδ	CYP2C9
14 nM (IC_{50})	2.7 μM (IC_{50})

In Vitro

IHMT-PI3Kδ-372 (Compound (S)-18; 0.03-3 μM; 1 hour; Raji cells) treatment inhibits PI3Kδ-mediated AKT T308 phosphorylation in Raji cells with an EC_{50} value of 67 nM[1].
IHMT-PI3Kδ-372 (compound (S)-18) shows moderate inhibition of CYP2C9 (IC_{50} of 2.7 μM) and no apparent inhibition against

CYP1A2, CYP2B6, CYP2C19, and CYP3A4 (IC_{50}s > 10 μM)[1].

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

Western Blot Analysis[1]

Cell Line:	Raji cells
Concentration:	0.03 μM, 0.1 μM, 0.3 μM, 1 μM, 3 μM
Incubation Time:	1 hour
Result:	Inhibited PI3Kδ-mediated AKT T308 phosphorylation in Raji cells with an EC_{50} value of 67 nM.

In Vivo

IHMT-PI3Kδ-372 (Compound (S)-18; 1-5 mg/kg; inhalation; daily; for 28 days) improves lung function and reduced the inflammatory patterns characteristic of COPD. The lung function parameters such as forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), and peak expiratory flow (PEF) are improved dose-dependently. The abnormally high level of leukocytes including the alveolar macrophages, neutrophils, and lymphocytes are also reduced. IHMT-PI3Kδ-372 decreases the inflammatory cell infiltration in a dose-dependent manner[1].

In rats, inhalation of 5 mg/kg dose of IHMT-PI3Kδ-372 (compound (S)-18) displays a half-life of 2.3 h, low exposure of 66 ng/mL, and high clearance of 348.5 mL/min/kg in plasma but high exposure of 5599 ng/g (6 h after inhalation) in lung tissue [1].

IHMT-PI3Kδ-372 is stable in human, rat, and mouse liver microsomes, while it has moderate stability in monkey and dog liver microsomes[1].

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

Animal Model:	Sprague-Dawley (SD) rats (5-week-old) induced with cigarette-smoke and LPS[1]
Dosage:	1 mg/kg, 3 mg/kg, and 5 mg/kg
Administration:	Inhalation; daily; for 28 days
Result:	Improved lung function and reduced the inflammatory patterns characteristic of COPD.

REFERENCES

[1]. Feng Li, et al. Discovery of (S)-2-(1-(4-Amino-3-(3-fluoro-4-methoxyphenyl)-1 H-pyrazolo[3,4- d]pyrimidin-1-yl)propyl)-3-cyclopropyl-5-fluoroquinazolin-4(3 H)-one (IHMT-PI3Kδ-372) as a Potent and Selective PI3Kδ Inhibitor for the Treatment of Chronic Obstructive Pulmonary Disease. J Med Chem. 2020 Nov 25;63(22):13973-13993.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA