产品名称：AZD6738
产品别名：Ceralasertib

生物活性：

Description	Ceralasertib (AZD6738) is an orally active and bioavailable inhibitor of **ATR** kinase with an **IC_{50}** of 1 nM.		
IC_{50} & Target	ATR	PI3Kδ	DYRK
	1 nM (IC_{50})	6.8 μM (IC_{50})	10.8 μM (IC_{50})
In Vitro	Ceralasertib (AZD6738) is a potent inhibitor of ATR kinase activity with an IC50 of 0.001 μM against the isolated enzyme and 0.074 μM against ATR kinase-dependent CHK1 phosphorylation in cells. Ceralasertib (AZD6738) induces cell death and senescence in non-small cell lung cancer (NSCLC) cell lines. Ceralasertib (AZD6738) impairs viability of four Kras mutant cell lines: H23, H460, A549, and H358. , with the lowest GI50 and greatest maximal inhibition in H460 and H23 cells (1.05 μM, 88.0% and 2.38 μM, 86.2%, respectively). Ceralasertib (AZD6738) potentiates the cytotoxicity of CDDP and NSC 613327 in NSCLC cell lines with intact ATM kinase signaling, and potently synergizes with CDDP in ATM-deficient NSCLC cells[1]. Ceralasertib (AZD6738) inhibits human breast cancer cell lines with IC50 values less than 1 μM using MTT assay. Ceralasertib (AZD6738) induces cell cycle arrest and apoptosis. It downregulates DNA damage response molecules and cell proliferative signaling molecules[2].		
In Vivo	Daily administration of Ceralasertib (AZD6738) and ATR kinase inhibition for 14 consecutive days is tolerated in mice and enhances the therapeutic efficacy of CDDP in xenograft models. Remarkably, the combination of CDDP and Ceralasertib (AZD6738) resolves ATM-deficient lung cancer xenografts[1].		

Solvent&Solubility

In Vitro:

DMSO : ≥ 38 mg/mL (92.12 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4242 mL	12.1209 mL	24.2418 mL
	5 mM	0.4848 mL	2.4242 mL	4.8484 mL
	10 mM	0.2424 mL	1.2121 mL	2.4242 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: ≥ 2.08 mg/mL (5.04 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (5.04 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (5.04 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (5.04 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (5.04 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (5.04 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Vendetti FP, et al. The orally active and bioavailable ATR kinase inhibitor AZD6738 potentiates the anti-tumor effects of CDDP to resolve ATM-deficient non-small cell lung cancer in vivo. [2]. Kim HJ, et al. Anti-tumor activity of the ATR inhibitor AZD6738 in HER2 positive breast cancer cells. Int J Cancer. 2017 Jan 1;140(1):109-119.

实验参考：

Cell Assay	Ceralasertib (AZD6738) is dissolved in DMSO at 30 mM and diluted in DMSO to desired working concentrations. The final DMSO concentration in media for all conditions and controls is 0.1% for Ceralasertib (AZD6738) dose response experiments, 0.05% for Ceralasertib (AZD6738) + chemotherapy viability experiments, and 0.025% for all experiments involving 0.3 μM and 1.0 μM doses of Ceralasertib (AZD6738)[1].
Animal Administration	Mice[1] Ceralasertib (AZD6738) is dissolved in DMSO at a concentration of 25 mg/mL or 50 mg/mL and diluted 1:5 in propylene glycol. Ceralasertib (AZD6738) is administered by oral gavage at 25 mg/kg (H23) or 50 mg/kg (H460) for 14 consecutive days. The dosing volume is 10 mL/kg.[1].
References	[1]. Vendetti FP, et al. The orally active and bioavailable ATR kinase inhibitor AZD6738 potentiates the anti-tumor effects of CDDP to resolve ATM-deficient non-small cell lung cancer in vivo. [2]. Kim HJ, et al. Anti-tumor activity of the ATR inhibitor AZD6738 in HER2 positive breast cancer cells. Int J Cancer. 2017 Jan 1;140(1):109-119.