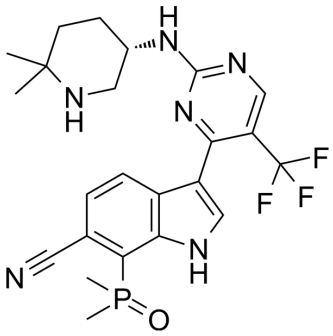
SY-5609

Cat. No.:	HY-138293
CAS No.:	2417302-07-7
Molecular Formula:	$C_{23}H_{26}F_3N_6OP$
Molecular Weight:	490.46
Target:	CDK; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Apoptosis
Storage:	4°C, stored under nitrogen * In solvent : -80°C, 2 years; -20°C, 1 year (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 40 mg/mL (81.56 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0389 mL	10.1945 mL	20.3890 mL
	5 mM	0.4078 mL	2.0389 mL	4.0778 mL
	10 mM	0.2039 mL	1.0195 mL	2.0389 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 4 mg/mL (8.16 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 4 mg/mL (8.16 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.10 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SY-5609 (CDK7-IN-3) is an orally active, highly selective, noncovalent CDK7 inhibitor with a K_D of 0.065 nM. SY-5609 shows poor inhibition on CDK2 (K_i=2600 nM), CDK9 (K_i=960 nM), CDK12 (K_i=870 nM). SY-5609 induces apoptosis in tumor cells and has antitumor activity[1][2].

IC_{50} & Target	CDK7	CDK2	CDK9	CDK12
	0.065 nM (Kd)	2600 nM (Ki)	960 nM (Ki)	870 nM (Ki)

In Vitro

SY-5609 (0.01-10000 nM; 72 hours) demonstrates strong antiproliferative effects in triple negative breast cancer (TNBC) and ovarian (OVA) cancer cells[1].

SY-5609 (100-500 nM; 48, 72 hours) induces apoptosis[1].
SY-5609 (100-500 nM; 48 hours) induces G2/M cell cycle arrest in HCC70 cells[1].
SY-5609 (25-500 nM; 6-48 hours) results in inhibition of the phosphorylation of CDK2 at Thr160 via loss of CAK function for 24 and 48 h[1].
SY-5609 (compound 101; 126.4 pM-4 μM; 72 hours) has an EC_{50} of 5.6 nM in HCC70 cell line[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	HCC70, MDA-MB453, COV504, A2780, OVCAR3, CAOV3 cells
Concentration:	0.01-10000 nM
Incubation Time:	72 hours
Result:	Demonstrated strong antiproliferative effects with IC_{50} of 1-6 nM.

Apoptosis Analysis[1]

Cell Line:	HCC70, MDA-MB-468, CAOV3 and OVCAR3 cells
Concentration:	100, 250, 500 nM
Incubation Time:	48 and 72 hours
Result:	Induced apoptosis.

Cell Cycle Analysis[1]

Cell Line:	HCC70 cells
Concentration:	100, 250, 500 nM
Incubation Time:	48 hours
Result:	Induced G2/M cell cycle arrest.

Western Blot Analysis[1]

Cell Line:	HCC70 cells
Concentration:	25, 50, 100, 250, 500 nM
Incubation Time:	6, 24, 48 hours
Result:	Resulted in inhibition of the phosphorylation of CDK2 at Thr160 via loss of CAK function for 24 and 48 h.

In Vivo

SY-5609 (2 mg/kg/day; orally; for 21 days) induces tumor regression over the 21-day dosing period[1].
Daily oral dosing of 2 mg/kg SY-5609 in mice provided a plasma exposure of 261.28 ng h/mL with a C_{max} of 50.67 ng/mL (103 nM) and an elimination half-life of 3.33 h[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Six-to-eight-week-old Balb/c nude female mice with HCC70 cell line[1]
Dosage:	2 mg/kg
Administration:	Orally; daily; for 21 days

Result:	Induced tumor regression over the 21-day dosing period and was well tolerated. No regrowth of tumor was observed out to day 28.

CUSTOMER VALIDATION

- bioRxiv. 2023 Apr 23.

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REFERENCES

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

[2]. Jason J Marineau, et al. Discovery of SY-5609: A Selective, Noncovalent Inhibitor of CDK7. J Med Chem. 2021 Nov 2.

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