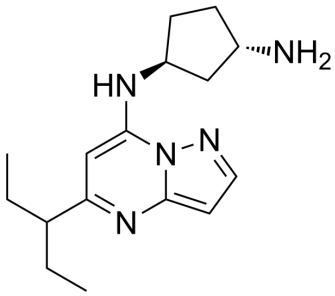
KB-0742

Cat. No.:	HY-137478
CAS No.:	2416873-83-9
Molecular Formula:	$C_{16}H_{25}N_5$
Molecular Weight:	287.4
Target:	CDK
Pathway:	Cell Cycle/DNA Damage
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	KB-0742 is a potent, selective and orally active CDK9 inhibitor with an IC_{50} of 6 nM for CDK9/cyclin T1. KB-0742 is selective for CDK9/cyclin T1 with >50-fold selectivity over other CDK kinases. KB-0742 has potent anti-tumor activity[1].
IC_{50} & Target	CDK9/cyclinT1 6 nM (IC_{50})

In Vitro

KB-0742 (6 hours; 0.1-10 μM; 22Rv1 cells) treatment significant reduction of downstream phosphorylation of RNA Pol II at Ser2 and Ser7, and diminished phosphorylation at Ser5. Global androgen receptor (AR)-FL and AR-V protein levels are significantly reduced starting at 6 h treatment time, which is accompanied by the reduction of phospho-AR levels (Ser81)[1].
KB-0742 (48-72 hours) treatment shows cytostatic effects in prostate cancer and leukemia cell lines. KB-0742 shows antiproliferative activity with GR_{50}s of 0.183 μM and 0.288 μM for 22Rv1 cells and MV-4-11 AML cells, respectively[1].
In 22Rv1 cells, KB-0742 rapidly downregulates nascent transcription, preferentially depleting short half-life transcripts and AR-driven oncogenic programs[1].

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

Western Blot Analysis[1]

Cell Line:	22Rv1 cells
Concentration:	0.1 μM, 0.5 μM, 1 μM, 10 μM
Incubation Time:	6 hours
Result:	Significant reduction of downstream phosphorylation of RNA Pol II at Ser2 and Ser7, and diminished phosphorylation at Ser5.

In Vivo

KB-0742 (3-30 mg/kg; p.o.; daily; over 21 days) is well tolerated even at high dose, while significantly reducing tumor burden in 22Rv1 human prostate cancer cell line-derived xenograft (CDX) models[1].

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Animal Model:	Male CB17-SCID mice injected with 22Rv1 human prostate cancer cells[1]
Dosage:	3 mg/kg, 10 mg/kg, and 30 mg/kg

Administration:	p.o.; daily; over 21 days
Result:	Significantly reduced tumor growth in castration-resistant prostate cancer (CRPC).

REFERENCES

[1]. André Richters, et al. Modulating Androgen Receptor-Driven Transcription in Prostate Cancer with Selective CDK9 Inhibitors. Cell Chem Biol. 2020 Oct 20;S2451-9456(20)30380-9.

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