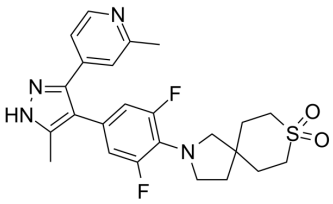
LRRK2-IN-5

Cat. No.:	HY-151441
CAS No.:	2892451-45-3
Molecular Formula:	$C_{24}H_{26}F_2N_4O_2S$
Molecular Weight:	472.55
Target:	LRRK2
Pathway:	Autophagy
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	LRRK2-IN-5 (compound 25) is a potent, orally active, selective leucine rich repeat protein kinase 2 gene (LRRK2) inhibitor with IC_{50} values of 1.2 and 16 μM for GS LRRK2 and WT LRRK2, respectively. LRRK2-IN-5 inhibits LRRK2 Ser1292 and Ser925 autophosphorylation. LRRK2-IN-5 can cross the blood-brain barrier[1].
IC_{50} & Target	IC50: 1.2 (GS LRRK2) and 16 μM (GS LRRK2)[1]

In Vitro

LRRK2-IN-5 (compound 25; 0-10000 nM; 24 h; HEK293 cells) has excellent potency and GS-LRRK2 selectivity[1].

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

Cell Viability Assay[1]

Cell Line:	HEK293 cells
Concentration:	0, 30, 100, 300, 1000, 3000, and 10000 nM
Incubation Time:	24 hours
Result:	Reduced GS-LRRK2 pSer935 and GS-LRRK2 pSer1292 autophosphorylation levels over WT-LRRK2.

In Vivo

LRRK2-IN-5 (compound 25; 0.5 mg/kg (i.v.) and 5 mg/kg (p.o.); CD-1 mice) has good pharmacokinetic parametershigh and high bioavailability[1].

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

Animal Model:	CD-1 mice[1]
Dosage:	0.5 mg/kg (i.v.) and 5 mg/kg (p.o.)
Administration:	Intravenous injection and oral administration

Result:

Route of Administration	IV	PO

Dose (mg/kg)	0.5	5
AUC_{inf} (μM*h)	0.51	1.44
C_{max} (μM)	0.61	0.60
T_{max} (h)	0.08	0.50
$T_{1/2}$ (h)	0.45	1.46
MRT (h)	0.65	2.35
CL (mL/min)	34.3	
F (%)		28

REFERENCES

[1]. Leśniak RK, et, al. Discovery of azaspirocyclic 1H-3,4,5-Trisubstitued pyrazoles as novel G2019S-LRRK2 selective kinase inhibitors. Eur J Med Chem. 2022 Nov 15;242:114693.

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