

GNE-7915

Catalog No: tcsc3094



Available Sizes

Size: 10mg

Size: 50mg

Size: 100mg

Size: 200mg



Specifications

CAS No:

1351761-44-8

Formula:

$C_{19}H_{21}F_4N_5O_3$

Pathway:

Autophagy

Target:

LRRK2

Form:

Off-white to light yellow (Solid)

Purity / Grade:

99.66%

Solubility:

DMSO : 14.33 mg/mL (32.32 mM; Need ultrasonic and warming)

Water:

Storage Instruction:

2-8°C

Alternative Names:

Methanone, [4-[[4-(ethylamino)-5-(trifluoromethyl)-2-pyrimidinyl]amino]-2-fluoro-5-methoxyphenyl]-4-morpholinyl

Observed Molecular Weight:

443.4

Protocol:

Animal administration [1] Thus, BAC transgenic mice expressing human LRRK2 protein with the G2019S Parkinson's disease mutation were given either a single oral dose (po) or intraperitoneal (ip) injection. Brain (hippocampus) and peripheral (spleen) tissues were harvested 1-24 h postdose to assess pSer1292 levels and compound concentration. The concentration-dependent knockdown of pLRRK2 in the brain after oral dosing with GNE-7915 at both 15 and 50 mg/kg and after ip dosing at both 10 and 50 mg/kg.

References

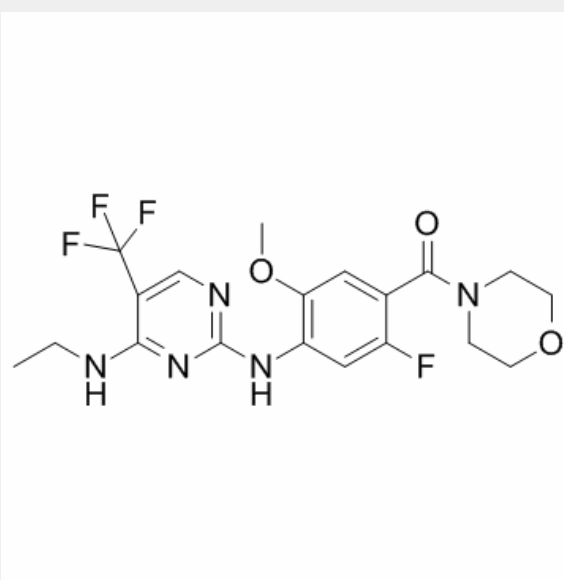
[1]. Kavanagh ME, et al. The development of CNS-active LRRK2 inhibitors using property-directed optimisation. *Bioorg Med Chem Lett.* 2013 Jul 1;23(13):3690-6. [2]. Estrada AA, et al. Discovery of highly potent, selective, and brain-penetrable leucine-rich repeat kinase 2 (LRRK2) small molecule inhibitors.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

Product Description

GNE-7915 is a potent, selective and brain-penetrant inhibitor of **LRRK2** with an **IC₅₀** of 9 nM.

IC50 & Target: IC50: 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 μM 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 μM. 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 μM. GNE-7915 and 19 are confirmed to be moderately potent 5-HT_{2B} antagonists in vitro functional assays^[2].



All products are for RESEARCH USE ONLY. Not for diagnostic & therapeutic purposes!