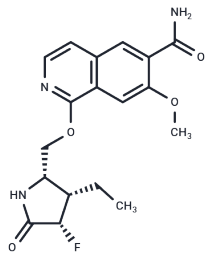
Data Sheet (Cat.No.TQ0167)

TargetMol

Zimlovisertib

Chemical Properties



CAS No. : 1817626-54-2

Formula: C18H20FN3O4

Molecular Weight: 361.37

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	Zimlovisertib (PF-06650833) is an effective, selective and orally active inhibitor of interleukin-1 receptor-associated kinase 4 (IRAK4) (IC50s: 0.2 and 2.4 nM in the cell and PBMC assay).
Targets(IC50)	IRAK
In vitro	The kinome selectivity profile of PF06650833 (Compound 40) is assessed in a panel of 278 kinases at 200 nM inhibitor concentration using the ATP Km for each kinase. Approximately 100% inhibition is observed for IRAK4. Lactam PF06650833 is assessed in a whole-cell functional VEGF2R assay (PAE-KDR cell line). No activity is observed at concentrations up to and including 30 μM. In a voltage clamp assay, PF06650833 inhibits hERG current by 25% at 100 μM.
In vivo	PF06650833 (0.3-30 mg/kg; p.o; for 2.5 hours; male SD rats) treatment significantly inhibits LPS-induced TNF-α in a dose dependent manner. Mean exposures of PF06650833 in plasma are 2.1 nM, 7.7 nM, 19 nM and 150 nM free, respectively, at 2.5 hours after oral administration of PF06650833 at 0.3, 1, 3, and 30 mg/kg. The fraction unbound in rat plasma of PF06650833 is 0.3.
Animal Research	Animal Model: Male Sprague-Dawley rats. Dosage: 0.1 mg/kg, 1 mg/kg, 3 mg/kg, 30 mg/kg. Administration: Oral administration; for 2.5 hours

Solubility Information

Solubility	DMSO: 150 mg/mL (415.09 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: 10 mg/mL (27.67 mM),Solution. 10% DMSO+90% Saline: < 10 mg/mL (27.67 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	2.7672 mL	13.8362 mL	27.6725 mL
5 mM	0.5534 mL	2.7672 mL	5.5345 mL
10 mM	0.2767 mL	1.3836 mL	2.7672 mL
50 mM	0.0553 mL	0.2767 mL	0.5534 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

Lee KL, et al. Discovery of Clinical Candidate 1-{[(2S,3S,4S)-3-Ethyl-4-fluoro-5-oxopyrrolidin-2-yl]methoxy}-7-methoxyisoquinoline-6-carboxamide (PF-06650833), a Potent, Selective Inhibitor of Interleukin-1 Receptor Associated Kinase 4 (IRAK4), by Fragment-Based Drug Design. J Med Chem. 2017 Jul 13;60(13):5521-5542.