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产品名称: **CO-1686 (hydrobromide)**
产品别名: **Rociletinib hydrobromide ; AVL-301 hydrobromide; CNX-419 hydrobromide**

生物活性:					
Description	Rociletinib hydrobromide (CO-1686 hydrobromide) is an orally delivered kinase inhibitor that specifically targets the mutant forms of EGFR including T790M, and the K_i values for EGFR ^{L858R/T790M} and EGFR ^{WT} are 21.5 nM and 303.3 nM, respectively.				
IC ₅₀ & Target	EGFR ^{L858R/T790M}	EGFR ^{T790M}			
	21.5 nM (K _i)	303.3 nM (K _i)			
In Vitro	Rociletinib (0.1 μM) inhibits EGFR potently and irreversibly, and inhibits more than 50% of 23 targets. Rociletinib potently and selectively inhibits growth of NSCLC cells expressing mutant EGFR and induces apoptosis. Rociletinib resistant NSCLC cell lines are sensitive to AKT inhibition ^[1] .				
In Vivo	Rociletinib (100 mg/kg/day, p.o.) demonstrates anti-tumor activity in NSCLC EGFR mutant xenograft models. Rociletinib (50 mg/kg bid, p.o.) demonstrates anti-tumor activity in human EGFR-L858R and EGFR-L858R-T790M expressing transgenic mice ^[1] .				
Solvent&Solubility	In Vitro: DMSO : ≥ 59 mg/mL (92.70 mM) H ₂ O : < 0.1 mg/mL (insoluble) * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
		1 mM	1.5712 mL	7.8560 mL	15.7119 mL
		5 mM	0.3142 mL	1.5712 mL	3.1424 mL
		10 mM	0.1571 mL	0.7856 mL	1.5712 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: ≥ 2.5 mg/mL (3.93 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.93 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 μL 25.0 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。				



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	2. 请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (3.93 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (3.93 mM) 的均匀悬浊液, 悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例, 取 100 μL 25.0 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。
References	[1]. Walter AO, et al. Discovery of a mutant-selective covalent inhibitor of EGFR that overcomes T790M-mediated resistance in NSCLC. Cancer Discov. 2013 Sep 25.
实验参考:	
Cell Assay	Cells are seeded at 3,000 cells/well in growth media supplemented with 5% FBS, 2 mM L-glutamine, and 1 % P/S, allowed to adhere overnight, and treated with a dilution series of test compound (Rociletinib) for 72 hr. Cell viability is determined by CellTiter Glo and results are represented as background-subtracted relative light units normalized to a DMSO-treated control. Growth inhibition (GI₅₀) values are determined by GraphPad Prism 5.04. Combination index (CI) data is generated using CalcuSyn. [1]
Animal Administration	Briefly, NCr nu/nu mice are sub-cutaneously implanted with 1×10⁷ tumor cells in 50% Matrigel (injection volume of 0.2 mL/mouse). Once tumors reached 100-200 mm³, Animals are dosed with compounds (Rociletinib) as outlined (N=10 animals/gp). The LUM1686 PDX xenograft study is performed by CrownBio. Briefly, LUM1686 PDX tumor fragments, harvested from donor mice, are inoculated into BALB/c nude mice. Administration of test compounds (Rociletinib) is initiated at a mean tumor size of approximately 160 mm³. Tumor growth is monitored over time to determine tumor growth inhibition of the experimental agent vs. vehicle. The endpoint of the experiment is a mean tumor volume (MTV) in control group of 2000 mm³. Percent TGI is defined as the difference between the MTV of the designated control group and the MTV of the drug-treated group, expressed as a percentage of the MTV of the designated control group. Data is presented as mean±standard error of the mean (SEM). [1]
References	[1]. Walter AO, et al. Discovery of a mutant-selective covalent inhibitor of EGFR that overcomes T790M-mediated resistance in NSCLC. Cancer Discov. 2013 Sep 25.