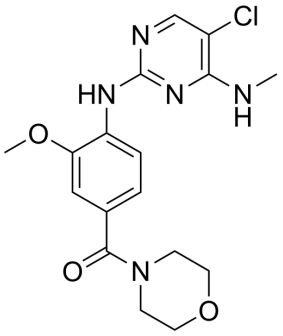
HG-10-102-01

Cat. No.:	HY-13488
CAS No.:	1351758-81-0
Molecular Formula:	$C_{17}H_{20}ClN_5O_3$
Molecular Weight:	377.83
Target:	LRRK2; MNK
Pathway:	Autophagy; MAPK/ERK Pathway
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 : ≥ 50 mg/mL (132.33 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6467 mL	13.2335 mL	26.4669 mL
5 mM	0.5293 mL	2.6467 mL	5.2934 mL
10 mM	0.2647 mL	1.3233 mL	2.6467 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 mg/mL (5.29 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2 mg/mL (5.29 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

HG-10-102-01 is a highly potent, selective, and brain-penetrable LRRK2 inhibitor, with IC_{50} values of 20.3 and 3.2 nM against wild-type LRRK2 and LRRK2[G2019S], respectively. HG-10-102-01 also inhibits MNK2 and MLK1, with IC_{50} values of 0.6 and 2.1 μM. HG-10-102-01 can be used for Parkinson's disease (PD) research[1][2].

IC_{50} & Target

IC50: 3.2 nM (LRRK2[G2019S]), 20.3 nM (wild-type LRRK2), 95.9 nM (LRRK2[G2019S+A2016T], 153.7 nM (LRRK2[A2016T]), 0.6 μM (MNK2), 2.1 μM (MLK1)[1]

In Vitro

HG-10-102-01 (0-3 μM, 90 min) substantially inhibits Ser910 and Ser935 phosphorylation of both wild-type LRRK2 and G2019S mutant[1].

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

Western Blot Analysis[1]

Cell Line:	HEK293 cells, Mouse Swiss 3T3 cells and Mouse embryonic fibroblast cells
Concentration:	0, 0.01, 0.03, 0.1, 0.3, 1, and 3 μM
Incubation Time:	90 min
Result:	Induced a dose-dependent inhibition of Ser910 and Ser935 phosphorylation in both wild-type LRRK2 and LRRK2[G2019S] stably transfected into HEK293 cells. Induced similar dose-dependent Ser910 and Ser935 dephosphorylation of endogenous LRRK2 in mouse Swiss 3T3 cells and mouse embryonic fibroblast cells.

In Vivo

HG-10-102-01 (0-100 mg/kg, IP, once) shows inhibition of LRRK2 Ser910/Ser935 phosphorylation in kidney, spleen, and brain of mice[1].

HG-10-102-01 (1 mg/kg, IV; 10 mg/kg, PO; once) shows good oral bioavailability (%F = 67), a short half-life of 0.13 h, and low plasma exposure[1].

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

Animal Model:	Wild type male C57BL/6 mice[1]
Dosage:	0, 3, 10, 30, 50, and 100 mg/kg
Administration:	IP, once
Result:	Showed near complete dephosphorylation of Ser910 and Ser935 of LRRK2 in all tissues including brain at 100 mg/kg and 50 mg/kg, but only partial inhibition in brain at the 30 and 10 mg/kg doses.

Animal Model:	Wild type male C57BL/6 mice[1]
Dosage:	1 mg/kg (IV); 10 mg/kg (PO)
Administration:	IV, PO; once (Pharmacokinetic Analysis)
Result:	Pharmacokinetic Parameters of HG-10-102-01 in male C57BL/6 mice[1].

	IV (1 mg/kg)	PO (10 mg/kg)
T_{max} (h)		0.25
C_{max} (ng/mL)	1330	1241
AUC_{last} (ng/mL·h)	74.85	502.34
AUC_{INF} (ng/mL·h)	75.06	503.41
$T_{1/2}$ (h)	0.13	
CL (mL/min/kg)	222.04	

Vss (L/kg)	1.68	
F (%)		67

CUSTOMER VALIDATION

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REFERENCES

[1]. Wang M, et al. Synthesis of [11C]HG-10-102-01 as a new potential PET agent for imaging of LRRK2 enzyme in Parkinson's disease. Bioorg Med Chem Lett. 2017 Mar 15;27(6):1351-1355.

[2]. Choi HG, et al. Brain Penetrant LRRK2 Inhibitor. ACS Med Chem Lett. 2012 Aug 9;3(8):658-662.

Caution: Product has not been fully validated for medical applications. For research use only.

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