产品名称：**BI-D1870**
产品别名：**BI-D1870**

生物活性：

Description	BI-D1870 is an ATP-competitive, cell permeable inhibitor of RSK isoforms, with IC_{50}s of 31 nM/24 nM/18 nM/15 nM for RSK1/SK2/SK3/SK4, respectively.
IC_{50} & Target	IC50: 31 nM (RSK1), 24 nM (RSK2), 18 nM (RSK3), 15 nM (RSK4)[1]
In Vitro	BI-D1870 inhibits a mutant of RSK2 lacking the C-terminal kinase catalytic domain (RSK21-389:S381E) with an IC50 of approx. 30 nM. BI-D1870 inhibits RSK1 and RSK2 with IC50 values of 10 nM and 20 nM respectively, when the kinase assays are performed with 100 μM ATP. When the assays are performed at a 10-fold lower ATP concentration, the IC50 of BI-D1870 is reduced to 5 nM for RSK1 and 10 nM for RSK2[1]. BI-D1870 inhibits PLK1 with an IC50 of 100 nM, whilst the IC50 values for Aurora B, DYRK1a, CDK2-A, Lck, CK1 and GSK3β are 10- to 100-fold higher than that of the RSK isoforms. BI-D1870 (10 μM) inhibits the PMA-induced phosphorylation of GSK3α and GSK3β in HEK-293 cells. In HEK-293 cells, BI-D1870 inhibits the EGF-induced phosphorylation of LKB1 at Ser431 with an IC50 of approx. 1 μM[1]. BI-D1870 does not affect the activation of ERK1/ERK2 and MSK1, nor does it inhibit the phosphorylation of CREB[1]. BI-D1870 is a potent RSK family kinase inhibitor (Kds: 10-100 nM), and also interact with BRD4(1) and PLK family, with Kds of 3.5 μM and appr 10 nM[2]. BI-D1870 (10 μM) strongly induces p70S6K activation in serum-starved LN-229 cells, and alao stimulates the phosphorylation of rpS6 and p70S6K in LN-18 cells. BI-D1870 (1 μM) potently inhibits rpS6 phosphorylation, and inhibits PMA-induced rpS6 phosphorylation at concentrations higher than 1 μM[4]. BI-D1870 (1-5 μM) induces a dose- and time-dependent inhibition of cell proliferation in all cell types. BI-D1870 (1-3 μM) induces apoptosis in SCC4 cells and HSC-3 cells. BI-D1870 (0-5) modulates cell survival signaling pathways including Akt and p38 MAPK dose-dependently[5].
In Vivo	BI-D1870 (0.5 mg/kg)-injected experimental autoimmune encephalomyelitis (EAE) mice exhibits a delayed neural deficit without obvious weight loss. Histopathological analyses shows inflammatory cell infiltration and demyelination in the spinal cord in control mice, but not in BI-D1870-treated mice. BI-D1870 protects against the infiltration of TH1 or TH17 cells into the CNS[3].

In Vitro:

DMSO : 100 mg/mL (255.48 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	2.5548 mL	12.7740 mL	25.5480 mL
	5 mM	0.5110 mL	2.5548 mL	5.1096 mL
	10 mM	0.2555 mL	1.2774 mL	2.5548 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：

Solvent&Solubility	——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 (6.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.39 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 (6.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.39 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 (6.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.39 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]. Sapkota GP, et al. BI-D1870 is a specific inhibitor of the p90 RSK (ribosomal S6 kinase) isoforms in vitro and in vivo. Biochem J. 2007 Jan 1;401(1):29-38. [2]. Ciceri P, et al. Dual kinase-bromodomain inhibitors for rationally designed polypharmacology. Nat Chem Biol. 2014 Mar 2. [3]. Takada I, et al. The ribosomal S6 kinase inhibitor BI-D1870 ameliorated experimental autoimmune encephalomyelitis in mice. Immunobiology. 2016 Feb;221(2):188-92. [4]. Roffe M, et al. Two widely used RSK inhibitors, BI-D1870 and SL0101, alter mTORC1 signaling in a RSK-independent manner. Cell Signal. 2015 Aug;27(8):1630-42. [5]. Chiu CF, et al. Antitumor effects of BI-D1870 on human oral squamous cell carcinoma. Cancer Chemother Pharmacol. 2014 Feb;73(2):237-47.

实验参考：

Cell Assay	Measurement of cell growth is assessed using the MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide] assay in six replicates. The cells (5×10^3/200 μL) are seeded in 96-well, flat-bottom plates for 24 h and then exposed to various concentrations of test agents for the indicated time intervals. After removing the culture medium, 200 μL of the medium containing MTT at a concentration of 0.5 mg/mL is added, and the cells are incubated at 37°C for 2 h. The medium is removed, and the reduced MTT dye in each well is dissolved in 200 μL DMSO. Absorbance is determined with a multimode microplate reader Synergy HT at 570 nm. [5]
	Myelin oligodendrocyte glycoprotein (MOG) peptide 35-55 MEVGWYRSPFSRVVHLYRNGK) (BEX) is used to induce EAE in C57/BL6J mice. Mice are injecteds.c. with 200 g of MOG peptide in 100 μL of PBS emulsified in 100 μL complete Freund's adjuvant (CFA) that is further supplemented with five

Animal Administration	mg/mL Mycobacterium tuberculosis. In addition, 500 ng pertussis toxin is injected i.p. on days zero and two. The RSK inhibitor (BI-D1870; 0.5 mg/kg) is injected i.p. into mice two days after immunization with MOG peptide, and injection is repeated every other day for 11 days. Mice that receive only dimethyl sulfoxide (DMSO) solution are used as controls. Paralysis is evaluated according to the following scale: zero, no disease; one, tail limpness; two, hind limb weakness; three, hind limb paralysis; four, fore limb weakness; five, quadriplegia; six, death. For histological analysis, CNS samples are fixed with 4% paraformaldehyde and sliced at 4 μm, and then hematoxylin & eosin (H & E) staining is performed. [3]
Kinase Assay	Purified His6-RSK1, His6-RSK2 or GST-RSK2$^{1\text{-}389:S381E}$ (1-2 units/mL) are assayed for 10 min at 30°C in a 50 μL assay mixture in Buffer A containing 30 μM substrate peptide (KEAKEKRQEQIAKRRRLSSLRASTSKSGGSQK), 10 mM magnesium acetate and 100 μM of [γ-^{32}P]ATP. Reactions are terminated and analysed. The amount of enzyme that catalysed the phosphorylation of 1 nmol of substrate peptide in 1 min is termed one unit. [1]
References	[1]. Sapkota GP, et al. BI-D1870 is a specific inhibitor of the p90 RSK (ribosomal S6 kinase) isoforms in vitro and in vivo. Biochem J. 2007 Jan 1;401(1):29-38. [2]. Ciceri P, et al. Dual kinase-bromodomain inhibitors for rationally designed polypharmacology. Nat Chem Biol. 2014 Mar 2. [3]. Takada I, et al. The ribosomal S6 kinase inhibitor BI-D1870 ameliorated experimental autoimmune encephalomyelitis in mice. Immunobiology. 2016 Feb;221(2):188-92. [4]. Roffe M, et al. Two widely used RSK inhibitors, BI-D1870 and SL0101, alter mTORC1 signaling in a RSK-independent manner. Cell Signal. 2015 Aug;27(8):1630-42. [5]. Chiu CF, et al. Antitumor effects of BI-D1870 on human oral squamous cell carcinoma. Cancer Chemother Pharmacol. 2014 Feb;73(2):237-47.