FTI-2148 diTFA

Cat. No.: HY-118916A

CAS No.: 817586-01-9

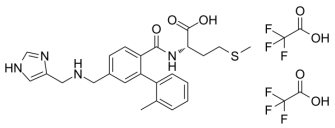
Molecular Formula: $C_{28}H_{30}F_6N_4O_7S$

Molecular Weight: 680.62

Target: Farnesyl Transferase

Pathway: Metabolic Enzyme/Protease

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



SOLVENT & SOLUBILITY

In Vitro

Ethanol : 5 mg/mL (7.35 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.4692 mL	7.3462 mL	14.6925 mL
	5 mM	0.2938 mL	1.4692 mL	2.9385 mL
	10 mM	---	---	---

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

In Vivo

1. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 0.5 mg/mL (0.73 mM); Clear solution
2. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.5 mg/mL (0.73 mM); Clear solution
3. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: ≥ 0.5 mg/mL (0.73 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

FTI-2148 diTFA is a RAS C-terminal mimetic dual farnesyl transferase (FT-1) and geranylgeranyl transferase-1 (GGT-1) inhibitor with IC_{50}s of 1.4 nM and 1.7 μM, respectively[1].

IC_{50} & Target

IC50: 1.4 nM (FT-1); 1.7 μM (GGT-1)[1]

In Vitro

FTI-2148 (30 μM) inhibits the farnesylation of the exclusively farnesylated protein HDJ2 in all 3 RAS-transformed NIH3T3 cells [1].

FTI-2148 diTFA is against P. falciparum PFT, Mammalian PFT and Mammalian PGGT-I with IC_{50} values of 15 nM; 0.82 nM and 1700 nM, respectively. PFT:protein farnesyltransferase; PGGT-I geranylgeranyltransferase-I[2].

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

Western Blot Analysis[1]

Cell Line:	KRAS HRAS, and NRAS-transformed NIH3T3 cells
Concentration:	30 μM
Incubation Time:	
Result:	Inhibited the prenylation of KRAS and NRAS.

In Vivo

FTI-2148 (intraperitoneal injection; 25 or 50 mpk/day with a mini-pump; started on day 15 and stopped on day 45 and restarted day 53-83) inhibits the tumor growth by 91% in human lung adenocarcinoma A-549 cells induced mouse model[1].
FTI-2148 (subcutaneous injection; 25 mpk/day with a mini-pump; 14 days) inhibits tumor growth by 77%by the end of the 2-week treatment in Human Xenograft Nude Mouse Model[1].
FTI-2148 (subcutaneous injection; 100 mg/kg/day; 14 days) results in breast tumor regression in a ras transgenic mouse model[3].
FTI-2148 (subcutaneous injection; 100 mg/kg/day; 4 days) results in 85–88% inhibition of FTase with no inhibition of GGTase I enzymatic activity in breast tumors from mice in vivo settings[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Ras transgenic mouse model[3]
Dosage:	100 mg/kg/day
Administration:	Subcutaneous injection; 100 mg/kg/day; 14 days
Result:	Reduced regression by 87 ± 3% of mammary carcinomas in mice.

REFERENCES

[1]. Sun J, et al. Antitumor efficacy of a novel class of non-thiol-containing peptidomimetic inhibitors of farnesyltransferase and geranylgeranyltransferase I: combination therapy with the cytotoxic agents cisplatin, Taxol, and gemcitabine.Cancer Res. 1999 Oct 1;59(19):4919-26.

[2]. Carrico D, et al.In vitro and in vivo antimalarial activity of peptidomimetic protein farnesyltransferase inhibitors with improved membrane permeability.Bioorg Med Chem. 2004 Dec 15;12(24):6517-26.

[3]. 3. Sun J, et al. Geranylgeranyltransferase I inhibitor GGTI-2154 induces breast carcinoma apoptosis and tumor regression in H-Ras transgenic mice.Cancer Res. 2003 Dec 15;63(24):8922-9.

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