产品名称：Molidustat
产品别名：BAY 85-3934

生物活性：

Description	Molidustat (BAY 85-3934) is a novel inhibitor of hypoxia-inducible factor prolyl hydroxylase (HIF-PH) with mean IC_{50}values of 480 nM for PHD1, 280 nM for PHD2, and 450 nM for PHD3.
IC_{50} & Target	IC50: 480 nM (PHD1), 280 nM (PHD2), 450 nM (PHD3)[1]
In Vitro	The mean IC50 values of BAY 85-3934 for PHD1, PHD2, and PHD3 are 480 nM, 280 nM, and 450 nM, respectively. Exposure of HeLa cells to 5 μM BAY 85-3934 for 20 min is sufficient to induce detectable concentrations of HIF-1α. In a cellular reporter assay, BAY 85-3934 induces the expression of the firefly luciferase reporter gene under the control of a hypoxia responsive element promoter at a mean (± SD) EC50 of 8.4±0.7 μM (n=4) [1].
In Vivo	HIF stabilization by oral administration of the HIF-PH inhibitor BAY 85-3934 (molidustat) results in dose-dependent production of EPO in healthy Wistar rats and cynomolgus monkeys. Molidustat therapy is aldo effective in the treatment of renal anemia in rats with impaired kidney function and, unlike treatment with rhEPO, resulted in normalization of hypertensive blood pressure in a rat model of CKD[1].

Solvent&Solubility

In Vitro:

DMSO : 5 mg/mL (**15.91 mM**; Need ultrasonic)

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	3.1817 mL	15.9084 mL	31.8167 mL
	5 mM	0.6363 mL	3.1817 mL	6.3633 mL
	10 mM	0.3182 mL	1.5908 mL	3.1817 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: ≥ 0.5 mg/mL (1.59 mM); Clear solution

此方案可获得 ≥ 0.5 mg/mL (1.59 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 5.0 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% (20% SBE-β-CD in saline)

Solubility: ≥ 0.5 mg/mL (1.59 mM); Clear solution

此方案可获得 ≥ 0.5 mg/mL (1.59 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 5.0 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: ≥ 0.5 mg/mL (1.59 mM); Clear solution 此方案可获得 ≥ 0.5 mg/mL (1.59 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 5.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Flamme I, et al. Mimicking hypoxia to treat anemia: HIF-stabilizer BAY 85-3934 (Molidustat) stimulates erythropoietin production without hypertensive effects. PLoS One. 2014 Nov 13;9(11):e111838.

实验参考：

Animal Administration	Rats: BAY 85-3934 is prepared as a solution in ethanol:Solutol HS 15:water (10:20:70). In a repeat-dose, 26-day experiment, male Wistar rats (240–340 g in body weight) are administered vehicle or BAY 85-3934 at doses of 0.5 mg/kg, 1.25 mg/kg, 2.5 mg/kg, and 5 mg/kg. The efficacy of BAY 85-3934 (2.5 mg/kg, once-daily, oral) is also compared with that of rhEPO (25 IU/kg, 50 IU/kg, and 100 IU/kg, twice-weekly, s.c. injection). The time-course of induction of EPO mRNA expression and plasma EPO is determined at baseline and 0.5 h, 1 h, 2 h, 4 h, 6 h, and 8 h after oral administration of a single dose of BAY 85-3934 (5 mg/kg)[1]. Monkey: BAY 85-3934 is prepared as a solution in 0.5% tylose. Male and female cynomolgus monkeys (2.8–5.6 kg in body weight) are administered at doses of 0.5 mg/kg and 1.5 mg/kg at 0 h, 24 h, 48 h, 72 h, and 96 h. Blood samples are taken at 7 h, 31 h, 55 h, 79 h, 103 h, and 168 h. Erythropoietic parameters are also evaluated after a 2-week treatment period with s.c. administration of rhEPO (100 IU/kg twice weekly at days 1, 4, 8, and 11) and BAY 85-3934 (1.5 mg/kg) once daily[1].
References	[1]. Flamme I, et al. Mimicking hypoxia to treat anemia: HIF-stabilizer BAY 85-3934 (Molidustat) stimulates erythropoietin production without hypertensive effects. PLoS One. 2014 Nov 13;9(11):e111838.