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产品名称：PF06650833
产品别名：PF06650833

生物活性：

Description	PF06650833 is a potent, selective and orally active inhibitor of interleukin-1 receptor associated kinase 4 (IRAK4) with IC50s of 0.2 and 2.4 nM in the cell and PBMC assay, respectively. PF06650833 is used to treat diseases such as rheumatoid arthritis, lupus, and lymphomas[1][2].
IC_{50} & Target	IRAK4
	0.2 nM (IC50)
In Vitro	The kinome selectivity profile of PF06650833 (Compound 40) is assessed in a panel of 278 kinases (Invitrogen) at 200 nM inhibitor concentration using the ATP K_m for each kinase. Approximately 100% inhibition is observed for IRAK4[1]. Lactam PF06650833 (Compound 40) is assessed in a whole cell functional VEGF2R assay (PAE-KDR cell line). No activity is observed at concentrations up to and including 30 μM. In a voltage clamp assay, PF06650833 inhibits hERG current by 25% at 100 μM[1]. The ability of PF06650833 (Compound 40) to inhibit five major CYP450 enzymes is assessed using pooled human liver microsomes and probe substrates for the CYP450 enzymes. At a concentration of 3 μM of PF06650833, less than 5% inhibition of CYPs 1A2, 2C8, 2C9, 2D6, and 3A4 is observed. Lactam PF06650833 is examined for time dependent inhibition effects on six major CYP450 enzymes (CYP1A2, 2B6, 2C8, 2C9, 2C19, and 2D6) using pooled human liver microsomes and probe substrates. At 100 μM of PF06650833, no time dependent CYP inhibition is observed. The potential induction of CYP3A by PF06650833 is assessed using cryopreserved human hepatocytes and afforded a 4.4-fold increase in mRNA at 10 μM[1].
In Vivo	PF06650833 (Compound 40; 0.3-30 mg/kg; oral administration; for 2.5 hours; male Sprague-Dawley rats) treatment significantly inhibits LPS-induced TNF-α in a dose dependent manner. Mean exposures of PF06650833 in plasma are 2.1 nM, 7.7 nM, 19 nM and 150 nM free, respectively, at 2.5 hours after oral administration of PF06650833 at 0.3, 1, 3, and 30 mg/kg. The fraction unbound in rat plasma of PF06650833 is 0.3[1].

Animal Model:	Male Sprague-Dawley rats[1]
Dosage:	0.1 mg/kg, 1 mg/kg, 3 mg/kg, 30 mg/kg
Administration:	Oral administration; for 2.5 hours
Result:	Significantly inhibited LPS-induced TNF-α in a dose dependent manner.

In Vitro:

DMSO： ≥ 100 mg/mL (276.72 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7672 mL	13.8362 mL	27.6725 mL
	5 mM	0.5534 mL	2.7672 mL	5.5345 mL
	10 mM	0.2767 mL	1.3836 mL	2.7672 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

Solvent&Solubility	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 (6.92 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.92 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 (6.92 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.92 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 (6.92 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.92 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]. Lee KL, et al. Discovery of Clinical Candidate 1-{[(2S,3S,4S)-3-Ethyl-4-fluoro-5-oxopyrrolidin-2-yl]methoxy}-7-methoxyisoquinoline-6-carboxamide (PF-06650833), a Potent, Selective Inhibitor of Interleukin-1 Receptor Associated Kinase 4 (IRAK4), by Fragment-Based Drug Design. J Med Chem. 2017 Jul 13;60(13):5521-5542. [2]. Seganish WM. Inhibitors of interleukin-1 receptor-associated kinase 4 (IRAK4): a patent review (2012-2015). Expert Opin Ther Pat. 2016 Aug;26(8):917-32.