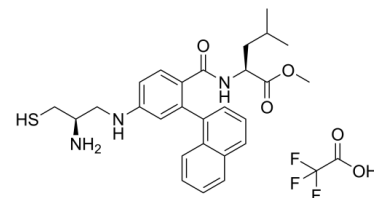


## Data Sheet

<b>Product Name:</b>	GGTI298 (Trifluoroacetate)
<b>Cat. No.:</b>	CS-7690
<b>CAS No.:</b>	1217457-86-7
<b>Molecular Formula:</b>	C <sub>29</sub> H <sub>34</sub> F <sub>3</sub> N <sub>3</sub> O <sub>5</sub> S
<b>Molecular Weight:</b>	593.66
<b>Target:</b>	Apoptosis
<b>Pathway:</b>	Apoptosis
<b>Solubility:</b>	DMSO : 100 mg/mL (ultrasonic)



### BIOLOGICAL ACTIVITY:

GGTI298 Trifluoroacetate is a CAAZ peptidomimetic geranylgeranyltransferase I (**GGTase I**) inhibitor, which can inhibit **Rap1A** with **IC<sub>50</sub>** of 3  $\mu$ M; little effect on **Ha-Ras** with **IC<sub>50</sub>** of >20  $\mu$ M. **IC<sub>50</sub> & Target:** IC<sub>50</sub>: 3  $\mu$ M (Rap1A, in vivo), > 20  $\mu$ M (Ha-Ras, in vivo)<sup>[3]</sup> *In Vitro*: RhoA inhibitor (GGTI298 Trifluoroacetate) significantly reduces cAMP agonist-stimulated apical K<sup>+</sup> conductance<sup>[1]</sup>. Knockdown of DR4 abolishes NF- $\kappa$ B activation, leading to sensitization of DR5-dependent apoptosis induced by the combination of GGTI298 Trifluoroacetate and TRAIL. GGTI298 Trifluoroacetate/TRAIL activates NF- $\kappa$ B and inhibits Akt. Knockdown of DR5, prevents GGTI298/TRAIL-induced I $\kappa$ B $\alpha$  and p-Akt reduction, suggesting that DR5 mediates reduction of I $\kappa$ B $\alpha$  and p-Akt induced by GGTI298/TRAIL. In contrast, DR4 knockdown further facilitates GGTI298/TRAIL-induced p-Akt reduction<sup>[2]</sup>. *In Vivo*: The vivo mouse ileal loop experiments show fluid accumulation is reduced in a dose-dependent manner by TRAM-34, GGTI298 Trifluoroacetate, or H1152 when inject together with cholera toxin into the loop<sup>[1]</sup>.

### PROTOCOL (Extracted from published papers and Only for reference)

**Kinase Assay:** <sup>[2]</sup>The given cells are lysed with reporter lysis buffer and subjected to luciferase activity assay using luciferase assay system in a luminometer. Relative luciferase activity is normalized to protein content<sup>[2]</sup>. **Cell Assay:** <sup>[2]</sup>Cells are seeded in 96-well cell culture plates and treated the next day with the agents (including GGTI298 Trifluoroacetate). The viable cell number is determined using the sulforhodamine B assay<sup>[2]</sup>. **Animal Administration:** <sup>[1]</sup>The ileal loop experiment is performed in 6-8-week-old mice by a modifying rabbit ileal loop assay. Following gut sterilization, the animals are kept fasted for 24 h prior to surgery and fed only water ad libitum. Anesthesia is induced by a mixture of ketamine (35 mg/kg of body weight) and xylazine (5 mg/kg of body weight). A laparotomy is performed, and the experimental loops of 5-cm length are constricted at the terminal ileum by tying with non-absorbable silk. The following fluids are instilled in each loop by means of a tuberculin syringe fitting with a disposable needle through the ligated end of the loop: pure CT (1  $\mu$ g; positive control), saline (negative control), CT (1  $\mu$ g)+TRAM-34 (different concentrations in  $\mu$ M), CT (1  $\mu$ g)+ H1152 (1  $\mu$ M), and CT (1  $\mu$ g)+GGTI298 Trifluoroacetate (different concentrations in  $\mu$ M), a specific inhibitor of Rap1A. The intestine is returned to the peritoneum, and the mice are sutured and returned to their cages. After 6 h, these animals are sacrificed by cervical dislocation, and the loops are excised<sup>[1]</sup>.

### References:

[1]. Sheikh IA, et al. The Epac1 signaling pathway regulates Cl<sup>-</sup> secretion via modulation of apical KCNN4c channels in diarrhea. J Biol Chem. 2013 Jul 12;288(28):20404-15.

[2]. Chen S, et al. Dissecting the roles of DR4, DR5 and c-FLIP in the regulation of geranylgeranyltransferase I inhibition-mediated augmentation of TRAIL-induced apoptosis. Mol Cancer. 2010 Jan 29;9:23.

[3]. McGuire TF, et al. Platelet-derived growth factor receptor tyrosine phosphorylation requires protein geranylgeranylation but not farnesylation. J Biol Chem. 1996 Nov 1;271(44):27402-7.

#### CAIndexNames:

(S)-methyl 2-(4-(((R)-2-amino-3-mercaptopropyl)amino)-2-(naphthalen-1-yl)benzamido)-4-methylpentanoate 2,2,2-trifluoroacetate

#### 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.O=C(O)C(F)(F)F

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

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