

Product Data Sheet

Product Name: PF-06882961

Cat. No.: GC38832

Chemical Properties

Cas. No. 2230198-02-2

SMILES OC(C1=CC=C(N=C(CN2CCC(C3=NC(OCC4=CC=C(C#N)C=C4F)=CC=C3)CC2)N5C[C@H]6OCC6)C5=C1)=O

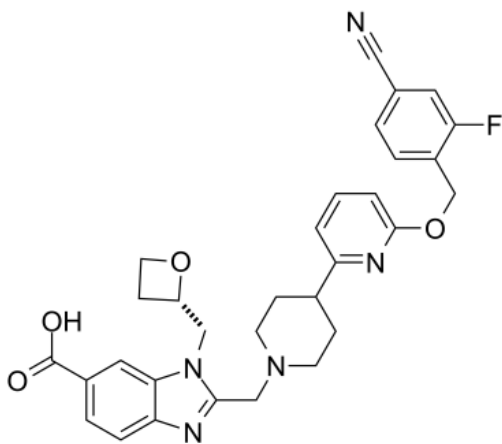
Formula $C_{31}H_{30}FN_5O_4$ M.Wt 555.6

Solubility DMSO: 125 mg/mL (224.98 mM) Storage Store at -20°C

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



Protocol

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

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Cell experiment [1]:

Cell lines neonatal rat cardiomyocytes (NRCMs)

75% alcohol sterilises the suckling Sprague–Dawley rat that has just been born for 1–2 days and quickly removes its heart, which was rinsed and minced into small pieces. Digest the ventricular myocardium of the neonatal rat hearts using 0.125% trypsin solution prepared with D-Hanks solution for 15min. This digestion process was repeated four times, after which 16mL of Dulbecco's modified Eagle's medium/nutrient mixture F12 containing 4mL of fetal bovine serum was added to terminate the digestion. The neonatal rat cardiomyocytes Preparation Method (NRCMs) were isolated using differential adhesion techniques and cultured in DMEM/F12 medium containing 15% FBS, 5-bromodeoxyuridine (0.1mM), and penicillin/streptomycin for 48h. Next, the cytotoxicity of PF-06882961 on cardiomyocytes was assessed. Cells were treated for 24h with various concentrations of PF-06882961 (0, 0.05, 0.1, 0.3, 0.9, 1.2µg/mL) or an equal volume of vehicle. Cell viability was then determined using the enhanced cell counting kit according to the manufacturer's protocol. Absorbance was measured at 450nm using a Synergy HT Multi-Detection Microplate Reader.

Reaction
Conditions 0-1.2µg/mL; 24h

Applications Treatment of phenylephrine (PE)-induced neonatal rat cardiomyocytes (NRCMs) with PF-06882961 significantly enhanced cardiomyocyte viability.

Animal experiment [1]:

Animal models C57BL/6 mice

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Adult male wild-type C57BL/6 mice (8–10 weeks old, body weight: 23.5–27.5g) were acclimated in laboratory environment for 1 week. Then, pressure overload (PO)-induced cardiac hypertrophy model in C57BL/6 mice was established using aortic banding (AB) surgery. Then AMPK α 2 knockout mice (AMPK α 2^{-/-}) were generated and bred. In the next experimental stage, we randomly assigned the experimental mice to four groups: WT ($n=10$), sham-AMPK α 2^{-/-} + PF-06882961 ($n=10$), AB-AMPK α 2^{-/-} + vehicle ($n=10$), and AB-AMPK α 2^{-/-} + PF-06882961 ($n=10$) with intragastric administration of PF-06882961 (1mg/kg/day) or saline for 8 weeks, which was initiated 3 days after AB surgery. After 8 weeks of feeding, the surviving mice were randomly selected for echocardiography to assess their cardiac function. Then the body weight, heart weight, lung weight, and tibial length of each mouse were measured and recorded after euthanized by administering excessive sodium pentobarbital (200mg/kg, i.p.). Hearts tissue were collected for further analyses.

Dosage form 1mg/kg/day; p.o.; 8 weeks

Applications PF-06882961 significantly improved cardiac function, attenuated cardiac hypertrophy and fibrosis, reduced heart weight to body weight (HW/BW), heart weight to tibia length (HW/TL), cardiomyocyte cross-sectional area (CSA) and collagen deposition.

References:

[1] Wang P, Guo Z, Kong CY, et al. Danuglipron Ameliorates Pressure Overload-Induced Cardiac Remodelling Through the AMPK Pathway. *J Cell Mol Med*. 2025;29(5):e70488.

Background

PF-06882961 is a potent, orally active glucagon-like peptide-1 receptor (GLP-1R) agonist^[1]. GLP-1R, a class B G-protein-coupled receptor mainly expressed in pancreatic β -cells and the central

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nervous system, binds GLP-1 to enhance glucose-dependent insulin secretion, suppress appetite, and delay gastric emptying^[2]. PF-06882961 is usually used in the research of metabolic diseases such as type 2 diabetes^{[3][4]}.

In vitro, treatment of phenylephrine (PE)-induced neonatal rat cardiomyocytes (NRCMs) with PF-06882961 (0-1.2µg/mL; 24h) significantly enhanced cardiomyocyte viability, attenuated PE-induced hypertrophy, reduced cell surface area, and decreased expression of hypertrophic markers (ANP, BNP, and β -MHC) without cytotoxicity^[5]. Treatment of monkey Flpin-HEK293 cells with PF-06882961 (0.37-30µM; 10min) showed moderate potency with an IC₅₀ value of 6.9µM in the hERG potassium ion channel assay^[6].

In vivo, PF-06882961 (1mg/kg/day; p.o.; 8 weeks) significantly improved cardiac function, attenuated cardiac hypertrophy and fibrosis, reduced heart weight to body weight (HW/BW), heart weight to tibia length (HW/TL), cardiomyocyte cross-sectional area (CSA) and collagen deposition, increased phosphorylated AMPK α and HSP70, decreased pro-apoptotic proteins (Bax and cleaved caspase-3), and enhanced autophagy marker Atg5 and anti-apoptotic Bcl-2 in a mouse model of aortic banding (AB)^[5]. PF-06882961 (2mg/kg; single oral administration; OGTT performed 1 hour post-dose) significantly reduced blood glucose levels in hGLP-1R knock-in mice during the oral glucose tolerance test^[7].

References:

- [1] Griffith DA, Edmonds DJ, Fortin JP, et al. A Small-Molecule Oral Agonist of the Human Glucagon-like Peptide-1 Receptor. *J Med Chem*. 2022;65(12):8208-8226.
- [2] Zheng Z, Zong Y, Ma Y, et al. Glucagon-like peptide-1 receptor: mechanisms and advances in therapy. *Signal Transduct Target Ther*. 2024;9(1):234.
- [3] Saxena AR, Gorman DN, Esquejo RM, et al. Danuglipron (PF-06882961) in type 2 diabetes: a randomized, placebo-controlled, multiple ascending-dose phase 1 trial. *Nat Med*. 2021;27(6):1079-1087.
- [4] Karakasis P, Patoulis D, Pamporis K, et al. Safety and efficacy of the new, oral, small-molecule, GLP-1 receptor agonists orforglipron and danuglipron for the treatment of type 2 diabetes and obesity: systematic review and meta-analysis of randomized controlled trials. *Metabolism*. 2023;149:155710.
- [5] Wang P, Guo Z, Kong CY, et al. Danuglipron Ameliorates Pressure Overload-Induced Cardiac

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Remodelling Through the AMPK Pathway. *J Cell Mol Med.* 2025;29(5):e70488.

[6] Sun J, Xiao Y, Hu X, et al. Toxicology profile of a novel GLP-1 receptor biased agonist-SAL0112 in nonhuman primates. *Toxicol Appl Pharmacol.* 2024;492:117125.

[7] Chen X, Xu S, Yang S, et al. Discovery of Selenium-Containing Derivatives as Potent and Orally Bioavailable GLP-1R Agonists. *J Med Chem.* 2025;68(3):3386-3408.

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