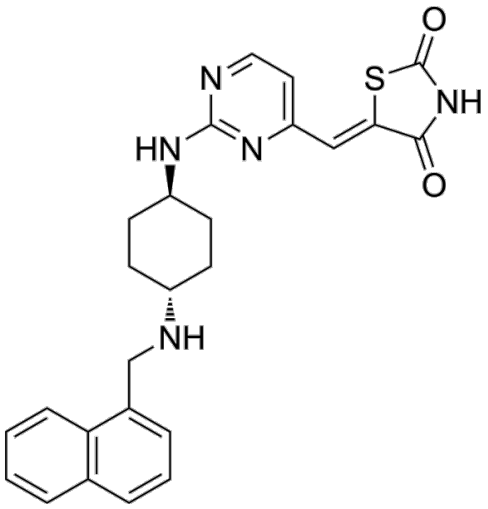
Product Data Sheet

Product Name: JP-11646
Cat. No.: GC79451

Chemical Properties

Cas. No.	1902983-63-4		
Formula	$C_{25}H_{25}N_5O_2S$	M.Wt	459.56
Solubility	DMSO: 100 mg/mL (217.60 mM; Need ultrasonic)	Storage	Store at 4°C, protect from light
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Background

JP-11646 is a pan-PIM inhibitor with increased potency against PIM2 (IC_{50} = 0.5 nM). JP11646 is freely reversible and ATP non-competitive. JP-11646 results in a decrease of PIM1, 2, and 3 mRNA.

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JP-11646 can effectively inhibit cell viability in small cell lung cancer (SCLC) and large cell neuroendocrine carcinomas of the lung (LCNEC). JP-11646 can cause a decrease in p-4EBP-1 protein, increasing the cleavage of caspases while decreasing caspase-3. JP-11646 induces apoptosis or necroptosis in cells. JP-11646 leads to reductions in MYC paralogs. JP-11646 can be used for the study of SCLC, LCNEC, human acute leukemia (AML), multiple myeloma (MM), and triple-negative breast cancer (TNBC) [1] [2] [3] [4] [5].

In Vivo, JP11646 (15 mg/kg, i.p., twice every week, 24-40 days) demonstrates broad-spectrum and potent antitumor activity in various mouse xenograft tumor in vivo models, with no significant toxic effects observed[3]. JP11646 (10-15 mg/kg, i.p., 2 or 3 times a week for 48 days) demonstrates potent dose-dependent antitumor activity in a mice model of multiple myeloma xenograft and significantly prolongs the median survival of tumor-bearing mice[4].

In Vitro, JP11646 (0.005 to 10 μM, 72 h) inhibits the proliferation of all tested cancer cell lines in a concentration-dependent manner, including head and neck cancer FaDu, ovarian cancer SK-OV-3, breast cancer MDA-MB-231 and BT549, prostate cancer PC-3, liver cancer HepG2, PDAC MIAPaCa-2 and PANC1, colorectal cancer DLD-1 and HT29, and NSCLC H1650, H661, H460 and A549 cell lines[3]. JP11646 (100-200 nM, 24 h) selectively downregulates the protein expression level of PIM2, but has no effect on PIM1 and PIM3, and induces the expression of the apoptosis marker cleaved PARP in MDA-MB-231 and BT549 cells[3]. JP11646 (100-200 nM, 48 h) significantly increases the apoptosis rate of MDA-MB-231 and BT549 cells[3]. JP11646 (20-200 nM, 0-24 h) gradually reduces the levels of p4EBP1 (S65) and pBAD (S112) in MM1.S and U266 cells over time, as do the total levels of these proteins. Furthermore, the levels of the potent phosphorylates form of the anti-apoptotic factor MCL1 (Ser159/Thr163) decrease in a dose-dependent manner[4]. JP11646 (0-1 μM, 72 h) shows the strongest antiproliferative effect against the MF characteristic cell line MM1.S (GI50 = 5 nM)[4]. JP11646 (20-200 nM, 24 h) can reverse (recombinant IL-6) rIL-6-induced PIM2 upregulation in MM1.S and U266 cells, while IL-6 does not affect PIM2 mRNA levels[4]. JP11646 (10-20 nM, 48 h) reverses the chemoprotective effect mediated by CD28 activation or DC co-culture; CTLA4-Ig enhances the cytotoxicity of JP11646[4]. JP11646 (20-200 nM, 0-24 h) dose- and time-dependently inhibits CD28-induced NF-κB activity in MM1.S and RPMI8226 cells[4].

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References:

[1]. Minton K, et al. P3. 02G. 04 JP11646-mediated PIM2 Inhibition Has Potent Antitumor Effects in Small Cell Lung Cancer and Large Cell Neuroendocrine Carcinoma of the Lung[J]. Journal of Thoracic Oncology, 2024, 19(10): S305-S306.
[2]. Krista E. et al. Translational pharmacology approaches to explore the novel mechanism of a pan-PIM kinase inhibitor, JP-11646, in acute myeloid leukemia. [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 681.
[3]. Katsuta E, et al. Targeting PIM2 by JP11646 results in significant antitumor effects in solid tumors[J]. International journal of oncology, 2022, 61(4): 114.
[4]. Nair JR, et al. Novel inhibition of PIM2 kinase has significant anti-tumor efficacy in multiple myeloma. Leukemia. 2017 Aug;31(8):1715-1726.
[5]. Mehta R, et al. Preclinical efficacy of the novel PIM2 kinase inhibitor, JP11646 in triple negative breast cancer models [abstract]. In: Proceedings of the 2016 San Antonio Breast Cancer Symposium; 2016 Dec 6-10; San Antonio, TX. Philadelphia (PA): AACR; Cancer Res 2017;77(4 Suppl):Abstract nr P6-11-10.

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