产品名称：**HMN-214**
产品别名：**IVX-214**

生物活性：

Description	HMN-214, an orally bioavailable prodrug of HMN-176, is an inhibitor of polo-like kinase-1 (plk1), with antitumor activity.
IC_{50} & Target	PLK1
In Vitro	HMN-214 is a prodrug of HMN-176. HMN-176 shows potent activities against 22 human tumor cell lines, with a mean IC50s of 118 nM[1]. HMN-176 (3-300 nM) inhibits luciferase expression driven by the MDR1 promoter in a dose dependent manner in HeLa cells. HMN-176 (30-3000 nM) also dose-dependently suppresses complex formation on the Y-box[3]. HMN-214 (3.3 μM) enhances luciferase expression relative to vehicle control with the 1,4C-1,4Bis polymer (11-fold) and PEI (37-fold) in PC3-PSMA cells. HMN-214 (≥ 3.3 μM) significantly reduces cell proliferation, causes considerable changes in cell morphology in MB49 cells[4].
In Vivo	HMN-214 (33 mg/kg, p.o.) converts to HMN-176 in rats. HMN-214 has no effect on the conduction velocity and the amplitude of action potentials in the aciatic and tibial nerves. HMN-214 (20 mg/kg, p.o.) exhibits antitumor activity in mice[1]. HMN-214 (10, 20 mg/kg, p.o.) decreases MDR1 mRNA expression in nude mice bearing KB- and KB-A.1.-derived tumors[3].
Solvent&Solubility	***In Vitro:*** **DMSO : 25 mg/mL (58.90 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3559 mL	11.7794 mL	23.5588 mL
	5 mM	0.4712 mL	2.3559 mL	4.7118 mL
	10 mM	0.2356 mL	1.1779 mL	2.3559 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 (5.89 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.89 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 (5.89 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.89 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 (5.89 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.89 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]. Takagi M, et al. In vivo antitumor activity of a novel sulfonamide, HMN-214, against human tumor xenografts in mice and the spectrum of cytotoxicity of its active metabolite, HMN-176. Invest New Drugs. 2003 Nov;21(4):387-99. [2]. Garland LL, et al. A phase I pharmacokinetic study of HMN-214, a novel oral stilbene derivative with polo-like kinase-1-interacting properties, in patients with advanced solid tumors. Clin Cancer Res. 2006 Sep 1;12(17):5182-9. [3]. Tanaka H, et al. HMN-176, an active metabolite of the synthetic antitumor agent HMN-214, restores chemosensitivity to multidrug-resistant cells by targeting the transcription factor NF-Y. Cancer Res. 2003 Oct 15;63(20):6942-7. [4]. Christensen MD, et al. Kinome-level screening identifies inhibition of polo-like kinase-1 (PLK1) as a target for enhancing non-viral transgene expression. J Control Release. 2015 Apr 28;204:20-9.

实验参考：

Cell Assay	Cell proliferation in case of different treatment conditions, relative to untreated control cells (treated as 100% viable, or a live control), is quantified using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), a yellow colored reagent which is converted to formazan (a purple dye) by living cells. For screening experiments, transfections are carried out in 96-well cell culture plates, that are seeded with 50,000 cells per well. Following 48 h of transfection, 10 μL of MTT reagent is added to the cells and incubated at 37°C for 2-4 h, and the cells are then lysed by adding 20 μL of MTT detergent and incubated for an additional 2 h at room temperature. Inhibitor dose-optimization transfections are carried out in 24-well plates that are seeded with 50,000 cells per well. After 48 h, 20 μL MTT reagent is added, followed by 100 μL of MTT detergent for lysis for 2 h[4].
Animal Administration	The ground HMN-214 is suspended with an agate pestle by gradually adding 0.5% methylcellulose 4000 solution to make a 3 mg/mL suspension. This is additionally diluted with methylcellulose 4000 solution to obtain suspensions of the appropriate concentration. Tumor tissue is grown in advance by s.c. transplantation into nude mice. The resulting tumors are removed, cut into cubic fragments of 8 mm^3, and transplanted s.c. into the right axillary region of nude mice with a trocar. When the theoretical volume of the tumor had reached about 145 mm^3, oral administration of HMN-214 is started (day 1)[3].
	[1]. Takagi M, et al. In vivo antitumor activity of a novel sulfonamide, HMN-214, against human tumor xenografts in mice and the spectrum of cytotoxicity of its active metabolite, HMN-176. Invest New Drugs. 2003 Nov;21(4):387-99. [2]. Garland LL, et al. A phase I pharmacokinetic study of HMN-214, a novel oral stilbene derivative with polo-like kinase-1-interacting properties, in patients with advanced solid tumors. Clin Cancer

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