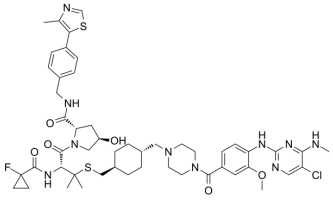
XL01126

Cat. No.:	HY-148030		
Molecular Formula:	$C_{50}H_{64}ClFN_{10}O_6S_2$		
Molecular Weight:	1019.69		
Target:	PROTACs; LRRK2		
Pathway:	PROTAC; Autophagy		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (98.07 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
	1 mM	0.9807 mL	4.9035 mL	9.8069 mL
	5 mM	0.1961 mL	0.9807 mL	1.9614 mL
	10 mM	0.0981 mL	0.4903 mL	0.9807 mL

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

BIOLOGICAL ACTIVITY

Description

XL01126 is a potent degrader of LRRK2 with DC_{50}s of 14 nM (G2019S LRRK2) and 32 nM (WT LRRK2), respectively. XL01126 can cross blood-brain barrier and be used as a degrader probe in Parkinson's disease research. XL01126 exerts function of study of non-catalytic and scaffolding functions of LRRK2[1].

IC_{50} & Target

DC50: 15-72 nM (LRRK2)[1]

In Vitro

XL01126 (300 nM; 4 h) exhibits strong degradation performance by forming a positively cooperative ternary complex with E3 ubiquitin ligase ligand VHL and target protein LRRK2[1].

XL01126 (10, 30, 100 nM; 24 h) increases mitophagy in immortalized mouse embryonic fibroblasts cells[1].

XL01126 (10 μM; 90 min) displays high permeability in Caco-2 cells[1].

XL01126 (10 μM; 0-60 min; every 15 min interval gradient) exhibits high stability in mouse plasma, liver microsome and hepatocyte[1].

Pharmacokinetic of XL01126 in vitro[1]

Parameter	Properties
$T_{1/2}$ in mouse plasma	108.29 min
$T_{1/2}$ in mouse liver microsome	3.65 min
Cl_{int} in mouse liver microsome	1494.62 mL/min/kg
$T_{1/2}$ in mose hepatocytes	314.33 min
Cl_{int} in mose hepatocytes	26.04 mL/min/kg

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

Western Blot Analysis[1]

Cell Line:	G2019S LRRK2 MEFs (mouse embryonic fibroblasts)
Concentration:	300 nM
Incubation Time:	4 hours
Result:	Resulted LRRK2 pSer935, Rab10 pThr73 decrease.

In Vivo

XL01126 (30 mg/kg; p.o.; single dose) shows oral activity with bioavailable value (F) of 15% and can penetrate the blood brain barrier after either oral or parenteral dosing in mice[1].

Pharmacokinetic property of XL01126 in mice[1]

Route	Dose (mg/kg)	CL (L/h/kg)	V_{ss} (L/kg)	T_{max} (h)	C_{max} (ng/mL)	$T_{1/2}$ (h)	AUC_{last} (h·ng/mL)	AUC_{inf} (h·ng/mL)	MRT (h)	F (%)
p.o.	30			2	3620	21.9	21337	109271		15
i.v.	5	0.208	0.511			1.52	23663	23981	2.45	
i.p.	30			0.25	7700	5.2	41434	64068		29.2

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

REFERENCES

[1]. Liu, Xingui, et al. Discovery of XL01126: A Potent, Fast, Cooperative, Selective, Orally Bi- oavailable and Blood Brain Barrier Penetrant PROTAC Degrader of Leucine Rich Repeat Kinase 2 (LRRK2). 2022.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA