CDK6/PIM1-IN-1

Cat. No.: HY-142696

CAS No.: 2677026-14-9

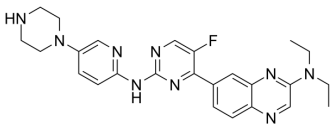
Molecular Formula: $C_{25}H_{28}FN_9$

Molecular Weight: 473.55

Target: CDK; Pim; Apoptosis

Pathway: Cell Cycle/DNA Damage; JAK/STAT Signaling; Apoptosis

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

CDK6/PIM1-IN-1 is a potent and balanced dual CDK6/PIM1 inhibitor with IC_{50} values of 39 and 88 nM, respectively. CDK6/PIM1-IN-1 inhibits CDK4 (IC_{50}=3.6 nM). CDK6/PIM1-IN-1 significantly inhibits acute myeloid leukemia (AML) cell proliferation, arrest cell cycle at the G1 phase, and promote cell apoptosis. CDK6/PIM1-IN-1 exhibits potent anti-AML activity[1].

IC_{50} & Target

CDK6/cyclinD1 39 nM (IC_{50})	CDK1/cyclinB >10 μM (IC_{50})	CDK2/cyclinA 2.274 μM (IC_{50})	CDK3/Cyclin E >10 μM (IC_{50})
Cdk4/cyclin D1 3.6 nM (IC_{50})	Cdk5/p25 >10 μM (IC_{50})	CDK7/Cyclin H/MNAT1 393 nM (IC_{50})	CDK9/cyclinT1 440 nM (IC_{50})
CDK12/Cyclin K >10 μM (IC_{50})	CDK13/Cyclin K >10 μM (IC_{50})	PIM1 88 nM (IC_{50})	PIM2 >10 μM (IC_{50})
PIM3 92 nM (IC_{50})			

In Vitro

CDK6/PIM1-IN-1 (compound 51) exhibits more than 10 times selectivity over CDK1 (IC_{50}>10 μM), CDK2 (IC_{50}=2.274 μM), CDK3 (IC_{50}>10 μM), CDK5 (IC_{50}>10 μM), CDK7 (IC_{50}=393 nM), CDK9 (IC_{50}=440 nM), CDK12 (IC_{50}>10 μM), and CDK13 (IC_{50}>10 μM). CDK6/PIM1-IN-1 shows inhibitory activity against PIM2 (IC_{50}>10 μM) and PIM3 (IC_{50}=92 nM)[1].

CDK6/PIM1-IN-1 inhibits proliferation in AML cells (K562 cell,GI_{50}=1.026 μM; HL-60 cell,GI_{50}=1.069 μM; MOLM13 cell, GI_{50} =1.362 μM)[1].

CDK6/PIM1-IN-1 (0.5, 1, 1.5 μM) causes a G1 arrest in a dose-dependent manner in K562 and HL-60 cell lines[1].

CDK6/PIM1-IN-1 (1, 2, 4 μM) promotes the apoptosis of K562 and HL-60 cell lines in a dose-dependent manner[1].

CDK6/PIM1-IN-1 (0.5, 1, 1.5 μM; for 24 h) reduces p-retinoblastoma (RB) and p-BAD levels in a concentration-dependent manner. CDK6/PIM1-IN-1 decreases the PIM1 level[1].

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

In Vivo

CDK6/PIM1-IN-1 (compound 51; orally; 60, 90 mg/kg/day; 17 days) displays more potent antitumor activity in BALB/c mice with K562 cell lines[1].

CDK6/PIM1-IN-1 (iv; 5 mg/kg) has the $t_{1/2}$, $MRT_{0-\infty}$, and $AUC_{0-\infty}$ values of 9.78 h, 14.61 h, and 1153.74 h·ng/mL, respectively in Sprague–Dawley (SD) rats[1].

CDK6/PIM1-IN-1 (po; 5 mg/kg) has the $t_{1/2}$, T_{max}, C_{max}, and $AUC_{0-\infty}$ of 15.81 h, 11 h, 152.31 ng/mL, and 5152.92 h·ng/mL,

	respectively in SD rats[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Kai Yuan, et al. Discovery of Dual CDK6/PIM1 Inhibitors with a Novel Structure, High Potency, and Favorable Druggability for the Treatment of Acute Myeloid Leukemia. J Med Chem. 2022 Jan 13;65(1):857-875.

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