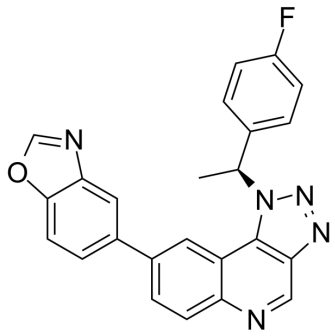
CLK1-IN-1

Cat. No.:	HY-103082
CAS No.:	2123491-32-5
Molecular Formula:	$C_{24}H_{16}FN_5O$
Molecular Weight:	409.42
Target:	CDK
Pathway:	Cell Cycle/DNA Damage
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (61.06 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4425 mL	12.2124 mL	24.4248 mL
5 mM	0.4885 mL	2.4425 mL	4.8850 mL
10 mM	0.2442 mL	1.2212 mL	2.4425 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.11 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CLK1-IN-1 is a potent and selective of Cdc2-like kinase 1 (CLK1) inhibitor, with an IC_{50} of 2 nM.

IC_{50} & Target

CLK1
2 nM (IC_{50})

In Vitro

CLK1 is the most potently inhibited kinase (IC_{50}: 2 nM). In addition to CLK1, only two kinases have an IC_{50} value less than 100 nM, namely CLK2 (IC_{50}: 31 nM) and CLK4 (IC_{50}: 8 nM), DYRK1A is the strongest off-target. The ability of CLK1-IN-1 to induce autophagy in BNL CL.2 and SKOV-3 (human ovarian cancer cell line) cells is also examined. The effects of CLK1-IN-1 on yellow LC3 puncta also displays obvious dose dependency, and a dose of 10 μM shows the best performance. In addition, in CLK1-IN-1-treated cells, the number of red LC3 puncta (mRFP signals only35) increases compared with that of DMSO-treated cells, indicating the formation of autolysosomes. Importantly, CLK1-IN-1 stimulats the degradation of SQSTM1/p62 and increases the ratio of red LC3 puncta to yellow LC3 puncta, both of which indicate an induction of autophagic flux by CLK1-

	IN-1[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	APAP exposure results in severe liver injury, and treatment with CLK1-IN-1 (ip, 30 mg/kg) imparts a significant hepatoprotective effect. The results show that treatment with CLK1-IN-1 decreases serum ALT and AST levels significantly such that both marker enzymes return to normal levels[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	BNL CL.2 (mouse embryonic liver cell line) is selected, and three concentrations (20 nM, 100 nM, and 10 μM) of CLK1-IN-1 are used[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Drug-induced liver injury (DILI) is a major public health concern and accounts for more than 50% of acute liver failure cases. APAP is a widely used antipyretic analgesic drug. Herein, the APAP-induced hepatotoxicity mouse model is used to examine the therapeutic effect of CLK1-IN-1 in vivo. Male C57BL/6 mice are given either saline (n=3, ip) or APAP (500 mg/kg) (n=15, ip). To examine the hepatoprotective effect, mice are injected (ip) with CLK1-IN-1 (25) (30 mg/kg), 30 (30 mg/kg, positive control), rapamycin (30 mg/kg, positive control), or solvent (12.5% ethanol and 12.5% castor oil, 10 mL/kg), immediately followed by APAP (500 mg/kg) injection (ip). All mice are sacrificed 6 h later. Liver sections are examined by H&E staining, and the serum from the blood samples is used for ALT and AST activity tests[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Sun QZ, et al. Discovery of Potent and Selective Inhibitors of Cdc2-Like Kinase 1 (CLK1) as a New Class of Autophagy Inducers. J Med Chem. 2017 Jul 27;60(14):6337-6352.

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