产品名称：CRT0066101 dihydrochloride
产品别名：CRT0066101 dihydrochloride

生物活性：

Description	CRT0066101 dihydrochloride is a potent and specific PKD inhibitor with IC50 values of 1, 2.5 and 2 nM for PKD1, 2, and 3 respectively.		
IC_{50} & Target	PKD1	PKD3	PKD2
	1 nM (IC_{50})	2 nM (IC_{50})	2.5 nM (IC_{50})
In Vitro	CRT0066101 specifically blocks PKD1/2 activity and does not suppress PKCα/PKCβ/PKCε activity in multiple cancer cell types including A549 (lung) and MiaPaCa-2 (pancreas). CRT0066101 significantly inhibits Panc-1 cell proliferation with an IC50 value of 1 μM. Treatment with CRT0066101 results in a 6-10 fold induction of apoptosis in Panc-1 cells. CRT0066101 significantly reduces cell proliferation of Colo357, Panc-1, 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[1].		
In Vivo	Optimal therapeutic concentrations (8 μM) of CRT0066101 are detectable 6 h after oral administration of this drug. CRT0066101 given orally (80 mg/kg/day) for 28 days significantly abrogates PaCa growth in Panc-1 subcutaneous xenograft model. Activated PKD1/2 expression in the treated tumor-explants is significantly inhibited with peak tumor concentration (12 μM) of CRT0066101 achieved within 2 h after oral administration. Further, CRT0066101 given orally (80 mg/kg/day) for 21 days in Panc-1 orthotopic model potently blocks tumor growth *in vivo*. CRT0066101 significantly reduces Ki-67+ proliferation index, increases TUNEL+ apoptotic cells ($p<0.05$), and abrogates expression of NF-κB-dependent proteins including cyclin D1, survivin, and cIAP-1[1].		
Solvent&Solubility	***In Vitro:***		
	H_2O : 50 mg/mL (133.38 mM; Need ultrasonic)		
	DMSO : ≥ 25 mg/mL (66.69 mM)		
	* "≥" means soluble, but saturation unknown.		

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6676 mL	13.3380 mL	26.6759 mL
	5 mM	0.5335 mL	2.6676 mL	5.3352 mL
	10 mM	0.2668 mL	1.3338 mL	2.6676 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

	1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 1 mg/mL (2.67 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (2.67 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 10.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 1 mg/mL (2.67 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (2.67 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 10.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 1 mg/mL (2.67 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (2.67 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 10.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. 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.

实验参考：

Animal Administration	Mice: Nineteen days after implantation of Panc-1 cells, tumor areas are, on average 0.3 cm^2 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 length by width. Therapy is given until tumors reached their designated size limits (1.44 cm^2) 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 with $p<0.05$[1]
References	[1]. 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.