

Product Data Sheet

Product Name: Roniciclib (BAY 1000394)

Cat. No.: GC33360

Chemical Properties

Cas. No. 1223498-69-8

SMILES C[C@@H](O)[C@H](OC1=NC(NC2=CC=C([S@@](=N)(C3CC3)=O)C=C2)=NC=C1C(F)(F)F)C

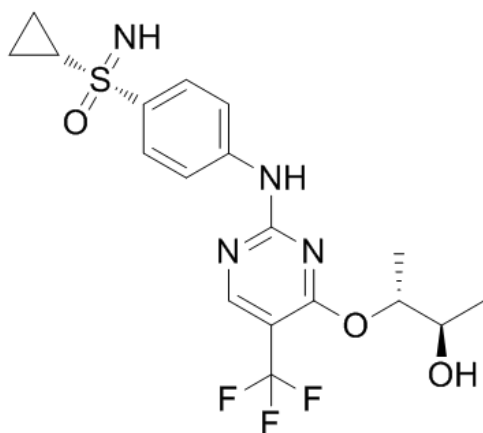
Formula $C_{18}H_{21}F_3N_4O_3S$ M.Wt 430.44

Solubility DMSO: ≥ 250 mg/mL (580.80 mM) Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

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Animal experiment: Mice[1]Athymic mice bearing established HeLa-MaTu xenograft tumors of approx. 25 mm² 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].

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.

Background

Roniciclib is an orally bioavailable pan-cyclin dependent kinase (CDK) inhibitor, with IC₅₀s of 5-25 nM for CDK1, CDK2, CDK3, CDK4, CDK7 and CDK9.

Roniciclib (BAY 1000394) inhibits the kinase activity of the cell-cycle CDKs CDK1/cyclin B, CDK2/cyclin E, and CDK4/cyclinD with IC₅₀ 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 IC₅₀ on human tumor cells: 16 nM)[2].

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 50mm² before start of treatment (day 8 after inoculation). Treatment with Roniciclib at doses of 1.5 and 1 mg/kg slow tumor

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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-1kg-1, respectively) [2].

[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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