产品名称：RO4929097
产品别名：RG-4733

生物活性：

Description	RO4929097 (RG-4733) is a γ secretase inhibitor with IC_{50} of 4 nM, inhibiting cellular processing of Aβ40 and Notch with EC_{50} of 14 nM and 5 nM, respectively.
IC_{50} & Target	IC50: 4 nM (γ secretase)
In Vitro	RO4929097 inhibits the production of ICN reducing the expression of the downstream Notch target, Hes1, producing a less transformed morphology in A549 cells. RO4929097 inhibits Notch processing in human tumor-derived cells[1]. RO4929097 (1 μM) inhibits the growth of breast cancer cells, and the inhibition is 20% for SUM149 and 10% for SUM190 cells. RO4929097 does not have a marked effect in invasiveness of SUM149 cells. RO4929097 significantly reduces colony formation by both cell lines with the effect being more notable in SUM149 than by SUM190 cells[2]. RO4929097 inhibits proliferation, anchorage independent growth, and sphere formation of primary melanoma cells in vitro[3].
In Vivo	RO4929097 (3-60 mg/kg, p.o.) results in significant tumor growth inhibition in nude mice bearing A549 NSCLC xenografts, compared with vehicle-treated animals. When mice are treated with 60 mg/kg RO4929097 twice daily with the 7+/14- schedule, treatment initially causes regression of established A549 tumors[1]. RO4929097 impairs the growth of primary melanoma cells in vivo. The percentage of secondary tumors formed by RO4929097-treated cells is lower; the secondary tumors formed by RO4929097-treated cells are smaller; a significant delay in tumor formation by the RO4929097-treated cells compared to the vehicle-treated ones is observed in mice injected with 10^4 cells in vivo[3].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 49 mg/mL (104.39 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1304 mL	10.6519 mL	21.3038 mL
	5 mM	0.4261 mL	2.1304 mL	4.2608 mL
	10 mM	0.2130 mL	1.0652 mL	2.1304 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 (5.33 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.33 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。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.33 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.33 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Luistro L, et al. Preclinical profile of a potent gamma-secretase inhibitor targeting notch signaling with in vivo efficacy and pharmacodynamic properties. Cancer Res. 2009, 69(19), 7672-7680. [2]. Debeb BG, et al. Pre-clinical studies of Notch signaling inhibitor RO4929097 in inflammatory breast cancer cells. Breast Cancer Res Treat. 2012. [3]. Huynh C, et al. The novel gamma secretase inhibitor RO4929097 reduces the tumor initiating potential of melanoma. PLoS One. 2011, 6(9), e25264.

实验参考：

Cell Assay	The IBC cell lines SUM149 and SUM190 are seeded at a density of 5 × 10^4 cells. The next day, they are treated with vehicle or increasing doses of RO4929097, ranging from 0.1 nM to 10 μM. After 72 hrs, cells are trypsinized and viable cells counted with a hemocytometer. [2]
Animal Administration	Mice: RO4929097-treated mice are orally dosed with suspensions at 3 to 60 mg/kg RO4929097 according to the indicated regimens. In the Calu-6 xenograft model, RO4929097 is dosed at 60 mg/kg/d every other week for 4 weeks (7+/7- × 2 cycles). For all other xenograft models, RO4929097 is dosed once daily at 10 mg/kg for 21 days. Statistical analysis is determined by Mann-Whitney rank-sum test, one-way ANOVA, and post hoc Bonferroni t test. Differences between groups are considered significant when P ≤ 0.05. A549 tumors from vehicle-treated and selected RO4929097-treated groups are collected and fixed in 10% zinc-formalin overnight, processed, paraffin-embedded, sectioned at 5 μM, and stained with H&E for histopathology assessment. An Olympus BX51 microscope (×40 objective) mounted with a Nikon DS-Fi1 using the NIS-Elements F2.20 program collected the histology pictures. For Western blot analysis, three A549 tumors from each group, 7 (60 mg/kg) or 21 days (3 and 30 mg/kg), are flash-frozen. Collagen type V is detected using the H-200 antibody at a dilution of 1:1,000, and MFAP5 is detected using the antibody at a dilution of 1:1,000. [1]
References	[1]. Luistro L, et al. Preclinical profile of a potent gamma-secretase inhibitor targeting notch signaling with in vivo efficacy and pharmacodynamic properties. Cancer Res. 2009, 69(19), 7672-7680. [2]. Debeb BG, et al. Pre-clinical studies of Notch signaling inhibitor RO4929097 in inflammatory breast cancer cells. Breast Cancer Res Treat. 2012. [3]. Huynh C, et al. The novel gamma secretase inhibitor RO4929097 reduces the tumor initiating potential of melanoma. PLoS One. 2011, 6(9), e25264.