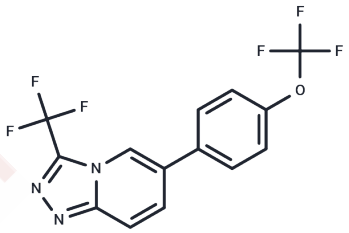
Data Sheet (Cat.No.T2049)

TargetMol

GS967

Chemical Properties



CAS No. : 1262618-39-2

Formula: C14H7F6N3O

Molecular Weight: 347.22

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	GS967 is a potent, and selective inhibitor of cardiac late sodium current (late INa).
Targets(IC50)	Sodium Channel
In vitro	GS967 at concentrations of 10, 100, and 300 nM fully counteracts ATX-II's (10 nM) ability to prolong and vary the action potential duration (APD) in ventricular myocytes. It demonstrates an approximate IC50 value of ~10 nM and reduces the beat-to-beat variability of APD[1].
In vivo	GS967 effectively mitigates and reverses the proarrhythmic consequences induced by the late INa enhancer ATX-II, the IKr inhibitor E-4031, as well as methoxamine, 1 clofilium, and ischemia-induced arrhythmias. It significantly reduces the proarrhythmic effects of these agents and suppresses ischemia-induced arrhythmias. Additionally, GS967 decreases INaP in a frequency-dependent manner, showcasing a use-dependent block (UDB) that is more potent than that of ranolazine and lidocaine, with an IC50 of 0.07 μM compared to 16 μM and 17 μM respectively. This compound also maintains its effectiveness against a common long QT syndrome mutation (delKPQ) and prevents ischemia-induced alternans in both the left atrium and ventricle, alongside reducing depolarization and repolarization heterogeneity induced by ischemia. Notably, GS967 does not affect heart rate, arterial blood pressure, PR and QT intervals, or QRS duration, although it slightly reduces contractility during ischemia, aligning with late INa inhibition effects.
Kinase Assay	The IC50 of LY-364947 at different enzyme concentrations are determined by the filter-binding assay. Typically, 40 μL reactions in 50 mM HEPES at pH 7.5, 1 mM NaF, 200 μM pKSmad3(-3), and 50 mM ATP containing a titration of each inhibitor with concentrations of 1600, 800, 400, 200, 100, 50, 25, and 0 nM are incubated at 30°C for 30 min. The IC50 is calculated using a nonlinear regression method with GraphPad Prism software. The binding type is determined by plotting the correlation between enzyme concentrations and IC50 values.

Solubility Information

Solubility	DMSO: 50 mg/mL (144 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Corn Oil: 2.5 mg/mL (7.2 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.880 mL	14.4001 mL	28.8002 mL
5 mM	0.576 mL	2.880 mL	5.760 mL
10 mM	0.288 mL	1.440 mL	2.880 mL
50 mM	0.0576 mL	0.288 mL	0.576 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

Belardinelli L, et al. A novel, potent, and selective inhibitor of cardiac late sodium current suppresses experimental arrhythmias. J Pharmacol Exp Ther. 2013 Jan;344(1):23-32.
Potet F, et al. Use-Dependent Block of Human Cardiac Sodium Channels by GS967. Mol Pharmacol. 2016 Jul;90(1): 52-60.
Bonatti R, et al. Selective late sodium current blockade with GS-458967 markedly reduces ischemia-induced atrial and ventricular repolarization alternans and ECG heterogeneity. Heart Rhythm. 2014 Oct;11(10):1827-35.