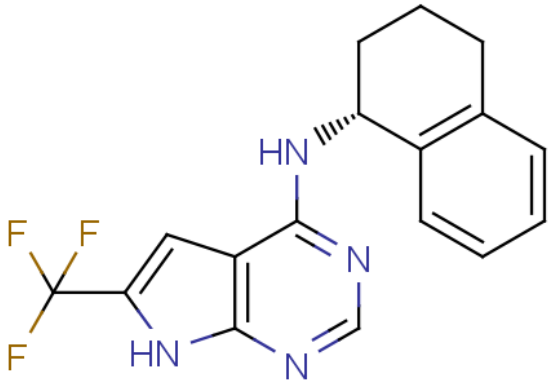
Name: MTK458 Cat#: EX-A8247

Target:: Mitophagy; Mitochondrial Metabolism; PINK1/Parkin
Pathway: Autophagy; Metabolic Enzyme/Protease; Neuronal Signaling

Chemical Structure:



Absolute stereochemistry shown

Chemical Name	7H-Pyrrolo[2,3-d]pyrimidin-4-amine, N-[(1R)-1,2,3,4-tetrahydro-1-naphthalenyl]-6-(trifluoromethyl)-

Molecular Weight	332.323	Storage	3 years -20°C powder 6 months -80°C in solvent Away from light
Formula	C17H15F3N4		
CAS No.	2499962-58-0	Synonyms	EP-0035985; EP0035985; MTK-458

Solubility (25°C) *	In vitro	DMSO	Soluble, >50mg/mL (Need ultrasonic)
		Ethanol	N/A
		Water	N/A
	In vivo （should be freshly prepared each time）		

* <1 mg/ml means slightly soluble or insoluble.
* Please note that Selleck tests the solubility of all compounds in-house, and the actual solubility may differ slightly from published values. This is normal and is due to slight batch-to-batch variations.

Preparing Stock Solutions:

Mass / Volume / Concentration	1 mg	5 mg	10 mg
1 mM	3.0091 mL	15.0457 mL	30.0915 mL
5 mM	0.6018 mL	3.0091 mL	6.0183 mL
10 mM	0.3009 mL	1.5046 mL	3.0091 mL

*The above data is based on the product molecular weight 332.32.

In Vivo (Solubility)	1. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (7.52 mM); Clear solution 2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.38 mg/mL (7.16 mM); Clear solution

Biological Activities:

Description	MTK458 is an orally active brain penetrant PINK1 activator. MTK458 binds to PINK1 and stabilizes an active heterocomplex, thereby increasing mitophagy. MTK458 can be used for research on Parkinson's disease[1].
In Vitro	MTK458 (25 μM) increases PINK1-mediated mitophagy to enhance clearance of intramitochondrial aggregates in Hela cells induced ΔOTC and YFP-Parkin[1]. MTK458 (0.1-25 μM) clears pS129 α-synuclein aggregates (12-250 kDa) in a dose-dependent manner in DIV9 and DIV12[1]. MTK458 (0-13 μM, 10 days) reduces α-synuclein pathology and the mitochondrial stress marker pUb in iPSC neurons[1].
In Vivo	MTK458 (50 mg/kg, p.o., daily, 6 months) drives clearance of pathologic α-synuclein in a dose-dependent manner in the stratum of mice injected with α-synuclein preformed fibrils (PFFs)[1]. MTK458 (50 mg/kg, p.o., 6 doses, 5 days) decreases plasma pS65-Ubiquitin (pUb) in wild-type Sprague-Dawley rats[1].

References	[1]. Chin RM, et al. Pharmacological PINK1 activation ameliorates Pathology in Parkinson's Disease models. bioRxiv [Preprint]. 2023 Feb 15:2023.02.14.528378.