Data Sheet (Cat.No.T4376)

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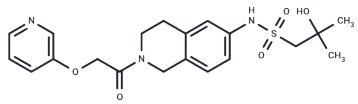
Nampt-IN-1

Chemical Properties



CAS No. : 1698878-14-6

Formula: C20H25N3O5S

Molecular Weight: 419.49

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Nampt-IN-1 (LSN3154567) (LSN3154567) is a potent and selective NAMPT inhibitor. Nampt-IN-1 inhibits purified NAMPT with an IC50 of 3.1 nM.
Targets(IC50)	c-Fms,NAMPT,CSF-1R
In vitro	LSN3154567 inhibits purified NAMPT with an IC50 of 3.1 nM. When tested against a panel of human kinases (>100; CEREP Kinase panel), it does not exhibit any significant activity (i.e.: IC50≥1 μM) against the kinases tested except CSF1R (IC50≈0.84 μM). To assess its anticancer activity, LSN3154567 is tested against a number of different types of cancer cell lines cultured in the absence or presence of nicotinic acid (NA) (10 μM). LSN3154567 exhibits a potent antiproliferative activity against many cell lines in the absence of NA.
In vivo	When dosed orally with 2 mg/kg in mice, it has an exposure of 195 nM*hour in the plasma with a peak concentration of 57 nM (at 0.25 hour) and an oral bioavailability of 39%. When dosed intravenously with 2 mg/kg, it has a hepatic clearance of 158.73 mL/min/kg and a volume of distribution at 7.1 L/kg. The half-life of terminal elimination is estimated to be 2.76 hours. LSN3154567 exhibits a dose-dependent inhibition of NAD+ formation with estimated TED50 value of 2.0 mg/kg. Dogs are treated with LSN3154567 at 1 and 2.5 mg/kg. At these dose levels, the retinal toxicity is observed. Degeneration of the outer nuclear layer occurred in all four animals, but is less pronounced in the animals treated with 1 mg/kg.
Cell Research	The cell lines used as following: A2780 and KM-12, KMS-11 and MKN-74, OPM-2 and Kelly; and all other cancer cells. Cells are seeded in 96-well plates, cultured overnight, and treated with LSN3154567 (0.03 to 1,000 nM)±NA (10 μM) in duplicate at 37°C in 5% CO2 for 72 hours. Staurosporine (10 μM) is used as positive control. Cell viability is determined by a CytoTox-Glo Cytotoxicity assay kit.
Animal Research	Male CD-1 mice are dosed with LSN3154567 at 2 mg/kg intravenously in 20% Captisol (w/v), 25 mmol/L NaPO4, pH 2, q.s. formulation or 2 mg/kg orally in the same vehicle in a cross over design with 3-d wash period in between two arms. Blood samples are obtained through retro orbital at 0, 0.08 (IV only), 0.25, 0.75, 2, 4, 8, and 24 hours and frozen until analysis. For exposure analysis, blood samples (≈20 μL) are obtained through tail clipping at 0.5, 1, 2, 4, 8, and 24 hours. The samples are collected into EDTA-coated capillary tubes and spotted onto Whatman DMPK-C DBS collection cards.

Solubility Information

Solubility	DMSO: 55 mg/mL (131.11 mM), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3838 mL	11.9192 mL	23.8385 mL
5 mM	0.4768 mL	2.3838 mL	4.7677 mL
10 mM	0.2384 mL	1.1919 mL	2.3838 mL
50 mM	0.0477 mL	0.2384 mL	0.4768 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.

Reference

Zhao G, et al. Discovery of a Highly Selective NAMPT Inhibitor That Demonstrates Robust Efficacy and Improved Retinal Toxicity with Nicotinic Acid Coadministration. Mol Cancer Ther. 2017 Dec;16(12):2677-2688.