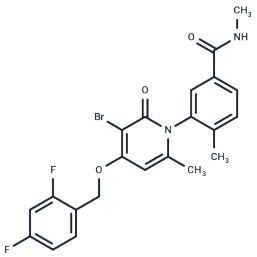
Data Sheet (Cat.No.T1974)

TargetMol

PH-797804

Chemical Properties



CAS No. : 586379-66-0

Formula: C22H19BrF2N2O3

Molecular Weight: 477.3

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	PH-797804 is a pyridinone inhibitor of p38α (IC50: 26 nM, in a cell-free assay); 4-fold more selective versus p38β and does not inhibit JNK2.
Targets(IC50)	Autophagy,p38 MAPK
In vitro	PH-797804 exhibits strong anti-inflammatory activity and is effective in treating arthritis induced by streptococcal cell walls and collagen in both mice and rats. A 10-day treatment regimen significantly reduces joint inflammation and associated bone loss. In human endotoxin challenge models, PH-797804 dose- and concentration-dependently inhibits the induction of IL-6, TNF-α, and MK-2 activities by lipopolysaccharides. Oral administration of PH-797804 effectively suppresses acute inflammatory responses induced by systemic administration of endotoxin in rats and crab-eating macaques, with an ED50 of 0.07 and 0.095 mg/kg, respectively.
In vivo	PH-797804 exhibits an IC50 value higher than 200 μM against several targets, including CDK2, ERK2, IKK1/2, IKKi, MAPKAP2/3, MKK7 (>100 μM), MNK, MSK (>164 μM), PRAK, RSK2, and TBK1. In the human monocytic U937 cell line, PH-797804 blocks the production of TNF-α and the activity of p38 kinase induced by lipopolysaccharide (LPS) with IC50 values of 5.9 and 1.1 nM, respectively. At a concentration of 1 μM, PH-797804 does not inhibit the JNK pathway (c-Jun phosphorylation) or the ERK pathway (ERK phosphorylation) in U937 cells. Additionally, in primary rat osteoclasts, PH-797804 displays a concentration-dependent inhibition of osteoclast formation induced by RANKL and M-CSF, achieving an IC50 of 3 nM.
Kinase Assay	P38 kinase assay: A resin capture assay method is used to determine the phosphorylation of epidermal growth factor receptor peptide (EGFRP) or GST-c-Jun by p38 kinases. Reactions mixtures contain 25 mM HEPES, pH 7.5, 10 mM magnesium acetate, ATP (at the indicated concentration), 0.05 to 0.3 μCi of [γ-33P]ATP, 0.8 mM dithiothreitol, and either 200 μM EGFRP or 10 μM GST-c-Jun for p38α kinase reactions. The reaction is initiated by the addition of 25 nM p38α kinase to give a final volume of 50 μl. The p38αkinase reactions are incubated at 25 °C for 30 minutes. Under these conditions, the formation of product for both p38αkinase is linear with time. The reaction is stopped, and the unreacted [γ-33P]ATP is removed by the addition of 150 μl of AG 1 × 8 ion exchange resin in 900 mM sodium formate, pH 3.0. Once thoroughly mixed, solutions are allowed to stand for 5 minutes. A 50-μl aliquot of head volume containing the phosphorylated substrate is removed from the mixture and transferred to

Kinase Assay	a 96-well plate. MicroScint-40 scintillation cocktail (150 μL) is added to each well and the radioactivity quantities using a TopCount NXT microplate scintillation and luminescence counter.

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 89.3 mg/mL (187.09 mM),Sonication is recommended. Ethanol: 7 mg/mL (14.67 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 8.93 mg/mL (18.71 mM),Solution. 10% DMSO+90% Saline: < 8.93 mg/mL (18.71 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0951 mL	10.4756 mL	20.9512 mL
5 mM	0.419 mL	2.0951 mL	4.1902 mL
10 mM	0.2095 mL	1.0476 mL	2.0951 mL
50 mM	0.0419 mL	0.2095 mL	0.419 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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