

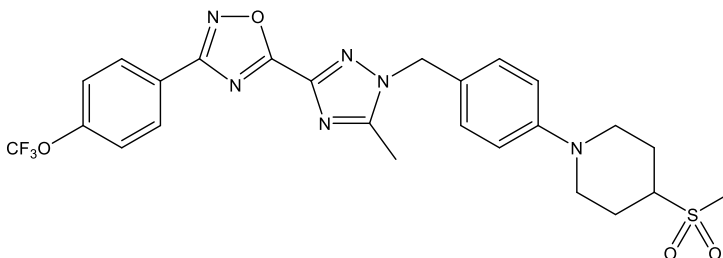
Catalog # 10-4475

IACS-010759

CAS# 1570496-34-2

5-[5-Methyl-1-[[3-(4-methylsulfonylpiperidin-1-yl)phenyl]methyl]-1,2,4-triazol-3-yl]-3-[4-(trifluoromethoxyphenyl)-1,2,4-oxadiazole

Lot # FBA849



IACS-010759 is a potent ($IC_{50} = 1.1$ nM isolated mouse complex I) and selective inhibitor of complex I of the mitochondrial electron transport chain (OXPHOS). IACS-010759 displayed *in vivo* efficacy in glycolysis-deficient glioblastoma and AML models without cytotoxicity to normal cells. The lack of cytotoxicity to normal cells, as opposed to other complex I inhibitors, is attributed to its unique binding location on complex I.² Complex I inhibition by IACS-010759 causes an ROS-induced decrease in the endogenous PP2A inhibitor CIP2A leading to cell death.³ It has also displayed potential in various chemotherapy-resistant cancer cell lines.⁴⁻⁷

- 1) Molina *et al.* (2018), *An inhibitor of oxidative phosphorylation exploits cancer vulnerability*; Nature Med. **24** 1036
- 2) Tsuji *et al.* (2020), *IACS-010759, a potent inhibitor of glycolysis-deficient hypoxic tumor cells, inhibits mitochondrial respiratory complex I through a unique mechanism*; J. Biol. Chem. **295** 7481
- 3) Cazzoli *et al.* (2023), *Endogenous PP2A inhibitor CIP2A degradation by chaperone-mediated autophagy contributes to the antitumor effect of mitochondrial complex I inhibition*; Cell Rep. **42** 112616
- 4) Gopal *et al.* (2019), *A Novel Mitochondrial Inhibitor Blocks MAPK Pathway and Overcomes MAPK Inhibitor Resistance in Melanoma*; Clin. Cancer Res. **25** 6429
- 5) Stuani *et al.* (2021), *Mitochondrial metabolism supports resistance to IDH mutant inhibitors in acute myeloid leukemia*; J. Exp. Med. **218** e20200924
- 6) Evans *et al.* (2021), *Oxidative Phosphorylation is a Metabolic Vulnerability in Chemotherapy-Resistant Triple-Negative Breast Cancer*; Cancer Res. **81** 5572
- 7) Fuhr *et al.* (2022), *CD52 and OXPHOS - potential targets in ibrutinib-treated mantle cell lymphoma*; Cell Death Discov. **8** 505

PHYSICAL DATA

Molecular Weight:	562.57
Molecular Formula:	C ₂₅ H ₂₅ F ₃ N ₆ O ₄ S
Purity:	>98% by HPLC
	NMR: (Conforms)
Solubility:	DMSO (>25 mg/ml)
Physical Description:	White solid
Storage and Stability:	Store as supplied at -20°C for up to 1 year from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 3 months.

Materials provided by Focus Biomolecules are for laboratory research use only and are not intended for human or veterinary applications.

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