产品名称：BPTES
产品别名：BPTES

生物活性：

Description	BPTES is an allosteric and selective glutaminase inhibitor with an IC_{50} of 0.16 μM.
IC_{50} & Target	Glutaminase[1]
In Vitro	BPTES (10 μM) exhibits inhibition of PDAC cell proliferation[1]. BPTES preferentially slows growth of mutant IDH1 cells without inducing apoptosis. BPTES (10 μM) reduces glutaminase activity in both WT and mutant IDH1 expressing cells, diminishes glutamate and α-KG levels, and increases glycolytic intermediates while leaving total 2-HG levels unaffected[2]. BPTES (10 μM) shows a clear synergistic anti-cancer effect with 10 μM of 5-FU in A549 and EKVX cell lines, and results in a growth reduction response not only in EKVX and A549 but also in most of the NSCLC cell lines[3]. BPTES (10 μM) effectively reduces the levels of the metabolites of the TCA cycle, with no changes in the levels of metabolites in glycolysis and the pentose phosphate pathway. BPTES treatment reduces about 30% ATP production under normoxia, and an additional 10% reduction of ATP production is observed under hypoxia in EKVX[4].
In Vivo	BPTES-NPs (BPTES nanoparticles, 1.2 mg BPTES in 100 μL nanoparticles, i.v.) significantly attenuates tumor growth in the patient-derived pancreatic orthotopic tumor model[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL (95.30 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9059 mL	9.5296 mL	19.0592 mL
	5 mM	0.3812 mL	1.9059 mL	3.8118 mL
	10 mM	0.1906 mL	0.9530 mL	1.9059 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 →90% corn oil

Solubility: ≥ 2.5 mg/mL (4.76 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.76 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]. Elgogary A, et al. Combination therapy with BPTES nanoparticles and metformin targets the metabolic heterogeneity of pancreatic cancer. Proc Natl Acad Sci U S A. 2016 Sep 6;113(36):E5328-36. [2]. Meghan J. Seltzer, et al. Inhibition of glutaminase preferentially slows growth of glioma cells with mutant IDH1. Cancer Res. 2010 Nov 15; 70(22): 8981-8987. [3]. Lee JS, et al. Glutaminase 1 inhibition reduces thymidine synthesis in NSCLC. Biochem Biophys Res Commun. 2016 Aug 26;477(3):374-82 [4]. Lee JS, et al. Dual targeting of glutaminase 1 and thymidylate synthase elicits death synergistically in NSCLC. Cell Death Dis. 2016 Dec 8;7(12):e2511.

实验参考：

Cell Assay	Cells are plated at a density of 500 cells/well in a 96-well black clear bottom plate. At 24 hrs, media is changed to the appropriate media (DMEM with 4.5 g/L, 1.5 g/L or 0.1 g/L glucose, 10% FBS, pencillin/streptomycin, and 4 mM glutamine with or without doxycyline). 48 hours after plating, compounds or DMSO are added. Media and alamarBlue is added to a volume of 200 µL in each well. Fluorescence is measured at 48 hrs or 72 hrs (EGCG) using a Victor3 plate-reader. [2]
Animal Administration	Four-week-old female Foxn1nuathymic nude mice are used for the assay. Freshly resected pancreatic tumor samples obtained from patients at the time of surgery are propagated from mouse to mouse as a live tumor bank. Once a tumor volume of 50 mm^3 is reached (4 wk postimplantation), mice are treated with 12.5 mg/kg BPTES by intraperitoneal injection, 200 mg/kg CB-839 twice per d by oral gavage, 54 mg/kg BPTES-NPs (1.2 mg BPTES in 100 µL nanoparticles per mouse) by intravenous injection, blank-NPs (100 µL per mouse) by intravenous injection, 25 mg/kg gemcitabine intraperitoneally, 250 mg/kg metformin intraperitoneally daily, or a combination of BPTES-NPs with gemcitabine or metformin. BPTES-NPs are injected once every 3 d for a total of six injections over 16 d. [1]
Kinase Assay	D54 cells are seeded in a T75 flask at 5×10^5 cells, and IDH1 expression is induced with doxycycline 48 hrs before assaying. Cells are collected and resuspended in PBS, 0.1% Triton X-100, and Halt-Protease Inhibitor. Cells are lysed for 30 min on ice and centrifuged for 30 min at 12000 rpm at 4°C. Protein concentration is measured using the BCA Assay. Varying amounts of protein are added to IDH activity assay buffer (33 mM Tris, pH 7.6, 0.33 mM EDTA, 0.1 mM $NADP^+$, 1.33 mM $MnCl_2$, and 1.3 mM isocitrate), and changes in absorbance at 340 nm after 5 min is documented for each protein amount. [2]
References	[1]. Elgogary A, et al. Combination therapy with BPTES nanoparticles and metformin targets the metabolic heterogeneity of pancreatic cancer. Proc Natl Acad Sci U S A. 2016 Sep 6;113(36):E5328-36. [2]. Meghan J. Seltzer, et al. Inhibition of glutaminase preferentially slows growth of glioma cells with mutant IDH1. Cancer Res. 2010 Nov 15; 70(22): 8981-8987. [3]. Lee JS, et al. Glutaminase 1 inhibition reduces thymidine synthesis in NSCLC. Biochem Biophys Res Commun. 2016 Aug 26;477(3):374-82 [4]. Lee JS, et al. Dual targeting of glutaminase 1 and thymidylate synthase elicits death synergistically in NSCLC. Cell Death Dis. 2016 Dec 8;7(12):e2511.