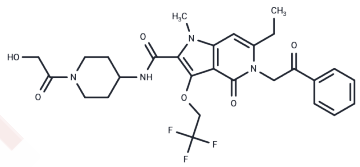
Data Sheet (Cat.No.T21325)

TAK-441

Chemical Properties



CAS No. : 1186231-83-3

Formula: C28H31F3N4O6

Molecular Weight: 576.56

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	TAK-441 is an orally active inhibitor of Hedgehog signaling(IC50 = 4.4 nM) with potent antitumor activity. TAK-441 suppresses transcription factor Gli1 mRNA expression and tumor growth.
Targets(IC50)	Hedgehog/Smoothened
In vitro	TAK-441 (0.03 nM-1 μM) inhibits Gli1 mRNA in the tumor and skin with IC50s of 45.7 and 113 μg/ml, respectively[3]. In LNCaP cells, TAK-441 (0.5-500 nM) delays the castration-resistant progression without affecting androgen withdrawal-induced Shh up-regulation or cell viability[4].
In vivo	In ptc1+/-p53-/- mice, oral administration of TAK-441 (1-25 mg/kg) shows strong and dose-dependent antitumor activity. In BALB/c-nu/nu mice, oral administration of TAK-441 (10-100 mg/kg) shows favorable exposure and good oral absorption[4].

Solubility Information

Solubility	DMSO: 45 mg/mL (78.05 mM),Sonication is recommended. H2O: Insoluble, (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.47 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.7344 mL	8.6721 mL	17.3442 mL
5 mM	0.3469 mL	1.7344 mL	3.4688 mL
10 mM	0.1734 mL	0.8672 mL	1.7344 mL
50 mM	0.0347 mL	0.1734 mL	0.3469 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Goldman J, et al. Phase 1 Dose-Escalation Trial of the Oral Investigational Hedgehog Signaling Pathway Inhibitor TAK-441 in Patients with Advanced Solid Tumors. Clin Cancer Res. 2014 Dec 12.

Naokazu Ibuki, et al. TAK-441, a novel investigational smoothened antagonist, delays castration-resistant progression in prostate cancer by disrupting paracrine hedgehog signaling. Int J Cancer. 2013 Oct 15;133(8):1955-66.

Kogame A, et al. Pharmacokinetic and pharmacodynamic modeling of hedgehog inhibitor TAK-441 for the inhibition of Gli1 messenger RNA expression and antitumor efficacy in xenografted tumor model mice. Drug Metab Dispos. 2013 Apr;41(4):727-34.

Tomohiro Ohashi, et al. Discovery of the investigational drug TAK-441, a pyrrolo[3,2-c]pyridine derivative, as a highly potent and orally active hedgehog signaling inhibitor: modification of the core skeleton for improved solubility. Bioorg Med Chem. 2012