Ozanimod hydrochloride

Cat. No.: HY-12288A

CAS No.: 1618636-37-5

Molecular Formula: $C_{23}H_{25}ClN_4O_3$

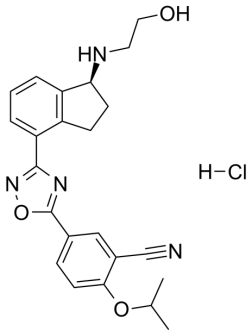
Molecular Weight: 440.92

Target: LPL Receptor

Pathway: GPCR/G Protein

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 : 200 mg/mL (453.60 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2680 mL	11.3399 mL	22.6798 mL
5 mM	0.4536 mL	2.2680 mL	4.5360 mL
10 mM	0.2268 mL	1.1340 mL	2.2680 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: ≥ 5 mg/mL (11.34 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5 mg/mL (11.34 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (11.34 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ozanimod (RPC-1063) hydrochloride, a sphingosine 1-phosphate (S1P) receptor modulator that binds with high affinity selectively to S1P receptor subtypes 1 (S1P1) and 5 (S1P5). Ozanimod hydrochloride has modulate effect for $hS1P_1$ and $hS1P_5$ receptor with EC_{50}s of 1.03 nM and 8.6 nM, respectively. Ozanimod hydrochloride can be used for the research of relapsing multiple sclerosis (MS) [1].

IC_{50} & Target

S1PR1	S1PR5
1.03 nM (EC50)	8.6 nM (EC50)

In Vitro

Ozanimod (RPC-1063) hydrochloride has potency and intrinsic activity of S1P receptor modulators for S1P5 across species

with [^{35}S]-GTPgS binding, and the EC_{50} values of 1.03 nM, 1.29 nM, 0.90 nM, 1.02 nM and 0.61 nM for Human $S1P_1$, Cynomolgus monkey $S1P_1$, Mouse $S1P_1$, Rat S1P1 and Canine $S1P_1$, respectively; and the EC_{50} values of 8.6 nM, 15.9 nM, 957.5 nM, 2032.7 nM and 1662.0 nM for Human $S1P_5$, Cynomolgus monkey $S1P_5$, Mouse $S1P_5$, Rat $S1P_5$ and Canine $S1P_5$, respectively[1].

Ozanimod hydrochloride restores the potency with EC_{50} from 958 nM for $mS1P_5$ to 6.7 nM for $mS1P_5$_A120T to closely mirror the EC_{50} for $hS1P_5$ of 8.6 nM by mutating the alanine in the mouse sequence[1].

Ozanimod hydrochloride has binding affinity with K_i values of 2.0 nM, 59.9 nM and 5.6 nM for $hS1P_5$, $mS1P_5$ and $mS1P_5$ _A120T, respectively[1].

Ozanimod hydrochloride has saturation binding of [^{3}H]-ozanimod to $hS1P_5$, and $mS1P_5$_A120T with K_D values of 6.56 nM, 7.35 nM, respectively and also has saturation binding for [^{3}H]-A971432 to $S1P_5$D value of 8.75 nM[1].

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

In Vivo

Ozanimod (RPC-1063) hydrochloride (oral gavage; 0.05, 0.2, or 1 mg/kg; once daily; for 14 consecutive days) exposures sufficient to engage $S1P_1$, but not $S1P_5$, resulted in reduced circulating lymphocytes, disease scores, and body weight loss; reduced inflammation, demyelination, and apoptotic cell counts in the spinal cord; and reduced circulating levels of the neuronal degeneration marker, neurofilament light[1].

Ozanimod hydrochloride (oral gavage; 5 mg/kg; once-daily) prevented axonal degradation and myelin loss during toxin challenge but did not facilitate enhanced remyelination after intoxication[1].

Ozanimod hydrochloride (oral, 1 or 5 mg/kg, for 7 days) has good pharmacokinetics in mice[1].

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Animal Model:	Experimental Autoimmune Encephalomyelitis Model[1]
Dosage:	0.05, 0.2, or 1 mg/kg
Administration:	oral gavage; 0.05, 0.2, or 1 mg/kg; once daily; for 14 consecutive days
Result:	Attenuated body weight loss, terminal disease scores were significantly attenuated with the 0.2 and 1 mg/kg doses and ALCs were significantly reduced in all dose groups. Reduced spinal cord inflammation and demyelination, as well as attenuated the number of spinal cord apoptotic cells, and significantly reduced the levels of circulating neurofilament light at the top dose of 1 mg/kg.

Animal Model:	Cuprizone/Rapamycin Demyelination Model[1]
Dosage:	5 mg/kg
Administration:	oral gavage; 5 mg/kg; once-daily
Result:	Protected neuronal axons, preventing breakage and ovoid formation in the corpus callosum of CPZ/Rapa treated mice. Significantly attenuated the extent to which the corpus callosum demonstrated reduced myelin content as visualized by MRI. Did not result in enhanced myelin content.

Animal Model:	Animal ModelC57BL/6J mice[1]
Dosage:	1 or 5 mg/kg
Administration:	oral, 1 or 5 mg/kg, for 7 days

Result:

Dose	Terminal body weight % versus day 1	Spinal cord inflammation Foci per 20 cells	Spinal cord demyelination Score 0–5	Spinal cord apoptotic cells Count per section	Plasma NfL pg/ml
Vehicle (5% DMSO, 5%Tween 20, 90% water)	86.4 ± 3.2	8.50 ± 1.21	2.00 ± 0.15	2.25 ± 0.53	4.37 ± 0.89
Ozanimod (0.05 mg/kg)	85.8 ± 2.7	5.00 ± 1.03*	0.91 ± 0.21***	1.08 ± 0.23*	3.53 ± 0.46
Ozanimod (0.2 mg/kg)	95.7 ± 3.1*	3.54 ± 0.49***	0.73 ± 0.14 ***	0.91 ± 0.28*	2.62 ± 0.46
Ozanimod (1 mg/kg)	102.8 ± 1.8*	2.67 ± 0.56***	0.33 ± 0.14 ***	0.60 ± 0.19**	1.91 ± 0.34**

CUSTOMER VALIDATION

- Mol Neurobiol. 2022 Nov 22.
- Research Square Preprint. 2021 Aug.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Julie V Selkirk, et al. Deconstructing the Pharmacological Contribution of Sphingosine-1 Phosphate Receptors to Mouse Models of Multiple Sclerosis Using the Species Selectivity of Ozanimod, a Dual Modulator of Human Sphingosine 1-Phosphate Receptor Subtyp

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