GNE-7915 tosylate

Cat. No.: HY-18163A

CAS No.: 2070015-00-6

Molecular Formula: $C_{26}H_{29}F_4N_5O_6S$

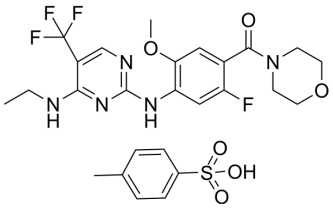
Molecular Weight: 615.6

Target: LRRK2

Pathway: Autophagy

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (81.22 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.6244 mL	8.1222 mL	16.2443 mL
5 mM	0.3249 mL	1.6244 mL	3.2489 mL
10 mM	0.1624 mL	0.8122 mL	1.6244 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 (4.06 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.06 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.06 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GNE-7915 tosylate is a potent, selective and brain-penetrant inhibitor of LRRK2 with an IC_{50} of 9 nM.

IC_{50} & Target

IC50: 9 nM[1] (LRRK2)

In Vitro

Maintaining the methoxy/fluoro arrangement at C-2′/C-5′ and varying aminoalkyl R1 substitution resultes 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) resultes 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, suggestes that GNE-7915 and 19 only inhibite 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].

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.

See more customer validations on www.MedChemExpress.com

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.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA