产品名称：GSK3787
产品别名：GSK3787

生物活性：

Description	GSK3787 is a selective and irreversible peroxisome proliferator-activated receptor δ (PPARδ) antagonist with $pIC_{50}$of 6.6.
IC_{50} & Target	PPARδ [1]
	6.6 nM (pIC_{50})
In Vitro	GSK3787 is identified as a potent and selective hPPARδ ligand (pIC50=6.6) with no measurable affinity for hPPARα or hPPARγ (pIC50 < 5) in our standard in vitro ligand displacement assay. GSK3787 is inactive against hPPARα and hPPARγ in similar functional antagonist assays. GSK3787 fails to activate the receptor in a standard hPPARδ-GAL4 chimera cell-based reporter assay. GSK3787 is a selective PPARδ antagonist with equipotent species activity against the human and mouse receptor[1].
In Vivo	GSK3787 has pharmacokinetic properties suitable for use as an in vivo PPARδ antagonist tool compound in mice. GSK3787 is administered intravenously (0.5 mg/kg) and orally (10 mg/kg) to male C57BL/6 mice. Mean clearance (CL) and volume of distribution at steady state (Vss) following iv administration are 39±11 (mL/min)/kg and 1.7±0.4 L/kg, respectively. Following oral administration, good exposure (Cmax=881±166 ng/mL, AUCinf=3343±332 h•ng/mL), half-life (2.7±1.1 h), and bioavailability (F=77±17%) are observed[1]. Oral administration of GSK3787 (10 mg/kg) leads to a serum Cmax of 2.2±0.4 μM in C57BL/6 male mice. Oral administration of GW0742 causes an increase in expression of Angptl4 and Adrp mRNA (known PPARβ/δ target genes) in wild-type mouse colon epithelium, and this effect is not found in Pparβ/δ-null mouse colon epithelium. Coadministration of GSK3787 with GW0742 effectively prevents the ligand-induced expression of both Angptl4 and Adrp mRNA in wild-type mouse colon epithelium, and this effect is not found in Pparβ/δ-null mouse colon epithelium. Oral administration of GSK3787 causes a modest increase in promoter occupancy of PPARβ/δ in the PPRE region of both the Angptl4 and Adrp genes, but coadministration of GSK3787 with GW0742 results in markedly less accumulation of PPARβ/δ in the PPRE region of both the Angptl4 and Adrp genes in wild-type mouse colon epithelium[2].
Solvent&Solubility	***In Vitro:***
	DMSO : ≥ 50 mg/mL (127.30 mM)
	H2O : < 0.1 mg/mL (insoluble)
	* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5460 mL	12.7298 mL	25.4595 mL
	5 mM	0.5092 mL	2.5460 mL	5.0919 mL
	10 mM	0.2546 mL	1.2730 mL	2.5460 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 (6.36 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (6.36 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 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% corn oil Solubility: ≥ 2.5 mg/mL (6.36 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.36 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]. Shearer BG, et al. Identification and characterization of 4-chloro-N-(2-{[5-trifluoromethyl)-2-pyridyl]sulfonyl}ethyl)benzamide (GSK3787), a selective and irreversible peroxisome proliferator-activated receptor delta (PPARdelta) antagonist. J Med Chem. 2010 Feb 25;53(4):1857-61. [2]. Palkar PS, et al. Cellular and pharmacological selectivity of the peroxisome proliferator-activated receptor-beta/delta antagonist GSK3787. Mol Pharmacol. 2010 Sep;78(3):419-30.

实验参考：

Animal Administration	Mice[2] For RNA and DNA analysis, male wild-type and Pparβ/δ-null mice are administered vehicle (corn oil), GW0742 (10 mg/kg), GSK3787 (10 mg/kg), or GW0742 and GSK3787 by oral gavage 3 h before euthanasia. After euthanasia, colons are carefully dissected. To isolate colon epithelium, colons are flushed with phosphate-buffered saline, and epithelial cells are scraped from mucosa using a razor blade. The isolated tissues are used for RNA isolation. For glucose-tolerance tests, male wild-type and Pparβ/δ-null mice are administered vehicle (corn oil), GW0742 (10 mg/kg), GSK3787 (10 mg/kg), or Rosiglitazone (20 mg/kg) by oral gavage once a day for 2 weeks.
References	[1]. Shearer BG, et al. Identification and characterization of 4-chloro-N-(2-{[5-trifluoromethyl)-2-pyridyl]sulfonyl}ethyl)benzamide (GSK3787), a selective and irreversible peroxisome proliferator-activated receptor delta (PPARdelta) antagonist. J Med Chem. 2010 Feb 25;53(4):1857-61. [2]. Palkar PS, et al. Cellular and pharmacological selectivity of the peroxisome proliferator-activated receptor-beta/delta antagonist GSK3787. Mol Pharmacol. 2010 Sep;78(3):419-30.