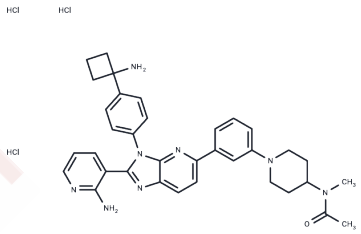
Data Sheet (Cat.No.T38846)

TargetMol

Vevorisertib trihydrochloride

Chemical Properties



CAS No. : 1416775-08-0

Formula: C35H41Cl3N8O

Molecular Weight: 696.12

Storage: Store at low temperature,Keep away from direct sunlight
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	Vevorisertib trihydrochloride (ARQ 751 trihydrochloride) is a selective and potent inhibitor of pan-AKT and AKT1-E17K mutations, inhibiting AKT1, AKT2 and AKT3. Vevorisertib trihydrochloride is used in the study of hepatocellular carcinoma and advanced solid tumours.
Targets(IC50)	Akt
In vitro	Vevorisertib trihydrochloride at concentrations ranging from 0 to 1000 nM over 2 hours inhibits the phosphorylation of AKT1-E17K. In NIH 3T3 cells transfected with pcDNAAKT-WT-GFP or pcDNA-E17K-GFP and treated with 1 μM of the compound for the same duration, it prevents the plasma membrane translocation of both AKT-WT and AKT1-E17K, regardless of growth factor presence. Additionally, a 5 μM concentration results in 57% inhibition of full-length AKT1. The compound demonstrates a dose-dependent impact on mTORC1 and AKT substrates, such as PRAS40, GSK3β, FOXO, BAD, and AS160 across various cancer cell lines with distinct concentrations (0 to 1 μM, 2 hours). It also exhibits significant anti-proliferative effects on esophageal, breast, and head and neck cancer cells, with GI 50 values below 1 μM, and showcases potent efficacy in PIK3CA mutant cell lines. Moreover, a combination of Vevorisertib trihydrochloride (MK-4440) and imatinib mesylate leads to cell cycle arrest and increased cell death in gastrointestinal stromal tumor cells. Western Blot analyses reveal the compound's effectiveness in inhibiting phosphorylation of AKT1-E17K and dose-dependent effects on mTORC1 and AKT substrates across different cell lines, including those with PIK3CA mutations and various cancer-related mutations.
In vivo	Vevorisertib trihydrochloride administered orally at doses of 25, 50, and 75 mg/kg for five consecutive days followed by a four-day break over a 20-day period demonstrated significant tumor growth inhibition rates of 68%, 78%, and 98%, respectively, in endometrial PDX mouse xenograft models featuring the AKT1-E17K mutation. When administered daily at varying doses (5, 10, 20, 40, 80, and 120 mg/kg) for ten days in AN3CA mouse xenograft models, it showed tumor growth inhibition rates ranging from 29% to 92%. The compound achieved C max plasma concentrations of ≥2 μM and was generally well-tolerated at all administered doses up to 120 mg/kg. Additionally, a combination of Vevorisertib trihydrochloride (MK-4440) and IM exhibited superior efficacy in an IM-sensitive preclinical GIST model compared to either agent alone,

In vivo	highlighting its potential as a robust therapeutic candidate in specific cancer models.

Solubility Information

Solubility	H2O: 20 mg/mL (28.73 mM),Sonication is recommended. DMSO: 100 mg/mL (143.65 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: 5 mg/mL (7.18 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	1.4365 mL	7.1827 mL	14.3653 mL
5 mM	0.2873 mL	1.4365 mL	2.8731 mL
10 mM	0.1437 mL	0.7183 mL	1.4365 mL
50 mM	0.0287 mL	0.1437 mL	0.2873 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

Kozinova M, et al. Combined Inhibition of AKT and KIT Restores Expression of Programmed Cell Death 4 (PDCD4) in Gastrointestinal Stromal Tumor. Cancers (Basel). 2021 Jul 23;13(15):3699.

Yu Y, et al. Targeting AKT1-E17K and the PI3K/AKT Pathway with an Allosteric AKT Inhibitor, ARQ 09PLoS One. 2015 Oct 15;10(10):e0140479.