产品名称：FK866 (APO866, Daporinad)
产品别名：达珀利奈 ；(E)-Daporinad

生物活性：

Description	(E)-Daporinad (FK866) is an effective inhibitor of nicotinamide phosphoribosyltransferase (NMPRTase; Nampt) with an IC_{50} of 0.09 nM.
IC_{50} & Target	IC50: 0.09 nM (NMPRTase)
In Vitro	Nampt inhibition with (E)-Daporinad (FK866) induces significant NAD^+ intracellular reduction and selectively kills MM cells. (E)-Daporinad (FK866)-induced cell death is associated with inhibition of Nampt activity, rather than protein expression, and higher NAD^+ baseline levels in MM cells than normal PBMCs confer (E)-Daporinad (FK866) sensitivity. (E)-Daporinad (FK866) abrogates the survival advantage conferred by the bone marrow microenvironment[1]. (E)-Daporinad (FK866) prevents the $[Ca^{2+}]i$ increase induced by different mitogens and reduces the Ca^{2+} content of TG-responsive Ca^{2+} stores in Jurkat and in activated PBLs. (E)-Daporinad (FK866) reduces the Ca^{2+} content of TG-responsive Ca^{2+} stores in Jurkat cells but not in Bcl2-Jurkat cells[2]. Inhibition of NAMPT by (E)-Daporinad (FK866), or inhibition of SIRT by nicotinamide decreases proliferation and triggered death of 293T cells involving the p53 acetylation pathway[3].
In Vivo	(E)-Daporinad (FK866) (30 mg/kg, i.p.) decreases the tumor burden in CB17-SCID mice, and the tumor tissue demonstrates a significant decrease in ERK phosphorylation and proteolytic cleavage of LC3[1].
Solvent&Solubility	***In Vitro:*** **DMSO： ≥ 50 mg/mL (127.71 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5542 mL	12.7711 mL	25.5421 mL
	5 mM	0.5108 mL	2.5542 mL	5.1084 mL
	10 mM	0.2554 mL	1.2771 mL	2.5542 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 (6.39 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.39 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 (6.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.39 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 (6.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.39 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]. Cea M, et al. Targeting NAD+ salvage pathway induces autophagy in multiple myeloma cells via mTORC1 and extracellular signal-regulated kinase (ERK1/2) inhibition. Blood. 2012 Oct 25;120(17):3519-29. [2]. Magnone M, et al. NAD+ levels control Ca2+ store replenishment and mitogen-induced increase of cytosolic Ca2+ by Cyclic ADP-ribose-dependent TRPM2 channel gating in human T lymphocytes. J Biol Chem. 2012 Jun 15;287(25):21067-81. [3]. Thakur BK, et al. Inhibition of NAMPT pathway by FK866 activates the function of p53 in HEK293T cells. Biochem Biophys Res Commun. 2012 Aug 3;424(3):371-7.

实验参考：

Cell Assay	MM1S cells (2×10^4 cells/well) are cultured for 72 and 96 hours in BMSC-coated 96-well plates in the presence or absence of drug. DNA synthesis is measured by (^{3}H)-thymidine uptake, with (^{3}H)-thymidine added (0.5 μCi/well) during the last 8 hours of cultures. [1]
Animal Administration	CB17-SCID mice (28-35 days old) are irradiated (200 cGy), and then inoculated subcutaneously in the right flank with 3×10^6 MM1S cells in 100 μL RPMI 1640. After detection of tumor (2 weeks after the injection), 7 mice are treated intraperitoneally with either vehicle or (E)-Daporinad (FK866) (30 mg/kg body weight) twice a day for 4 days, repeated weekly over 3 weeks. Caliper measurements of the longest perpendicular tumor diameters are performed twice a week to estimate the tumor volume using the following formula: length×width^2×0.5. Tumor growth inhibition (TGI) is calculated. Animals are killed when tumors reach 2 cm^3 or the mice appear moribund. Survival is evaluated from the first day of treatment until death. [1]
References	[1]. Cea M, et al. Targeting NAD+ salvage pathway induces autophagy in multiple myeloma cells via mTORC1 and extracellular signal-regulated kinase (ERK1/2) inhibition. Blood. 2012 Oct 25;120(17):3519-29. [2]. Magnone M, et al. NAD+ levels control Ca2+ store replenishment and mitogen-induced increase of cytosolic Ca2+ by Cyclic ADP-ribose-dependent TRPM2 channel gating in human T lymphocytes. J Biol Chem. 2012 Jun 15;287(25):21067-81. [3]. Thakur BK, et al. Inhibition of NAMPT pathway by FK866 activates the function of p53 in HEK293T cells. Biochem Biophys Res Commun. 2012 Aug 3;424(3):371-7.