

Product Data Sheet

Product Name: CDKI-73

Cat. No.: GC19096

Chemical Properties

Cas. No. 1421693-22-2

SMILES CNC1=NC(C)=C(C2=C(F)C=NC(NC3=CC(S(=O)(N)=O)=CC=C3)=N2)S1

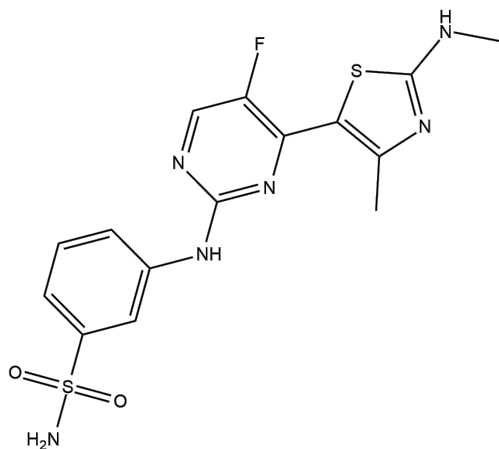
Formula $C_{15}H_{15}FN_6O_2S_2$ M.Wt 394.45

Solubility DMSO : ≥ 52 mg/mL (131.83 mM); Water : < 0.1 mg/mL (insoluble) 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



Background

CDKI-73 is a potent CDK9 inhibitor with K_i of 4 nM; shows selective toxicity to CLL cells ($\text{LD}_{50}=80$ nM) versus normal B cell and normal CD34+ cell ($\text{LD}_{50}>20$ μM). IC_{50} value: 4 nM/80 nM (K_i/LD_{50}) [1] Target: CDK9 inhibitor in vitro: CDKI-73 was cytotoxic to all of the CLL samples tested ($n = 38$) with a mean LD_{50} value of $0.08 \mu\text{M} \pm 0.10 \mu\text{M}$ following exposure to drug for 48h. In contrast, normal B-

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lymphocytes (n = 10) and CD34+ normal bone marrow cells (n = 5) were significantly less susceptible to the cytotoxic effects of CDKI-73. Treatment of CLL cells with 0.1 μ M CDKI-73 for 4h inhibited the phosphorylation of cdk9 and ser2 of RNA polymerase II. CDKI-73 induces a rapid loss of MCL1 protein and this is mediated by significant inhibition at the level of gene transcription. However, this inhibition is not restricted to MCL1 as similar reductions in XIAP and CCND2 were also observed following exposure to CDKI-73 for 4h [1]. CDKI-73 rapidly inhibited cellular CDK9 kinase activity and down-regulated the RNAPII phosphorylation. CDK9 shRNA was also found to down-regulate the Mnk1 expression. Both CDKI-73 and CDK9 shRNA decreased anti-apoptotic proteins Mcl-1 and Bcl-2 and induced apoptosis [2]. in vivo: CDKI-73 exhibited a favorable pharmacokinetic profile with oral bioavailability of F = 56% following a single intravenous bolus dose at 2 mg/kg and an oral dose at 10 mg/kg in mice [1].

References:

- [1]. Xie S, et al. Antitumor action of CDK inhibitor LS-007 as a single agent and in combination with ABT-199 against human acute leukemia cells. *Acta Pharmacol Sin.* 2016 Nov;37(11):1481-1489.
- [2]. Lam F, et al. Targeting RNA transcription and translation in ovarian cancer cells with pharmacological inhibitor CDKI-73. *Oncotarget.* 2014 Sep 15;5(17):7691-704.

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