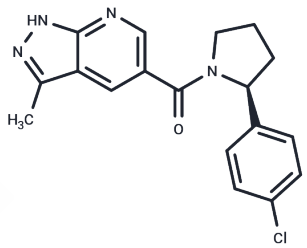
Data Sheet (Cat.No.TQ0266)

TargetMol

MSC2530818

Chemical Properties



CAS No. : 1883423-59-3

Formula: C18H17ClN4O

Molecular Weight: 340.81

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	MSC2530818 is an effective, selective and orally available CDK8 inhibitor (IC50: 2.6 nM).
Targets(IC50)	CDK
In vitro	MSC2530818 binds to CDK8 and CDK19 with a similar affinity (4 nM) and shows potent inhibition of phospho-STAT1SER727, a biomarker of CDK8 activity, in SW620 human colorectal carcinoma cells (pSTAT1SER727 IC50=8±2 nM). It also inhibits WNT-dependent transcription in human cancer cell lines with activated WNT signaling, including LS174T (β-catenin mutant, IC50=32±7 nM), COLO205 (APC mutant, IC50=9±1 nM), and WNT3a ligand-dependent reporter readout in PA-1 cells (IC50=52±30 nM). Moreover, MSC2530818 exhibits a low efflux ratio in Caco-2 cells and does not inhibit any cytochrome P450 subtypes.
In vivo	Treatment with MSC2530818 in mice carrying tumors resulted in a notable reduction of tumor growth, presenting T/C ratios of 49% and 57%. This compound was well accepted, showing no impact on the body weight of mice under a daily (qd) administration regimen, aside from controllable body weight loss. Additionally, its pharmacokinetic profile in humans indicates a low clearance (0.14 L/h/kg) and a small volume of distribution at steady-state (0.48 L/kg), leading to a brief estimated terminal half-life of 2.4 hours. Moreover, physiologically based pharmacokinetic simulations predict that MSC2530818 could achieve an oral bioavailability of at least 75% when administered up to a daily dose of 500 mg.
Animal Research	MSC2530818 is assessed in an established SW620 human colorectal cancer xenograft model in female NCr athymic mice. Tumor-bearing mice are treated orally with MSC2530818 (50 mg/kg bid or 100 mg/kg qd) for 16 days. Tumor weights are measured and body weights are monitored [1].

Solubility Information

Solubility	DMSO: 120 mg/mL (352.1 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4 mg/mL (11.74 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.9342 mL	14.6709 mL	29.3419 mL
5 mM	0.5868 mL	2.9342 mL	5.8684 mL
10 mM	0.2934 mL	1.4671 mL	2.9342 mL
50 mM	0.0587 mL	0.2934 mL	0.5868 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Czodrowski P, et al. Structure-Based Optimization of Potent, Selective, and Orally Bioavailable CDK8 Inhibitors Discovered by High-Throughput Screening. J Med Chem. 2016 Oct 27;59(20):9337-9349.

Li J, Bai Y, Liu Y, et al.Transcriptome-based chemical screens identify CDK8 as a common barrier in multiple cell reprogramming systems.Cell Reports.2023, 42(6).

Jiang L, Yu Y, Li Z, et al.BMS-265246, a Cyclin-Dependent Kinase Inhibitor, Inhibits the Infection of Herpes Simplex Virus Type 1.Viruses.2023, 15(8): 1642.

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