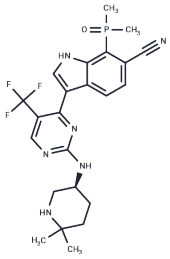
Data Sheet (Cat.No.T36038)

TargetMol

SY-5609

Chemical Properties



CAS No. : 2417302-07-7

Formula: C23H26F3N6OP

Molecular Weight: 490.46

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	SY-5609 (CDK7-IN-3) is a selective non-covalent CDK7 inhibitor (Kd value is 0.07 nM), with weak inhibitory activity against CDK2, CDK9 and CDK12 with IC50 values of 5.5, 1.9 and 1.7 μM, respectively, and has anti-tumor activity and inhibits cell apoptosis.
Targets(IC50)	Apoptosis,CDK
In vitro	**METHODS**: HCC70 cells were treated with SY-5609 （CDK7-IN-3） (25, 50, 100, 250, 500 nM), and protein samples were collected at 6, 24 and 48 h after treatment. Immunoblotting was used to detect the protein levels of Phospho-CDK2 T160, total CDK2, c-MYC, MCL1, cyclinB1, RNAPII Ser5 phosphorylation and total RNAPII; HCC70, MDA-MB-468, CAOV3, OVCAR3 and HDF cells were treated with SY-5609 （CDK7-IN-3） (100, 250, 500 nM) for 48 and 72 h, and Annexin V-FITC and propidium iodide (PI) were used to detect cell apoptosis. **RESULTS** Treatment of HCC70 cells with SY-5609 （CDK7-IN-3） for 24 and 48 hours inhibited phosphorylation of CDK2 at Thr160 by loss of CAK function; inhibition of CDK7 in TFIIH resulted in reduced phosphorylation of Ser5 in the C-terminal heptad repeat of RNA polymerase II and decreased cMyc levels; SY-5609 （CDK7-IN-3） treatment resulted in a mild reduction in MCL1 protein only at 48 h; SY-5609 （CDK7-IN-3） induced apoptosis and cell cycle arrest at G2/M in multiple cancer cell lines at 48 and 72 h, as detected by Annexin V/PI staining, but not in primary fibroblast cell lines. [1]
In vivo	**METHODS**: SY-5609 (CDK7-IN-3) (2 mg/kg, orally, once daily, for 21 days) was administered to HCC70 cell line-derived xenograft models, and tumor volume and body weight were measured twice weekly. One-tailed t test was used to evaluate the significance of the anti-tumor effect of SY-5609 (CDK7-IN-3). **RESULTS** The plasma exposure in mice treated with SY-5609 (CDK7-IN-3) was 261.28 ng h/mL, Cmax was 50.67 ng/mL (103 nM), and the elimination half-life was 3.33 h. During the 21-day dosing period, the tumor regressed and was well tolerated, with no tumor regrowth on day 28. [1]

Solubility Information

Solubility	DMSO: 16.7 mg/mL (34.05 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: 2 mg/mL (4.08 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	2.0389 mL	10.1945 mL	20.389 mL
5 mM	0.4078 mL	2.0389 mL	4.0778 mL
10 mM	0.2039 mL	1.0195 mL	2.0389 mL
50 mM	0.0408 mL	0.2039 mL	0.4078 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

Marineau JJ,et al. Discovery of SY-5609: A Selective, Noncovalent Inhibitor of CDK7. J Med Chem. 2022 Jan 27;65(2): 1458-1480.

Michael Bradley, et al. Inhibitors of cyclin-dependent kinase 7 (cdk7). WO2020093011A1.