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产品名称：(1,3-苯并噻唑-2-基)[2-[4-[(吗啉-4-基)甲基]苄氧基]嘧啶-4-基]乙腈
产品别名：Bentamapimod；AS 602801

生物活性：

Description	Bentamapimod (AS 602801) is an ATP-competitive JNK inhibitor with IC50 of 80 nM, 90 nM, and 230 nM for JNK1, JNK2, and JNK3, respectively.		
IC_{50} & Target	JNK1	JNK2	JNK3
	80 nM (IC_{50})	90 nM (IC_{50})	230 nM (IC_{50})
In Vitro	Bentamapimod (AS 602801) treatment induces cell death and accordingly decreased the number of viable cells in all three cell lines in a dose-dependent manner, suggesting that Bentamapimod (AS 602801) may have selective cytotoxic activity against neoplastic cells. Bentamapimod (AS 602801) exhibits cytotoxicity against both serum-cultured non-stem cancer cells and cancer stem cells derived from human pancreatic cancer, non-small cell lung cancer, ovarian cancer and glioblastoma at concentrations that did not decrease the viability of normal human fibroblasts. Bentamapimod (AS 602801) also inhibits the self-renewal and tumor-initiating capacity of cancer stem cells surviving Bentamapimod (AS 602801) treatment[2].		
In Vivo	Treatment of nude mice bearing xenografts biopsied from women with endometriosis (BWE) with 30 mg/kg Bentamapimod (AS 602801) causes 29% regression of lesion. Medroxyprogesterone acetate (MPA) or progesterone (PR) alone did not cause regression of BWE lesions, but combining 10 mg/kg Bentamapimod (AS 602801) with MPA caused 38% lesion regression. In human endometrial organ cultures (from healthy women), treatment with Bentamapimod (AS 602801) or MPA reduced matrix metalloproteinase-3 (MMP-3) release into culture medium. In organ cultures established with BWE, PR or MPA failed to inhibit MMP-3 secretion, whereas AS 602801 alone or MPA + Bentamapimod (AS 602801) suppresses MMP-3 production. In an autologous rat endometriosis model, AS 602801 causes 48% regression of lesions compared to GnRH antagonist Antide (84%). Bentamapimod (AS 602801) reduces inflammatory cytokines in endometriotic lesions, while levels of cytokines in ipsilateral horns are unaffected. Furthermore, Bentamapimod (AS 602801) enhances natural killer cell activity, without apparent negative effects on uterus[3].		
Solvent&Solubility	***In Vitro:*** **DMSO : 14.29 mg/mL (31.23 mM;** Need ultrasonic)		

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	2.1856 mL	10.9278 mL	21.8555 mL
	5 mM	0.4371 mL	2.1856 mL	4.3711 mL
	10 mM	0.2186 mL	1.0928 mL	2.1856 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: 1.43 mg/mL (3.13 mM); Suspended solution; Need ultrasonic 此方案可获得 1.43 mg/mL (3.13 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 14.299999 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。
References	[1]. Messoussi A, et al. Recent progress in the design, study, and development of c-Jun N-terminal kinase inhibitors as anticanceragents. Chem Biol. 2014 Nov 20;21(11):1433-43. [2]. Okada M, et al. The novel JNK inhibitor AS602801 inhibits cancer stem cells in vitro and in vivo. Oncotarget. 2016 May 10;7(19):27021-32. [3]. Palmer SS, et al. Bentamapimod (JNK Inhibitor AS602801) Induces Regression of Endometriotic Lesions in Animal Models. Reprod Sci. 2016 Jan;23(1):11-23.

实验参考：

Cell Assay	PANC-1, A2780, and A549 human cancer cells and IMR90 human normal fibroblasts are treated without (control) or with the indicated concentrations of Bentamapimod (AS 602801) (2.5, 5, and 7.5 μM) for 3 days. The number of viable cells (left panels) and the percentage of dead cells (right panels) are determined using trypan blue as a vital dye[2].
Animal Administration	Mice[3] The 5-week-old athymic (ncr/nude) ovariectomized mice are anesthetized with isoflurane and subcutaneously implanted with a silastic capsule containing 8 μg estradiol. Twenty-four hours later, mice received subcutaneous or intraperitoneal injection with a phosphate-buffered saline (PBS) suspension of 8 to 10 human endometrial tissue fragments/mouse (biopsies obtained from volunteers or patients) on the ventral midline just below the umbilicus. For 24 hours immediately preceding injection, tissue fragments are established as organ cultures treated with 1 nM estradiol, PR, or MPA. Oral administration of Bentamapimod (AS 602801) is initiated 10 to 12 days following the injection of tissue. Progesterone is provided via a slow-release silastic capsule containing 25 μg PR, and MPA is given by twice-weekly injections (200 mg/kg) along the right flank using a tuberculin syringe. Bentamapimod (AS 602801) is administered by gavage at a dose of 10 mg/kg and 30 mg/kg/animal for 30 days. Following the completion of treatment, mice are again anesthetized and sacrificed by cervical dislocation for direct examination of lesion size and number. Uteri are measured and weighed, and excised lesions rapidly frozen for further analysis[3].
References	[1]. Messoussi A, et al. Recent progress in the design, study, and development of c-Jun N-terminal kinase inhibitors as anticanceragents. Chem Biol. 2014 Nov 20;21(11):1433-43. [2]. Okada M, et al. The novel JNK inhibitor AS602801 inhibits cancer stem cells in vitro and in vivo. Oncotarget. 2016 May 10;7(19):27021-32. [3]. Palmer SS, et al. Bentamapimod (JNK Inhibitor AS602801) Induces Regression of Endometriotic Lesions in Animal Models. Reprod Sci. 2016 Jan;23(1):11-23.