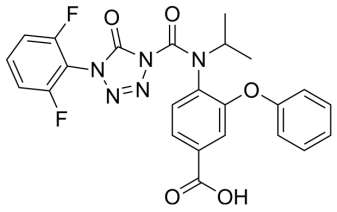
IPI-9119

Cat. No.:	HY-124628
CAS No.:	1346564-56-4
Molecular Formula:	$C_{24}H_{19}F_2N_5O_5$
Molecular Weight:	495
Target:	Fatty Acid Synthase (FASN)
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (202.02 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0202 mL	10.1010 mL	20.2020 mL
5 mM	0.4040 mL	2.0202 mL	4.0404 mL
10 mM	0.2020 mL	1.0101 mL	2.0202 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 (4.20 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.20 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.20 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

IPI-9119 is an orally active, selective and irreversible FASN inhibitor with an IC_{50} of 0.3 nM in vitro biochemical assay. IPI-9119 inhibits tumor growth of castration-resistant prostate cancer (CRPC) xenografts mouse models[1][2].

IC_{50} & Target

IC50: 0.3 nM (FASN)[1]

In Vitro

IPI-9119 inhibits FASN in cellular occupancy assays (IC_{50}-10nM), and shows more than 400-fold selectivity against several additional serine hydrolases[2].

IPI-9119 (0.1-0.5 μM; 6 days) inhibits cell growth and induces cell cycle arrest, apoptosis[1].
IPI-9119 (0.05-5 μM; 6 days) inhibits AR-FL and AR-V7 protein expression[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	Prostate cancer (PCa) cells (AD LNCaP, AI C4-2, LNCaP-95 and 22Rv1 AI cells)
Concentration:	0.1, 0.5 μM
Incubation Time:	6 days
Result:	Inhibited PCa cell growth. Had no growth inhibition in FASN KO PCa cells.

Cell Cycle Analysis[1]

Cell Line:	PCa cells
Concentration:	0.1, 0.5 μM
Incubation Time:	6 days
Result:	Reduced the proportion of S-phase cells and increased that of G0/G1-, sub-G1–phase cells and decreased expression of cyclin A2.

Western Blot Analysis[1]

Cell Line:	PCa cells
Concentration:	0.05, 0.1, 0.25, 0.5, 5 μM
Incubation Time:	6 days
Result:	Significantly decreased AR-FL protein levels in AD LNCaP, AI C4-2 cells (expressing only AR-FL) and reduced the expression of AR-V7 in LNCaP-95, 22Rv1 AI cells driven by this variant.

In Vivo

IPI-9119 (SC pump infusion; 0.5 μL/h; 100 mg/mL; for 28 days) inhibits tumor growth of CRPC xenografts mouse models[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	8-10-week male Ncr Nu Castrated mice or castrated NOD male SCID with 22Rv1 or LNCaP-95 cells[1]
Dosage:	100 mg/mL
Administration:	SC pump infusion (0.5 μL/h; 100 mg/mL); for 28 days
Result:	Inhibited tumor growth of castration-resistant prostate cancer (CRPC) xenografts mouse models.

REFERENCES

[1]. Giorgia Zadra, et al. Inhibition of de novo lipogenesis targets androgen receptor signaling in castration-resistant prostate cancer. Proc Natl Acad Sci U S A. 2019 Jan 8;116(2):631-640.

[2]. Erin Broph, et al. Abstract 1891: Pharmacological target validation studies of fatty acid synthase in carcinoma using the potent, selective and orally bioavailable

inhibitor IPI-9119.

Caution: Product has not been fully validated for medical applications. For research use only.

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