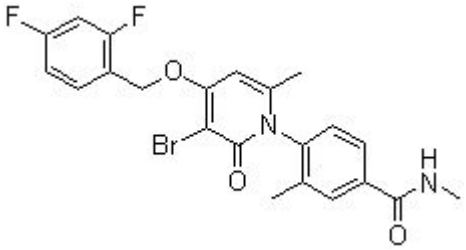
Product Introduction

PH-797804

PH-797804 is a novel pyridinone inhibitor of **p38α** with **IC50** of 26 nM; 4-fold more selective versus p38β and does not inhibit JNK2. Phase 2.

Technical Data:

Molecular Weight (MW):	477.3	
Formula:	C22H19BrF2N2O3	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 96 mg/mL	
	Water <1 mg/mL	
	Ethanol 7 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	586379-66-0	

Biological Activity

PH-797804 blocks LPS-induced TNF-α production and p38 kinase activity in the human monocytic U937 cell line, with comparable IC50 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] IC50 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]

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]

References

[1] Hope HR, et al, J Pharmacol Exp Ther, 2009, 331(3), 882-895.
[2] Xing L, et al. Biochemistry, 2009, 48(27), 6402-6411.

Note： Products protected by valid patents are not offered for sale in countries where the sale of such products constitutes a patent infringement and its liability is at buyer’s risk. This item is only for R&D purpose not for commercial business in kilos. Buyers should overview the patent issue in their countries.