# Roniciclib

**Cat. No.:** HY-13914

**CAS No.:** 1223498-69-8

**Molecular Formula:** $C_{18}H_{21}F_3N_4O_3S$

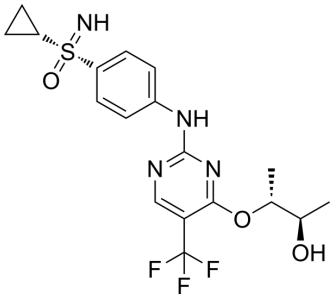
**Molecular Weight:** 430.44

**Target:** CDK

**Pathway:** Cell Cycle/DNA Damage

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 2 years |
| | -20°C | 1 year |



## 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<br>7 nM ($IC_{50}$) | CDK2/cyclinE<br>9 nM ($IC_{50}$) | CDK4/cyclin D<br>11 nM ($IC_{50}$) | CDK9/cyclinT1<br>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].<br>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].<br>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 50$mm^2$ 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].<br>Roniciclib has low blood clearance rates in mouse, rat, and dog (0.51, 0.78, and 0.50 $Lh^{-1}kg^{-1}$, respectively) [2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

| | |
|---|---|
| **Animal Administration** [1] | Mice[1]<br>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].<br>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.





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