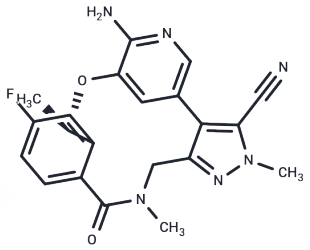
Data Sheet (Cat.No.T3061)

TargetMol

Lorlatinib

Chemical Properties



CAS No. : 1454846-35-5

Formula: C21H19FN6O2

Molecular Weight: 406.41

Storage: Keep away from moisture,Store under nitrogen,Store at low temperature
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	Lorlatinib (PF-6463922) is an orally available, ATP-competitive inhibitor of the receptor tyrosine kinases, anaplastic lymphoma kinase (ALK) and C-ros oncogene 1 (Ros1), with potential antineoplastic activity.
Targets(IC50)	Apoptosis,ALK,ROS,ROS Kinase,Tyrosine Kinases
In vitro	PF-06463922 effectively inhibits cell proliferation and induces apoptosis in HCC78 human NSCLC cells containing SLC34A2-ROS1 fusions and in BaF3-CD74-ROS1 cells expressing human CD74-ROS1. It also demonstrates this inhibitory action on cell proliferation and induces apoptosis in NSCLC cells with either non-mutated or mutated ALK fusions. PF-06463922 exhibits significant cellular activity against ALK and a wide range of ALK clinical mutations (IC50=0.2-77 nM).
In vivo	In NIH3T3 xenograft models expressing human CD74-ROS1 and Fig-ROS1, PF-06463922 inhibits cell proliferation by repressing ROS1 phosphorylation and downstream signaling molecules, including Cyclin D1. Furthermore, PF-06463922 demonstrates significant antitumor activity in mice bearing tumor grafts that overexpress EML4-ALK, EML4-ALK-L1196M, EML4-ALK-G1269A, EML4-ALK-G1202R, or NPM-ALK.
Kinase Assay	Recombinant human wild-type and mutant ALK kinase domain proteins (amino acids 1093–1411) are produced in-house using baculoviral expression, preactivated via autophosphorylation with MgATP, and assayed for kinase activity using a microfluidic mobility shift assay. The reactions contained 1.3 nM wild-type ALK or 0.5 nM mutant ALK (appropriate to produce 15-20% phosphorylation of peptide substrate after 1 h of reaction), 3 μM 5-FAM-KKSRGDYMTMQIG-CONH2), 5 mM MgCl2, and the Km level of ATP in 25 mM Hepes, pH 7.1. The inhibitors are shown to be ATP-competitive from kinetic and crystallographic studies. The Ki values are calculated by fitting the conversion (%) to a competitive inhibition equation. ROS1 enzyme is assayed as described above for ALK, except using 0.25 nM recombinant human ROS1 catalytic domain (amino acids 1883-2347). Kinase inhibitor selectivity is evaluated using a 206-kinase panel.
Cell Research	Cells are seeded in 96-well plates in growth medium containing 10% FBS and are cultured overnight at 37°C. The following day, serial dilutions of PF-06463922 or appropriate controls are added to the designated wells, and cells are incubated at 37°C for 72 h. A CellTiter-Glo assay is performed to determine the relative cell numbers. IC50 values are calculated by concentration-response curve fitting using a four-parameter

Cell Research	analytical method.

Solubility Information

Solubility	Ethanol: 40.6 mg/mL (99.9 mM),Sonication is recommended. DMSO: 13 mg/mL (31.99 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: 2 mg/mL (4.92 mM),Sonication is recommended. *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	2.4606 mL	12.3028 mL	24.6057 mL
5 mM	0.4921 mL	2.4606 mL	4.9211 mL
10 mM	0.2461 mL	1.2303 mL	2.4606 mL
50 mM	0.0492 mL	0.2461 mL	0.4921 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

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