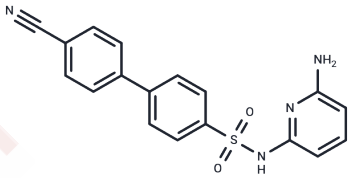
Data Sheet (Cat.No.T16510)

TargetMol

PF-915275

Chemical Properties



CAS No. : 857290-04-1

Formula: C18H14N4O2S

Molecular Weight: 350.39

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	PF-915275 is an effective and selective inhibitor of human 11β-hydroxysteroid dehydrogenase type 1 (11βHSD1, Ki = 2.3 nM, EC50 = 15 nM in vitro HEK293 cells). The dose-dependent effect of PF-915275 on conversion of cortisone to cortisol in primary human and monkey hepatocytes, with an EC50 of 20 and 100 nM, respectively.
Targets(IC50)	Others,Dehydrogenase
In vitro	PF-915275 is a poor inhibitor of 11βHSD1 in rat FAO hepatoma cells (EC50: 14,500 nM), consistent with the species differences between humans and rodents observed in biochemical assays. PF-915275 is a potent inhibitor of 11βHSD1 (in vitro HEK293, EC50 of 15 nM) in this human 11βHSD1 overexpressed cell line when coincubated in the presence of 300 nM enzyme substrate. PF-915275 does not significantly inhibit 11βHSD2 (only 1.5% inhibition when tested at 10 μM). PF-915275 shows species-dependent potency for inhibiting the cellular conversion of cortisone to cortisol in a dog, monkey, and human in primary hepatocytes, with activity in human hepatocytes/monkey hepatocytes/dog hepatocytes [1].
In vivo	PF-915275 dose-dependently inhibits the 11βHSD1-mediated conversion of prednisone to prednisolone. A maximum of 87% inhibition is observed, with the highest tested dose of 3 mg/kg. The inhibition of either cortisone or prednisone turnover with PF-915275 yields similar EC50 values to that in human hepatocytes (EC50 by PF-915275 is 18 and 13 nM using cortisone and prednisone substrates, respectively) in vivo 11βHSD1 activity. The half-life of PF-915275 is 22 hours in the monkey. Plasma insulin levels are significantly lowered (by 54 and 60%, respectively) at 1 and 3 mg/kg PF-915275 treatment. Plasma glucose or lipid levels are not altered with treatment. PF-915275 (0.1-3 mg/kg; p.o.; for 8 hours; male cynomolgus monkeys) treatment displays a trend in dose-dependent lowering of fed plasma insulin after 8 h of dosing in these monkeys [1].

Solubility Information

Solubility	DMSO: 60 mg/mL (171.24 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 1 mg/mL (2.85 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one.*

In vivo Formulation	*Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.854 mL	14.2698 mL	28.5396 mL
5 mM	0.5708 mL	2.854 mL	5.7079 mL
10 mM	0.2854 mL	1.427 mL	2.854 mL
50 mM	0.0571 mL	0.2854 mL	0.5708 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Bhat BG, et al. Demonstration of proof of mechanism and pharmacokinetics and pharmacodynamic relationship with 4'-cyano-biphenyl-4-sulfonic acid (6-amino-pyridin-2-yl)-amide (PF-915275), an inhibitor of 11 - hydroxysteroid dehydrogenase type 1, in cynomolgus monkeys. J Pharmacol Exp Ther. 2008 Jan;324(1):299-305.
Siu M, et al. N-(Pyridin-2-yl) arylsulfonamide inhibitors of 11beta-hydroxysteroid dehydrogenase type 1: Discovery of PF-915275. Bioorg Med Chem Lett. 2009 Jul 1;19(13):3493-7.
Courtney R, et al. Modulation of 11beta-hydroxysteroid dehydrogenase (11betaHSD) activity biomarkers and pharmacokinetics of PF-00915275, a selective 11betaHSD1 inhibitor. J Clin Endocrinol Metab. 2008 Feb;93(2):550-6.