产品名称：BAY 87-2243
产品别名：BAY 87-2243

生物活性：

Description	BAY 87-2243 is a highly potent and selective hypoxia-inducible factor-1 (HIF-1) inhibitor.
IC_{50} & Target	HIF-1α[1]
In Vitro	BAY 87-2243 inhibits luciferase activity with a calculated IC50 value of ~0.7 nM. Hypoxic induction of the HIF target gene CA9 on protein level in HCT116luc cells is inhibited by BAY 87-2243 with an IC50 value of ~2 nM. BAY 87-2243 inhibits mitochondrial oxygen consumption measured by using the oxygen sensitive fluorescence dye LUX-MitoXpress with an IC50 value of ~10 nM[1]. BAY-87-2243 inhibits nuclear HIF-1α protein expression. Administration of BAY-87-2243 for about 18 days significantly reduces HIF-1α protein expression as well as pimonidazole hypoxic fraction (pHF) (mean 2.4% (BAY-87-2243) vs. 17.6% (carrier), p<0.0001), and necrotic fraction (NF) (mean 9% vs. 35.6%, p=0.0002), whereas relative vascular area (RVA) and perfused vessels (PF) remained unchanged[2].
In Vivo	Nude mice are inoculated with H460 cells subcutaneously and after tumors have been established, animals are treated with BAY 87-2243 (0.5, 1, 2, and 4 mg/kg) for 3 weeks by daily oral gavage. BAY 87-2243 reduced tumor weight dose dependently in line with a dose-dependent reduction of the mRNA expression levels of the HIF-1 target genes CA9, ANGPTL4, and EGLN3, whereas the mRNA expression levels of hypoxia-insensitive EGLN2 gene and of HIF-1α itself are not affected by compound treatment in vivo[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 25 mg/mL (47.57 mM;** Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9028 mL	9.5142 mL	19.0284 mL
5 mM	0.3806 mL	1.9028 mL	3.8057 mL
10 mM	0.1903 mL	0.9514 mL	1.9028 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 (4.76 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.76 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 (4.76 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (4.76 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]. Ellinghaus P, et al. BAY 87-2243, a highly potent and selective inhibitor of hypoxia-induced gene activation has antitumor activities by inhibition of mitochondrial complex I. Cancer Med. 2013 Oct;2(5):611-24. [2]. Helbig L, et al. BAY 87-2243, a novel inhibitor of hypoxia-induced gene activation, improves local tumor control after fractionated irradiation in a schedule-dependent manner in head and neck human xenografts. Radiat Oncol. 2014 Sep 19;9:207.

实验参考：

Cell Assay	Luciferase activity is given in % of DMSO-treated cells. To evaluate the cytotoxicity of BAY 87-2243, 2.000 cells of the respective cell lines are seeded in 96-well plates and cultured in the appropriate growth medium containing 10% FCS. BAY 87-2243 at various concentrations is added at 24 h after seeding for additional 48 h and cell viability is determined using Cell Titer Glow Assay[1].
Animal Administration	Mice[1] Tumor xenograft experiment is carried out on female immune-deficient, athymic NMRI nude mice, aged 7-9 weeks, weighing 20-25 g. The lung carcinoma xenograft mouse model is established by subcutaneous injection into the right flank with 0.1 mL H460 tumor cells (1.5×10^6) mixed 1:1 with Matrigel. Mice are randomized into control and BAY 87-2243 (0.5, 1, 2, and 4 mg/kg) groups when tumors reach a size of more than 40 mm^2. Body weight is monitored as a measure for treatment-related, acute toxicity. Tumor area (measured by caliper) or tumor weight (measured when mice are sacrificed 21 days after cell injection) is calculated by the formula 100-100×(tumor weight/area of treatment group)/(tumor weight/area of vehicle group). Tumor Statistical analysis is performed using the one-way analysis of variance.
References	[1]. Ellinghaus P, et al. BAY 87-2243, a highly potent and selective inhibitor of hypoxia-induced gene activation has antitumor activities by inhibition of mitochondrial complex I. Cancer Med. 2013 Oct;2(5):611-24. [2]. Helbig L, et al. BAY 87-2243, a novel inhibitor of hypoxia-induced gene activation, improves local tumor control after fractionated irradiation in a schedule-dependent manner in head and neck human xenografts. Radiat Oncol. 2014 Sep 19;9:207.