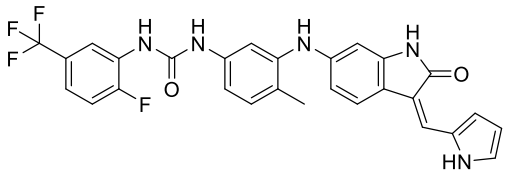
Product data sheet

MedKoo Cat#: 406427 Name: GNF-5837 CAS#: 1033769-28-6 Chemical Formula: $C_{28}H_{21}F_4N_5O_2$ Exact Mass: 535.16314 Molecular Weight: 535.49225	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
GNF-5837 is a potent, selective, and orally bioavailable pan-TRK inhibitor that inhibited tumor growth in a mouse xenograft model derived from RIE cells expressing both TRKA and NGF. The properties of GNF-5837 make it a good tool for the elucidation of TRK biology in cancer and other nononcology indications.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	32	59.76

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.87 mL	9.34 mL	18.67 mL
5 mM	0.37 mL	1.87 mL	3.73 mL
10 mM	0.19 mL	0.93 mL	1.87 mL
50 mM	0.04 mL	0.19 mL	0.37 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Chen Y, Wang H, Chen Y, Wang M, Ding G, Li T. Trk inhibitor GNF-5837 suppresses the tumor growth, survival and migration of renal cell carcinoma. Oncol Rep. 2019 Nov;42(5):2039-2048. doi: 10.3892/or.2019.7296. Epub 2019 Aug 28. PMID: 31485624.

2. Aristizabal Prada ET, Heinzle V, Knösel T, Nölting S, Spöttl G, Maurer J, Spitzweg C, Angele M, Schmidt N, Beuschlein F, Stalla GK, Blaser R, Kuhn KA, Auernhammer CJ. Tropomyosin receptor kinase: a novel target in screened neuroendocrine tumors. Endocr Relat Cancer. 2018 May;25(5):547-560. doi: 10.1530/ERC-17-0201. Epub 2018 Mar 21. PMID: 29563190.

In vivo study

1. Albaugh P, Fan Y, Mi Y, Sun F, Adrian F, Li N, Jia Y, Sarkisova Y, Kreusch A, Hood T, Lu M, Liu G, Huang S, Liu Z, Loren J, Tuntland T, Karanewsky DS, Seidel HM, Molteni V. Discovery of GNF-5837, a Selective TRK Inhibitor with Efficacy in Rodent Cancer Tumor Models. ACS Med Chem Lett. 2012 Jan 1;3(2):140-5. doi: 10.1021/ml200261d. PMID: 24900443; PMCID: PMC4025649.

7. Bioactivity
Biological target:

Product data sheet

GNF-5837 is a potent, selective, and orally bioavailable pan-tropomyosin receptor kinase (TRK) inhibitor which display antiproliferative effects in cellular Ba/F3 assays (IC50 values of 7 nM, 9 nM and 11 nM for cells containing the fusion proteins Tel-TrkC, Tel-TrkB and Tel-TrkA, respectively).

In vitro activity

GNF-5837, an inhibitor of TrkA and TrkB, suppressed the cell viability of renal carcinoma 786O and Caki-2 cells in a concentration-dependent manner. GNF-5837 treatment led to decreased activities of TrkA and TrkB signaling, accompanied by reduced phosphorylation levels of AKT and extracellular signal-regulated kinase (ERK) kinases, which was detected by western blot assay. GNF-5837 induced G0/G1-phase arrest and apoptosis. Consistently, GNF-5837 affected the expression of p21, c-Myc, and survivin proteins. Meanwhile, a wound healing assay showed that GNF-5837 inhibited the migration ability of RCC cells by impairing Rac1 activity. GNF-5837 also enhanced the cytotoxic effects of sunitinib via inhibition of ERK kinase.

Reference: Oncol Rep. 2019 Nov;42(5):2039-2048. https://www.spandidos-publications.com/or/42/5/2039

In vivo activity

To determine the in vivo PK data, GNF-5837 (compound 22) was administered intravenously to male Balb/c mice and Sprague–Dawley rats, and the drug clearance was found to be low and the volume of distribution moderate (mice) to high (rat). When administered orally by gavage, it gave moderate biovailability in both mice and rats due to poor absorption deriving from a combination of poor permeability and low aqueous solubility (Table 3). In the mice, the drug concentration in the brain after oral delivery was below the limit of quantitation, suggesting that the compound does not effectively cross the blood–brain barrier. To demonstrate in vivo efficacy, compound 22 was administered at ascending doses once daily for 10 days in mice (Figure 2) with established tumor xenografts derived from RIE cells expressing both TRKA and NGF. In this study, 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.

Reference: ACS Med Chem Lett. 2012 Jan 1;3(2):140-5. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24900443/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.