产品名称：CB-5083
产品别名：CB-5083

生物活性：

Description	CB-5083 is a potent, selective and orally bioavailable **p97** inhibitor with an **IC_{50}** value of 11 nM.
IC_{50} & Target	IC50: 11 nM (p97)[1]
In Vitro	Treatment of tumor cells with CB-5083 leads to significant accumulation of markers associated with inhibition of ubiquitin−proteasome system and endoplasmic reticulum-associated degradation functions, which induces irresolvable proteotoxic stress and cell death[1]
In Vivo	In tumor bearing mice, oral administration of CB-5083 causes rapid accumulation of markers of the unfolded protein response and subsequently induces apoptosis leading to sustained antitumor activity in in vivo xenograft models of both solid and hematological tumors. CB-5083 has been taken into phase 1 clinical trials in patients with multiple myeloma and solid tumors[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (241.86 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4186 mL	12.0928 mL	24.1856 mL
	5 mM	0.4837 mL	2.4186 mL	4.8371 mL
	10 mM	0.2419 mL	1.2093 mL	2.4186 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 (6.05 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.05 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% (20% SBE-β-CD in saline)

Solubility: ≥ 2.5 mg/mL (6.05 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.05 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 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: ≥ 2.5 mg/mL (6.05 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.05 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]. Zhou HJ, et al. Discovery of a First-in-Class, Potent, Selective, and Orally Bioavailable Inhibitor of the p97 AAA ATPase (CB-5083). J Med Chem. 2015 Dec 24;58(24):9480-97.

实验参考：

Cell Assay	A549 and other tumor cell lines are cultured according to ATCC guidelines. Cells are cultured in black or white, clear-bottomed, tissue culture-treated 384-well plates. Cells are treated with 10-point dose titration of the compound (CB-5083) in well duplicates. After a 72 h treatment, CellTiter-Glo is added to the white plates to measure cell viability[1]
Animal Administration	Mice: Tumor-bearing mice are used to evaluate pharmacokinetics and pharmacodynamics effect and antitumor activity. Both molecules (CB-5083 and compoud 69) are administered orally as a suspension in 0.5% methylcellulose aqueous suspensions at the fixed dose strength of 150 mg/kg; plasma and tumor samples at multiple time points (2, 6, 16, and 24 h) are harvested for pharmacokinetics and pharmacodynamics analysis[1]
Kinase Assay	The ATPase assay is performed to determine the IC_{50} value. compounds (CB-5083) are diluted in DMSO with a 3-fold 10-point serial dilution starting at 10 μM. The assay is done in a 384-well plate with each row as a single dilution[1]
References	[1]. Zhou HJ, et al. Discovery of a First-in-Class, Potent, Selective, and Orally Bioavailable Inhibitor of the p97 AAA ATPase (CB-5083). J Med Chem. 2015 Dec 24;58(24):9480-97.