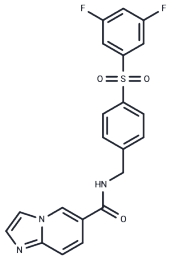
Data Sheet (Cat.No.T4335)

TargetMol

GNE-617

Chemical Properties



CAS No. : 1362154-70-8

Formula: C21H15F2N3O3S

Molecular Weight: 427.42

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	GNE-617, a specific NAMPT inhibitor(IC50=5 nM), shows potency in xenograft models of cancer.
Targets(IC50)	NAMPT
In vitro	In A549 cell, GNE-617 inhibits NAMPT (IC50=18.9 nM) .
In vivo	In rat studies, GNE-617 hydrochloride (QD) and GNE-875 (BID) demonstrated greater retinal toxicity at comparable exposures and durations of dosing than did GMX-1778 (BID). The efficacy studies in mice, which evaluated GNE-617, GNE-618, and GMX-1778, also opportunistically investigated retinal toxicity. NAMPTi-induced retinal toxicity was identified in cases involving GNE-617 and GMX-1778. However, varying study durations for GNE-617 and GMX-1778 preclude a direct comparison of their retinal toxicity profiles.
Kinase Assay	For RNA interference (RNAi), A549 cells are plated at 1,500 cells per well in 96-well plates, allowed to adhere for 24 hours, and transfected with 25 nM siRNA oligonucleotide using Dharmafect 4. Transfected cells are treated with the indicated concentrations of GNE-617 (0.1, 1 , 10 , 100 , and 1000 nM) for 72 hours and viability is evaluated with CellTiter-Glo. Lysates for detection of NAPRT1 protein are collected 72 hours after transfection of 1 million A549 cells in 10 cm dishes. For NAPRT1 re-expression, RERF-LC-MS cells are transfected with pCMV6-AC.NAPRT1 and empty vector pCMV6-AC using Amaxa Nucleofector technology and selected with Geneticin
Cell Research	GNE-617 is dissolved in DMSO and stored, and then diluted with appropriate media before use.Cells are grown in RPMI-1640 medium supplemented with 10% FBS and 2 mM glutamine and passaged not more than 20 times after thawing. To determine the IC50 values and nicotinic acid rescue status, cells are treated with nine point dose titrations of GNE-617 with or without 10 μM nicotinic acid. At 96 hours post-drug addition, the GNE-617-treated cells are evaluated using CyQUANT Direct Cell Proliferation Assay followed by CellTiter-Glo Luminescent Cell Viability Assay quantified with a Wallac EnVision 2104 Multilabel Reader. IC50 values are calculated using XLfit 5.1. To examine the protein level, cells are lysed in ice-cold radioimmunoprecipitation assay buffer, run on SDS-PAGE (4%-12% Bis-Tris), and evaluated by Western blotting using antibodies directed against NAPRT1 and β-actin

Animal Research	Male na?ve Sprague Dawley rats are administered once daily via oral gavage with GNE-617(30?mg/kg), formulated as a solution in the vehicle of 60% polyethylene glycol (PEG 400)/10% ethanol/30% 5% dextrose in water (D5W) .

Solubility Information

Solubility	DMSO: 25 mg/mL (58.49 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: 1 mg/mL (2.34 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	2.3396 mL	11.6981 mL	23.3962 mL
5 mM	0.4679 mL	2.3396 mL	4.6792 mL
10 mM	0.234 mL	1.1698 mL	2.3396 mL
50 mM	0.0468 mL	0.234 mL	0.4679 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

Shames DS, et al. Loss of NAPRT1 Expression by Tumor-specific Promoter Methylation Provides a Novel Predictive Biomarker for NAMPT Inhibitors. Clin Cancer Res. 2013 Dec 15;19(24):6912-23.
Zabka TS, et al. Retinal toxicity, in vivo and in vitro, associated with inhibition of nicotinamide phosphoribosyltransferase. Toxicol Sci. 2015 Mar;144(1):163-72.