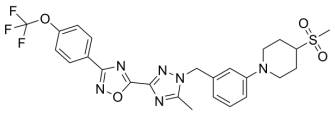
IACS-010759

Cat. No.:	HY-112037
CAS No.:	1570496-34-2
Molecular Formula:	$C_{25}H_{25}F_3N_6O_4S$
Molecular Weight:	562.56
Target:	Apoptosis; Mitochondrial Metabolism; Oxidative Phosphorylation
Pathway:	Apoptosis; Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (88.88 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7776 mL	8.8879 mL	17.7759 mL
	5 mM	0.3555 mL	1.7776 mL	3.5552 mL
	10 mM	0.1778 mL	0.8888 mL	1.7776 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.08 mg/mL (3.70 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.70 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

IACS-010759 is an orally active, potent mitochondrial complex I of oxidative phosphorylation (OXPHOS) inhibitor. IACS-010759 inhibits proliferation and induces apoptosis in models of brain cancer and acute myeloid leukemia (AML) reliant on OXPHOS. IACS-010759 has the potential for relapsed/refractory AML and solid tumors research[1][2].

IC_{50} & Target

OXPHOS[1]

In Vitro

IACS-010759 (10, 30, 100 nM; for 4 or 5 days) reduces viability and induces apoptosis in primary AML[1].
IACS-010759 (0.001, 0.01, 0.1, 1, 10, 100, 1000 nM; 72 hurs) robustly inhibits both OCR and galactose-dependent H460 cell viability and has nearly identical IC_{50} values of 1.4 nM[1].
IACS-010759 is similarly active in mouse (average IC_{50} = 5.6 nM), rat (IC_{50} = 12.2 nM), and cynomolgus monkey (IC50 = 8.7 nM)

	cell lines[1]. IACS-010759 (0.01-10 μM) yieldes a maximal reduction of growth of > 50% in the majority of cancer cell lines (24 of 30 pancreatic (PDAC), 19 of 20 ovarian, 13 of 16 triple-negative breast (TNBC), 8 of 10 non-small-cell lung (NSCLC)) and a subset (11of 30 PDAC, 10 of 20 ovarian, 5 of 16 TNBC, 2 of 10 NSCLC) exhibited > 100% growth inhibition[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	IACS-010759 (5, 10, 25 mg/kg/day; oral; for 21 d) results in tumor regression with minimal body weight loss at the 5 or 10 mg/kg dose in mice bearing NB-1 (PGD-null) subcutaneous xenografts. IACS-010759 at the 25 mg/kg dose is not tolerated[1]. IACS-010759 HCl (10 mg/kg; orally; QD (daily) or QD×5 (5 d on/2 d off); for 35 d) increases median survival from 28 d to longer than 60 d, whereas less-frequent dosing schedules (Q2D or Q3D) enhances survival to a lesser extent[1]. IACS-010759 (0.3 mg/kg for iv; 1 mg/kg for oral) has low plasma clearance with a high volume of distribution, resulting in a prolonged terminal half-life (>24 h)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Discov. 2022 Oct 6;8(1):102.
- Nat Commun. 2023 Jul 14;14(1):4221.
- Cell Rep Med. 2022 Nov 3;100802.
- Biochem Biophys Res Commun. 2023 Jun 1.
- Biochem Biophys Res Commun. 2021 Mar 16;552:23-29.

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REFERENCES

[1]. 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. doi:10.1158/1538-7445.AM2015-4380

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

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