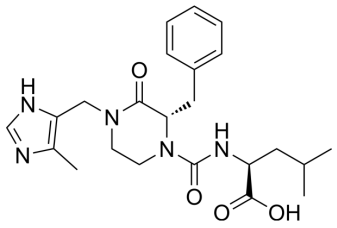
GGTI-2418

Cat. No.:	HY-16231
CAS No.:	501010-06-6
Molecular Formula:	$C_{23}H_{31}N_5O_4$
Molecular Weight:	441.52
Target:	Apoptosis
Pathway:	Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (283.11 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2649 mL	11.3245 mL	22.6490 mL
5 mM	0.4530 mL	2.2649 mL	4.5298 mL
10 mM	0.2265 mL	1.1325 mL	2.2649 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: ≥ 2.08 mg/mL (4.71 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.71 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.71 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GGTI-2418 is a highly potent, competitive, and selective geranylgeranyltransferase I (GGTase I) inhibitor. GGTI-2418 inhibits GGTase I and FTase activities with IC_{50}s of 9.5 nM and 53 μM, respectively. GGTI-2418 also increases p27(Kip1) and induces significant regression of breast tumors[1].

IC_{50} & Target

IC50: 9.5 nM (GGTase I), 53 μM (FTase)[1]

In Vitro

GGTI-2418 inhibits GGTase I and FTase activities with IC_{50}s of 9.5±2.0 nM and 53±11 μM, respectively, a 5,600-fold selectivity

toward inhibition of GGTase I versus FTase. GGTI-2418 demonstrates competitive inhibition of GGTase I against the H-Ras-CVLL protein with a K_i of 4.4±1.6 nM[1].
GGTi-2418 (10-15 μM; 16 hours) treatment delocalizes FBXL2 and stabilizes IP3R3[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[2]

Cell Line:	HeLa cells
Concentration:	10-15 μM
Incubation Time:	16 hours
Result:	Delocalized FBXL2 and stabilized IP3R3.

In Vivo

GGTI-2418 (100 mg/kg daily or 200 mg/kg every third day; 15 days) significantly inhibits the growth of breast tumor xenografts in nude mice with MDA-MB-231 xenografts[1].
GGTI-2418 (100 mg/kg daily; 5 days) induces regression of ErbB2-driven mammary tumors in ErbB2 transgenic mice[1].
GGTI-2418 inhibits the geranylgeranylation of Rap1 and causes a dramatic decrease in S473 phosphorylation of Akt. GGTI-2418 also upregulates p27 levels in vivo[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Nude mice implanted with MDA-MB-231 breast cancer tumors[1]
Dosage:	100 mg/kg daily or 200 mg/kg every third day
Administration:	Injected intraperitoneally; 15 days
Result:	Inhibited the growth of breast tumor xenografts.

Animal Model:	ErbB2 transgenic mice[1]
Dosage:	100 mg/kg/day
Administration:	Subcutaneously; 5 days
Result:	Halted tumor growth and induced massive tumor regression. Tumor decreased by 76% following GGTI-2418 treatment.

REFERENCES

[1]. Kazi A, et al. Blockade of protein geranylgeranylation inhibits Cdk2-dependent p27Kip1 phosphorylation on Thr187 and accumulates p27Kip1 in the nucleus: implications for breast cancer therapy. Mol Cell Biol. 2009 Apr;29(8):2254-63.

[2]. Kuchay S, et al. PTEN counteracts FBXL2 to promote IP3R3- and Ca^{2+}-mediated apoptosis limiting tumour growth. Nature. 2017 Jun 22;546(7659):554-558.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA