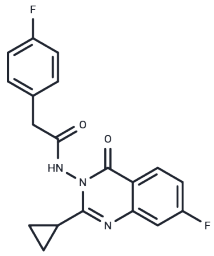
Data Sheet (Cat.No.T11606)

TargetMol

ICA-105665

Chemical Properties



CAS No. : 2694728-63-5

Formula: C19H15F2N3O2

Molecular Weight: 355.34

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	ICA-105665 (PF-04895162) is a potent and orally active opener of neuronal Kv7.2/7.3 and Kv7.3/7.5 potassium channels. ICA-105665 had low cytotoxic potential in human hepatocytes but inhibited liver mitochondrial function and bile salt export protein (BSEP) transport (IC50 of 311 μM). ICA-105665 can penetrate the central nervous system (CNS) and has antiseizure effects [1][2][3][4].
Targets(IC50)	Others,Potassium Channel
In vitro	ICA-105665 (PF-04895162) shows minimal cytotoxic effects in THLE and HepG2 cell lines, with IC 50 values of approximately 192 μM and 130 μM after 72 hours, respectively, and exhibits negligible cell loss in human hepatocytes, with an AC 50 of over 125 μM as determined by three assessments across two hepatocyte batches (LBN and HU4165) [1]. Furthermore, it impairs mitochondrial respiratory capacity in human hepatocytes at concentrations exceeding 11 μM when exposed for 25 minutes [1].
In vivo	ICA-105665 (PF-04895162) exhibited dose-dependent alanine aminotransferase (ALT) elevations in a 7-day rat toxicity study, suggesting potential liver toxicity. Nonetheless, no histological liver injury was observed, and subsequent 7-day studies did not confirm ALT elevations. Further, both 28-day and 6-month rat studies, as well as up to 9-month toxicity studies in cynomolgus monkeys, showed no transaminase elevations or liver toxicity. Additionally, ICA-105665 (PF-04895162) has shown broad-spectrum antiseizure efficacy across several animal models, including maximal electroshock, 6 Hz seizures, pentylenetetrazole, and electrical kindling, at doses ranging from <1 to 5 mg/kg [3].

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.8142 mL	14.071 mL	28.1421 mL
5 mM	0.5628 mL	2.8142 mL	5.6284 mL
10 mM	0.2814 mL	1.4071 mL	2.8142 mL
50 mM	0.0563 mL	0.2814 mL	0.5628 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

Aleo MD, et al. Phase I study of PF-04895162, a Kv7 channel opener, reveals unexpected hepatotoxicity in healthy subjects, but not rats or monkeys: clinical evidence of disrupted bile acid homeostasis. Pharmacol Res Perspect. 2019 Feb;7(1):e00467.

Generaux G, et al. Quantitative systems toxicology (QST) reproduces species differences in PF-04895162 liver safety due to combined mitochondrial and bile acid toxicity. Pharmacol Res Perspect. 2019 Oct 9;7(6):e00523.

Kasteleijn-Nolst Trenité DG, et al. Kv7 potassium channel activation with ICA-105665 reduces photoparoxysmal EEG responses in patients with epilepsy. Epilepsia. 2013 Aug;54(8):1437-43.

Bialer M, et al. Progress report on new antiepileptic drugs: a summary of the Eleventh Eilat Conference (EILAT XI). Epilepsy Res. 2013 Jan;103(1):2-30.

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