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Zuschläge

- Mindermengenzuschlag
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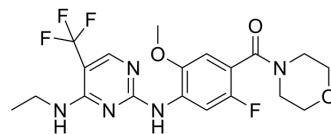
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GNE-7915

Cat. No.:	HY-18163
CAS No.:	1351761-44-8
Molecular Formula:	C ₁₉ H ₂₁ F ₄ N ₅ O ₃
Molecular Weight:	443.4
Target:	LRRK2
Pathway:	Autophagy
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro	DMSO : 100 mg/mL (225.53 mM; Need ultrasonic)					
	Preparing Stock Solutions	Solvent Concentration	Mass	1 mg	5 mg	10 mg
		1 mM		2.2553 mL	11.2765 mL	22.5530 mL
		5 mM		0.4511 mL	2.2553 mL	4.5106 mL
		10 mM		0.2255 mL	1.1277 mL	2.2553 mL
Please refer to the solubility information to select the appropriate solvent.						
In Vivo	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.5 mg/mL (5.64 mM); Clear solution					
	2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (5.64 mM); Suspended solution; Need ultrasonic					
	3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (5.64 mM); Clear solution					
	4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline Solubility: ≥ 2.5 mg/mL (5.64 mM); Clear solution					

BIOLOGICAL ACTIVITY

Description	GNE-7915 is a potent, selective and brain-penetrant inhibitor of LRRK2 with an IC ₅₀ of 9 nM.
IC ₅₀ & Target	IC ₅₀ : 9 nM ^[1] (LRRK2)
In Vitro	Maintaining the methoxy/fluoro arrangement at C-2'/C-5' and varying aminoalkyl R1 substitution results in single-digit

nanomolar LRRK2 cellular activities for GNE-7915 and compound 19. Expanded Invitrogen kinase profiling (187 kinases) at 0.1 μ M for both GNE-7915 (100-fold over LRRK2 Ki) and 19 (250-fold over LRRK2 Ki) results in only TTK showing greater than 50% inhibition. Selectivity profiling using the DiscoverX KinomeScan55 competitive binding assay panel, which includes 392 unique kinases, is also performed for GNE-7915 at 0.1 μ M. Binding of >50% probe displacement is detected for 10 kinases and of >65% for only LRRK2, TTK, and ALK, further supporting the excellent LRRK2 selectivity for GNE-7915. Cerep receptor profiling, including expanded brain panels, suggests that GNE-7915 and 19 only inhibit 5-HT_{2B} with >70% inhibition at 10 μ M. GNE-7915 and 19 are confirmed to be moderately potent 5-HT_{2B} antagonists in vitro functional assays^[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Stem Cell Reports. 2022 Sep 12;S2213-6711(22)00423-4.
- Hum Mol Genet. 2017 Jul 15;26(14):2747-2767.
- bioRxiv. 2023 Jan 9.
- bioRxiv. 2020 Apr.
- Programa Oficial de Doctorado en Biomedicina. Universidad de Granada. 5-Jul-2017.

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REFERENCES

- [1]. Kavanagh ME, et al. The development of CNS-active LRRK2 inhibitors using property-directed optimisation. Bioorg Med Chem Lett. 2013 Jul 1;23(13):3690-6.
- [2]. Estrada AA, et al. Discovery of highly potent, selective, and brain-penetrable leucine-rich repeat kinase 2 (LRRK2) small molecule inhibitors. J Med Chem. 2012 Nov 26;55(22):9416-33.

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

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