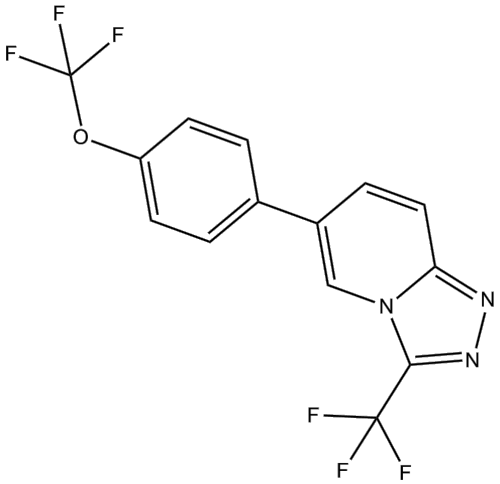
Product Data Sheet

Product Name: GS967
Cat. No.: GC10830

Chemical Properties

Cas. No.	1262618-39-2		
Chemical Name	6-(4-(trifluoromethoxy)phenyl)-3-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyridine		
SMILES	FC(F)(F)C1=NN=C2C=CC(C3=CC=C(OC(F)(F)F)C=C3)=CN21		
Formula	$C_{14}H_7F_6N_3O$	M.Wt	347.22
Solubility	≥ 13.35mg/mL in DMSO	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

Animal experiment [1]:

Animal models $Scn1a^{+/-}$ mice

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Preparation Method	On the 18th day after birth (P18), the Scn1a $^{+/-}$ mice were weaned and then randomly assigned to the GS967 group or the control group. Mice in the GS967 treatment group were fed food containing GS967 (at a dose of 1.5mg/kg/day). The survival rate of the mice was monitored until 8 weeks of age. At 8 weeks of age, the GS967 treatment was stopped, and the survival rate of the mice was monitored until 12 weeks of age.
Dosage form	1.5mg/kg/day for 38 days; p.o.
Applications	GS967 treatment improved the survival of Scn1a $^{+/-}$ mice.

References:
[1] Anderson L L, Hawkins N A, Thompson C H, et al. Unexpected efficacy of a novel sodium channel modulator in Dravet syndrome[J]. Scientific reports, 2017, 7(1): 1682.

Background

GS967 is a potent and selective inhibitor of late sodium current (late I_{Na}) in ventricular myocytes and isolated hearts with IC_{50} values of 0.13 and 0.21μM, respectively [1]. GS967 can induce a hyperpolarized shift of steady-state channel inactivation and slowe both recovery from fast inactivation and onset of slow inactivation[2]. GS967 has been widely used in various models to block cardiac sodium channels, exhibiting antiarrhythmic effects [3].

In vitro, GS967 treatment inhibited peak sodium current (I_{NaP}) with use-dependent block (UDB) in cardiomyocytes derived from pluripotent stem cells within 400milliseconds, with an IC_{50} value of 0.07μM[4].

In vivo, GS967 treatment via oral administration at a dose of 1.5mg/kg/day for 38 days significantly prolonged the survival rate of Scn1a$^{+/-}$ mice and reduced seizure frequency[5]. For two consecutive days, administering a daily dose of 1.5mg/kg/day of GS967 significantly reduced the seizure frequency in Scn2a^{Q54} mice and prevented the loss of pulmonary ganglion neurons [6]. Oral

administration of 1mg/kg/day dose of GS967 for 5 consecutive weeks significantly reduced the left ventricular mass and lung edema of Dahl salt-sensitive (DSS) rats on a high-salt diet, without affecting blood pressure or left ventricular contractility[7].

References:

[1] Belardinelli L, Liu G, Smith-Maxwell C, et al. A novel, potent, and selective inhibitor of cardiac late sodium current suppresses experimental arrhythmias[J]. The Journal of pharmacology and experimental therapeutics, 2013, 344(1): 23-32.
[2] Baker E M, Thompson C H, Hawkins N A, et al. The novel sodium channel modulator GS-458967 (GS 967) is an effective treatment in a mouse model of SCN 8A encephalopathy[J]. Epilepsia, 2018, 59(6): 1166-1176.
[3] Vos M A, Houtman M, Antoons G, et al. GS967, By Blocking the Late Sodium Current (INaL), Has Strong Action Potential–Stabilizing Properties in Isolated Remodeled Ventricular Canine Cells[J]. Heart Rhythm, 2013, 10(11): 1742.
[4] Potet F, Egecioglu D E, Burridge P W, et al. GS-967 and eleclazine block sodium channels in human induced pluripotent stem cell–derived cardiomyocytes[J]. Molecular pharmacology, 2020, 98(5): 540-547.
[5] Anderson L L, Hawkins N A, Thompson C H, et al. Unexpected efficacy of a novel sodium channel modulator in Dravet syndrome[J]. Scientific reports, 2017, 7(1): 1682.
[6] Anderson L L, Thompson C H, Hawkins N A, et al. Antiepileptic activity of preferential inhibitors of persistent sodium current[J]. Epilepsia, 2014, 55(8): 1274-1283.
[7] Chi L, Belardinelli L, Zeng A, et al. Inhibition of late Na+ current, a novel target to improve diastolic function and electrical abnormalities in Dahl salt-sensitive rats[J]. American Journal of Physiology-Heart and Circulatory Physiology, 2016, 310(10): H1313-H1320.

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