GNE-900

Cat. No.: HY-15883

CAS No.: 1200126-26-6

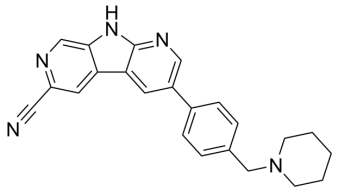
Molecular Formula: $C_{23}H_{21}N_5$

Molecular Weight: 367.45

Target: Checkpoint Kinase (Chk); Apoptosis

Pathway: Cell Cycle/DNA Damage; Apoptosis

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (272.15 mM; ultrasonic and warming and heat to 80°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7215 mL	13.6073 mL	27.2146 mL
	5 mM	0.5443 mL	2.7215 mL	5.4429 mL
	10 mM	0.2721 mL	1.3607 mL	2.7215 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 (6.80 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

GNE-900 is a an ATP-competitive, selective, and orally active ChK1 inhibitor with IC_{50}s of 0.0011, 1.5 μM for ChKl, ChK2, respectively. GNE-900 abrogates the G2-M checkpoint, enhances DNA damage, and induces Apoptosis. gemcitabine (HY-17026) and GNE-900 administration shows anti-tumor activity[1].

IC_{50} & Target

Chk1	Chk2
0.0011 μM (IC_{50})	1.5 μM (IC_{50})

In Vitro

GNE-900 (1 μM; 1-48 h) induces apoptosis with increases in the expression of cleaved PARP when combined with gemcitabine (50 nM) in HT-29 cells[1].

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

Apoptosis Analysis[1]

Cell Line:	HT-29 cells

Concentration:	1 μM
Incubation Time:	1-48 h
Result:	Inducesd apoptosis with increased the expression of cleaved PARP when combination with gemcitabine (50 nM).

In Vivo

GNE-900 (2.5-40 mg/kg; p.o.; once) decreases the tumor volume and increases DNA damage, γ-H2AX levels when combinated with gemcitabine (HY-17026) in rats[1].

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

Animal Model:	Sprague-Dawley rats (HT-29 tumor xenografts)[1]
Dosage:	2.5-40 mg/kg (received a dose of gemcitabine 120 mg/kg)
Administration:	P.o.; once
Result:	Decreased the tumor volume and resulted in significant enhancement of DNA damage, increased γ-H2AX levels.

REFERENCES

[1]. Blackwood E, et al. Combination drug scheduling defines a "window of opportunity" for chemopotentiation of gemcitabine by an orally bioavailable, selective ChK1 inhibitor, GNE-900. Mol Cancer Ther. 2013 Oct;12(10):1968-80.

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