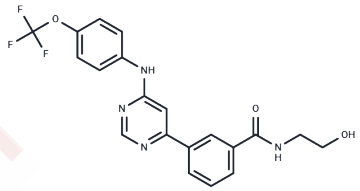
Data Sheet (Cat.No.T1803)

TargetMol

GNF-5

Chemical Properties



CAS No. : 778277-15-9

Formula: C20H17F3N4O3

Molecular Weight: 418.37

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	GNF-5 is a specific non-ATP competitive inhibitor of Bcr-Abl (IC50: 0.22±0.1 uM, Wild-type Abl). It is an analog of GNF-2 with improved pharmacokinetic properties.
Targets(IC50)	Bcr-Abl,SARS-CoV
In vitro	Concurrent administration of GNF-5 (75 mg/kg) with nilotinib (50 mg/kg) has been shown to increase the overall survival rate in a T315I Bcr-Abl BMT model. Additionally, GNF-5 (100 mg/kg) demonstrated therapeutic efficacy against both wild-type and T315I Bcr-Abl-dependent proliferation in xenograft and bone marrow transplantation models.
In vivo	GNF-5 exhibits strong antiproliferative activities, inhibiting the proliferation of cells expressing wild-type Bcr-Abl (EC50: 430 nM) and its E255K mutant variant (EC50: 580 nM). When used in combination with nilotinib or imatinib, GNF-5 suppresses the emergence of resistant mutations in vitro and demonstrates enhanced inhibitory effects against the Bcr-Abl T315I mutant in both cell-based and biochemical assays.
Kinase Assay	Kinetic characterization of Abl inhibition: The ATP/NADH-coupled assay system in a 96-well format is used to determine the initial velocity of Abl tyrosine kinase catalyzed peptide phosphorylation. The reaction mixture contained 20 mM Tris-HCl, (pH 8.0), 50 mM NaCl, 10 mM MgCl2, 2 mM PEP [2-(Phosphonooxy)- 2-propenoic acid) and 20 μg Abl peptide substrate (EAIYAAPFAKKK), fixed or varied (to determine inhibitor kinetic parameters) concentration of inhibitor applied, 1/50 of the final reaction mixture volume of PK/LDH enzyme (pyruvate kinase/lactic dehydrogenase enzymes from rabbit muscle), 160 μM NADH, 0.16 μM Abl, and ATP added last to start the reaction. Absorbance data are collected every 20s at 340 nm using a SpectraMax M5 Microplate Reader.
Cell Research	Ba/F3.p210 cells are obtained by transfecting the IL-3-dependent murine hematopoietic Ba/F3 cell line with a pEYK vector containing p210BCR-ABL and Bcr-Abl mutations. All cell lines are cultured with 5% CO2 at 37 °C in RPMI 1640 with 10% fetal bovine serum (FBS) and supplemented with 1% l-glutamine. Parental Ba/F3 cells are similarly cultured with 10% WEHI-conditioned medium as a source of IL-3. Transfected cell lines are cultured in media supplemented with 25 μg/mL zeocin. The 48 h cell proliferation studies are obtained using the CellTiter-Glo assay.(Only for Reference)

Solubility Information

Solubility	Ethanol: 16 mg/mL (38.24 mM),Sonication is recommended. DMSO: 16.67 mg/mL (39.85 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3902 mL	11.9511 mL	23.9023 mL
5 mM	0.478 mL	2.3902 mL	4.7805 mL
10 mM	0.239 mL	1.1951 mL	2.3902 mL
50 mM	0.0478 mL	0.239 mL	0.478 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.

Reference

Zhang J, et al. Nature. 2010, 463(7280), 501-506.
Deng X, et al. J Med Chem. 2010, 53(19), 6934-6946.