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产品名称：RET Kinase inhibitor 1
产品别名：GSK3179106

生物活性：

Description	GSK3179106 is a potent and selective RET kinase inhibitor with an IC50 of 0.4 nM[1].
IC_{50} & Target	IC50: 0.4±0.2 nM (Human RET), 0.2±0.1 nM (Rat RET)[1]
In Vitro	GSK3179106 (10 nM-100 μM; 8 days for TT cells, 3 days for SK-N-AS and A549 cells) inhibits the proliferation of the RET-dependent TT cell line with a mean IC_{50} value of 25.5 nM however has no effect on the proliferation of the RET-independent SK-NAS and A549 cell lines (mean IC_{50}>10 μM and IC_{30}>17 μM, respectively)[1]. GSK3179106 inhibits RET phosphorylation in SK-N-AS cells and TT cells with mean IC_{50}s of 4.6 nM and 11.1 nM, respectively[1].
	Cell Viability Assay[1]
	Cell Line: TT, SK-N-AS and A549 cells
	Concentration: 10 nM-100 μM
	Incubation Time: 8 days for TT cells, 3 days for SK-N-AS and A549 cells
	Result: Inhibited the proliferation of TT cell line with a mean IC50 value of 25.5 nM however had no effect on the proliferation of the SK-NAS and A549 cell lines (mean IC50>10 μM and IC30>17 μM, respectively).
In Vivo	GSK3179106 (3 or 10 mg/kg; orally; for 3.5 days BID) reduces the visceromotor response (VMR) in comparison to rats given an acetic acid enema and dosed with vehicle[1].
	Animal Model: Seventy male Sprague Dawley rats (225-250 g, ~7-8 weeks old); Fifty male Fischer 344 rats (225-250 g, ~10-12 weeks old); Sprague Dawley female rats[1]
	Dosage: 3 and 10 mg/kg
	Administration: Oral gavage ; administered BID at 8:00 and 16:00 for 3.5 days
	Result: Reduced the visceral motor response. Led to a 34-43% inhibition in VMR to colorectal distension (CRD) at 10 mg/kg.

In Vitro:

DMSO : ≥ 100 mg/mL (213.94 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1394 mL	10.6972 mL	21.3945 mL
	5 mM	0.4279 mL	2.1394 mL	4.2789 mL
	10 mM	0.2139 mL	1.0697 mL	2.1394 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。-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

Solvent&Solubility	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 (5.35 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.35 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 (5.35 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.35 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 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.35 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.35 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 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 玉米油中，混合均匀。
References	[1]. Russell JP, et al. Exploring the Potential of RET Kinase Inhibition for Irritable Bowel Syndrome: A Preclinical Investigation in Rodent Models of Colonic Hypersensitivity. J Pharmacol Exp Ther. 2019 Feb;368(2):299-307. [2]. Russell JP, et al. Enteric RET inhibition attenuates gastrointestinal secretion and motility via cholinergic signaling in rat colonic mucosal preparations. Neurogastroenterol Motil. 2019 Apr;31(4):e13479.