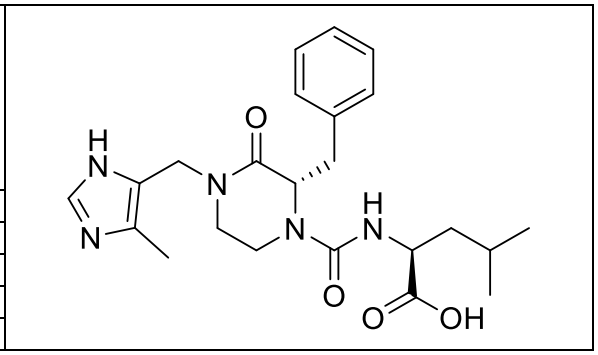
Product data sheet

MedKoo Cat#: 205472 Name: GGTI-2418 CAS: 501010-06-6 (free acid) Chemical Formula: $C_{23}H_{31}N_5O_4$ Exact Mass: 441.2376 Molecular Weight: 441.532	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

GGTI-2418, also known as PTX100, is a synthetic peptidomimetic inhibitor of geranylgeranyltransferase I (GGTase I) that appears to induce apoptosis by downregulating several pivotal oncogenic and tumor survival pathways. GGTase I catalyzes the lipid posttranslational modification which is required for the function of Rho GTPases (frequently found aberrantly activated in human cancer). GGTase I inhibitors block Rho function in cancer cells and induce a G1 phase cell cycle arrest by a mechanism involving induction of the CDK inhibitors p21waf and p27kip, CDK2 and CDK4 inhibition and hypophoshorylation of the tumor suppressor Rb. GGTase I inhibitors also induce apoptosis by a mechanism involving downregulation of the expression of survivin and suppression of the activation of PI3K/Akt.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	125.0	283.11

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.26 mL	11.32 mL	22.65 mL
5 mM	0.45 mL	2.26 mL	4.53 mL
10 mM	0.23 mL	1.13 mL	2.26 mL
50 mM	0.05 mL	0.23 mL	0.45 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Kazi A, Carie A, Blaskovich MA, Bucher C, Thai V, Moulder S, Peng H, Carrico D, Pusateri E, Pledger WJ, Berndt N, Hamilton A, Sebti SM. 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. doi: 10.1128/MCB.01029-08. Epub 2009 Feb 9. PMID: 19204084; PMCID: PMC2663293.

In vivo study

1. Kazi A, Carie A, Blaskovich MA, Bucher C, Thai V, Moulder S, Peng H, Carrico D, Pusateri E, Pledger WJ, Berndt N, Hamilton A, Sebti SM. 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. doi: 10.1128/MCB.01029-08. Epub 2009 Feb 9. PMID: 19204084; PMCID: PMC2663293.

7. Bioactivity

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Biological target:

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.

In vitro activity

In vitro, GGTI-2418 inhibited GGTase I and FTase activities with 50% inhibitory concentrations (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 demonstrated competitive inhibition of GGTase I against the H-Ras-CVLL protein with a K_i value of 4.4 ± 1.6 nM (Fig. 1C).

Reference: Mol Cell Biol. 2009 Apr;29(8):2254-63. https://pubmed.ncbi.nlm.nih.gov/19204084/

In vivo activity

In contrast, treatment with GGTI-2418 at 100 mg/kg/day not only halted tumor growth, but also actually induced massive tumor regression within a few days. Figures 5B and C show a representative example of a tumor that decreased by 76% following GGTI-2418 treatment. The degree of regression was independent of the size of the tumor before initiation of treatment; in seven mice with a total of 17 tumors, treatment with 100 mg/kg GGTI-2418 resulted in tumor regression between 34 and 100%, with an average of 60% ± 4% (standard error of the mean) (see Table S1 in the supplemental material).

Reference: Mol Cell Biol. 2009 Apr;29(8):2254-63. https://pubmed.ncbi.nlm.nih.gov/19204084/