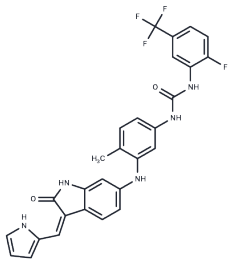
Data Sheet (Cat.No.T6097)

TargetMol

GNF-5837

Chemical Properties



CAS No. : 1033769-28-6

Formula: C28H21F4N5O2

Molecular Weight: 535.49

Appearance: no data available

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

Biological Description

Description	GNF-5837 is a specific, and orally bioavailable pan-TRK inhibitor for TrkA/TrkB (IC50: 8/12 nM).
Targets(IC50)	c-Kit,PDGFR,Trk receptor
In vitro	In Ba/F3 cells overexpressing the constitutively active Tel-TRKC fusion, GNF-5837 shows potent anti-Trk activity and potent antiproliferation activity with IC50 of 0.042 μM. [1]
In vivo	In both male Balb/c mice and Sprague-Dawley rats, GNF-5837 has the low drug clearance, and moderate biovailability. In mice bearing Rie xenografts expressing TrkA and NGF, GNF-5837 (100 mg/kg/d p.o.) significantly inhibits tumor growth. [1]
Kinase Assay	Inhibition of biochemical TrkA,TrkB and TrkC: TrkA and TrkC biochemical assays are carried out by HTRF method.The reaction mixtures contains 1 μM peptide substrate,1 μM ATP,and either 1.8 nM TrkA or 34 nM TrkC in the reaction buffer (50 mM HEPES pH 7.1,10 mM MgCl2,2 mM MnCl2,0.01% BSA,2.5 mM DTT and 0.1 mM Na3VO4) at a final volume of 10 μL.All reactions are carried out at room temperature in white ProxiPlate? 384-well Plus plates and are quenched with 5 μL of 0.2 mM EDTA at 60 min.Five μL of the detection reagents (2.5 ng PT66K and 0.05 μg SAXL per well) are added,the plates are incubated at room temperature for 1 h and then read in EnVision reader.Compounds are diluted into assay mixture (final DMSO 0.5%),and IC50 values are determined by 12-point (from 50 to 0.000282 μM) inhibition curves in duplicate under the assay conditions. TrkB biochemical assay is carried out by caliper microfluidic method.The reaction mixtures contained 1 μM peptide substrate,10 μM ATP,and 2 nM TrkB in a reaction buffer containing 100 mM HEPES,pH 7.5,5 mM MgCl2,0.01% Triton X-100,0.1% BSA,1 mM DTT,10 μMNa3VO4,and 10 μMBeta-Glycerophosphate.The reactions are carried out at room temperature for 3 hrs,and the products are determined by Caliper EZ-reader. Compounds are diluted into assay mixture (final DMSO 1%),and IC50 values are determined by 12-point (from 50 to 0.000282 μM) inhibition curves in duplicate under the assay conditions.
Cell Research	Compounds are tested for their ability to inhibit the proliferation of wt Ba/F3 cells and Ba/F3 cells transformed with constitutively expressed luciferase reporter and BCR-ABL or Tel-KDR or other Tel fusion kinases. Parental Ba/F3 cells are maintained in media containing recombinant mouse IL3 and the kinase transformed Ba/F3 cells are maintained in media without IL-3. 7.5 nL of compounds are spotted to each well of 1536-well assay plates by Liquid handling System Echo 555 (Labcyte). 700 cells are then

plated into each well of the assay plates in 7 μL culture media per well and compounds are tested at 0.17 nM to 10 uM in 3-fold serial dilutions. The cells were then incubated for 48 hours at 37 °C. 3 μL of Bright-Glo® is added to each well and the plates are read using ViewLux. (Only for Reference)

Solubility Information

Solubility	Ethanol: 5.4 mg/mL (10.08 mM),Sonication is recommended. DMSO: 40 mg/mL (74.7 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.8674 mL	9.3372 mL	18.6745 mL
5 mM	0.3735 mL	1.8674 mL	3.7349 mL
10 mM	0.1867 mL	0.9337 mL	1.8674 mL
50 mM	0.0373 mL	0.1867 mL	0.3735 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

Albaugh P, et al. ACS Med Chem Lett. 2012, 3(2), 140-145.
Qin Q, Fu Q, Wang X, et al.Design, synthesis and biological evaluation of novel indolin-2-one derivatives as potent second-generation TRKs inhibitors.European Journal of Medicinal Chemistry.2023: 115291.