产品名称：**GNF-5837**
产品别名：**GNF-5837**

生物活性：			
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 (IC50 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].		
	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].		
	Animal Model:	Mouse xenograft model[1]	
	Dosage:	25 mg/kg, 50 mg/kg, 100 mg/kg	
	Administration:	Oral administration; once daily; for 10 days	

<table>
<tr><td></td><td>Result:</td><td>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.</td></tr>
<tr><td>Solvent&Solubility</td><td colspan="2">
In Vitro:
DMSO : ≥ 32 mg/mL (59.76 mM)
H_2O : < 0.1 mg/mL (insoluble)
* "≥" means soluble, but saturation unknown.
<table>
<tr><td rowspan="4">Preparing Stock Solutions</td><td>Solvent / Mass / Concentration</td><td>1 mg</td><td>5 mg</td><td>10 mg</td></tr>
<tr><td>1 mM</td><td>1.8674 mL</td><td>9.3372 mL</td><td>18.6745 mL</td></tr>
<tr><td>5 mM</td><td>0.3735 mL</td><td>1.8674 mL</td><td>3.7349 mL</td></tr>
<tr><td>10 mM</td><td>0.1867 mL</td><td>0.9337 mL</td><td>1.8674 mL</td></tr>
</table>
*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。
储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。
In Vivo:
请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：
——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶
1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline
Solubility: ≥ 2.5 mg/mL (4.67 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (4.67 mM，饱和度未知) 的澄清溶液。
以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)
Solubility: 2.5 mg/mL (4.67 mM); Suspended solution; Need ultrasonic
此方案可获得 2.5 mg/mL (4.67 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。
以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。
</td></tr>
<tr><td>References</td><td colspan="2">
[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.
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