产品名称：4-[4-[(4'-氯[1,1'-联苯]-2-基)甲基]-1-哌嗪基]-N-[[4-[[(1R)-3-(二甲基氨基)-1-[(苯硫基)甲基]丙基]氨基]-3-硝基苯基]磺酰基]苯甲酰胺
产品别名： ABT-737

生物活性：

Description

ABT-737 is a selective and BH3 mimetic Bcl-2, Bcl-xL and Bcl-w inhibitor with EC_{50}s of 30.3 nM, 78.7 nM, and 197.8 nM, respectively.

IC_{50} & Target [3]

Bcl-2	Bcl-xL	Bcl-W	Bcl-B	Autophagy	Mitophagy
30.3 nM (EC_{50})	78.7 nM (EC_{50})	197.8 nM (EC_{50})	1820 nM (EC_{50})		

In Vitro

ABT-737 and ATO inhibits proliferation and induces apoptosis in SGC-7901 and MGC-803 cells in concentration- and time-dependent manner, and shows a synergistic effect. ABT-737 disturbs the binding of B cell lymphoma (Bcl)-2 homologous antagonist killer and Bcl-extra large[1]. ABT-737 induces a BAX/BAK-dependent impairment of maximal O_2 consumption rate in sensitive cells. Stable BCL-2 overexpression in MCF10A cells induces an ABT-737-sensitive primed for death state. ABT-737 induces dose-dependent impairment of maximal O_2 consumption rate in B-cell lymphoma cells[2]. ABT-737 induces apoptosis and synergizes with chemotherapy,and disrups BCL-2/BAX heterodimerization and induces BAX conformational change in AML cells[3].

In Vivo

ABT-737 (50 mg/kg, i.p.) and ATO significantly suppress SGC-7901 xenograft growth, synergistically inhibit tumour growth and induce apoptosis in vivo[1]. ABT-737 suppresses the leukemia burden by 48% and 53% at the 20 and 30 mg/kg dose levels, respectively[3].

Solvent&Solubility

In Vitro:

DMSO : 50 mg/mL (61.47 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.2294 mL	6.1468 mL	12.2936 mL
	5 mM	0.2459 mL	1.2294 mL	2.4587 mL
	10 mM	0.1229 mL	0.6147 mL	1.2294 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 (3.07 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (3.07 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

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 (3.07 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (3.07 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 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 (3.07 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.07 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]. Sun XP, et al. ABT-737 Induces Apoptosis of Gastric Carcinoma Cells In Vitro and In Vivo.J Int Med Res. 2012;40(4):1251-64. [2]. Clerc P, et al. Polster BM.Rapid Detection of an ABT-737-Sensitive Primed for Death State in Cells Using Microplate-Based Respirometry.PLoS One. 2012;7(8):e42487. Epub 2012 Aug 3. [3]. Konopleva M, et al. Mechanisms of apoptosis sensitivity and resistance to the BH3 mimetic ABT-737 in acute myeloid leukemia. Cancer Cell. 2006 Nov;10(5):375-88.

实验参考：

Cell Assay	Cells are treated with ABT-737, ABT-263, or vehicle (DMSO) for 4 h in XF24 assay medium (6×10^4 MCF10A cells, see medium composition below) or RPMI 1640 medium (1×10^6 B-cell lymphoma cells) and apoptosis is analyzed by Annexin-V-binding/PI exclusion or by sub-diploid nuclei determination. FACS analysis is performed on Becton Dickinson FACScan or FACScalibur instruments. Data analysis is performed with CellQuest software.［2］
Animal Administration	For intraperitoneal (i.p.) administration, 1 g/mL stock solution of ABT-737 in DMSO is added to a mixture of 30% propylene glycol, 5% Tween 80, 65% D5W (5% dextrose in water) (pH 4−5; final concentration of DMSO ≤ 1%). Mice injected with FD/ΔRaf-1:ER cells are treated with either ABT-737 (20 and 30 mg/kg/mouse every day i.p. for 21 days starting on day 1 post-cell injection (n=9-10 mice per group) or vehicle or left untreated (control); mice injected with human KG-1 cells are treated with 30 mg/kg ABT-737 starting on day 18 post-cell injection. For noninvasive imaging of FD/ΔRaf-1:ER-luc cells, anesthetized mice are injected with 150 mg/kg of D-luciferin and placed for imaging in the In Vivo Imaging System with total imaging time of 2 min. [3]
Kinase Assay	To determine the binding affinity of GST-BCL-2 family proteins to the FITC-conjugated BH3 domain of BIM (FITC-Ahx-DMRPEIWIAQELRRIGDEFNAYYAR), FPAs are performed as follows. Briefly, 100 nM of GST-BCL-2 family fusion proteins are incubated with serial dilutions of ABT-737 in PBS for 2 min. Then, 20 nM of FITC-BIM BH3 peptide (FITC-Ahx-DMRPEIWIAQELRRIGDEFNAYYAR) is added. Fluorescence polarization is measured using an Analyst TM AD Assay Detection System after 10 min using the 96-well black plate. IC_{50}s are determined using GraphPad Prism software. [3]
References	[1]. Sun XP, et al. ABT-737 Induces Apoptosis of Gastric Carcinoma Cells In Vitro and In Vivo.J Int Med Res. 2012;40(4):1251-64. [2]. Clerc P, et al. Polster BM.Rapid Detection of an ABT-737-Sensitive Primed for Death State in Cells Using Microplate-Based Respirometry.PLoS One. 2012;7(8):e42487. Epub 2012 Aug 3.

	[3]. Konopleva M, et al. Mechanisms of apoptosis sensitivity and resistance to the BH3 mimetic ABT-737 in acute myeloid leukemia. Cancer Cell. 2006 Nov;10(5):375-88.