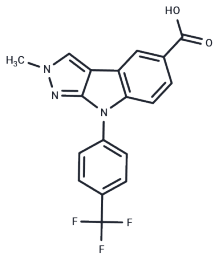
Data Sheet (Cat.No.T60148)

TargetMol

MSC-4106

Chemical Properties



CAS No. : 2738542-58-8

Formula: C18H12F3N3O2

Molecular Weight: 359.3

Storage: Keep away from direct sunlight
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	MSC-4106, an orally active and potent YAP/TAZ-TEAD inhibitor, disrupts TEAD1 and TEAD3 auto-palmitoylation and demonstrates significant efficacy in the NCI-H226 tumor xenograft model [1].
Targets(IC50)	YAP
In vitro	MSC-4106, at a concentration of 10 μM, demonstrated notable effects in various assays related to cancer cell viability and interaction inhibition within a certain time frame. Specifically, after 24 hours of treatment, it significantly reduced the viability of SK-HEP-1 reporter and NCI-266 cells, with IC50 values measuring at 4 nM and 14 nM, respectively. Additionally, within 6 hours, it was observed to crystalize in the P-site of TEAD1, markedly inhibiting TEAD1 and TEAD3 palmitoylation in TEAD-overexpressing HEK293 cells by 97.3% and 75.9%, correspondingly. A four-day exposure to MSC-4106 also suggested its targeting action on TEAD through a diminished viability in NCI-H226 cells, indicative of its potential mechanistic pathways. Further evaluation via a Cell Viability Assay on NCI-H226 (YAP dependent) and SW620 YAP/TAZ KO (YAP-independent) cells exposed to varying concentrations of MSC-4106 for 96 hours revealed an inhibitory effect on NCI-H226 and a general cytotoxicity towards SW620 with an IC50 greater than 30 μM. Immunofluorescence studies in SK-HEP-1 cells after 24 hours of treatment confirmed the inhibition of YAP-TEAD interaction, showcasing MSC-4106's multifaceted biochemical activities.
In vivo	MSC-4106 (P.O.; 100 mg/kg once daily; 7 days) demonstrates anti-tumor effects with controlled tumor volume and good tolerability, maintaining stable body weight in mice [1]. MSC-4106 (P.O.; 1, 5, 100 mg/kg once daily; 6, 24, 30, 48, and 72 h) down-regulates Cyr61 (cysteine-rich angiogenic inducer 61) expression, a TEAD-regulated target gene, in tumor lysates at all time points at 100 mg/kg and at 24 h at 5 mg/kg [1]. Pharmacokinetic (PK) profiles in different species [1]: - Mouse: Cl (0.2 l/h/kg), PO t 1/2 (45 h), PO AUC (45 μg h/mL), V ss (2 L/kg), F (>90%). - Rat: Cl (0.7 l/h/kg), PO t 1/2 (40 h), PO AUC (10 μg h/mL), V ss (5 L/kg), F (80%). - Dog: Cl (0.05 l/h/kg), PO t 1/2 (3.6 h), PO AUC (33 μg h/mL), V ss (0.3 L/kg), F (18%). Note: PO studies at 10 mg/kg; MSC-4106 formulated in 20% Kleptose in 50 mM PBS, pH 7.4. Animal model: NCI-H226 xenograft in H2d Rag2 female mice (9-week-old) [1].

In vivo	Dosage: 5, 100 mg/kg Oral gavage, once daily for 32 days, resulting in controlled tumor growth at 5 mg/kg and tumor regression at 100 mg/kg after 32 days of treatment.

Solubility Information

Solubility	DMSO: 225 mg/mL (626.22 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.7832 mL	13.9159 mL	27.8319 mL
5 mM	0.5566 mL	2.7832 mL	5.5664 mL
10 mM	0.2783 mL	1.3916 mL	2.7832 mL
50 mM	0.0557 mL	0.2783 mL	0.5566 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

Timo Heinrich, et al. Optimization of TEAD P-site binding fragment hit into in vivo active lead MSC-4106. J. Med. Chem. 2022, 65, 13, 9206-9229.

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