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产品名称：Afuresertib (hydrochloride)
产品别名：GSK2110183 hydrochloride

生物活性：

Description	Afuresertib hydrochloride (GSK 2110183 hydrochloride) is an orally bioavailable, selective, ATP-competitive and potent pan-Akt kinase inhibitor with Kis of 0.08/2/2.6 nM for Akt1/Akt2/Akt3 respectively[1][2].

IC_{50} & Target

Akt	Akt1	Akt2	Akt3	Akt1 E17K mutant
	0.08 nM (Ki)	2 nM (Ki)	2.6 nM (Ki)	0.2 nM (IC_{50})
PKCη	PKC-βI	ROCK	PKCθ	
210 nM (IC_{50})	430 nM (IC_{50})	100 nM (IC_{50})	510 nM (IC_{50})	

In Vitro

Afuresertib (GSK 2110183) exhibits favorable tumor-suppressive effects on malignant pleural mesothelioma (MPM) cells. Afuresertib significantly increases caspase-3 and caspase-7 activities and apoptotic cell number among ACC-MESO-4 and MSTO-211H cells. Afuresertib strongly arrests the cell cycle in the G_1 phase.

Western blotting analysis shows that Afuresertib increases the expression of $p21^{WAF1/CIP1}$ and decreases the phosphorylation of Akt substrates, including GSK-3β and FOXO family proteins. Afuresertib-induced p21 expression promotes G_1 phase arrest by inducing FOXO activity. Afuresertib significantly enhances cisplatin-induced cytotoxicity. Afuresertib modulates the expression *E2F1* and *MYC*, which are associated with fibroblast core serum response[1].

In Vivo

Mice bearing BT474 breast tumor xenografts are dosed orally with either vehicle or GSK2110183 at 10, 30 or 100 mg/kg daily for 21 days which result in 8, 37 and 61% TGI, respectively. Mice tolerated GSK2110183 well, with 1-3% body weight loss reported after 5 days of dosing which recover over the course of the study. Other tumor xenograft models which possess an activation of the Akt pathway are explored to further demonstrate compound efficacy. Mice treated with GSK2110183 at 10, 30 and 100 mg/kg result in 23, 37 and 97% TGI, respectively, of SKOV3 xenografts[2]

In Vitro:

DMSO : 100 mg/mL (215.62 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1562 mL	10.7810 mL	21.5619 mL
5 mM	0.4312 mL	2.1562 mL	4.3124 mL
10 mM	0.2156 mL	1.0781 mL	2.1562 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

Solvent&Solubility	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 (5.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.39 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 (5.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.39 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 (5.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.39 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]. Yamaji M, et al. Novel ATP-competitive Akt inhibitor Afuresertib suppresses the proliferation of malignant pleural mesothelioma cells. Cancer Med. 2017 Nov;6(11):2646-2659. [2]. Dumble M, et al. Discovery of novel AKT inhibitors with enhanced anti-tumor effects in combination with the MEK inhibitor. PLoS One. 2014 Jun 30;9(6):e100880

实验参考：

Cell Assay	MPM cells are seeded in 96-well plates (cell density, 2.5×10^3 cells/well) and are incubated for 24 h at 37°C. Next, the cells are incubated in a medium containing indicated concentrations of Akt inhibitors (e.g., Afuresertib ; 50, 20, 10, 5, 2, 1, 0.5, 0.2, 0.1, and 0.01 μM) for 72 h. Next, MTT solution is added to each well, and the cells are incubated for 4 h. Finally, the cells are incubated overnight with lysis buffer (10% SDS in 0.01 mol/L hydrogen chloride). Absorbance is measured at 550 nm using SpectraMAX M5 spectrophotometer[1].
References	[1]. Yamaji M, et al. Novel ATP-competitive Akt inhibitor Afuresertib suppresses the proliferation of malignant pleural mesothelioma cells. Cancer Med. 2017 Nov;6(11):2646-2659. [2]. Dumble M, et al. Discovery of novel AKT inhibitors with enhanced anti-tumor effects in combination with the MEK inhibitor. PLoS One. 2014 Jun 30;9(6):e100880