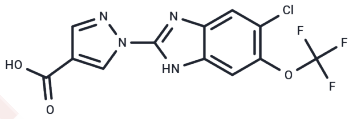
Data Sheet (Cat.No.T3180)

TargetMol

JNJ-42041935

Chemical Properties



CAS No. : 1193383-09-3

Formula: C12H6ClF3N4O3

Molecular Weight: 346.65

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	JNJ-42041935 (HIF-PHD Inhibitor II) is a potent (pKi = 7.3-7.9), 2-oxoglutarate competitive, reversible, and selective inhibitor of PHD enzymes.
Targets(IC50)	HIF/HIF Prolyl-Hydroxylase
In vitro	JNJ-42041935 is the most potent inhibitor of PHD2181-417 with a pIC50 value of 7.0±0.03. JNJ-42041935 also inhibits full-length PHD1, PHD2, and PHD3 enzymes (pKi values 7.91±0.04, 7.29 ±0.05, and 7.65±0.09, respectively) [1].
In vivo	JNJ-42041935 has been evaluated for its capability to selectively inhibit prolyl hydroxylase domain (PHD) enzymes compared to the effect of intermittent, high doses (50 μg/kg i.p.) of an erythropoietin receptor agonist in a rat model of inflammation-induced anemia. The study demonstrates that JNJ-42041935, administered at a dose of 100 μmol/kg orally once daily for 14 days, successfully ameliorates inflammation-induced anemia, whereas erythropoietin shows no efficacy. Further, a 5-day consecutive oral administration of JNJ-42041935 at 100 μmol/kg led to a doubling in reticulocyte count, a 2.3 g/dl increase in hemoglobin levels, and a 9% rise in hematocrit values. Additionally, a single oral dose of 300 μmol/kg of JNJ-42041935 resulted in a 2.2 ± 0.3-fold increase in peritoneal bioluminescence, relative to luciferase-treated vehicle controls in mice, indicating enhanced activity two hours post-administration [1].
Kinase Assay	The potency of JNJ-42041935 for inhibition of the structurally related enzyme FIH is assessed by methods similar to those described for PHD2. In brief, activity of FIH is determined using purified glutathione transferase-tagged full-length FIH amino acids 1 to 350 and a synthetic HIF-1α peptide corresponding to residues Asp788 to Leu822. Compounds are preincubated with 17.1 nM FIH for 30 min, followed by a 10-min incubation with 1 μM [2-14C]2-oxoglutarate, in the presence of 10 μM FeNH4SO4 in reaction buffer. The selectivity of JNJ-42041935 for inhibition of a range of other targets available for testing in commercial assays is also assessed at concentrations of 1 and 10 μM[1].

Solubility Information

Solubility	DMSO: 50 mg/mL (144.24 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: 2 mg/mL (5.77 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. 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	2.8848 mL	14.4238 mL	28.8475 mL
5 mM	0.577 mL	2.8848 mL	5.7695 mL
10 mM	0.2885 mL	1.4424 mL	2.8848 mL
50 mM	0.0577 mL	0.2885 mL	0.577 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

Barrett TD, et al. Pharmacological characterization of 1-(5-chloro-6-(trifluoromethoxy)-1H-benzoimidazol-2-yl)-1 H-pyrazole-4-carboxylic acid (JNJ-42041935), a potent and selective hypoxia-inducible factor prolyl hydroxylase inhibitor. Mol Pharmacol. 2011