GSK2578215A

Cat. No.: HY-13237

CAS No.: 1285515-21-0

Molecular Formula: $C_{24}H_{18}FN_3O_2$

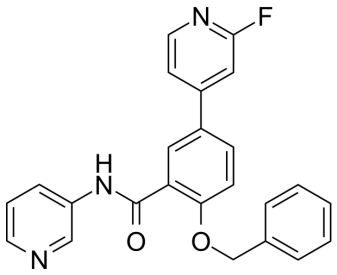
Molecular Weight: 399

Target: LRRK2; Autophagy; Mitophagy

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 : 50 mg/mL (125.31 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5063 mL	12.5313 mL	25.0627 mL
	5 mM	0.5013 mL	2.5063 mL	5.0125 mL
	10 mM	0.2506 mL	1.2531 mL	2.5063 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.27 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK2578215A is a potent and highly selective LRRK2 inhibitor, which exhibits IC_{50}s of around 10 nM against both wild-type LRRK2 and the G2019S mutant.

In Vitro

GSK2578215A (0-1 μM, 90 min) inhibits Ser910 and Ser935 phosphorylation in HEK293 cells stably transfected with wild-type LRRK2 and LRRK2[G2019S], as well as in mouse Swiss 3T3 cells[1].

GSK2578215A (1 nM, 12 h) induces autophagy (increased level of LC3 and p62 protein) in SH-SY5Y cells[2].

GSK2578215A (1 nM, 12 h) induces Drp1-mediated mitochondrial fission in SH-SY5Y cells, and induces mitophagy (12 and 24 h)[2].

GSK2578215A (1 nM, 24 h) induces oxidative stress, indicated by the accumulation of 4-HNE in SH-SY5Y cells, and induces apoptotical cell death[2].

GSK2578215A (1 μM, 24 h) inhibits homologous recombination in OVCAR8 cells[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

GSK2578215A (5 mg/kg, i.p.) with Olaparib (HY-10162) (50 mg/kg, i.p., T.I.W for 3 weeks) effectively inhibits the tumor growth in mice bearing OVCAR8 xenografts[3].

GSK2578215A (IV, 1 mg/kg, or PO, 10 mg/kg) achieves an exposure in the brain with a brain to plasma ratio of 1.4 (IV) and 2.4 (PO), and shows low oral bioavailability (IV, 12.2%), a half-life of 1.14 h (IV) and plasma exposure (PO, 635.3 h ng/mL, AUC_{last}) [1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	mice bearing OVCAR8 xenografts[3]
Dosage:	5 mg/kg, with Olaparib (50 mg/kg)
Administration:	i.p., for 3 weeks
Result:	Inhibited the tumor growth and increased DNA damage in tumors more potently than Olaparib or GSK2578215A alone.

CUSTOMER VALIDATION

- J Vis Exp. 2017 Dec 14:(130):56688.

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REFERENCES

[1]. Saez-Atienzar S, et al. The LRRK2 inhibitor GSK2578215A induces protective autophagy in SH-SY5Y cells: involvement of Drp-1-mediated mitochondrial fission and mitochondrial-derived ROS signaling. Cell Death Dis. 2014 Aug 14;5(8):e1368.

[2]. Chen L, et al. LRRK2 inhibition potentiates PARP inhibitor cytotoxicity through inhibiting homologous recombination-mediated DNA double strand break repair. Clin Transl Med. 2021 Mar;11(3):e341.

[3]. Reith AD, et al. GSK2578215A; a potent and highly selective 2-arylmethyloxy-5-substitutent-N-arylbenzamide LRRK2 kinase inhibitor. Bioorg Med Chem Lett. 2012 Sep 1;22(17):5625-9.

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