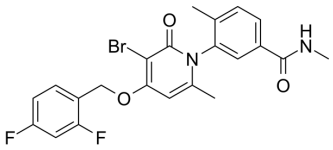
PH-797804

Cat. No.:	HY-10403
CAS No.:	586379-66-0
Molecular Formula:	$C_{22}H_{19}BrF_2N_2O_3$
Molecular Weight:	477
Target:	p38 MAPK; Autophagy
Pathway:	MAPK/ERK 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 (104.82 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0964 mL	10.4822 mL	20.9644 mL
5 mM	0.4193 mL	2.0964 mL	4.1929 mL
10 mM	0.2096 mL	1.0482 mL	2.0964 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: ≥ 3 mg/mL (6.29 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.24 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PH-797804 is a ATP-competitive, selective p38α/p38β inhibitor (IC_{50}=26 nM and K_i=5.8 nM for p38α; K_i=40 nM for p38β) and does not inhibit JNK2.

IC_{50} & Target

IC50: 26 nM (p38α)[1]
Ki: 5.8 nM (p38α), 40 nM (p38β)[2]

In Vitro

PH-797804 blocks LPS-induced TNF-α production and p38 kinase activity in the human monocytic U937 cell line, with comparable IC_{50} of 5.9 nM and 1.1 nM. PH-797804 has no inhibitory effect on either the JNK pathway (c-Jun phosphorylation) or ERK pathway (ERK phosphorylation) in U937 cells at concentrations up to 1 μM. PH-797804 inhibits RANKL- and M-CSF-induced osteoclast formation in a concentration-dependent manner, with IC50 of 3 nM in primary rat

	bone marrow cells[1]. IC_{50} values for PH-797804 against the following targets have been determined to be greater than 200 μM (unless specified): CDK2, ERK2, IKK1, IKK2, IKKi, MAPKAP2, MAPKAP3, MKK7 (>100 μM), MNK, MSK (>164 μM), PRAK, RSK2, and TBK1, which means the activity of PH-797804 is specific[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Orally dosing of PH-797804 effectively inhibits acute inflammatory responses induced by systemically administered endotoxin in both rat and cynomolgus monkeys. PH-797804 treatment for 10 days demonstrates robust anti-inflammatory activity in chronic disease models, significantly reducing both joint inflammation and associated bone loss in streptococcal cell wall-induced arthritis in rats and mouse collagen-induced arthritis. Dose-response analysis resulted in ED50 values of 0.07 mg/kg and 0.095 mg/kg in rat and cynomolgus monkeys, respectively. PH-797804 inhibits LPS-induced TNF-α, IL-6, and MK-2 activity in a dose- and concentration-dependent manner in a human endotoxin challenge model[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cell Death Dis. 2021 Oct 23;12(11):994.
- Cell Death Dis. 2018 Apr 27;9(5):500.
- Osteoarthritis Cartilage. 2022 May 2;S1063-4584(22)00718-X.
- bioRxiv. 2023 Feb 8.

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REFERENCES

[1]. Hope HR, et al. Anti-inflammatory properties of a novel N-phenyl pyridinone inhibitor of p38 mitogen-activated protein kinase: preclinical-to-clinical translation. J Pharmacol Exp Ther, 2009, 331(3), 882-895.

[2]. Xing L, et al. Structural bioinformatics-based prediction of exceptional selectivity of p38 MAP kinase inhibitor PH-797804. Biochemistry, 2009, 48(27), 6402-6411.

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