Data Sheet (Cat.No.TQ0104)

TargetMol

CRT0066101 dihydrochloride

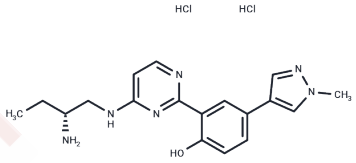
Chemical Properties

CAS No. : 1883545-60-5

Formula: C18H22N6O.2HCl

Molecular Weight: 411.33

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	CRT0066101 dihydrochloride is an effective and selective PKD inhibitor (IC50s: 1, 2.5 and 2 nM for PKD1, 2, and 3).
Targets(IC50)	Apoptosis,Pim,Serine/threonin kinase
In vitro	CRT0066101 specifically blocks PKD1/2 activity and does not suppress PKCα/PKCβ/PKCε activity in multiple cancer cell types including A549 and MiaPaCa-2. CRT0066101 significantly inhibits Panc-1 cell proliferation (IC50: 1 μM). Treatment with CRT0066101 results in a 6-10 fold induction of apoptosis in Panc-1 cells. CRT0066101 significantly reduces cell proliferation of Panc-1, Colo357, MiaPaCa-2, and AsPC-1 cells but has a modest effect in Capan-2 cells. CRT0066101 (5 μM) blocks both the basal and NT-induced pS916-PKD1/2 (activated PKD1/2) in Panc-1 and Panc-28 cells. CRT0066101 reduces PKD-dependent NF-κB activation and NF-κB-dependent gene expressions in Panc-1.
In vivo	Optimal therapeutic concentrations of CRT0066101 (8 μM) are achieved 6 h post-oral administration. A 28-day oral regimen of CRT0066101 (80 mg/kg/day) markedly reduces Panc-1 subcutaneous xenograft growth, with a significant inhibition of activated PKD1/2 expression observed. The peak tumor concentration of CRT0066101 (12 μM) is reached within 2 h, indicating rapid absorption. Additionally, administering CRT0066101 orally (80 mg/kg/day) for 21 days in a Panc-1 orthotopic model effectively inhibits tumor growth in vivo. This intervention significantly decreases the Ki-67+ proliferation index, increases TUNEL+ apoptotic cell counts, and suppresses the expression of NF-κB-dependent proteins, including cyclin D1, survivin, and cIAP-1.
Animal Research	Nineteen days after implantation of Panc-1 cells, tumor areas are, on average 0.3 cm2 and are randomized into the following groups (n=8 mice per group): (a) vehicle (control) 5% dextrose administered by oral gavage once daily and (b) 80 mg/kg CRT0066101 dissolved in 5% dextrose administered by oral gavage once daily. Tumors are measured in 2 dimensions every 2 to 3 days by calipers and area is calculated by multiplying the length by width. Therapy is given until tumors reached their designated size limits (1.44 cm2) or until day 24 in CRT0066101 treated group. Final tumor areas are compared among groups using a Student's t-test and Fisher's exact test.

Solubility Information

Solubility	DMSO: 23 mg/mL (55.92 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: 1 mg/mL (2.43 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	2.4311 mL	12.1557 mL	24.3114 mL
5 mM	0.4862 mL	2.4311 mL	4.8623 mL
10 mM	0.2431 mL	1.2156 mL	2.4311 mL
50 mM	0.0486 mL	0.2431 mL	0.4862 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

Harikumar KB, et al. A novel small-molecule inhibitor of protein kinase D blocks pancreatic cancer growth in vitro and in vivo. Mol Cancer Ther. 2010 May;9(5):1136-46.