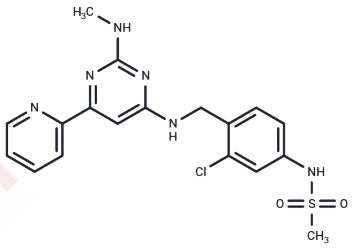
Data Sheet (Cat.No.T4648)

TargetMol

TC-G-1008

Chemical Properties



CAS No. : 1621175-65-2

Formula: C18H19ClN6O2S

Molecular Weight: 418.9

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	TC-G-1008 (GPR39-C3) is a zinc receptor agonist with EC50 values of 0.4 nM for rat GPR39 and 0.8 nM for human GPR39.
Targets(IC50)	GHSR
In vitro	TC-G-1008 demonstrates selectivity over a panel of kinases (IC50s>10 μM) and lacks significant binding affinity for the related ghrelin and neurotensin-1 receptors (IC50s>30 μM)[1]. GPR39-C3 acts as a positive allosteric modulator in HEK293-GPR39 cells, activating cAMP production (downstream of Gs), IP1 accumulation (downstream of Gq), SRF-RE-dependent transcription (downstream of G12/13), and β-arrestin recruitment, and induces dose- and time-dependent loss of response in cAMP production upon second challenge[2].
In vivo	Rat and mouse plasma protein binding for TC-G-1008 is 99.3% and 99.1%, respectively. TC-G-1008 is the first potent GPR39 agonist (EC50s ≤ 1 nM for human and rat receptor) that is orally bioavailable in mice and significantly induces acute GLP-1 levels. Following single oral doses of 10, 30, and 100 mg/kg of aqueous suspensions in 0.5% methylcellulose/0.1% Tween 80, TC-G-1008 achieves maximal exposures of 1.4, 6.1, and 25.3 μM, respectively, between 1 and 1.5 hours[1].
Kinase Assay	HEK293-GPR39 cells are plated and cultured in poly-d-lysine-coated, white, 384-well plates (4000 cells/well) in the growth medium overnight at 37°C in the presence of 5% CO2. For pretreatment of the cells with GPR39 ligands (TCG-1008) or vehicle control (DMSO), the culture medium is removed and the cells are stimulated with GPR39 ligands in assay buffer for the indicated time at 37°C. Then, the compound solution is removed and washed twice with PBS containing 0.1% BSA. For measurement of intracellular cAMP, the cells are stimulated with drugs in stimulation buffer for 30 min at 37°C. The intracellular cAMP level is determined by using HTRF cAMP dynamic 2 kit[2] .
Animal Research	Mice: Mice are given single oral doses of 10, 30, and 100 mg/kg of TC-G-1008[1] .

Solubility Information

Solubility	DMSO: 255 mg/mL (608.74 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.77 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	2.3872 mL	11.936 mL	23.872 mL
5 mM	0.4774 mL	2.3872 mL	4.7744 mL
10 mM	0.2387 mL	1.1936 mL	2.3872 mL
50 mM	0.0477 mL	0.2387 mL	0.4774 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

Peukert S, et al. Discovery of 2-Pyridylpyrimidines as the First Orally Bioavailable GPR39 Agonists. ACS Med Chem Lett. 2014 Aug 4;5(10):1114-8.

Shimizu Y, et al. Rho kinase-dependent desensitization of GPR39; a unique mechanism of GPCR downregulation. Biochem Pharmacol. 2017 Sep 15;140:105-114.