产品名称：**OTS-964**
产品别名：**OTS964 hydrochloride**

生物活性：		
Description	OTS964 hydrochloride is an orally active, high affinity and selective TOPK (T-lymphokine-activated killer cell-originated protein kinase) inhibitor with an IC50 of 28 nM[1]. OTS964 hydrochloride is also a potent inhibitor of the cyclin-dependent kinase CDK11, which binds to CDK11B with a Kd of 40 nM[2].	
IC_{50} & Target	TOPK	CDK11B
	28 nM (IC_{50})	40 nM (Kd)
In Vitro	OTS964 hydrochloride (10 nM; 48 hours) suppresses cancer cell proliferation[1]. OTS964 hydrochloride (10 nM; 48 hours) increases cancer cell death[1]. OTS964 (0.1-2 μM; 24 and 48 hours) increases the expression of LC3-II and decreases the expression of P62, both in a dose-dependent manner[3].	
	Cell Proliferation Assay[1].	
	Cell Line:	LU-99 cells
	Concentration:	10 nM
	Incubation Time:	48 hours
	Result:	Suppressed cancer cell proliferation.
	Apoptosis Analysis[1].	
	Cell Line:	LU-99 cells
	Concentration:	10 nM
	Incubation Time:	48 hours
	Result:	Increased cancer cell death.
	Western Blot Analysis[3]..	
	Cell Line:	Hs683 cells, H4 cells
	Concentration:	0.1, 1, 2 μM
	Incubation Time:	24 and 48 hours
	Result:	Increased the expression of LC3-II and decreased the expression of P62, both in a dose-dependent manner.
In Vivo	OTS964 hydrochloride (intravenously; 40 mg/kg on days 1, 4, 8, 11, 15, and 18) makes tumors shrinking even after the treatment and finally revealing complete regression[1]. OTS964 hydrochloride (oral administration; 50 or 100 mg/kg/day for 2 weeks) ultimately achieves complete tumor regression[1].	
	Animal Model:	Nude mice bearing LU-99 lung cancer cells[1]
	Dosage:	40 mg/kg
	Administration:	Intravenously; on days 1, 4, 8, 11, 15, and 18
	Result:	The tumors continued shrinking even after the treatment and finally revealed complete regression.
	Animal Model:	Nude mice bearing LU-99 lung cancer cells[1]
	Dosage:	50 or 100 mg/kg
	Administration:	Oral administration; once every day for 2 weeks
	Result:	Achieved complete tumor regression.

Solvent&Solubility

In Vitro:

DMSO : ≥ 83.33 mg/mL (194.26 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3312 mL	11.6558 mL	23.3117 mL
	5 mM	0.4662 mL	2.3312 mL	4.6623 mL
	10 mM	0.2331 mL	1.1656 mL	2.3312 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 (5.83 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.83 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 (5.83 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.83 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 (5.83 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.83 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 ofcytokinesis. Sci Transl Med. 2014 Oct 22;6(259):259ra145.

[2]. Lin A, et al. Off-target toxicity is a common mechanism of action of cancer drugs undergoing clinical trials. Sci Transl Med. 2019 Sep 11;11(509).

[3]. Lu H, et al. TOPK inhibits autophagy by phosphorylating ULK1 and promotes glioma resistance to TMZ. Cell Death Dis. 2019 Aug 5;10(8):583.