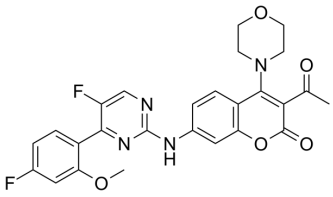
CDK9-IN-19

Cat. No.:	HY-150562
CAS No.:	2479306-60-8
Molecular Formula:	$C_{26}H_{22}F_2N_4O_5$
Molecular Weight:	508.47
Target:	CDK
Pathway:	Cell Cycle/DNA Damage
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

CDK9-IN-19 is a highly potent and selective CDK9 inhibitor with an IC_{50} value of 2.0 nM. CDK9-IN-19 has excellent cellular antiproliferative activity, moderate pharmacokinetic property and low hERG inhibition. CDK9-IN-19 significantly induces tumour growth inhibition in an MV4-11 xenograft mice model. CDK9-IN-19 can be used for researching acute myeloid leukaemia (AML)[1].

IC_{50} & Target

CDK9/cyclinT1
2 nM (IC_{50})

In Vitro

CDK9-IN-19 (compound 30i) has antiproliferative activity against a panel of human tumor cell lines with IC_{50} ranks of 0.08~0.64 μM (for example: Hep G2, HCT-116, SW620, A549, MV-4-11, et al.)[1].
CDK9-IN-19 has low hERG inhibitory activity (IC_{50}=10080 nM) and over 5000-fold selectivity for CDK9[1].
CDK9-IN-19 (0.1-0.8 μM; 24 h) reduces the expression levels of Mcl-1 and c-Myc[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	MV4-11
Concentration:	0.1, 0.2, 0.4 and 0.8 μM
Incubation Time:	24 h
Result:	Clearly reduced the expression levels of Mcl-1 and c-Myc at 0.1 μM, and completely reduced at 0.2-0.8 μM.

In Vivo

CDK9-IN-19 (10, 20 or 40 mg/kg; IV, for 32 days) significantly suppresses the tumour progression in MV4-11 xenograft model [1].

Pharmacokinetic Parameters of CDK9-IN-19 in ICR mice[1].

	PO (30 mg/kg)	IV (2 mg/kg)
$T_{1/2}$ (h)	NR	0.23

T_{max} (h)	0.25	-
C_0 (ng/mL)	-	3060
C_{max} (ng/mL)	665	-
AUC_{0-t} (ng/mL·h)	1200	560
$AUC_{0-\infty}$ (ng/mL·h)	NR	561
CL (L/h/kg)	-	3.56
Vd_{SS} (L/kg)	-	0.67
F (%)	14.3	-

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

Animal Model:	Female BALB/c nude mice (injected with MV4-11)[1]
Dosage:	10, 20 or 40 mg/kg
Administration:	IV, for 32 days
Result:	Significantly suppressed the tumour progression and tumour growth inhibition (TGI) values up to 100% from days 14-32 at 40 mg/kg.

REFERENCES

[1]. Xu J, et al. Discovery of coumarin derivatives as potent and selective cyclin-dependent kinase 9 (CDK9) inhibitors with high antitumour activity. Eur J Med Chem. 2020 Aug 15;200:112424.

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