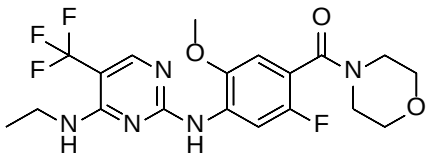
Product data sheet

MedKoo Cat#: 510257 Name: GNE-7915 CAS#: 1351761-44-8 (free base) Chemical Formula: $C_{19}H_{21}F_4N_5O_3$ Exact Mass: 443.1581 Molecular Weight: 443.40	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
GNE-7915 is a potent LRRK2 kinase inhibitor, which possess an ideal balance of LRRK2 cellular potency, broad kinase selectivity, metabolic stability, and brain penetration across multiple species. GNE-7915 was reported as a potent (IC50=9 nM) selective (1/187 kinases), brain-penetrant and non-toxic inhibitor of LRRK2.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	10.0	22.55
Ethanol	1.0	2.25

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.26 mL	11.28 mL	22.55 mL
5 mM	0.45 mL	2.26 mL	4.51 mL
10 mM	0.23 mL	1.13 mL	2.26 mL
50 mM	0.05 mL	0.23 mL	0.45 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Howlett EH, Jensen N, Belmonte F, Zafar F, Hu X, Kluss J, Schüle B, Kaufman BA, Greenamyre JT, Sanders LH. LRRK2 G2019S-induced mitochondrial DNA damage is LRRK2 kinase dependent and inhibition restores mtDNA integrity in Parkinson's disease. Hum Mol Genet. 2017 Nov 15;26(22):4340-4351. doi: 10.1093/hmg/ddx320. PMID: 28973664; PMCID: PMC5886254.

In vivo study

1. Qin Q, Zhi LT, Li XT, Yue ZY, Li GZ, Zhang H. Effects of LRRK2 Inhibitors on Nigrostriatal Dopaminergic Neurotransmission. CNS Neurosci Ther. 2017 Feb;23(2):162-173. doi: 10.1111/cns.12660. Epub 2016 Dec 9. PMID: 27943591; PMCID: PMC5248597.

7. Bioactivity
Biological target: GNE-7915 is an inhibitor of LRRK2 with an IC50 of 9 nM.

In vitro activity

Whether LRRK2 G2019S-induced mtDNA damage is kinase dependent was investigated. A pretreatment paradigm in which primary midbrain neuronal cultures were treated with vehicle or GNE-7915 for 24 h and then transduced with either GFP or LRRK2 G2019S for 24 h was used. Pretreatment with GNE-7915 was able to prevent LRRK2 G2019S-induced mtDNA damage (Fig. 4A).

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Mitochondrial DNA copy number was unaffected by treatments (Fig. 4B). Importantly, treatment of GNE-7915 by itself did not alter mtDNA damage levels or copy number (Supplementary Material, Fig. S2). It was also confirmed that treatment with GNE-7915 reduced levels of LRRK2 pSer935, as these sites may be modulated indirectly by LRRK2 kinase activity and dephosphorylation occurs with LRRK2 kinase inhibitor exposure (Supplementary Material, Fig. S3).

Reference: Hum Mol Genet. 2017 Nov 15;26(22):4340-4351. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5886254/

In vivo activity

The effects of LRRK2 inhibitor GNE-7915 on R1441G Tg mice were examined to see whether GNE-7915 could alleviate DA (dopamine) transmission deficits. When treated with 1 μM GNE-7915 for 2 h, a significant increase of PPR (pair-pulse ratio) was observed (PPR/5s, control: 0.45 ± 0.01, treated: 0.48 ± 0.01, n = 10, $P < 0.05$; PPR/10s, control: 0.61 ± 0.005, treated: 0.66 ± 0.008, n = 10, $P < 0.01$; PPR/20s, control: 0.80 ± 0.015, treated: 0.84 ± 0.002, n = 10, $P < 0.001$, Figure 6). Single-pulse-evoked DA release was also enhanced (control: 1.93 ± 0.15 μM, n = 10; treated: 2.17 ± 0.19 μM, n = 10, $P < 0.05$, Figure 6).

Reference: CNS Neurosci Ther. 2017 Feb;23(2):162-173. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5248597/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.