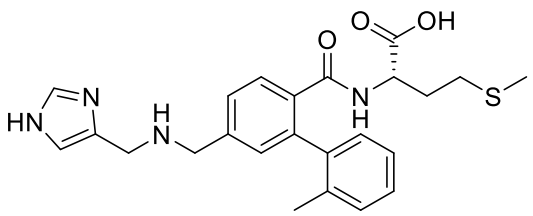
Product data sheet

MedKoo Cat#: 406425 Name: FTI-2148 free base CAS#: 251577-09-0 (free base) Chemical Formula: $C_{24}H_{28}N_4O_3S$ Exact Mass: 452.18821 Molecular Weight: 452.573	
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:
FTI-2148 is a potent farnesyltransferase inhibitor with potential antitumor activity. FTI-2148 is highly selective for FTase (IC50, 1.4 nM) over GGTase I (IC50, 1700 nM). FTI-2148 suppressed the growth of the human lung adenocarcinoma A-549 cells in nude mice by 33, 67, and 91% in a dose-dependent manner. Combination therapy of FTI-2148 with either cisplatin, gemcitabine, or Taxol resulted in a greater antitumor efficacy than monotherapy.

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	TBD	TBD

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.21 mL	11.05 mL	22.10 mL
5 mM	0.44 mL	2.21 mL	4.42 mL
10 mM	0.22 mL	1.10 mL	2.21 mL
50 mM	0.04 mL	0.22 mL	0.44 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. Sun J, Blaskovich MA, Knowles D, Qian Y, Ohkanda J, Bailey RD, Hamilton AD, Sebti SM. 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. PMID: 10519405.
2. Kazi A, Xiang S, Yang H, Chen L, Kennedy P, Ayaz M, Fletcher S, Cummings C, Lawrence HR, Beato F, Kang Y, Kim MP, Delitto A, Underwood PW, Fleming JB, Trevino JG, Hamilton AD, Sebti SM. Dual Farnesyl and Geranylgeranyl Transferase Inhibitor Thwarts Mutant KRAS-Driven Patient-Derived Pancreatic Tumors. Clin Cancer Res. 2019 Oct 1;25(19):5984-5996. doi: 10.1158/1078-0432.CCR-18-3399. Epub 2019 Jun 21. PMID: 31227505; PMCID: PMC6774803.

In vivo study

1. Sun J, Blaskovich MA, Knowles D, Qian Y, Ohkanda J, Bailey RD, Hamilton AD, Sebti SM. 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. PMID: 10519405.
2. Sun J, Ohkanda J, Coppola D, Yin H, Kothare M, Busciglio B, Hamilton AD, Sebti SM. 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. PMID: 14695209.

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7. Bioactivity

Biological target:

FTI-2148 is a RAS C-terminal mimetic dual farnesyl transferase (FT-1) and geranylgeranyl transferase-1 (GGT-1) inhibitor with IC50s of 1.4 nM and 1.7 μM, respectively.

In vitro activity

To determine the potency and selectivity of FTI-2148, its ability to inhibit the transfer of farnesyl from [3H]FPP and [3H]GGPP to H-Ras CVLS and H-Ras CVLL, respectively, was evaluated. Table 1 shows IC50s of the inhibitors. FTI-2148 (IC50, 1.4 nm) is 2.5 times more potent than GGTI-297 (IC50, 55 nm). Table 1 also shows that FTI-2148 (1200-fold) is highly selective for FTase over GGTase. hus, for FTIs, replacement of reduced cysteine by the imidazole derivative and the phenyl substituent by tolyl (Fig. 1) resulted in much higher selectivity with little loss of potency. Although FTI-2148 alone was capable of inhibiting human tumor growth, drug removal resulted in tumor regrowth.

Reference: Cancer Res. 1999 Oct 1;59(19):4919-26. https://cancerres.aacrjournals.org/content/59/19/4919.long

In vivo activity

To evaluate the effects of replacing the reduced cysteine by an imidazole derivative and the phenyl group by a tolyl, the antitumor potency of FTI-2148 and FTI-276 (both i.p. and s.c. delivery) were compared in the human lung adenocarcinoma A-549 cell nude mouse model. Fig. 5 A ⇓ shows that, over a period of 83 days, tumors from animals that were treated with vehicle reached an average size of 839.56 ± 162.66 mm3, whereas those treated with FTI-276 or FTI-2148 grew to average sizes of 193.21 ± 61.88 mm3 or 122.95 ± 17.36 mm3, respectively. Thus, FTI-276 and FTI-2148 inhibited A-549 tumor growth by 82 and 91%, respectively. This suggested that the effect of FTI-276 and FTI-2148 on A-549 tumor growth in nude mice is cytostatic. To confirm this, A-549 cell-bearing nude mice were treated with FTI-276 or FTI-2148 (25 mpk/day for 14 days) and followed tumor growth for an additional 15 days after drug cessation. Fig. 5B ⇓ shows that FTI-276 and FTI-2148 delivered via s.c. mini-pumps at a rate of 25 mpk/day for 14 days inhibited tumor growth by 50 and 77%, respectively, by the end of the 2-week treatment. Furthermore, after drug treatment was stopped, the tumors from the FTI-276 group grew faster than those from the FTI-2148 group. Thus, the data show that FTI-2148 is more effective than FTI-276.

Reference: Cancer Res. 1999 Oct 1;59(19):4919-26. https://cancerres.aacrjournals.org/content/59/19/4919.long

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.