产品名称：**XMD17-109**
产品别名：**XMD17-109**

生物活性：

Description	XMD17-109 is a novel, specific ERK-5 inhibitor, with an IC50 of 162 nM.	
IC_{50} & Target	ERK5	LRRK2[G2019S]
	162 nM (IC_{50})	339 nM (IC_{50})
In Vitro	XMD17-109 (Compound 26) inhibits ERK5 biochemically with an IC_{50} of 0.162 ± 0.006 μM, and blocks pidermal growth factor induced ERK5 autophosphorylation with an EC_{50} of 0.09 ± 0.03 μM in cells. XMD17-109 also inhibits LRRK2[G2019S] with an IC_{50} of 339 nM[1]. XMD17-109 demonstrats low nanomolar cellular activity judged by the significant dose-dependent reduction of mobility shifted phosphorylated ERK5 bands from sorbitol stimulated cells. XMD17-109 completely inhibits the ERK5-mediated AP1 transcriptional activity at 30 μM and has an EC_{50} of 4.2 μM[2].	

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (156.54 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5654 mL	7.8272 mL	15.6544 mL
	5 mM	0.3131 mL	1.5654 mL	3.1309 mL
	10 mM	0.1565 mL	0.7827 mL	1.5654 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 (3.91 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (3.91 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 (3.91 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (3.91 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 (3.91 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.91 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]. Deng X, et al. Structural determinants for ERK5 (MAPK7) and leucine rich repeat kinase 2 activities of benzo[e]pyrimido-[5,4-b]diazepine-6(11H)-ones. Eur J Med Chem. 2013;70:758-67. [2]. Elkins, Jonathan M., et al. X-ray Crystal Structure of ERK5 (MAPK7) in Complex with a Specific Inhibitor. Journal of Medicinal Chemistry (2013), 56(11), 4413-4421. [3]. Wilhelmsen K, et al. Extracellular signal-regulated kinase 5 promotes acute cellular and systemic inflammation. Sci Signal. 2015 Aug 25;8(391):ra86.

实验参考：

Cell Assay	HeLa cells are maintained in DMEM supplemented with 10% FBS, 2 mM l-glutamine, 50 U/mL penicillin G, and 50 μg/mL streptomycin. Before use HeLa cells are serum starved for 16 h in DMEM supplemented with 2 mM l-glutamine, 50 U/mL penicillin G, and 50 μg/mL streptomycin. HeLa cells are then incubated with ERK5-IN-1 at the indicated concentrations for 1 h prior to stimulation with 0.5mol/Lsorbitol for 30 min. Cells are lysed in Triton lysis buffer (50 mM Tris-HCl, pH 7.5, 1 mM EGTA, 1 mM EDTA, 1 mM sodium orthovanadate, 50 mM sodium fluoride, 1 mM sodium pyrophosphate, 0.27mol/Lsucrose, 1 μM microcystin-LR, 1% (v/v) Triton X-100, 0.1% (v/v) 2-mercaptoethanol) and 20 μg of protein loaded per well. Samples are run on 8% polyacrylamide gels using standard methods. Proteins are transferred onto nitrocellulose membranes and specific proteins detected by immunoblotting. [2]
References	[1]. Deng X, et al. Structural determinants for ERK5 (MAPK7) and leucine rich repeat kinase 2 activities of benzo[e]pyrimido-[5,4-b]diazepine-6(11H)-ones. Eur J Med Chem. 2013;70:758-67. [2]. Elkins, Jonathan M., et al. X-ray Crystal Structure of ERK5 (MAPK7) in Complex with a Specific Inhibitor. Journal of Medicinal Chemistry (2013), 56(11), 4413-4421. [3]. Wilhelmsen K, et al. Extracellular signal-regulated kinase 5 promotes acute cellular and systemic inflammation. Sci Signal. 2015 Aug 25;8(391):ra86.