

产品名称: **GDC-0994**
 产品别名: **Ravoxertinib**

生物活性:					
Description	Ravoxertinib (GDC-0994) is an orally bioavailable ERK kinase inhibitor with an IC₅₀ of 6.1 nM and 3.1 nM for ERK1 and ERK2 , respectively.				
IC ₅₀ & Target	ERK2	ERK1	p-RSK		
	3.1 nM (IC ₅₀)	6.1 nM (IC ₅₀)	12 nM (IC ₅₀)		
In Vitro	Ravoxertinib (GDC-0994) also inhibits p90RSK with an IC50 of 12 nM[1]. Ravoxertinib (GDC-0994) is highly selective for ERK1 and ERK2, with biochemical potency of 1.1 nM and 0.3 nM, respectively[2].				
In Vivo	In CD-1 mice, a 10 mg/kg oral dose of Ravoxertinib (GDC-0994) is sufficient to achieve the desired target coverage for at least 8 h[1]. Daily, oral dosing of Ravoxertinib results in significant single-agent activity in multiple in vivo cancer models, including KRAS-mutant and BRAF-mutant human xenograft tumors in mice[2].				
Solvent&Solubility	In Vitro: DMSO : ≥ 35 mg/mL (79.39 mM) * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	<div>Solvent / Mass / Concentration</div>	1 mg	5 mg	10 mg
		1 mM	2.2683 mL	11.3415 mL	22.6829 mL
		5 mM	0.4537 mL	2.2683 mL	4.5366 mL
		10 mM	0.2268 mL	1.1341 mL	2.2683 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℃, 6 months; -20℃, 1 month。 -80℃ 储存时, 请在 6 个月内使用, -20℃ 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: ≥ 1.67 mg/mL (3.79 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (3.79 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 μL 16.699999 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: ≥ 1.67 mg/mL (3.79 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (3.79 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 μL 16.699999 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水中, 混合均匀。				

	<p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil</p> <p>Solubility: ≥ 1.67 mg/mL (3.79 mM); Clear solution</p> <p>此方案可获得 ≥ 1.67 mg/mL (3.79 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。</p> <p>以 1 mL 工作液为例，取 100 μL 16.699999 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</p>
References	<p>[1]. Blake JF, et al. Discovery of (S)-1-(1-(4-Chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one (GDC-0994), an Extracellular Signal-Regulated Kinase 1/2 (ERK1/2) Inhibitor in Early Clinical Developme</p> <p>[2]. Kirk Robarge, et al. Abstract DDT02-03: Discovery of GDC-0994, a potent and selective ERK1/2 inhibitor in early clinical development. Proceedings: AACR Annual Meeting 2014; April 5-9, 2014.</p> <p>[3]. Huang X, et al. Targeting Epigenetic Crosstalk as a Therapeutic Strategy for EZH2-Aberrant Solid Tumors. Cell. 2018 Sep 20;175(1):186-199.e19.</p>
实验参考：	
Animal Administration	<p>Mice[1]</p> <p>PK/PD data for Ravoxertinib (GDC-0994) in the HCT116 mouse xenograft model. HCT116 tumors are established in nude mice to a tumor volume of 400-600 mm³. Mice are treated with a single oral dose of 22 at 15, 30, or 100 mg/kg versus vehicle control alone (40% PEG400/60% (10% HPβCD)) follow by tumor and plasma collection at 2, 8, 16, and 24 h postdose. Tumor levels of phosphorylated p90RSK (pRSK) relative total p90RSK (tRSK) are measured by quantitative Western blot and are normalized to vehicle control at 2 h postdose (set to 100%). Plasma and tumor concentrations are measured by LC-MS.</p>
References	<p>[1]. Blake JF, et al. Discovery of (S)-1-(1-(4-Chloro-3-fluorophenyl)-2-hydroxyethyl)-4-(2-((1-methyl-1H-pyrazol-5-yl)amino)pyrimidin-4-yl)pyridin-2(1H)-one (GDC-0994), an Extracellular Signal-Regulated Kinase 1/2 (ERK1/2) Inhibitor in Early Clinical Developme</p> <p>[2]. Kirk Robarge, et al. Abstract DDT02-03: Discovery of GDC-0994, a potent and selective ERK1/2 inhibitor in early clinical development. Proceedings: AACR Annual Meeting 2014; April 5-9, 2014.</p> <p>[3]. Huang X, et al. Targeting Epigenetic Crosstalk as a Therapeutic Strategy for EZH2-Aberrant Solid Tumors. Cell. 2018 Sep 20;175(1):186-199.e19.</p>