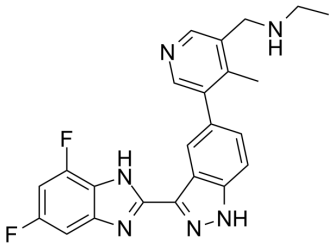
AG-024322

Cat. No.:	HY-15491
CAS No.:	837364-57-5
Molecular Formula:	$C_{23}H_{20}F_2N_6$
Molecular Weight:	418.44
Target:	COX; Apoptosis
Pathway:	Immunology/Inflammation; Apoptosis
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 (238.98 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3898 mL	11.9491 mL	23.8983 mL
5 mM	0.4780 mL	2.3898 mL	4.7797 mL
10 mM	0.2390 mL	1.1949 mL	2.3898 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 (5.97 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.97 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AG-024322 is a potent ATP-competitive pan-CDK inhibitor against cell cycle kinases CDK1, CDK2, and CDK4 with K_i values in the 1-3 nM range[1]. AG-024322 displays broad-spectrum anti-tumor activity and clear target modulation in vivo. AG-024322 induces cell apoptosis[3].

IC_{50} & Target

COX-1	COX-2	COX-4
2.3 nM (Ki)	3 nM (Ki)	2.9 nM (Ki)

In Vitro

AG-024322 (0.1-30 μM; 24 hours) is less toxic at concentrations below 3 μM, the viability of human PBMCs as measured by ATP content with a TC_{50} value of 1.4 μM for human PBMCs[2].

AG-024322 (0-120 nM) exhibits growth inhibition effects on HCT-116 cells. It is slightly less potent in the functional cellular

assay with an IC_{50} of 120 nM[2].

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

In Vivo

AG-024322 (intravenous infusion; 2, 6, and 10 mg/kg; 5 days) exhibits no-adverse-effect at 2 mg/kg with mean plasma AUC (0-24.5) of 2.11 g.h/mL. At 6 mg/kg produces pancytic bone marrow hypocellularity, lymphoid depletion. And vascular injury at the injection site renal tubular degeneration occurs at 10 mg/kg[1].

AG-024322 (20 mg/kg) inhibits the growth of established human tumor xenografts of different origins with tumor growth inhibition (TGI) ranging from 32% to 86.4%.It also exhibits anti-tumor effects as a dose-pdependent manner[3].

AG-024322 (20 mg/kg) causes a 65% TGI in the MV522 tumor model. It results a 52% TGI at 1/2 of the maximum tolerated dose (MTD) and only slight anti-tumor activity at 1/4 of the MTD[3].

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

Animal Model:	Male and female cynomolgus monkeys[1]
Dosage:	2, 6, and 10 mg/kg (Toxicity analysis)
Administration:	Intravenous infusion; 5 days
Result:	Resulted in dose-dependent pancytic bone marrow hypocellularity and lymphoid depletion in lymph nodes, spleen, and/or thymus at >6 mg/kg.

REFERENCES

[1]. Brown AP, et al. Toxicity and toxicokinetics of the cyclin-dependent kinase inhibitor AG-024322 in cynomolgus monkeys following intravenous infusion.Cancer Chemother Pharmacol. 2008 Nov;62(6):1091-101.

[2]. Jessen BA,et al. Peripheral white blood cell toxicity induced by broad spectrum cyclin-dependent kinase inhibitors.J Appl Toxicol. 2007 Mar-Apr;27(2):133-42.

[3]. Cathy C. Zhang, et al. AG-024322 is a multi-targeted CDK inhibitor with potent antitumor activity in vivo. Cellular and Molecular Biology 53: Cell Cycle Control and Cancer 1

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