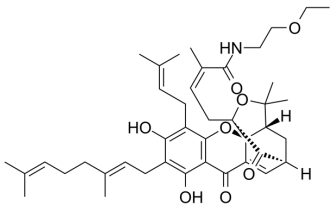
GNA002

Cat. No.:	HY-101508
CAS No.:	1385035-79-9
Molecular Formula:	$C_{42}H_{55}NO_8$
Molecular Weight:	701.89
Target:	Histone Methyltransferase
Pathway:	Epigenetics
Storage:	-20°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (35.62 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4247 mL	7.1236 mL	14.2472 mL
	5 mM	0.2849 mL	1.4247 mL	2.8494 mL
	10 mM	0.1425 mL	0.7124 mL	1.4247 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (1.78 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 1.25 mg/mL (1.78 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

GNA002 is a highly potent, specific and covalent EZH2 (Enhancer of zeste homolog 2) inhibitor with an IC_{50} of 1.1 μM. GNA002 can specifically and covalently bind to Cys668 within the EZH2-SET domain, triggering EZH2 degradation through COOH terminus of Hsp70-interacting protein (CHIP)-mediated ubiquitination. GNA002 efficiently reduces EZH2-mediated H3K27 trimethylation, reactivates polycomb repressor complex 2 (PRC2)-silenced tumor suppressor genes[1].

IC_{50} & Target

EZH2
1.1 μM (IC_{50})

In Vitro

GNA002 (10 μM; 72 hours) clearly inhibits the proliferation of numerous cancer cell lines with IC_{50}s of 0.070 μM and 0.103 μM for MV4-11 and RS4-11[1].
GNA002 (2 μM; 24 hours) demonstrates an elevated capacity to induce cell death in human cancer cells[1].

GNA002 (0.1-4 μM; 48 hours) efficiently reduces EZH2-mediated H3K27 trimethylation in Cal-27 head and neck cancer cells[1].

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

Cell Proliferation Assay[1]

Cell Line:	Numerous cancer cell lines
Concentration:	10 μM
Incubation Time:	72 hours
Result:	Inhibited the proliferation of numerous cancer cell lines with IC50s of 0.070 μM and 0.103 μM for MV4-11 and RS4-11.

Apoptosis Analysis[1]

Cell Line:	HN-4 and Cal-27 head and neck cancer cells
Concentration:	2 μM
Incubation Time:	24 hours
Result:	Induced cellular apoptosis in human cancer cells.

Western Blot Analysis[1]

Cell Line:	Cal-27 head and neck cancer cells
Concentration:	0.1, 0.2, 0.5, 1, 2, 4 μM
Incubation Time:	48 hours
Result:	Reduced H3K27Me3 levels.

In Vivo

GNA002 (oral administration; 100 mg/kg; daily) significantly decreases the volumes of Cal-27-derived tumors and reduces H3K27Me3 levels in tumor tissues. GNA002 also significantly suppresses the in vivo tumor growth derived from the xenografted A549 lung cancer cells, Daudi and Pfeiffer cells. GNA002 inhibits the aberrant oncogenic functions of EZH2, thus inhibiting tumor growth in vivo, at least in the xenograft experimental model[1].

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

Animal Model:	Male BALB/C Nude mice aged 30-35 days and weighing 18-22 g, bearing Cal-27 xenograft tumors[1]
Dosage:	100 mg/kg
Administration:	Oral administration; daily
Result:	Decreased the size and weight of tumors formed by Cal-27 cells.

REFERENCES

[1]. Wang X, et al. A covalently bound inhibitor triggers EZH2 degradation through CHIP-mediated ubiquitination. EMBO J. 2017 May, 36(9):1243-1260.

Caution: Product has not been fully validated for medical applications. For research use only.

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