产品名称：**TWS119**
产品别名：**TWS119**

生物活性：

Description	TWS119 is a specific inhibitor of GSK-3β, with an IC_{50} of 30 nM, and activates the wnt/β-catenin pathway.
IC_{50} & Target	GSK-3β
	30 nM (IC_{50})
In Vitro	TWS119 induces neuronal differentiation in P19 EC cells and primary mouse ESCs. TWS119 binds to GSK-3β with KD of 126 nM, and modulates the activity of the complex, triggering downstream transcriptional events that lead the neuronal induction[1]. TWS119 (< 4 μM) significantly enhances the proliferation and survival of γδT cells via activation of the mammalian target of rapamycin (mTOR) pathway, upregulation of the expression of anti-apoptotic protein Bcl-2 and inhibition of cleaved caspase-3. TWS119 (0-8 μM) induces the generation of $CD62L^+$γδT or $CCR5^+$γδT cell phenotypes. TWS119 (0.5, 1.0 and 2 μM) increases the expression level of granzyme B in a dose-dependent manner. TWS119 also enhances the cytolytic activity of γδT cells against tumour cells in vitro[3].
In Vivo	TWS119 (30 mg/kg, i.p.) improves the neurologic function and decreases neurologic deficit dcore in rtPA-treated MCAO rats. TWS119 effectively relieves cerebral edema, and reduces cerebral infarction in rats treated with rtPA. TWS119 also effectively decreases blood-brain barrier permeability in rtPA-Treated MCAO Rats and attenuates rtPA-induced hemorrhage in ischemic brain tissue. Futhermore, TWS119 activates the Wnt/β-Catenin signaling pathway and increases the expression of Claudin-3 and ZO-1[2].
Solvent&Solubility	***In Vitro:***
	DMSO : ≥ 50 mg/mL (157.07 mM)
	* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1414 mL	15.7070 mL	31.4139 mL
	5 mM	0.6283 mL	3.1414 mL	6.2828 mL
	10 mM	0.3141 mL	1.5707 mL	3.1414 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 (7.85 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (7.85 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 (7.85 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.85 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。
References	[1]. Ding S, et al. Synthetic small molecules that control stem cell fate. Proc Natl Acad Sci U S A. 2003 Jun 24;100(13):7632-7. Epub 2003 Jun 6. [2]. Wang W, et al. GSK-3β inhibitor TWS119 attenuates rtPA-induced hemorrhagic transformation and activates the Wnt/β-catenin signaling pathway after acute ischemic stroke in rats. Mol Neurobiol. 2016 Dec;53(10):7028-7036. Epub 2015 Dec 15. [3]. Chen YQ, et al. Wnt pathway activator TWS119 enhances the proliferation and cytolytic activity of human γδT cells against colon cancer. Exp Cell Res. 2017 Nov 16. pii: S0014-4827(17)30587-6.

实验参考：

Cell Assay	PBMCs are cultured with pamidronate disodium for 8 days and then cells are labelled with or without 1.5 μM carboxyfluorescein succinimidyl ester (CFSE) and CFSE-labelled cells are then seeded in 6-well plates (2.5 × 10^6 cells/well) followed by treatment with various concentrations of TWS119 for 72 h. The total number of cultured cells is evaluated using an automated cell counter and the γδT cell proliferation is examined by flow cytometry[3].
Animal Administration	All rats are randomly divided into four groups as follows: Sham group-rats undego the same surgical procedure, but the filament is not inserted and they receive 1 mL of dimethyl sulfoxide (1 % DMSO in saline); Vehicle group-rats undergo MCAO and receive 1 mL of DMSO; rtPA group-rats underwent MCAO and receive rtPA (10 mg/kg, Actilyse®) at 4 h after MCAO; and rtPA+TWS119 group-rats undergo MCAO and receive intraperitoneal TWS119 (30 mg/kg, dissolved in 1 mL 1 % DMSO) immediately after rtPA injection at 4 h after MCAO[2].
References	[1]. Ding S, et al. Synthetic small molecules that control stem cell fate. Proc Natl Acad Sci U S A. 2003 Jun 24;100(13):7632-7. Epub 2003 Jun 6. [2]. Wang W, et al. GSK-3β inhibitor TWS119 attenuates rtPA-induced hemorrhagic transformation and activates the Wnt/β-catenin signaling pathway after acute ischemic stroke in rats. Mol Neurobiol. 2016 Dec;53(10):7028-7036. Epub 2015 Dec 15. [3]. Chen YQ, et al. Wnt pathway activator TWS119 enhances the proliferation and cytolytic activity of human γδT cells against colon cancer. Exp Cell Res. 2017 Nov 16. pii: S0014-4827(17)30587-6.