GSK3179106

Cat. No.: HY-100459

CAS No.: 1627856-64-7

Molecular Formula: $C_{22}H_{21}F_4N_3O_4$

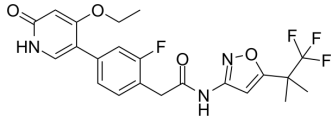
Molecular Weight: 467.41

Target: RET

Pathway: Protein Tyrosine Kinase/RTK

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 (213.94 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1394 mL	10.6972 mL	21.3945 mL
5 mM	0.4279 mL	2.1394 mL	4.2789 mL
10 mM	0.2139 mL	1.0697 mL	2.1394 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 (5.35 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.35 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.35 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK3179106 is an orally active and selective RET kinase inhibitor with IC_{50}s of 0.4 nM, 0.2 nM for human RET and rat RET, respectively. GSK3179106 has the potential for irritable bowel syndrome (IBS) through the attenuation of post-inflammatory and stress-induced visceral hypersensitivity[1].

IC_{50} & Target

IC50: 0.4 nM (human RET), 0.2 nM (rat RET)[1]

In Vitro

GSK3179106 (10 nM-100 μM; 8 days for TT cells, 3 days for SK-N-AS and A549 cells) inhibits the proliferation of the RET-dependent TT cell line with a mean IC_{50} value of 25.5 nM however has no effect on the proliferation of the RET-independent SK-NAS and A549 cell lines (mean IC_{50}>10 μM and IC_{30}>17 μM, respectively)[1].

GSK3179106 inhibits RET phosphorylation in SK-N-AS cells and TT cells with mean IC_{50}s of 4.6 nM and 11.1 nM, respectively [1].

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

Cell Viability Assay[1]

Cell Line:	TT, SK-N-AS and A549 cells
Concentration:	10 nM-100 μM
Incubation Time:	8 days for TT cells, 3 days for SK-N-AS and A549 cells
Result:	Inhibited the proliferation of TT cell line with a mean IC50 value of 25.5 nM however had no effect on the proliferation of the SK-NAS and A549 cell lines (mean IC50>10 μM and IC30>17 μM, respectively).

In Vivo

GSK3179106 (3 or 10 mg/kg; orally; for 3.5 days BID) reduces the visceromotor response (VMR) in comparison to rats given an acetic acid enema and dosed with vehicle[1].

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

Animal Model:	Seventy male Sprague Dawley rats (225-250 g, ~7-8 weeks old); Fifty male Fischer 344 rats (225-250 g, ~10-12 weeks old); Sprague Dawley female rats[1]
Dosage:	3 and 10 mg/kg
Administration:	Oral gavage ; administered BID at 8:00 and 16:00 for 3.5 days
Result:	Reduced the visceral motor response. Led to a 34-43% inhibition in VMR to colorectal distension (CRD) at 10 mg/kg.

CUSTOMER VALIDATION

- Cell Metab. 2022 Nov 11;S1550-4131(22)00490-9.
- Cell Prolif. 2020 Oct;53(10):e12889.
- Mol Cell Neurosci. 2021 Jul 14;103655.

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REFERENCES

[1]. Russell JP, et al. Exploring the Potential of RET Kinase Inhibition for Irritable Bowel Syndrome: A Preclinical Investigation in Rodent Models of Colonic Hypersensitivity. J Pharmacol Exp Ther. 2019 Feb;368(2):299-307.

[2]. Russell JP, et al. Enteric RET inhibition attenuates gastrointestinal secretion and motility via cholinergic signaling in rat colonic mucosal preparations. Neurogastroenterol Motil. 2019 Apr;31(4):e13479.

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

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