产品名称：CH5183284
产品别名：CH5183284

生物活性：

Description

CH5183284 is an orally available and selective **FGFR** inhibitor with **IC_{50}**s of 9.3, 7.6, and 22 nM for FGFR1, FGFR2, FGFR3, and FGFR4, respectively.

IC_{50} & Target

FGFR1	FGFR2	FGFR3	FGFR4
9.3 nM (IC_{50})	7.6 nM (IC_{50})	22 nM (IC_{50})	290 nM (IC_{50})

In Vitro

CH5183284 is well balanced in cellular antiproliferative activity against SNU-16 and stability in human liver microsome. The selectivity of 8 to inhibit FGFR over KDR is suggested to be caused by the difference in the interaction with M535 in FGFR1 and L889 in KDR[1]. The IC50 of CH5183284/Debio 1347 is 29 nM for FGF-dependent proliferation and 780 nM for VEGF-dependent proliferation[2].

In Vivo

CH5183284 treatment shows a dose-dependent tumor regression (tumor growth inhibition (TGI)=106% at 30 mg/kg and 147% at 100 mg/kg) without apparent body weight loss. CH5183284 treatment also shows significant in vivo efficacy in xenograft mice models with FGFR genetic alterations, such as KG1 (leukemia, FGFR1OP-FGFR1 fusion), MFE280 (endometrial cancer, FGFR2 S252W mutation), UM-UC-14 (bladder cancer, FGFR3 S249C mutation), and RT112/84 (bladder cancer, FGFR3-TACC3 fusion)[1].

Solvent&Solubility

In Vitro:

DMSO : 25 mg/mL (70.15 mM; ultrasonic and warming and heat to 50°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8060 mL	14.0300 mL	28.0599 mL
	5 mM	0.5612 mL	2.8060 mL	5.6120 mL
	10 mM	0.2806 mL	1.4030 mL	2.8060 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: ≥ 2.08 mg/mL (5.84 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (5.84 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (5.84 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (5.84 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (5.84 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (5.84 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Nakanishi Y, et al. The fibroblast growth factor receptor genetic status as a potential predictor of the sensitivity to CH5183284/Debio 1347, a novel selective FGFR inhibitor. Mol Cancer Ther. 2014 Nov;13(11):2547-58. [2]. Nakanishi Y, et al. Mechanism of Oncogenic Signal Activation by the Novel Fusion Kinase FGFR3-BAIAP2L1. Mol Cancer Ther. 2015 Mar;14(3):704-12. [3]. Nakanishi Y, et al. ERK Signal Suppression and Sensitivity to CH5183284/Debio 1347, a Selective FGFR Inhibitor. Mol Cancer Ther. 2015 Dec;14(12):2831-9.

实验参考：

Cell Assay	The cell lines are added to the wells of 96-well plates containing 0.076−10,000 nM tested compounds (CH5183284) and incubated at 37°C. After 4 days' incubation, Cell Counting Kit-8 solution is added, and after incubation for several more hours, absorbance at 450 nm is measured. The antiproliferative activity is calculated using the formula (1-T/C) × 100 (%), where T and C represent absorbance at 450 nm of the cells treated with drugs (T) and that of untreated control cells (C)[1].
Animal Administration	Rats: Male Wistar rats (340-390 g) implanted with a telemetry transmitter are used for the assessment of effects on blood pressure (BP). Vehicle (0.5% carmellose sodium, 0.5% polysorbate 20, and 0.9% benzyl alcohol in purified water) or CH5183284/Debio 1347 (10 and 30 mg/kg) are administered by oral gavage once a day for 4 consecutive days. Data for blood pressure are automatically analyzed and continuously recorded at 5-minute intervals[2]. Mice: The in vivo efficacy is evaluated in mice bearing an SNU-16 xenograft. CH5183284 is orally administered once daily for 11 days, and the body weight of mice and the volume of the tumors are measured twice a week[1].
References	[1]. Nakanishi Y, et al. The fibroblast growth factor receptor genetic status as a potential predictor of the sensitivity to CH5183284/Debio 1347, a novel selective FGFR inhibitor. Mol Cancer Ther. 2014 Nov;13(11):2547-58. [2]. Nakanishi Y, et al. Mechanism of Oncogenic Signal Activation by the Novel Fusion Kinase FGFR3-BAIAP2L1. Mol Cancer Ther. 2015 Mar;14(3):704-12. [3]. Nakanishi Y, et al. ERK Signal Suppression and Sensitivity to CH5183284/Debio 1347, a Selective FGFR Inhibitor. Mol Cancer Ther. 2015 Dec;14(12):2831-9.