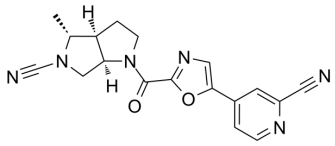
MTX115325

Cat. No.:	HY-160019
CAS No.:	2750895-97-5
Molecular Formula:	$C_{18}H_{16}N_6O_2$
Molecular Weight:	348.36
Target:	Deubiquitinase; Mitophagy
Pathway:	Cell Cycle/DNA Damage; Autophagy
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (717.65 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8706 mL	14.3530 mL	28.7059 mL
	5 mM	0.5741 mL	2.8706 mL	5.7412 mL
	10 mM	0.2871 mL	1.4353 mL	2.8706 mL

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

BIOLOGICAL ACTIVITY

Description

MTX115325 (Example 1) is an orally active, brain-penetrating USP30 inhibitor (IC_{50}=12 nM) with neuroprotective activity. MTX115325 increases ubiquitination (EC_{50}=32 nM) of the mitochondrial outer membrane protein TOM20 (a USP30 substrate), increasing mitophagy. MTX115325 prevents dopaminergic neuron loss and preserves striatal dopamine[1].

IC_{50} & Target

IC50: 12 nM (USP30)
EC50: 32 nM (TOM20, the outer mitochondrial membrane protein)[1]

In Vitro

MTX115325 (37 nM-1 μM; 72 h) shows promotion of mitochondrial autophagy in SH-SY5Y cells[1].
MTX115325 (10 nM-1 μM; 90 min) promotes ubiquitination of TOM20 and inhibits USP30 activity in both HeLa cells and YFP-Parkin overexpressing HeLa cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

MTX115325 (i.g.; 15 mg/kg and 50 mg/kg; twice daily for 10 weeks) reduces phosphorylated S129-αSyn levels and decreases the total area of GFAP staining in AAV-A53T-SNCA Mouse Model, indicating lower astrocyte activation[1].
MTX115325 (i.g.; 10 mg/kg; single dose) demonstrates excellent oral bioavailability (98%) and good CNS penetration with a brain partition coefficient (Kpu,u) of approximately 0.4[1].

MTX115325 (i.g.; single dose) has a C_{max} of 7546.9 ng/mL at 15 mg/kg and a C_{max} of 16374.3 ng/mL at 50 mg/kg. At a 50 mg/kg dosage, the drug concentration consistently remained above the EC_{50} for TOM20 ubiquitination[1].

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Animal Model:	AAV-A53T-SNCA Mouse Model [1]
Dosage:	15 mg/kg and 50 mg/kg
Administration:	i.g.; twice daily for 10 weeks
Result:	Reduced the loss of dopaminergic neurons in the substantia nigra (SN) and preserved dopamine levels in the striatum. Increased the percentage of tyrosine hydroxylase (TH)+ neurons.

REFERENCES

[1]. Fang TZ et al. Knockout or inhibition of USP30 protects dopaminergic neurons in a Parkinson's disease mouse model. Nat Commun. 2023 Nov 13;14(1):7295.

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