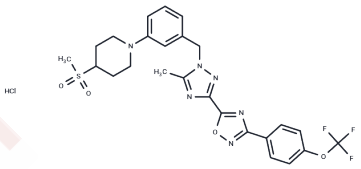
Data Sheet (Cat.No.T27568)

TargetMol

IACS-010759 hydrochloride

Chemical Properties



CAS No. : 1807523-99-4

Formula: C25H26ClF3N6O4S

Molecular Weight: 599.03

Storage: Store at low temperature
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	IACS-010759 hydrochloride is an orally potent and selective OXPHOS inhibitor that inhibits proliferation and induces apoptosis in OXPHOS-dependent brain cancer and acute myeloid leukaemia models for the study of relapsed/refractory AML and advanced solid tumours.
Targets(IC50)	Apoptosis,OXPHOS,Mitochondrial Metabolism
In vitro	IACS-010759 hydrochloride shows potent in vitro activity by reducing AML cell viability and inducing apoptosis at concentrations of 10-100nM over 4-5 days. It also inhibits mitochondrial OCR and oxidative phosphorylation-dependent viability in H460 cells, with an average IC_{50} of 1.4nM over 72h. Similar potency was observed in cells from mice (IC_{50} = 5.6nM), rats (12.2nM), and cynomolgus monkeys (8.7nM)[1].
In vivo	In NB-1 neuroblastoma xenograft mice, oral IACS-010759 hydrochloride at 5-10mg/kg for 21 days significantly reduced tumor size, although 25mg/kg was not well tolerated. In another model, daily or alternate-day dosing at 10mg/kg for 35 days extended survival from 28 to over 60 days, and lower-frequency dosing (e.g., 2×/week) also improved outcomes. Pharmacokinetic studies showed that a 0.3mg/kg dose had low clearance, limited distribution, and a prolonged half-life (>24h)[1].

Solubility Information

Solubility	DMSO: 50 mg/mL (83.47 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble) (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	2% DMSO+40% PEG300+5% Tween 80+53% Saline: 1 mg/mL (1.67 mM),Suspension. *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	1.6694 mL	8.3468 mL	16.6937 mL
5 mM	0.3339 mL	1.6694 mL	3.3387 mL
10 mM	0.1669 mL	0.8347 mL	1.6694 mL
50 mM	0.0334 mL	0.1669 mL	0.3339 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

Protopopova M. IACS-10759: A novel OXPHOS inhibitor which selectively kill tumors with metabolic vulnerabilities. [abstract]. In: Proceedings of the 106th Annual Meeting of the American Association for Cancer Research; 2015 Apr 18-22; Philadelphia, PA. Philadelphia (PA): AACR; Cancer Res 2015;75(15 Suppl):Abstract nr 4380.

Molina JR, et al. An inhibitor of oxidative phosphorylation exploits cancer vulnerability. Nat Med. 2018 Jul;24(7): 1036-1046.

Lissanu Deribe Y, et al. Mutations in the SWI/SNF complex induce a targetable dependence on oxidative phosphorylation in lung cancer. Nat Med. 2018 Jul;24(7):1047-1057.

Vangapandu HV, et al. Biological and metabolic effects of IACS-010759, an OxPhos inhibitor, on chronic lymphocytic leukemia cells. Oncotarget. 2018 May 18;9(38):24980-24991.