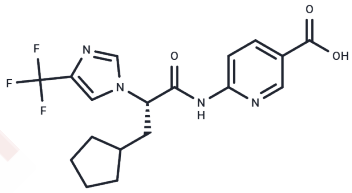
Data Sheet (Cat.No.T16480)

TargetMol

PF-04991532

Chemical Properties



CAS No. : 1215197-37-7

Formula: C18H19F3N4O3

Molecular Weight: 396.36

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-04991532 is a hepatoselective glucokinase activator that reduces plasma glucose and AMP concentrations in the Goto-Kakizaki rat model, with human and rat EC50 values of 80 and 100 nM respectively.
Targets(IC50)	Glucokinase
In vitro	PF-04991532 is a Phase 2 clinical candidate. PF-04991532 reduces the production of glucose from 1-[14C]-lactate in a dose-dependent manner (EC50=0.626 μM). PF-04991532 enhances the expression of G6Pase compare to cells treated only with 100 nM glucagon, in isolated rat hepatocytes. The greatest increase in G6Pase mRNA expression is in the presence of 25 mM glucose, 100 nM glucagon, and PF-04991532. Mechanistic experiments conducted in freshly isolated primary rat hepatocytes treated for 1 hour with PF-04991532 display increased 2-[14C]-deoxyglucose uptake (EC50=1.261 μM) and increased glucose oxidation (EC50=5.769 μM) [1].
In vivo	PF-04991532 (a single dose) enhances the glucose infusion rate in order to maintain hyperglycemia. PF-04991532 (in rats) treatment, there is increased expression of lipogenic gene expression such as acetyl-CoA carboxylase (ACC), ATP citrate lyase (ACLY), and fatty acid synthase (FAS). Despite the elevations in plasma triglycerides, hepatic triglycerides in rats dosed with 19 days of PF-04991532 are identical to vehicle-treated GK rats. Identical hepatic lipid concentrations are observed between vehicle and rats dosed with PF-04991532 (Vehicle: 9.89±0.31; PF-04991532 100 mg/kg: 9.91±0.31), in an additional cohort treated for 28 days [1].

Solubility Information

Solubility	DMSO: 100 mg/mL (252.3 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: 3.3 mg/mL (8.33 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	2.523 mL	12.6148 mL	25.2296 mL
5 mM	0.5046 mL	2.523 mL	5.0459 mL
10 mM	0.2523 mL	1.2615 mL	2.523 mL
50 mM	0.0505 mL	0.2523 mL	0.5046 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

Erion DM, et al. The hepatoselective glucokinase activator PF-04991532 ameliorates hyperglycemia without causing hepatic steatosis in diabetic rats. PLoS One. 2014 May 23;9(5):e97139.