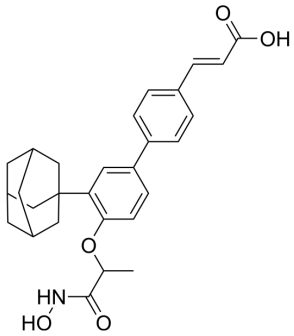
GEM144

Cat. No.:	HY-143411
CAS No.:	2487526-28-1
Molecular Formula:	$C_{28}H_{31}NO_5$
Molecular Weight:	461.55
Target:	HDAC; Apoptosis; DNA/RNA Synthesis
Pathway:	Cell Cycle/DNA Damage; Epigenetics; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

GEM144 is a potent and orally active DNA polymerase α (POLA1) and HDAC 11 dual inhibitor. GEM144 induces acetylation of p53, activation of p21, G1/S cell cycle arrest, and apoptosis. GEM144 has significant antitumor activity in human orthotopic malignant pleural mesothelioma xenografts[1].

IC_{50} & Target

HDAC11
8.23 μM (IC_{50})

In Vitro

GEM144 (0-10 μM; 24 hours) exhibits antiproliferative activity in tested cancer cell lines with IC_{50}s of 0.26 ~ 2.2 μM[1].
GEM144 (0.1 - 0.4 μM; 24 hours) strongly increases levels of H2AX phosphorylation on Ser 39 (γH2AX), and strongly upregulates p21 expression in a dose-dependent manner[1].
GEM144 (0.26 μM in NCI-H4609, 0.95 μM in A2780 and 1.4 μM in MM473; 72 hours) induced G1/S cell cycle arrest[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay

Cell Line:	NCI-H460, H460-R9A, A2780 and A2780-DX[1]
Concentration:	0-10 μM
Incubation Time:	24 hours (further 48 h growth in drug-free medium)
Result:	Exhibited antiproliferative activity in tested cancer cell lines with IC_{50}s of 0.26 ~ 2.2 μM.

Western Blot Analysis

Cell Line:	NCI-H460[1]
Concentration:	0.1 μM, 0.25 μM and 0.4 μM
Incubation Time:	24 hours
Result:	Strongly increased levels of H2AX phosphorylation on Ser 39 (γH2AX), and strongly upregulated p21 expression in a dose-dependent manner.

Cell Cycle Analysis

Cell Line:	NCI-H4609, A2780 and MM473[1]
Concentration:	0.26 μM in NCI-H4609, 0.95 μM in A2780 and 1.4 μM in MM473
Incubation Time:	72 hours
Result:	Induced G1/S cell cycle arrest.

In Vivo

GEM144 (50 mg/kg; p.o., bid, 5 days a week, for 3-4 weeks) significantly reduces tumor burden of MM487 with TGI of 72% in xenografts mice[1].

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Animal Model:	Female CD-1 nude mice (injected with MM473 and MM487)[1]
Dosage:	50 mg/kg
Administration:	PO, bid, 5 days a week, for 3-4 weeks
Result:	Significantly reduced tumor burden of MM487 with TGI of 72%.

REFERENCES

[1]. Dallavalle S, et al. Antitumor activity of novel POLA1-HDAC11 dual inhibitors. Eur J Med Chem. 2022;228:113971.

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