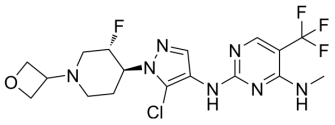
GNE-9605

Cat. No.:	HY-12282
CAS No.:	1536200-31-3
Molecular Formula:	$C_{17}H_{20}ClF_4N_7O$
Molecular Weight:	449.83
Target:	LRRK2
Pathway:	Autophagy
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (222.31 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2231 mL	11.1153 mL	22.2306 mL
	5 mM	0.4446 mL	2.2231 mL	4.4461 mL
	10 mM	0.2223 mL	1.1115 mL	2.2231 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.62 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.62 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.62 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GNE-9605 is a potent, orally active, selective Leucine-rich repeat kinase 2 (LRRK2) inhibitor with an IC_{50} value of 18.7 nM. GNE-9605 inhibits LRRK2 Ser1292 autophosphorylation. GNE-9605 can be used in research of Parkinson's disease (PD) [1].

In Vivo

GNE-9605 (10 and 50 mg/kg; i.p.; once) inhibits LRRK2 Ser1292 autophosphorylation in BAC transgenic mice expressing human LRRK2 protein[1].

GNE-9605 (1 mg/kg, p.o.; 0.5 mg/kg, i.v.; once) displays LRRK2 K_i in the biochemical assay of 2 nM as well as a cellular IC_{50} of 19 nM. GNE-9605 has a total plasma clearance with excellent oral bioavailability[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	BAC transgenic mice expressing human LRRK2 protein[1].
Dosage:	10 and 50 mg/kg
Administration:	Intraperitoneal injection; once
Result:	Inhibited LRRK2 Ser1292 autophosphorylation in a dose-dependent manner.

Animal Model:	BAC transgenic mice expressing human LRRK2 protein[1].
Dosage:	1 mg/kg, p.o.; 0.5 mg/kg, i.v.
Administration:	Oral administration and intravenous injection; once
Result:	Demonstrated a total plasma clearance of 26 mL min^{-1} kg^{-1} with excellent oral bioavailability (90%).

REFERENCES

[1]. Estrada AA, et, al. Discovery of highly potent, selective, and brain-penetrant aminopyrazole leucine-rich repeat kinase 2 (LRRK2) small molecule inhibitors. J Med Chem. 2014 Feb 13;57(3):921-36.

[2]. Kumar S, et, al. Exploring the focal role of LRRK2 kinase in Parkinson's disease. Environ Sci Pollut Res Int. 2022 May;29(22):32368-32382.

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