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Lieferung & Zahlungsart

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Zuschläge

- Mindermengenzuschlag
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SZABO-SCANDIC HandelsgmbH

Quellenstraße 110, A-1100 Wien

T. +43(0)1 489 3961-0

F. +43(0)1 489 3961-7

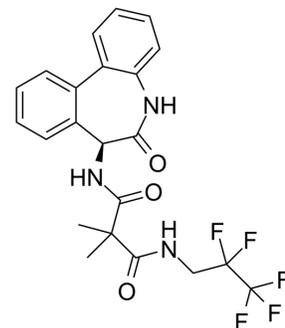
mail@szabo-scandic.com

www.szabo-scandic.com

[linkedin.com/company/szaboscandic](https://www.linkedin.com/company/szaboscandic) 

RO4929097

Cat. No.:	HY-11102
CAS No.:	847925-91-1
Molecular Formula:	C ₂₂ H ₂₀ F ₅ N ₃ O ₃
Molecular Weight:	469.4
Target:	γ-secretase; Notch
Pathway:	Neuronal Signaling; Stem Cell/Wnt
Storage:	4°C, stored under nitrogen * In solvent : -80°C, 1 year; -20°C, 6 months (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 49 mg/mL (104.39 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (5.33 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (5.33 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

RO4929097 (RG-4733) is a γ secretase inhibitor with IC₅₀ of 4 nM, inhibiting cellular processing of Aβ40 and Notch with EC₅₀ of 14 nM and 5 nM, respectively^[1].

IC₅₀ & Target

IC₅₀: 4 nM (γ secretase)^[1]

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].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[2]

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 μ M. After 72 hrs, cells are trypsinized and viable cells counted with a hemocytometer.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^[1]

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- \times 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 $P \leq 0.05$. 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 μ M, and stained with H&E for histopathology assessment. An Olympus BX51 microscope ($\times 40$ 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.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Theranostics. 2019 Oct 12;9(25):7566-7582.
- J Exp Clin Cancer Res. 2019 Dec 30;38(1):505.
- Cell Syst. 2018 Apr 25;6(4):424-443.e7.
- Cell Chem Biol. 2022 Jun 9;S2451-9456(22)00204-5.
- Cell Commun Signal. 2021 Nov 15;19(1):112.

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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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898

Fax: 609-228-5909

E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA