产品名称：**PF-06447475**
产品别名：**PF-06447475**

生物活性：

Description	PF-06447475 is a highly potent, selective and brain penetrant LRRK2 inhibitor with an IC50 of 3 nM.
IC_{50} & Target	IC50: 3 nM (LRRK2)[1].
In Vitro	PF-06447475 inhibits LRRK2 enzyme and LRRK2 in the whole cell assay with IC50s of 3 and 25 nM, respectively[1]. Cells incubated with PF-06447475 alone (0.5, 1, 3 μM) or in the presence of ROT significantly reduces (S935)-LRRK2 kinase phosphorylation to control. PF-06447475 significantly preserves the nucleus morphology and ΔΨm of NLCs exposed to ROT compared to untreated and control. PF-475 significantly diminishes ROT-induced ROS generation to a similar extent to cells exposed to PF-475 alone[2].
In Vivo	In G2019S+ rats treated with PF-06447475, a significant reduction in microgliosis to levels found in wild-type rats could be observed. The proinflammatory marker MHC-II expressed on myeloid cells but not neurons also appears to be less abundant in confocal sections in G2019S+ rats treated with PF-06447475. PF-06447475 treatment in G2019S+ rats significantly lowers the number of CD68 cells recruited to the SNpc. PF-06447475 successfully blocks the enhanced neuroinflammation associated with G2019S-LRRK2 expression. Treatment of G2019S+ rats with PF-06447475 preserves TH expression in the dorsal striatum, consistent with drug attenuating neurodegeneration in the SNpc[3]. PF-06447475 is well tolerated in rats[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 33 mg/mL (108.08 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.2751 mL	16.3757 mL	32.7515 mL
	5 mM	0.6550 mL	3.2751 mL	6.5503 mL
	10 mM	0.3275 mL	1.6376 mL	3.2751 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。

References

[1]. Henderson JL, et al. Discovery and preclinical profiling of 3-[4-(morpholin-4-yl)-7H-pyrrolo[2,3-d]pyrimidin-5-yl]benzonitrile (PF-06447475), a highly potent, selective, brain penetrant, and in vivo active LRRK2 kinase inhibitor. J Med Chem. 2015 Jan 8;58(1):419-32.

[2]. Mendivil-Perez M, et al. Neuroprotective Effect of the LRRK2 Kinase Inhibitor PF-06447475 in Human Nerve-Like Differentiated Cells Exposed to Oxidative Stress Stimuli: Implications for Parkinson's Disease. Neurochem Res. 2016 Oct;41(10):2675-2692.

[3]. Daher JP, et al. Leucine-rich Repeat Kinase 2 (LRRK2) Pharmacological Inhibition Abates α-Synuclein Gene-induced Neurodegeneration. J Biol Chem. 2015 Aug 7;290(32):19433-44.

实验参考：

Animal Administration	Rats: PF-06447475 are administered to the desired amount in a suspension solution consisting of 10% propylene glycol, 20% PEG-400, and 70% 0.5% methylcellulose. To determine the potency of PF-06447475 in blocking brain LRRK2 kinase activity, wild-type Sprague-Dawley rats are treated at 3 and 30 mg/kg PF-06447475 (p.o. b.i.d.) for 14 days, and total and phospho-LRRK2 are subsequently measured from brain tissue lysates[3].
References	[1]. Henderson JL, et al. Discovery and preclinical profiling of 3-[4-(morpholin-4-yl)-7H-pyrrolo[2,3-d]pyrimidin-5-yl]benzonitrile (PF-06447475), a highly potent, selective, brain penetrant, and in vivo active LRRK2 kinase inhibitor. J Med Chem. 2015 Jan 8;58(1):419-32. [2]. Mendivil-Perez M, et al. Neuroprotective Effect of the LRRK2 Kinase Inhibitor PF-06447475 in Human Nerve-Like Differentiated Cells Exposed to Oxidative Stress Stimuli: Implications for Parkinson's Disease. Neurochem Res. 2016 Oct;41(10):2675-2692. [3]. Daher JP, et al. Leucine-rich Repeat Kinase 2 (LRRK2) Pharmacological Inhibition Abates α-Synuclein Gene-induced Neurodegeneration. J Biol Chem. 2015 Aug 7;290(32):19433-44.