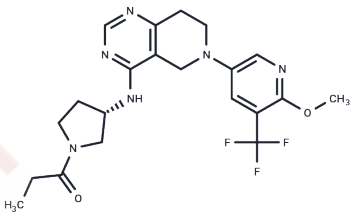
Data Sheet (Cat.No.T5166)

TargetMol

Leniolisib

Chemical Properties



CAS No. : 1354690-24-6

Formula: C21H25F3N6O2

Molecular Weight: 450.46

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	Leniolisib (CDZ173) (CDZ173) is a potent and selective PI3Kδ inhibitor (IC50: 11 nM).
Targets(IC50)	DNA-PK,PI3K
In vitro	Leniolisib (CDZ173) inhibits a large spectrum of immune cell functions, as demonstrated in B and T cells, neutrophils, monocytes, basophils, plasmocytoid dendritic cells, and mast cells [1]. Treatment with CDZ173 caused dose-dependent suppression of PI3Kδ pathway hyperactivation (measured as phosphorylation of AKT/S6) in cell lines ectopically expressing APDS-causative p110δ variants and in T-cell blasts derived from patients [2].
In vivo	In vivo, CDZ173 inhibits B cell activation in rats and monkeys in a concentration- and time-dependent manner. After prophylactic or therapeutic dosing, CDZ173 potently inhibited antigen-specific antibody production and reduced disease symptoms in a rat collagen-induced arthritis model [1]. Oral leniolisib led to a dose-dependent reduction in PI3K/AKT pathway activity assessed ex vivo and improved immune dysregulation. After 12 weeks of treatment, all patients showed amelioration of lymphoproliferation with lymph node sizes and spleen volumes reduced by 39% and 40%, respectively [2].
Cell Research	Studies in transfected Rat-1 fibroblasts and in primary immune cells isolated from patients with APDS were done to assess the in vitro potency of leniolisib on endogenously activated PI3Kδ. PIK3CD mutants encoding published forms of p110δ variants were generated by site-directed mutagenesis using human PIK3CD complementary DNA and transiently transfected in mammalian Rat-1 fibroblasts. The effects of leniolisib and mTOR inhibition on endogenous PI3K/AKT pathway activity in the transfectants were evaluated by measuring phosphorylated AKT (pAKT; S473) using homogeneous time-resolved fluorescence. T-cell blasts from healthy donors as well as APDS patients were generated from isolated T cells by stimulation with anti-CD3 and anti-CD28 antibodies for 3 days. Cells were then incubated with titrated amounts of leniolisib, stimulated with anti-CD3, and the phosphorylation of AKT(S473) and S6 (S240/244) was determined by flow cytometry [2].
Animal Research	Female wild-type Sprague Dawley rats were kept in standard cages and conditions according to Swiss Animal Welfare guidelines (12h light/dark cycles, RT at 22-24 °C, humidity at least 45 % but <70 %) with free access to Ringer solution (glucose 5%, NaCl 0.9% and KCl 0.5%) and pelleted rodent chow. 96-120 hours before administration of the

Animal Research	test substance the animals were anesthetized with isoflurane and catheters were surgically implanted under aseptic precautions (use of sterile instruments and surgical material in combination with local antibiotic prophylaxis) into the femoral artery and vein. The catheters were exteriorized in the neck region, connected to a Harvard swivel system and filled with 0.9% saline containing 100 U/mL heparin. After recovery from anesthesia, the animals were housed individually in special cages with free access to food and tap water until and throughout the experiment. Analgesic treatment with Temgesic (10 µg/kg s.c., application volume 1 mL/kg) was performed in the evening following surgery and in the next morning. Compound administration was in the morning (6-8 AM). Blood samples were collected at various time points from the femoral artery catheter into Eppendorf tubes coated with sodium EDTA. Blood samples were immediately frozen at -20 °C until final processing (maximum storage was 8 days). Intravenous and oral dosing was performed in the same animals after a 48 h wash-out interval between the single dose applications. The test substance was administered intravenously as a solution in 1-methyl-2-pyrrolidone and polyethylene glycol 200 (30: 70, v/v) at a dose of 1 mg/kg and orally as a homogenous aqueous suspension in Tween 80 and carboxymethyl cellulose sodium 0.5/0.5/99 (w/w) at a dose of 3 mg/kg [1].

Solubility Information

Solubility	Ethanol: 10 mg/mL (22.2 mM),Sonication is recommended. DMSO: 16.67 mg/mL (37.01 mM),Sonication is recommended. H2O: Insoluble, (< 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 (4.44 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	2.220 mL	11.0998 mL	22.1995 mL
5 mM	0.444 mL	2.220 mL	4.4399 mL
10 mM	0.222 mL	1.110 mL	2.220 mL
50 mM	0.0444 mL	0.222 mL	0.444 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

Hoegenauer K, et al. Discovery of CDZ173 (Leniolisib), Representing a Structurally Novel Class of PI3K Delta-Selective Inhibitors. ACS Med Chem Lett. 2017 Aug 25;8(9):975-980.
Rao V, et al. Effective 'Activated PI3Kd Syndrome' -targeted therapy with PI3Kd inhibitor leniolisib. The New England journal of medicine: NEJM. ISSN 20028-4793; 1533-4406

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