

产品名称: **Verdinexor (KPT-335)**

产品别名: **Verdinexor**

**生物活性:**

**Description**

Verdinexor(KPT-335) is a novel, orally bioavailable selective inhibitor of nuclear export (SINE), inhibits nuclear export protein Exportin 1(XPO1/CRM1) against canine tumor cell lines; also reduce influenza virus replication in vitro and in vivo. IC50 value: Target: SINE; XPO1/CRM1 in vitro: potently and selectively inhibit vRNP export and effectively inhibited the replication of various influenza virus A and B strains in vitro, including pandemic H1N1 virus, highly pathogenic H5N1 avian influenza virus, and the recently emerged H7N9 strain [1]. KPT-335 inhibited proliferation, blocked colony formation, and induced apoptosis of treated cells at biologically relevant concentrations of drug. Additionally, KPT-335 downregulated XPO1 protein while inducing a concomitant increase in XPO1 messenger RNA. Lastly, KPT-335 treatment of cell lines upregulated the expression of both protein and mRNA for the tumor suppressor proteins p53 and p21, and promoted their nuclear localization [3]. in vivo: Prophylactic and therapeutic administration of verdinexor protected mice against disease pathology following a challenge with influenza virus A/California/04/09 or A/Philippines/2/82-X79, as well as reduced lung viral loads and proinflammatory cytokine expression, while having minimal toxicity [1]. A dose expansion study was performed in 6 dogs with NHL given 1.5 mg/kg KPT-335 Monday/Wednesday/Friday; CB was observed in 4/6 dogs with a median TTP for responders of 83 days (range 35-354 days). Toxicities were primarily gastrointestinal consisting of anorexia, weight loss, vomiting and diarrhea and were manageable with supportive care, dose modulation and administration of low dose prednisone; hepatotoxicity, anorexia and weight loss were the dose limiting toxicities [2]. Inhibition of XPO1 with KPT-335 attenuated cyst growth in vivo in the PKD1 mutant mouse model Pkd1v/v [4].

***In Vitro:***

**DMSO :  $\geq 100$  mg/mL (226.08 mM)**

\* " $\geq$ " means soluble, but saturation unknown.

	Solvent Mass Concentration		1 mg	5 mg	10 mg
	1 mM				
Preparing	1 mM		2.2608 mL	11.3040 mL	22.6081 mL
Stock Solutions	5 mM		0.4522 mL	2.2608 mL	4.5216 mL
	10 mM		0.2261 mL	1.1304 mL	2.2608 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℃，6 months；-20℃，1 month。 -80℃ 储存时，请在 6 个月内使用，-20℃ 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:  $\geq 2.5$  mg/mL (5.65 mM); Clear solution

此方案可获得  $\geq 2.5$  mg/mL (5.65 mM，饱和度未知) 的澄清溶液。

**Solvent&Solubility**

	<p>以 1 mL 工作液为例，取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 <math>\mu</math>L PEG300 中，混合均匀向上述体系中加入 50 <math>\mu</math>L Tween-80，混合均匀；然后继续加入 450 <math>\mu</math>L 生理盐水定容至 1 mL。</p> <p>2.请依序添加每种溶剂： 10% DMSO <math>\rightarrow</math>90% corn oil Solubility: <math>\geq</math> 2.5 mg/mL (5.65 mM); Clear solution</p> <p>此方案可获得 <math>\geq</math> 2.5 mg/mL (5.65 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。</p> <p>以 1 mL 工作液为例，取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中，混合均匀。</p>
References	<p>[1]. Munuce MJ, et al. Effects of ulipristal acetate on sperm DNA fragmentation during in vitro incubation. <u>Eur J Contracept Reprod Health Care</u>. 2013 Oct;18(5):355-63.</p> <p>[2]. Pohl O, et al. Carcinogenicity and chronic rodent toxicity of the selective progesterone receptor modulator ulipristal acetate. <u>Curr Drug Saf</u>. 2013 Apr;8(2):77-97.</p> <p>[3]. Pohl O, et al. A 39-week oral toxicity study of ulipristal acetate in cynomolgus monkeys. <u>Regul Toxicol Pharmacol</u>. 2013 Jun;66(1):6-12.</p> <p>[4]. Attardi BJ, et al. In vitro antiprogestational/antiglucocorticoid activity and progestin and glucocorticoid receptor binding of the putative metabolites and synthetic derivatives of CDB-2914, CDB-4124, and mifepristone. <u>J Steroid Biochem Mol Biol</u>. 2004 Mar;88(3):277-88.</p> <p>[5]. Ciarmela P, et al. Ulipristal acetate modulates the expression and functions of activin a in leiomyoma cells. <u>Reprod Sci</u>. 2014 Sep;21(9):1120-5.</p>

源叶生物