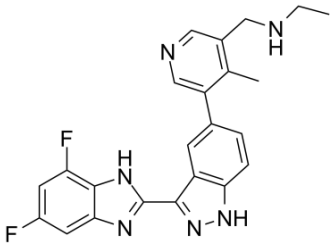
AG-024322

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:	Please store the product under the recommended conditions in the Certificate of Analysis.



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

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