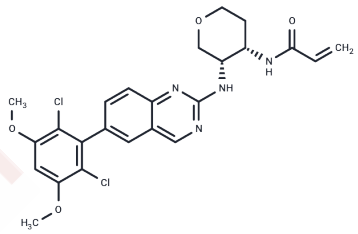
Data Sheet (Cat.No.T3456)

TargetMol

Fisogatinib

Chemical Properties



CAS No. : 1707289-21-1

Formula: C24H24Cl2N4O4

Molecular Weight: 503.38

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	Fisogatinib (BLU-554) is a highly potent, selective and orally active FGFR4 inhibitor with an IC50 value of 5 nM and significant anti-tumor activity in hepatocellular carcinoma models dependent on FGFR4 signaling.
Targets(IC50)	FGFR
In vitro	**METHODS**: Transepithelial drug transport was assessed using polarized monolayers of MDCK-II parental cells and their subclones overexpressing hABCB1, hABCG2, or mAbcg2 treated with Fisogatinib (BLU-554) (5 μM). **RESULTS** Fisogatinib (BLU-554) was moderately transported by hABCB1 and slightly transported by mAbcg2. [4]
In vivo	**METHODS**: A preliminary experiment was conducted in which male wild-type and Oatp1a/1b−/− mice were given Fisogatinib (BLU-554) (10 mg/kg, oral) and the plasma concentration before 4 hours and the liver-to-plasma ratio at 4 hours were analyzed. **RESULTS** Oatp1a/1b protein had little effect on the oral efficacy or liver distribution of Fisogatinib (BLU-554) in mice. [4]
Kinase Assay	The Ki value and mode of inhibition of LY2801653 for the MET kinase activity are determined using a radiometric filter-binding assay. Reactions are carried out in 96-well plates in Enzyme dilution buffer (EDB) compose of 50 mM Tris HCl pH 7.5, 2 mM DTT, 0.005% Triton X-100, 10 mM MgCl2, and 250 ?M EDTA. Serially diluted LY2801653 (final concentration 250 to 0 nM) are followed by the addition of a series of 8 concentrations of 33P-γ-ATP (final concentration 400 to 10 μM ATP), and 5 nM enzyme (final concentration). After a 2-hour incubation, PolyGluTyr synthetic protein substrate (final 150 μg/mL) is added to initiate the 30-minute kinase reaction. Reactions are quenched with 10% H3PO4, transfer to a pre-wetted Multiscreen anionic phosphocellulose 96-well filter plate, and washed; radioactivity is measured with a scintillation counter. The experimental data are fit to a global mix model inhibition equation using GraphPad Prism softwar to generate an alpha value to determine the modality of inhibition and to calculate the Ki value for LY2801653[1].

Solubility Information

Solubility	Ethanol: 2 mg/mL (3.97 mM),Sonication is recommended. DMSO: 250 mg/mL (496.64 mM),Sonication is recommended.

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 3.3 mg/mL (6.56 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	1.9866 mL	9.9329 mL	19.8657 mL
5 mM	0.3973 mL	1.9866 mL	3.9731 mL
10 mM	0.1987 mL	0.9933 mL	1.9866 mL
50 mM	0.0397 mL	0.1987 mL	0.3973 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

Dogan-Topal B, et al. Quantification of FGFR4 inhibitor BLU-554 in mouse plasma and tissue homogenates using liquid chromatography-tandem mass spectrometry. J Chromatogr B Analyt Technol Biomed Life Sci. 2019 Mar 15; 1110-1111:116-123.

Tao Z, Cui Y, Xu X, et al. FGFR redundancy limits the efficacy of FGFR4-selective inhibitors in hepatocellular carcinoma. Proceedings of the National Academy of Sciences. 2022, 119(40): e2208844119.

Blueprint Medicines. 50th th international liver congress. 2015.

Richard Kim, et al. First-in-human study of BLU-554, a potent, highly selective FGFR4 inhibitor designed for hepatocellular carcinoma (HCC) with FGFR4 pathway activation. EJC. December 2016, Volume 69, Supplement 1, Page S41.

Li W, et al. P-glycoprotein (ABCB1/MDR1) limits brain accumulation and Cytochrome P450-3A (CYP3A) restricts oral availability of the novel FGFR4 inhibitor fisogatinib (BLU-554). Int J Pharm. 2020 Jan 5;573:118842.