Plogosertib

Cat. No.: HY-147298

CAS No.: 1137212-79-3

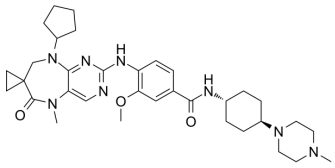
Molecular Formula: $C_{34}H_{48}N_8O_3$

Molecular Weight: 616.8

Target: Polo-like Kinase (PLK)

Pathway: Cell Cycle/DNA Damage

Storage: 4°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (162.13 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6213 mL	8.1064 mL	16.2127 mL
	5 mM	0.3243 mL	1.6213 mL	3.2425 mL
	10 mM	0.1621 mL	0.8106 mL	1.6213 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 (4.05 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.05 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.05 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Plogosertib (CYC140) is a selective, potent, and orally active ATP-competitive PLK1 inhibitor (IC_{50}: 3 nM). Plogosertib is an anti-cancer agent with anti-proliferative activity. Plogosertib can be used in the research of several tumors, including esophageal, gastric, leukemia, non–small cell lung cancer, ovarian, and squamous cell cancers[1][2].

IC_{50} & Target

PLK1	PLK2	PLK3
3 nM (IC_{50})	149 nM (IC_{50})	393 nM (IC_{50})

In Vitro

Plogosertib (CYC140) selectively inhibits PLK1 (IC_{50}: 3 nM), and is >50 fold more potent against PLK2 and PLK3 (IC_{50}s: 149 nM

and 393 nM, respectively)[2].
Plogosertib (0-4 μM, 2 h) reduces phosphorylation of the PLK1 substrate, pSer4-nucleophosmin (p-NPM) in KYSE-410 cells[2].
Plogosertib (100 nM, 24 h) increases in the proportion of mitotic cells, with increased monopolar spindles in HeLa cells[2].
Plogosertib (72 h) preferentially inhibits cell proliferation in malignant cell lines (IC_{50}s: 14-21 nM), and is less toxic against none-malignant cell lines (IC_{50}: 82 nM)[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[2]

Cell Line:	KYSE-410 cells
Concentration:	0, 0.07, 0.15, 0.3, 0.6, 1.25 μM
Incubation Time:	72 h
Result:	Inhibited cell proliferation in a concentration-dependent manner.

Western Blot Analysis[2]

Cell Line:	KYSE-410 cells
Concentration:	0, 0.01, 0.025, 0.05, 0.1, 0.25, 0.5, 1, 2, 4 μM
Incubation Time:	2 h (p-NPM), 24 h (p-HH3), 72 h (cPARP)
Result:	Reduced phosphorylation of the PLK1 substrate (p-NPM). Increased in the mitotic marker pSer10 histone H3 (p-HH3), and the cleavage of PARP (cPARP, an indicator of cell death).

In Vivo

Plogosertib (CYC140, oral administration, 40 mg/kg, qd 5/2/5) inhibits tumor growth in preclinical xenograft models of acute leukemia and solid tumors[2].Plogosertib (Coumpond A7, 1 mg/kg, mouse) shows pharmacokinetic parameters: C_{max} (453 ng/mL), AUC (377 hr•ng/mL), Cl (2445 mL/h/kg)[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	HL60 promyelocytic leukemia xenograft[2]
Dosage:	40, 54, 67 mg/kg, qd 5/2/5
Administration:	Oral administration
Result:	Inhibited tumor growth (>87%) without significant loss in body weight.

Animal Model:	OE19 esophageal xenograft[2]
Dosage:	40 mg/kg, qd 5/2
Administration:	Oral administration
Result:	Inhibited tumor growth (61 % inhibition).

REFERENCES

[1]. Sylvie Moureau, et al. Abstract 4178: The novel PLK1 inhibitor, CYC140: Identification of pharmacodynamic markers, sensitive target indications and potential combinations. Cancer Res (2017) 77 (13_Supplement): 4178.

[2]. Moureau S, et al. Therapeutic potential of novel PLK1 inhibitor CYC140 in esophageal cancer and acute leukemia[J]. European Journal of Cancer, 2016, 1(69): S117.

[3]. Susan Davis, et al. Treatment of proliferative diseases with pyrimidodiazepinones. Patent US20150320762A1.

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