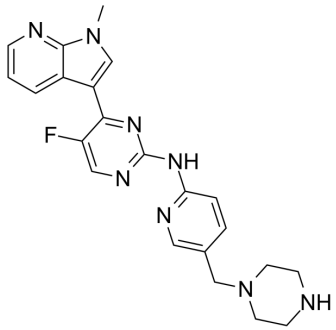
CDK4/6-IN-10

Cat. No.:	HY-115993
CAS No.:	2688098-11-3
Molecular Formula:	$C_{22}H_{23}FN_8$
Molecular Weight:	418.47
Target:	CDK; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

CDK4/6-IN-10 is a potent, selective and orally active CDK4 and CDK6 inhibitor with IC_{50}s of 22 nM and 10 nM, respectively. CDK4/6-IN-10 shows antitumor activity. CDK4/6-IN-10 has the potential for the research of Multiple myeloma (MM)[1].

IC_{50} & Target

CDK4	CDK6/cyclinD1
22 nM (IC_{50})	10 nM (IC_{50})

In Vitro

CDK4/6-IN-10 (compouns 32) (1 μM) shows kinase selectivity with IC_{50}s of 22 nM and 10 nM for CDK4 and CDK6, respectively [1].

CDK4/6-IN-10 (72 h) shows antiproliferative activity (GI_{50}s of 2.028, 5.802, 2.286, 2.238, 1.526, 11.381 μM for RPMI-8226, U266, K562, HL-60, 22RV1, HEK-293 cells, respectively)[1].

CDK4/6-IN-10 (0, 1.5, 3, 6 μM, 24 h) induces cell cycle arrest at the G1 phase in a concentration-dependent manner[1].

CDK4/6-IN-10 (0, 1, 2, 3 μM, 24 h) induces apoptosis of RPMI-8226 cells in a concentration-dependent manner[1].

CDK4/6-IN-10 (0, 1.5, 3, 6 μM, 24 h) reduces the CDK4/6 activity by decreases the expression level of p-RB, c-MYC and BCL-2[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	RPMI-8226, U266, K562, HL-60, 22RV1, HEK-293 cells
Concentration:	
Incubation Time:	72 h
Result:	Shows antiproliferative activity (GI_{50}s of 2.028, 5.802, 2.286, 2.238, 1.526, 11.381 μM for RPMI-8226, U266, K562, HL-60, 22RV1, HEK-293 cells, respectively).

Cell Cycle Analysis[1]

Cell Line:	RPMI-8226 cells
Concentration:	0, 1.5, 3, 6 μM
Incubation Time:	24 h
Result:	Cells were arrested at the G1 phase in a concentration-dependent manner.

Apoptosis Analysis[1]

Cell Line:	RPMI-8226 cells
Concentration:	0, 1.5, 3, 6 μM
Incubation Time:	24 h
Result:	Reduced the CD4/K activity by decreased the expression level of p-RB, c-MYC and BCL-2.

In Vivo

CDK4/6-IN-10 (1000, 5000, 10000 mg/kg; p.o.) shows safety profile with LD_{50} much higher than 10,000 mg/kg[1].
CDK4/6-IN-10 (10 mg/kg; p.o.) shows oral bioavailability (F=51%) in SD rats[1].
CDK4/6-IN-10 (100, 200 mg/kg; p.o., once a day for 19 days) shows antitumor potency and favorable safety profile[1].
Pharmacokinetic Parameters of CDK4/6-IN-10 in SpragueeDawley rats[1].

Compd	Admin.	C_{max} (ng/mL)	AUC_{0-t} (h·ng/mL)	MRT_{0-t} (h)	T_{max} (h)	$t_{1/2}$ (h)	CL (mL/h/kg)	F (%)
32	i.v.	355	960	5.9	0.033	8.9	641	-
	p.o.	257	4,878	12.8	10.7	>24	524	51

SprageueDawley rats, 10 mg/kg, p.o.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	ICR mice[1]
Dosage:	1000, 5000, 10000 mg/kg
Administration:	p.o.
Result:	Showed safety profile with LD_{50} much higher than 10,000 mg/kg.

Animal Model:	SprageueDawley rats[1]
Dosage:	10 mg/kg
Administration:	p.o.
Result:	Showed oral bioavailability (F=51%).

Animal Model:	BALB/c nude mice (6-8 weeks) (MM xenograft model)[1]
Dosage:	100, 200 mg/kg
Administration:	p.o., once a day, 19 days
Result:	Showed antitumor potency and favorable safety profile.

REFERENCES

[1]. Yuan K, et al. Discovery of novel and orally bioavailable CDK 4/6 inhibitors with high kinome selectivity, low toxicity and long-acting stability for the treatment of multiple myeloma. Eur J Med Chem. 2022; 228:114024.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA