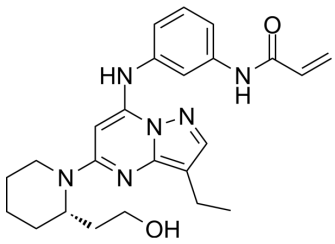
CDK12-IN-E9

Cat. No.:	HY-117203A
CAS No.:	2020052-55-3
Molecular Formula:	$C_{24}H_{30}N_6O_2$
Molecular Weight:	434.53
Target:	CDK
Pathway:	Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (287.67 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3013 mL	11.5067 mL	23.0134 mL
	5 mM	0.4603 mL	2.3013 mL	4.6027 mL
	10 mM	0.2301 mL	1.1507 mL	2.3013 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 20.83 mg/mL (47.94 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.79 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CDK12-IN-E9 is a potent and selective covalent CDK12 inhibitor and a non-covalent CDK9 inhibitor, while avoiding ABC transporter-mediated efflux. CDK12-IN-E9 has weak binding ability to CDK7/CyclinH complex with an IC_{50}> 1 μM[1].

IC_{50} & Target				
	CDK12	CDK9/cyclinT1 23.9 nM (IC_{50})	cdk2/cyclin A 932 nM (IC_{50})	CDK7/Cyclin H/MNAT1 1210 nM (IC_{50})

In Vitro

CDK12-IN-E9 (E9; 10 nM-10 μM; 72 hours; Kelly, LAN5, SK-N-BE2, PC-9, NCI-H82 and NCI-H3122 cells) treatment shows potent antiproliferative activity in $THZ1^R$ NB and lung cancer cells, with IC_{50} values ranging from 8 to 40 nM[1].
CDK12-IN-E9 (E9; 0-3000 nM; 6 hours; Kelly, PC-9, and NCI-H82 cells) treatment leads to a dose-dependent decrease in phosphorylated and total RNAPII in $THZ1^r$ NB and lung cancer models, accompanied by decreased MYC and MCL1

expression[1].

CDK12-IN-E9 also results in increased PARP cleavage, and an increase in the subGI population in THZ1^r lung cancer cells, while in NB cells, more of a G2/M arrest is seen after a 24-hr exposure to CDK12-IN-E9[1].

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

Cell Proliferation Assay[1]

Cell Line:	Kelly, LAN5, SK-N-BE2, PC-9, NCI-H82 and NCI-H3122 cells
Concentration:	10 nM-10 μM
Incubation Time:	72 hours
Result:	Showed potent antiproliferative activity in THZ1^R NB and lung cancer cells, with IC_{50} values ranging from 8 to 40 nM.

Western Blot Analysis[1]

Cell Line:	Kelly, PC-9, and NCI-H82 cells
Concentration:	0 nM, 30 nM, 100 nM, 300 nM, 1000 nM, 3000 nM
Incubation Time:	6 hours
Result:	Led to a dose-dependent decrease in phosphorylated and total RNAPII in THZ1^r NB and lung cancer models.

REFERENCES

[1]. Gao Y, et al. Overcoming Resistance to the THZ Series of Covalent Transcriptional CDK Inhibitors. Cell Chem Biol. 2018 Feb 15;25(2):135-142.e5.

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