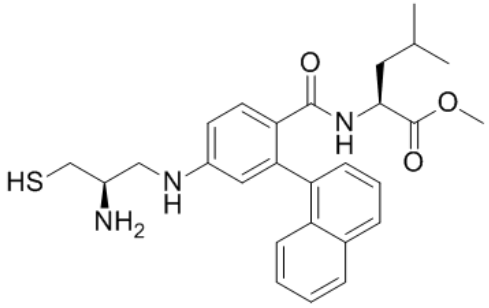
Product Data Sheet

Product Name: GGTI298
Cat. No.: GC36134

Chemical Properties

Cas. No.	180977-44-0		
SMILES	CC(C)C[C@@H](C(OC)=O)NC(C1=CC=C(NC[C@@H](N)CS)C=C1C2=C3C=CC=CC3=CC=C2)=O		
Formula	$C_{27}H_{33}N_3O_3S$	M.Wt	479.63
Solubility	DMSO: 100 mg/mL (208.49 mM); Water: < 0.1 mg/mL (insoluble)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines A549 cells

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Preparation Method	A549 cells were seeded (5×10^3 cells per well in 100μL DMEM with 10% FBS) in a 96-well flat-bottomed plate at 24h prior to treatment. A549 cells were treated with gefitinib (5μM) and/or GGTI298 (concentration indicated) for 48h at 37°C in a humidified (5% CO_2, 95% air) incubator. Following incubation at 37°C, cell growth was measured using a Cell Counting Kit-8.
Reaction Conditions	2.5-5μM; 48h
Applications	Gefitinib and GGTI298 have synergistic anti-proliferative effects on cells.

Animal experiment [2]:

Animal models	Luc-G33 cells xenograft mice model
Preparation Method	The nude mice were initially weighed and anesthetized intraperitoneally with 10% chloral hydrate at 0.1ml/30g live weight. The operative area was prepared with iodine. Each mouse was then given an intraosseous (1×10^6) and a subcutaneous injection (3×10^6) of Luc-G33 cells in hydrogel into the tibia and under the dorsal skin, respectively. A preliminary study had been proceeded on eight mice for observing the duration of the BLI signals from the Luc-G33 cells in the mice in vivo. Thirty-two mice after Luc-G33 implantation were randomly divided into four groups (8 mice/group) with equal average body weight and drugs were given to each mice three days after cell injection. Group 1 was then given 0.9% sodium chloride (Abbott) as the vehicle control treatment; Groups 2–4 were given Zoledronate (ZOL) and GGTI298 treatments at the following dosages: group 2 treated with ZOL alone at 400mg/kg; group 3 with GGTI298 alone at 1.16mg/kg; and group 4 with the combination of ZOL at 400mg/kg and GGTI298 at 1.16mg/kg.

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Dosage form	1.16mg/kg; sc; 35d
Applications	Combination treatment with Zoledronate and GGTI298 both reduced tumor proliferation.

References:
[1]. Liu B S, Dai X Y, Xia H W, et al. Geranylgeranyl transferase 1 inhibitor GGTI-298 enhances the anticancer effect of gefitinib[J]. Molecular Medicine Reports, 2018, 18(4): 4023-4029.
[2]. Lau C P Y, Wong K C, Huang L, et al. A mouse model of luciferase-transfected stromal cells of giant cell tumor of bone[J]. Connective tissue research, 2015, 56(6): 493-503.

Background

GGTI298 is a selective, irreversible inhibitor of geranylgeranyl transferase I (GGTase-I) (IC_{50} = 3μM) [1]. By inhibiting GGTase-I, GGTI298 blocks geranylgeranylation of small GTPases such as RhoA, leading to cell cycle arrest at the G0/G1 phase and induction of apoptosis [2-3]. GGTI298 is primarily used to treat non-small cell lung cancer [4].

In A549 cells, Gefitinib and GGTI298 (2.5-5μM; 48h) have synergistic anti-proliferative effects on cells [5]. In A549 cells, GGTI298 (15μM; 48h) induces cell apoptosis [6].

In Luc-G33 cells xenograft mice model, combination treatment with Zoledronate and GGTI298 (1.16mg/kg; sc; 35d) both reduced tumor growth [7].

References:
[1]. Dan H C, Jiang K, Coppola D, et al. GGTI 298[J]. Oncogene, 2004, 23: 706-715.
[2]. Peterson Y K, Kelly P, Weinbaum C A, et al. A novel protein geranylgeranyltransferase-I inhibitor with high potency, selectivity, and cellular activity[J]. Journal of Biological Chemistry, 2006, 281(18): 12445-12450.
[3]. Vogt A, Sun J, Qian Y, et al. The geranylgeranyltransferase-I inhibitor GGTI-298 arrests human tumor cells in G0/G1 and induces p21WAF1/CIP1/SDI1 in a p53-independent manner[J]. Journal of Biological Chemistry, 1997, 272(43): 27224-27229.

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[4]. Chen S, Fu L, Raja S M, et al. Dissecting the roles of DR4, DR5 and c-FLIP in the regulation of geranylgeranyltransferase I inhibition-mediated augmentation of TRAIL-induced apoptosis[J]. Molecular cancer, 2010, 9(1): 23.
[5]. Liu B S, Dai X Y, Xia H W, et al. Geranylgeranyl transferase 1 inhibitor GGTI-298 enhances the anticancer effect of gefitinib[J]. Molecular Medicine Reports, 2018, 18(4): 4023-4029.
[6]. Miquel K, Pradines A, Sun J, et al. GGTI-298 induces G0-G1 block and apoptosis whereas FTI-277 causes G2-M enrichment in A549 cells[J]. Cancer research, 1997, 57(10): 1846-1850.
[7]. Lau C P Y, Wong K C, Huang L, et al. A mouse model of luciferase-transfected stromal cells of giant cell tumor of bone[J]. Connective tissue research, 2015, 56(6): 493-503.

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