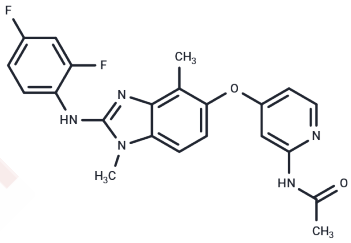
Data Sheet (Cat.No.TQ0061)

TargetMol

CHZ868

Chemical Properties



CAS No. : 1895895-38-1

Formula: C22H19F2N5O2

Molecular Weight: 423.42

Storage: 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	CHZ868 is a type II JAK inhibitor with potential antitumor activity that reverses the persistence of type I JAK inhibitors and can be used to study leukemia.
Targets(IC50)	JAK
In vitro	CHZ868 effectively inhibits constitutive phosphorylation of JAK2 and STAT5 in JAK2V617F SET2 cells. The compound demonstrates potent inhibition of SET2 cell proliferation (GI50=59nM) and exhibits 6-fold lower growth inhibitory activity against CMK cells (GI50=378nM)[1]. At a concentration of 100 nM, CHZ868 shows activity against 26 kinases, including JAK2 and TYK2. It is believed that CHZ868 interacts with the hinge region of JAK2 through two hydrogen bonds, formed between the amino-pyridine of CHZ868 and the backbone-NH/CO of L932, while the pyridine occupies the adenine pocket of the ATP binding site. CHZ868 effectively suppresses the growth of CRLF2-rearranged human B-ALL cells and disrupts JAK2 signaling[1].
In vivo	Characterized by high passive permeability, good metabolic stability, and low water solubility, CHZ868 also exhibits moderate blood clearance and good oral bioavailability, rendering it suitable for in vivo applications. In mice with human or murine B-ALL, CHZ868 enhances survival. When used in combination with dexamethasone, CHZ868 synergistically induces apoptosis in JAK2-dependent B-ALLs, leading to improved survival compared to CHZ868 alone[1].
Cell Research	CHZ868 is dissolved in DMSO to make 10 mM stock solution and diluted in culture media. Cells are treated with CHZ868 (0, 0.05, 0.1, 0.2 μM) or vehicle (DMSO). After 48 hr (Ba/F3 cells) or 72 hr (MHH-CALL4 and PDX cells), CellTiter-Glo Luminescent Cell Viability Assay is added (10 μL undiluted or 25 μL of a 1:2 dilution in each well) and plates are read [2].
Animal Research	CHZ868 is reconstituted in 0.5% methylcellulose / 0.5% Tween-80 and administered at doses of 10 or 30 mg/kg/day by oral gavage. Pharmacokinetic/pharmacodynamic and efficacy studies in the mouse model of rhEpo-induced polycythemia are carried out essentially. Detection of STAT5 phosphorylation in spleen lysates by Meso Scale Discovery is performed [2].

Solubility Information

Solubility	DMSO: 50 mg/mL (118.09 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: 2 mg/mL (4.72 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	2.3617 mL	11.8086 mL	23.6172 mL
5 mM	0.4723 mL	2.3617 mL	4.7234 mL
10 mM	0.2362 mL	1.1809 mL	2.3617 mL
50 mM	0.0472 mL	0.2362 mL	0.4723 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

Wu SC, et al. Activity of the Type II JAK2 Inhibitor CHZ868 in B Cell Acute Lymphoblastic Leukemia. Cancer Cell. 2015 Jul 13;28(1):29-41.

Meyer SC, et al. CHZ868, a Type II JAK2 Inhibitor, Reverses Type I JAK Inhibitor Persistence and Demonstrates Efficacy in Myeloproliferative Neoplasms. Cancer Cell. 2015 Jul 13;28(1):15-28.