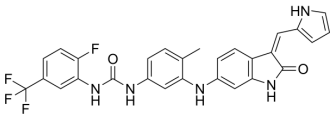
GNF-5837

Cat. No.:	HY-13491
CAS No.:	1033769-28-6
Molecular Formula:	$C_{28}H_{21}F_4N_5O_2$
Molecular Weight:	535.49
Target:	Trk Receptor
Pathway:	Neuronal Signaling; Protein Tyrosine Kinase/RTK
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 32 mg/mL (59.76 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.67 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.67 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

GNF-5837 is a potent, selective, and orally bioavailable pan-tropomyosin receptor kinase (TRK) inhibitor which display antiproliferative effects in cellular Ba/F3 assays (IC_{50} values of 7 nM, 9 nM and 11 nM for cells containing the fusion proteins Tel-TrkC, Tel-TrkB and Tel-TrkA, respectively) [1].

IC_{50} & Target

TrkB	TrkC	TrkA
9 nM (IC_{50})	7 nM (IC_{50})	11 nM (IC_{50})

In Vitro

GNF-5837 (0.1-500 nM; 72-144 hours; GOT1 cells) treatment decreases cell viability in a time- and dose-dependent manner in GOT1 cells[2].

?GNF-5837 (5-500 nM; 24 hours; GOT1 cells) causes downregulation of PI3K-Akt-mTOR signaling, Ras-Raf-MEK-ERK signaling [2].

?GNF-5837 (5-500 nM; 72 hours; GOT1 cells) treatment induces G1 cell cycle arrest[2].

?GNF-5837 (500 nM; 144 hours; GOT1 cells) treatment increases apoptotic cell death[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	GOT1 cells
Concentration:	0.1 nM , 0.5 nM , 1 nM , 5 nM , 10 nM , 50 nM , 100 nM and 500 nM
Incubation Time:	72 hours, 96 hours and 144 hours
Result:	Cell viability assay determined a clear decrease of GOT1 cell viability in a time- and dose-dependent manner.

Western Blot Analysis[2]

Cell Line:	GOT1 cells
Concentration:	5 nM, 50 nM and 500 nM
Incubation Time:	24 hours
Result:	Significant levels of TrkA expression, faint TrkC expression and no TrkB expression.

Cell Cycle Analysis[2]

Cell Line:	GOT1 cells
Concentration:	5 nM, 500 nM
Incubation Time:	72 hours
Result:	Induced G1 cell cycle arrest.

Apoptosis Analysis[2]

Cell Line:	GOT1 cells
Concentration:	500 nM
Incubation Time:	144 hours
Result:	Induced apoptosis.

In Vivo

GNF-5837 (25-100 mg/kg; oral administration; once daily; for 10 days; mice) treatment inhibits tumor growth in a mouse xenograft model derived from RIE cells expressing both TRKA and NGF[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Mouse xenograft model[1]
Dosage:	25 mg/kg, 50 mg/kg, 100 mg/kg
Administration:	Oral administration; once daily; for 10 days
Result:	72 and 100% tumor regression was observed at 50 and 100 mg/kg, respectively. At 25

	mg/kg, only partial tumor growth inhibition was achieved.

CUSTOMER VALIDATION

- J Hazard Mater. 2023 Sep 5, 457, 131831.
- BMC Complement Altern Med. 2017 Aug 12;17(1):401.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Albaugh, P. et al. Discovery of GNF-5837, a Selective TRK Inhibitor with Efficacy in Rodent Cancer Tumor Models. ACS MEDICINAL CHEMISTRY LETTERS, 2012; 3 (2): 140

[2]. Aristizabal Prada ET, et al. Tropomyosin receptor kinase: a novel target in screened neuroendocrine tumors. Endocr Relat Cancer. 2018 May;25(5):547-560.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA