

Product Data Sheet

Product Name: ICA-105665

Cat. No.: GC64965

Chemical Properties

Cas. No. 2694728-63-5

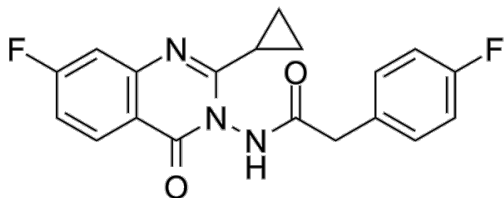
Formula C₁₉H₁₅F₂N₃O₂ M.Wt 355.34

Solubility DMSO : 250 mg/mL (703.55 mM; Storage Store at -20°C
Need ultrasonic)

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



Background

ICA-105665 (PF-04895162) is a potent and orally active neuronal Kv7.2/7.3 and Kv7.3/7.5 potassium channels opener. ICA-105665 inhibits liver mitochondrial function and bile salt export protein (BSEP)

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

transport (IC₅₀ of 311 μ M). ICA-105665 can penetrate the blood-brain barrier and has antiseizure effects[1][2][3][4].

ICA-105665 (PF-04895162) does not display potent cytotoxic properties in THLE and HepG2 cell lines (IC₅₀ ~192 μ M and 130 μ M after 72 hours, respectively) or in human hepatocytes (AC₅₀ for cell loss at 48 hours was >125 μ M based on results in three assessments in two different human hepatocyte lots (LBN and HU4165)[1]. Mitochondrial respiratory reserve is compromised in human hepatocytes treated with ICA-105665 (PF-04895162) at concentrations >11 μ M for 25 minutes[1].

For ICA-105665 (PF-04895162), in a 7-day rat toxicity study, dose-dependent alanine aminotransferase (ALT) elevations, potentially indicative of liver toxicity, were observed. However, no histological evidence of liver injury was identified, and ALT elevations were not confirmed in a repeat 7-day study. Further, 28 day and 6 month toxicity studies in rats were negative for transaminase elevations and liver toxicity, and toxicity studies up to 9 months duration in cynomolgus monkeys were also negative[2]. ICA-105665 (PF-04895162) has demonstrated broad spectrum antiseizure activity in multiple animal models including maximal electroshock, 6 Hz seizures, pentylenetetrazole, and electrical kindling at doses from <1 to 5 mg/kg[3].

[1]. 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.

[2]. 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.

[3]. Kasteleijn-Nolst Trenit  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.

[4]. 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.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA