Web: www.taiclone.com
Tel: +886-2-2735-9682
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PF-04991532

Catalog No: tcsc0018176

Available Sizes

Size: 5mg

Size: 10mg

Specifications

CAS No:
1215197-37-7

Formula:
$C_{18}H_{19}F_3N_4O_3$

Pathway:
Metabolic Enzyme/Protease

Target:
Glucokinase

Purity / Grade:
>98%

Solubility:
10 mM in DMSO

Observed Molecular Weight:
396.36

Product Description

PF-04991532 is a potent, hepatoselective **glucokinase** activator with **EC_{50}**s of 80 and 100 nM in human and rat, respectively.

IC50 & Target: EC50: 80 nM (glucokinase in human), 100 nM (glucokinase in rat)[1]

In Vitro: PF-04991532 is a potent, hepatoselective glucokinase activator with EC_{50}s of 80 nM in human and 100 nM in rat and also a Phase 2 clinical candidate. Mechanistic experiments conducted in freshly isolated primary rat hepatocytes treated for 1 hour with PF-

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04991532 show increased 2-[^{14}C]-deoxyglucose uptake (EC_{50}=1.261 μM) and increased glucose oxidation (EC_{50}=5.769 μM). Additionally, PF-04991532 decreases the production of glucose from 1-[^{14}C]-lactate in a dose dependent manner (EC_{50}=0.626 μM). In isolated rat hepatocytes, PF-04991532 increases the expression of G6Pase compare to cells treated only with 100 nM glucagon, and the greatest increase in G6Pase mRNA expression is in the presence of 25 mM glucose, 100 nM glucagon and PF-04991532[1].

In Vivo: A single dose of PF-04991532 increases the glucose infusion rate in order to maintain hyperglycemia. Despite the elevations in plasma triglycerides, surprisingly, hepatic triglycerides in rats dosed with 19 days of PF-04991532 are identical to vehicle treated GK rats. In an additional cohort treated for 28 days, 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 rats treated with PF-04991532, there is increased expression of lipogenic gene expression such as acetyl-CoA carboxylase (ACC), ATP citrate lyase (ACLY), and fatty acid synthase (FAS)[1].