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产品名称：ARRY-520
产品别名：Filanesib

生物活性：

Description	Filanesib (ARRY-520) is a synthetic kinesin spindle protein (KSP) inhibitor with IC50 of 6 nM.
IC_{50} & Target	KSP
	6 nM (IC_{50})
In Vitro	Filanesib (ARRY-520) retains activity in multidrug-resistant cell lines. The EC50s of Filanesib (ARRY-520) for inhibition of proliferation of HCT-15, NCI/ADR-RES and K562/ADR cells are 3.7, 14 and 4.2 nM respectively. Filanesib (ARRY-520) (10 nM) blocks a majority of cells in mitosis with the monopolar spindle structure typical of KSP inhibition[1]. Filanesib (ARRY-520) (10 nM) induces mitotic arrest as judged by both increased phosphorylation of histone H3 (pHH3) and accumulation of cyclin B1 in four cells[2]. Filanesib (ARRY-520) and Paclitaxel exhibit the same cytotoxic effect on Type I and II cells. The GI50 at 48 h for Type II EOC cells is 0.0015 μM for ARRY-520. For Type I EOC cells, the GI50 at 48 h is > 3 μM for ARRY-520[3]. Filanesib (ARRY-520) (1 nM) induces significant G2M cell cycle block in OCI-AML3 cells at 24 hours[4].
In Vivo	Filanesib (ARRY-520) (10, 15, 20, 30 mg/kg, i.p.) is active in UISO-BCA-1 xenograft, and also superior to paclitaxel in mice bearing subcutaneous HT-29, HCT-116, MDA-MB-231 and A2780 xenografts. ARRY-520 is superior to docetaxel in the androgen receptor-negative prostate cancer xenograft model PC-3, and is also superior to docetaxel in the DU145 prostate xenograft model[1]. RPMI 8226 tumor xenografts are particularly sensitive to low doses of ARRY-520 (12.5 mg/kg, i.p.)[2]. ARRY-520 significantly inhibits tumor growth in HL60 and MV4-11 xenografts of SCID mice at concentrations of 27 mg/kg and 20 mg/kg, respectively[4].
Solvent&Solubility	***In Vitro:***
	DMSO : ≥ 100 mg/mL (237.82 mM)
	* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3782 mL	11.8912 mL	23.7823 mL
5 mM	0.4756 mL	2.3782 mL	4.7565 mL
10 mM	0.2378 mL	1.1891 mL	2.3782 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 (5.95 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.95 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 (5.95 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.95 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 (5.95 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.95 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]. Woessner R, et al. ARRY-520, a novel KSP inhibitor with potent activity in hematological and taxane-resistant tumor models. Anticancer Res. 2009 Nov;29(11):4373-80. [2]. Tunquist BJ, et al. Mcl-1 stability determines mitotic cell fate of human multiple myeloma tumor cells treated with the kinesin spindle protein inhibitor ARRY-520. Mol Cancer Ther. 2010 Jul;9(7):2046-56. [3]. Kim KH, et al. KSP inhibitor ARRY-520 as a substitute for Paclitaxel in Type I ovarian cancer cells. J Transl Med. 2009 Jul 20;7:63. [4]. Carter BZ, et al. Inhibition of KSP by ARRY-520 induces cell cycle block and cell death via the mitochondrial pathway in AML cells. Leukemia. 2009 Oct;23(10):1755-62.

实验参考：

Cell Assay	Exponentially growing cells (0.4×10^6/mL) are treated with Filanesib (ARRY-520) for up to 48 hours. For combination, HL-60 and HL-60Bcl-2 cells (0.4×10^6/mL) are incubated with Filanesib (ARRY-520), ABT-737, or both for up to 96 hours. DMSO is used as the control agent. Apoptosis is estimated by flow cytometry measurements of phosphatidyl serine with the Annexin-V-FLUOS Staining Kit. Membrane integrity is simultaneously assessed by 7-amino-actinomycin D (7-AAD). To measure changes in the mitochondrial membrane potential (MMP), cells are loaded with CMXRos (300 nM) and MitoTracker Green (500 nM) for 1 hour at 37°C. The loss of MMP is then assessed by measuring CMXRos retention while simultaneously adjusting for mitochondrial mass. [4]
Animal Administration	Subcutaneous tumor xenografts are allowed to grow to a volume of 250-350 mm^3. The mice are randomized into groups of 3-4 based on tumor size, and are given a single dose of Filanesib (ARRY-520) i.p. At various time-points after administration of the drug, the mice are euthanized by CO_2 inhalation and the tumors excised and placed in 10% neutral buffered formalin. The formalin-fixed tumors are processed and paraffin embedded by standard procedures. Spindle morphology is analyzed by staining tumor sections for α-tubulin, and apoptosis is analyzed by

	TUNEL stain. Monopolar/abnormal spindles and TUNEL positive (apoptotic) cells are counted in three ×40 fields from each sample, analyzed using algorithms developed in ImagePro software. [1]
References	[1]. Woessner R, et al. ARRY-520, a novel KSP inhibitor with potent activity in hematological and taxane-resistant tumor models. Anticancer Res. 2009 Nov;29(11):4373-80. [2]. Tunquist BJ, et al. Mcl-1 stability determines mitotic cell fate of human multiple myeloma tumor cells treated with the kinesin spindle protein inhibitor ARRY-520. Mol Cancer Ther. 2010 Jul;9(7):2046-56. [3]. Kim KH, et al. KSP inhibitor ARRY-520 as a substitute for Paclitaxel in Type I ovarian cancer cells. J Transl Med. 2009 Jul 20;7:63. [4]. Carter BZ, et al. Inhibition of KSP by ARRY-520 induces cell cycle block and cell death via the mitochondrial pathway in AML cells. Leukemia. 2009 Oct;23(10):1755-62.