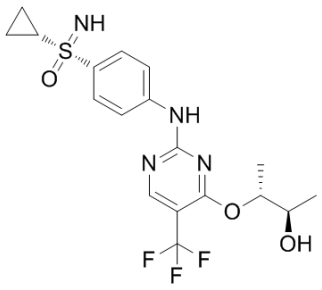
Roniciclib

Cat. No.:	HY-13914
CAS No.:	1223498-69-8
Molecular Formula:	$C_{18}H_{21}F_3N_4O_3S$
Molecular Weight:	430.44
Target:	CDK
Pathway:	Cell Cycle/DNA Damage
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 : ≥ 250 mg/mL (580.80 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3232 mL	11.6160 mL	23.2320 mL
5 mM	0.4646 mL	2.3232 mL	4.6464 mL
10 mM	0.2323 mL	1.1616 mL	2.3232 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: ≥ 2.08 mg/mL (4.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.83 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Roniciclib is an orally bioavailable pan-cyclin dependent kinase (CDK) inhibitor, with IC_{50}s of 5-25 nM for CDK1, CDK2, CDK3, CDK4, CDK7 and CDK9.

IC_{50} & Target

Cdk1/cyclin B 7 nM (IC_{50})	CDK2/cyclinE 9 nM (IC_{50})	CDK4/cyclin D 11 nM (IC_{50})	CDK9/cyclinT1 5 nM (IC_{50})
CDK7/Cyclin H/MAT1			

	25 nM (IC_{50})
In Vitro	Roniciclib (BAY 1000394) inhibits the kinase activity of the cell-cycle CDKs CDK1/cyclin B, CDK2/cyclin E, and CDK4/cyclinDwith IC_{50} values of 7, 9, and 11 nM, respectively. The transcriptional CDKs CDK9/cyclin T1 and CDK7/cyclin H/MAT1 are inhibited in a similar range (5 and 25 nM)[1]. Roniciclib potently inhibits the proliferation of various human and murine tumor cell lines with a very balanced profile (mean IC_{50} on human tumor cells: 16 nM)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tumor growth is strongly inhibited in a dose-dependent manner with T/C values of 0.19 at the lower dose and of 0.02 (tumor regression) at the higher dose. Furthermore, Roniciclib strongly inhibits growth of HeLa-MaTu tumors that have been grown to a size of approximately 50mm^2 before start of treatment (day 8 after inoculation). Treatment with Roniciclib at doses of 1.5 and 1 mg/kg slow tumor growth to T/C values of 0.15 and 0.62, respectively. Addition of Roniciclib to cisplatin result in a strong tumor growth inhibition with T/C values of 0.01 (1.0 mg/kg Roniciclib) and -0.02 (1.5 mg/kg Roniciclib)[1]. Roniciclib has low blood clearance rates in mouse, rat, and dog (0.51, 0.78, and 0.50 $Lh^{-1}kg^{-1}$, respectively) [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice[1] Athymic mice bearing established HeLa-MaTu xenograft tumors of approx. 25 mm^2 in size are treated orally with Roniciclib (BAY 1000394) at doses of 0.5, 1.0, 1.5, and 2.0 mg/kg once daily for 21 days. Treatment is well tolerated as no body weight loss below the initial body weight is observed. Additional groups of mice are treated on a cyclic intermittent dosing schedule at doses of 1.5, 2.0, and 2.5 mg/kg twice daily for 2 days followed by 5 days without treatment (2 on/5 off). In total, 3 treatment cycles are completed[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Siemeister G, et al. BAY 1000394, a novel cyclin-dependent kinase inhibitor, with potent antitumor activity in mono- and in combination treatment upon oral application. Mol Cancer Ther. 2012 Oct;11(10):2265-73.

[2]. Lücking U, et al. The lab oddity prevails: discovery of pan-CDK inhibitor (R)-S-cyclopropyl-S-(4-{[4-{[(1R,2R)-2-hydroxy-1-methylpropyl]oxy}-5-(trifluoromethyl)pyrimidin-2-yl]amino}phenyl)sulfoximide (BAY 1000394) for the treatment of cancer. ChemMedChem. 2013 Jul;8(7):1067-85.

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