

Product Data Sheet

Product Name: PIPE-791

Cat. No.: GC79293

Chemical Properties

Cas. No. 2901868-37-7

Formula $C_{24}H_{29}F_2N_3O_5$

M.Wt 477.5

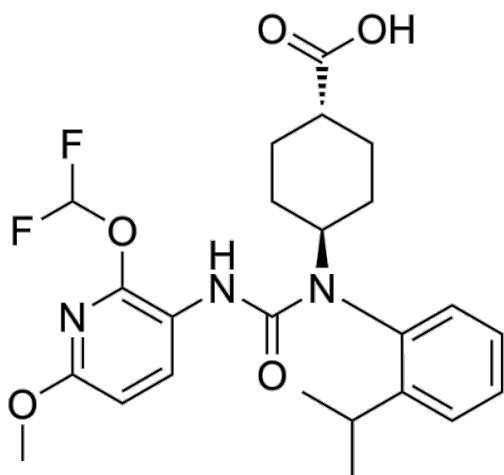
Solubility

Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Background

PIPE-791 is an orally active, blood-brain barrier-permeable selective antagonist of LPAR1. PIPE-791 inhibits LPA-induced calcium mobilization, collagen expression, histamine release, and the activation of fibroblasts, microglia and macrophages. PIPE-791 induces oligodendrocyte precursor cell differentiation, myelination and remyelination, and increases the number of microglia in the retina of normotensive rats. PIPE-791 protects mature oligodendrocytes from cytokine-induced death, reduces the levels of pulmonary fibrosis markers and alleviates neuroinflammation in preclinical models. PIPE-791 can be used in the research of glaucoma, neuroinflammatory diseases, chronic osteoarthritis pain, idiopathic pulmonary fibrosis and multiple sclerosis [1] [2] [3] [4].

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In Vivo, PIPE-791 (30-1000 mg/kg/day; oral administration; once daily; for 28 consecutive days) is well tolerated in Sprague-Dawley rats and Göttingen minipigs, with no evidence of genotoxicity, hepatobiliary toxicity or neurotoxicity^[2]. PIPE-791 (0.03-3 mg/kg; p.o.; daily administration; for 15 consecutive days) dose-dependently improves body weight, increases survival rate, and reduces the levels of multiple fibrosis markers and pulmonary collagen in a mouse model of pulmonary fibrosis induced by oropharyngeal administration of Bleomycin^[3]. PIPE-791 (3 mg/kg; p.o.; once daily; for 29 consecutive days) reduces pulmonary collagen levels to those of the control group in a mouse model of subcutaneous Bleomycin-induced chronic pulmonary fibrosis^[3]. PIPE-791 (0.003-3 mg/kg; p.o.; single administration or daily administration for 4 consecutive days) exhibits long-term LPAR1 receptor binding kinetics in healthy mice. Its receptor occupancy potency at 24 h after single administration is 20-fold higher than that at 3 h, and receptor occupancy can be maintained at steady state at low doses^[3]. PIPE-791 (3 mg/kg; p.o.; single administration) increases mature oligodendrocytes in healthy mice by 163%^[4]. PIPE-791 (0.03-3 mg/kg; p.o.; single dose/once daily; up to 4 days) achieves dose-dependent, long-lasting LPA1 receptor occupancy in mouse brains, with an ED50 of 0.17-0.19 mg/kg for a single dose and an ED50 of 0.03 mg/kg at steady state. Moreover, receptor occupancy persists for up to 7 days after a single 3 mg/kg dose^[4]. PIPE-791 (3 mg/kg; p.o.; once daily; for 11 consecutive days) reduces Bleomycin-induced macrophage activation and IL-1 β secretion in a mouse model of pulmonary fibrosis established by intratracheal injection of Bleomycin^[3]. PIPE-791 (0.3-3 mg/kg; p.o.; single administration or daily administration for 4 days) dose-dependently inhibits LPA-induced mast cell histamine release in healthy mice, with the pharmacodynamic effect lasting for 24 hours after administration and enhanced under steady-state conditions^[3]. PIPE-791 (0.3-3 mg/kg; p.o.; once daily; for 25 consecutive days) significantly reduces disease severity, improves myelination, restores visual evoked potential latency, and decreases microglial activation in MOG-EAE mouse models of multiple sclerosis^[4].

In Vitro, PIPE-791 can bind strongly to the cell membrane of human LPAR1 overexpressing cells, with a K_i value of 0.752 nM and a K_d value of 0.341 nM; it can also inhibit LPA-induced calcium mobilization in human LPAR1 overexpressing cells, and its efficacy increases with pre-incubation time, with IC_{50} decreasing from 91.8 nM to 9.9 nM^[2]. PIPE-791 (100 pM-10 μ M; 3 h) acts as a selective LPAR1 antagonist in transiently transfected HEK293T cells, with an LPAR1 IC_{50} value of

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8.0 nM^[2]. PIPE-791 exhibits inhibitory activity against PDE3A with an IC₅₀ of 9.0 μM; it also acts as a partial agonist for CNR1 with an EC₅₀ of 15.1 μM, and shows no significant activity against most other screened targets^[2]. PIPE-791 induces CYP3A4 in cryopreserved human hepatocytes with an EC₅₀ of 25.6 μM; it directly and time-dependently inhibits CYP2C8, with IC₅₀ values of 17.4 μM and 7.73 μM^[2]. PIPE-791 inhibits OATP1B1 (IC₅₀ = 3.5 μM), OAT3 (IC₅₀ = 23.0 μM), OATP1B3 (IC₅₀ = 20.7 μM) and BSEP (IC₅₀ = 24.4 μM), and shows no obvious inhibitory activity against most other tested human transporters. Its IC₅₀ value against LPAR1 reaches 8 nM in HEK293T cells. It potently suppresses LPA-triggered chemotaxis (IC₅₀ = 1.5 nM) and COL1A1 expression (IC₅₀ = 1.1 nM) in primary adult pulmonary fibroblasts. Besides, it blocks myofibroblast transformation induced by TGFβ1 or LPA^[2]. PIPE-791 (0.03-3 μM; 48 h-6 days) reduces the expression of key fibrotic genes (COL1A1, COL3A1, SERPINE1, TIMP1) in 6-day cultures of precision-cut lung slices (PCLS) derived from pulmonary fibrosis donors, and decreases the levels of secreted C3M and Pro-C6 biomarkers in 48-hour cultures of fresh PCLS derived from pulmonary fibrosis donors^[3]. PIPE-791 potently binds to human LPA1 receptors in recombinant membranes, with a K_i value of 0.752 nM and an IC₅₀ value of 2.63 nM. It binds to LPA1 receptors in native human brain homogenate with a K_d value of 0.68 nM, and binds to LPA1 receptors in native mouse brain homogenate with a K_d value of 1.7 nM^[4]. PIPE-791 induces the differentiation of primary rat O4+ oligodendrocyte precursor cells (OPCs) into mature oligodendrocytes in a dose-dependent manner, with an EC₅₀ of 108 nM; it promotes functional myelination of axons by oligodendrocytes in primary rat cortical culture systems, with an EC₅₀ of 2.6 nM^[4]. PIPE-791 (300 nM; 48 h) reverses the inhibitory effect of macrophages on the differentiation of primary rat oligodendrocyte precursor cells (OPC)^[4]. PIPE-791 (3 μM; 2 h pre-incubation, 3 h with LPA) inhibits lysophosphatidic acid (LPA)-induced activation of microglia and maintains their branched morphology in hippocampal slices from postnatal day 20 mice^[4]. PIPE-791 (0.001 μM-3 μM; 72 h) dose-dependently protects mature rat oligodendrocytes against TNFα/IFNγ-induced cell death, with an EC₅₀ of 125 nM^[4]. PIPE-791 (0.001 nM-1 μM; 72 h, 5 days) promotes remyelination in postnatal day 17 mouse cortical slices demyelinated by lysophosphatidylcholine, with an EC₅₀ value of 12.1 nM for Mbp transcript induction, 74 nM for the increase in MBP-positive areas, and 17.9 nM for the increase in Caspr punctate structure count^[4]. PIPE-791 (0.3 nM-300 nM; 9 days) dose-dependently induces oligodendrocyte differentiation in adult cortical slices, with an EC₅₀ of 4.2 nM for inducing Mbp transcripts, and the number of CC1+ oligodendrocytes increases significantly at 300

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nM^[4]. PIPE-791 (0.001 nM-1 μ M; 15 h+5 h for rat cells, 6 h+4 h for human cells) inhibits lysophosphatidic acid (LPA)-induced activation of rat and human meningeal fibroblasts, with IC₅₀ values of 31.8 nM and 4.5 nM, respectively^[4]. PIPE-791 inhibits LPS-induced IL-1 β secretion in primary human alveolar macrophages in vitro^[3].

References:

- [1]. Kocherlakota S, et al. Pharmacological Blockade of LPAR1 Does Not Provide Neuroprotection in a Rat Model of Ocular Hypertensive Glaucoma. Translational vision science & technology. 2026 Jan 05;15(1):11.
- [2]. Chen A, et al. Discovery of, A Potent and Brain-Penetrant Lysophosphatidic Acid Receptor 1 Antagonist with Slow Tight Binding Characteristics for the Treatment of Neuroinflammatory Disorders. Journal of medicinal chemistry. 2026 Jul 09;69(13):15888-15927.
- [3]. Poon M, et al. The LPAR1 antagonist, PIPE-791 produces antifibrotic effects in models of lung fibrosis. Respiratory research. 2025 Aug 31;26(1):265.
- [4]. Poon MM, et al. Discovery of a brain penetrant small molecule antagonist targeting LPA1 receptors to reduce neuroinflammation and promote remyelination in multiple sclerosis. Scientific reports. 2024 May 08;14(1):10573.

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