上海源叶生物科技有限公司
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产品名称：Nirogacestat dihydrobromide
CAS 号：1962925-29-6
产品货号：S34237

生物活性：

Description	Nirogacestat dihydrobromide (PF-3084014 dihydrobromide) 是一种有效的，具有口服活性的，可逆的非竞争性的选择性的 γ-secretase 抑制剂，IC50 为 6.2 nM。Nirogacestat dihydrobromide 抑制 Notch 信号通路，同时最小化胃肠道毒性。可用于研究 Notch 受体依赖性肿瘤.
In Vitro	The IC50 of Nirogacestat (PF-03084014) for γ-secretase enzyme inhibition in cell-free assay for Aβ production using detergent solubilized membranes derived from HeLa cells is determined to be 6.2 nM. When tested for inhibition of Notch receptor cleavage in cellular assays using HPB-ALL cells that harbor mutations in both the heterodimerization and PEST domains in Notch1, the cell IC50 is determined to be 13.3 nM. Nirogacestat causes a significant increase in caspase-3 activities in HPB-ALL and TALL-1 cells as well as an induction of cleaved PARP and cleaved caspase-3 after a 7-day treatment[1].
In Vivo	Nirogacestat (PF-03084014) shows robust antitumor activity in this model on 14-day twice daily dosing. Tumor growth inhibition is dose dependent, with maximal tumor growth inhibition of ~92% obtained at high dose levels (150 mg/kg). In tumor growth inhibition studies where mice receive repetitive twice daily dosing for more than a week, Nirogacestat is well tolerated at dose levels below 100 mg/kg as no significant weight loss, morbidity, or mortality is observed. When the dose is increased to 150 mg/kg, however, mice have diarrhea and show weight loss (10-15%) approximately 10 days after compound administration. The body weight of treated animals usually returns to normal if dosing holidays are given, suggesting that the toxicity of Nirogacestat is reversible[1].
Solvent&Solubility	**细胞实验:** DMSO 中的溶解度 ：80 mg/mL (122.80 mM; 超声助溶; 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5350 mL	7.6750 mL	15.3499 mL
	5 mM	0.3070 mL	1.5350 mL	3.0700 mL
	10 mM	0.1535 mL	0.7675 mL	1.5350 mL

*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 (sealed storage, away from moisture)。-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。

参考文献

[1]. Wei P, et al. Evaluation of selective gamma-secretase inhibitor PF-03084014 for its antitumor efficacy and gastrointestinal safety to guide optimal clinical trial design. Mol Cancer Ther. 2010 Jun;9(6):1618-28.

完整储备液配制表：

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。

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可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	**1 mM**	1.5350 mL	7.6750 mL	15.3499 mL	38.3748 mL
	5 mM	0.3070 mL	1.5350 mL	3.0700 mL	7.6750 mL
	10 mM	0.1535 mL	0.7675 mL	1.5350 mL	3.8375 mL
	15 mM	0.1023 mL	0.5117 mL	1.0233 mL	2.5583 mL
	20 mM	0.0767 mL	0.3837 mL	0.7675 mL	1.9187 mL
	25 mM	0.0614 mL	0.3070 mL	0.6140 mL	1.5350 mL
	30 mM	0.0512 mL	0.2558 mL	0.5117 mL	1.2792 mL
	40 mM	0.0384 mL	0.1919 mL	0.3837 mL	0.9594 mL
	50 mM	0.0307 mL	0.1535 mL	0.3070 mL	0.7675 mL
	60 mM	0.0256 mL	0.1279 mL	0.2558 mL	0.6396 mL
	80 mM	0.0192 mL	0.0959 mL	0.1919 mL	0.4797 mL
	100 mM	0.0153 mL	0.0767 mL	0.1535 mL	0.3837 mL