产品名称：OTS514
产品别名：OTS514

生物活性：

Description	OTS514 is a highly potent **TOPK** inhibitor, which inhibits TOPK kinase activity with a median inhibitory concentration ($\mathbf{IC_{50}}$) value of 2.6 nM.
IC_{50} & Target	IC50: 2.6 nM (TOPK)[1]
In Vitro	To confirm the specificity of OTS514 against TOPK, a panel of 60 diverse human protein kinases is used. The activity of each kinase is measured after a 2 hour incubation with 0.2 μM OTS514. The highest inhibition is observed for TOPK (83.5% inhibition), whereas the mean and the SD of the inhibitory effects against other kinases are 11.5 and 18.5%, respectively, indicating the specificity of the TOPK inhibitory effect of OTS514. TOPK expression is examined in cancer cell lines derived from various cancer types, such as lung cancer (A549, LU-99), breast cancer (DU4475, MDA-MB-231, and T47D), Burkitt lymphoma (Daudi), bladder cancer (UM-UC-3), colon cancer (HCT-116 and HT29), gastric cancer (MKN1 and MKN45), liver cancer (HepG2), pancreatic cancer (MIAPaca-2), and prostate cancer (22Rv1). High expression of TOPK is observed in all of these cell lines except HT29. The growth inhibitory effects of OTS514 are examined ton each cell line and strong growth inhibitory effects are found with low IC50 values ranging from 1.5 to 14 nM for the TOPK-positive cancer cell lines. On the other hand, the IC50 value for HT29 cells, in which TOPK expression is hardly detectable, is significantly higher at 170 nM (P=5.92×10-11).[1].
In Vivo	The in vivo antitumor effect of OTS514 is first investigated t in a xenograft model of A549 cells (TOPK-positive lung cancer cells). Intravenous administration of free OTS514 at 1, 2.5, and 5 mg/kg once a day for 2 weeks results in tumor growth inhibition (TGI) of 5.7, 43.3, and 65.3% on day 15, respectively, without any body weight loss. The antitumor effect of OTS514 is further investigated in another lung cancer xenograft model of LU-99 cells. Intravenous administration of OTS514 (5 mg/kg) once a day for 2 weeks achieve good growth-suppressive effect with TGI of 104% without any body weight loss. However, although the antitumor effect against LU-99 xenograft is stronger than that against A549 xenograft, the treatment still causes a significant reduction of white blood cells (WBCs) (P<0.01)[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 100 mg/mL** (**274.38 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7438 mL	13.7189 mL	27.4379 mL
	5 mM	0.5488 mL	2.7438 mL	5.4876 mL
	10 mM	0.2744 mL	1.3719 mL	2.7438 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 (6.86 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.86 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 (6.86 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.86 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 (6.86 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.86 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]. Matsuo Y, et al. TOPK inhibitor induces complete tumor regression in xenograft models of human cancer through inhibition of cytokinesis. Sci Transl Med. 2014 Oct 22;6(259):259ra145.

实验参考：

Cell Assay	$CD34^+$ HSCs are cultured in RPMI supplemented with 20% fetal bovine serum and 1× StemSpan CC100. Cells are treated with OTS514 (20 or 40 nM) or OTS-964 (100 or 200 nM) for 48 hours. Collected cells are washed with phosphate-buffered saline (PBS) and resuspended in 100 μL of PBS followed by staining with CD41a antibody for 20 min at room temperature. Finally, the cells are washed with PBS again and then analyzed for CD41a staining by flow cytometry on the BD FACSCalibur. Expression of STAT5 is examined by Western blot with an anti-STAT5 antibody[1].
Animal Administration	Mice[1] A549 (1×10^7 cells) or LU-99 cells (5×10^6 or 1×10^7 cells) are injected subcutaneously in the left flank of female BALB/cSLC-nu/nu mice. When A549 xenografts have reached an average volume of 200 mm^3 or when LU-99 xenografts have reached an average volume of 150 or 200 mm^3, animals are randomized into groups of six mice. The in vivo antitumor effect of OTS514 is first investigated in a xenograft model of A549 cells (TOPK-positive lung cancer cells). OTS514 is administered to mice bearing A549 cells after the tumor size reaches about 200 mm^3. Mice are intravenously treated with OTS514 (1, 2.5, and 5 mg/kg) once a day for 2 weeks. The tumor size is measured as a surrogate marker of drug response, and the percentage of tumor growth inhibition (TGI) is calculated. The antitumor effect of OTS514 is further investigated tin another lung cancer xenograft model of LU-99 cells. OTS514 is administered to mice bearing LU-99 cancer cells after the tumor size reaches about 200 mm^3. Mice are intravenously treated with OTS514 (5 mg/kg) once a day for 2 weeks. Tumor volumes are determined using a caliper. The weight of the mice is determined as an indicator of tolerability on the same days [1].

References	[1]. Matsuo Y, et al. TOPK inhibitor induces complete tumor regression in xenograft models of human cancer through inhibition of cytokinesis. Sci Transl Med. 2014 Oct 22;6(259):259ra145.