产品名称：1(2H)-Phthalazinone, 4-[[4-fluoro-3-[(4-methoxy-1-piperidinyl)carbonyl]phenyl]methyl]-
产品别名：AZD2014；Vistusertib

生物活性：

Description	AZD2014 is an ATP competitive mTOR inhibitor with an IC_{50} of 2.81 nM. AZD2014 inhibits both mTORC1 and mTORC2 complexes.

IC_{50} & Target	mTOR	mTORC1	mTORC2	PI3Kα	Autophagy
	2.81 nM (IC_{50})			3.766 μM (IC_{50})	

In Vitro	The inhibitory effects of Vistusertib (AZD2014) are measured against isolated recombinant mTOR enzyme (IC50 of 2.81 nM) as well as in cellular assays measuring both mTORC1 and mTORC2 activities. In MDAMB468 cells, Vistusertib (AZD2014) decreases the phosphorylation of the mTORC1 substrate ribosomal protein S6 (Ser235/236) with a mean IC50 value of 210 nM and the mTORC2 substrate AKT (Ser473) with a mean IC50 value of 78 nM[1].
In Vivo	Vistusertib (AZD2014) induces dose-dependent tumor growth inhibition in several xenograft and primary explant models. The antitumor activity of Vistusertib (AZD2014) is associated with modulation of both mTORC1 and mTORC2 substrates, consistent with its mechanism of action. The pharmacokinetics of Vistusertib (AZD2014) in mice is tested upon administration of doses between 7.5 and 15 mg/kg. A dose-dependent increase in Cmax and AUC is observed following single dose and repeat dosing of AZD2014: Cmax range from 1 to 16 μM and AUC range from 220 to 5,042 μM·h across this dose range. The pharmacodynamic effect of Vistusertib (AZD2014) against an mTORC1 biomarker (phosphorylation of S6) and an mTORC2 biomarker (phosphorylation of AKT) is assessed in SCID mice bearing MCF7 xenografts following administration of 3.75, 7.5, and 15 mg/kg AZD2014. There is a good relationship between the drug plasma concentrations and biomarker levels (estimated p-AKT IC50 of 0.119 μM total, 53% SE, and estimated p-S6 IC50 0.392 μM, 28.8% SE)[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (108.10 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	2.1620 mL	10.8099 mL	21.6198 mL
	5 mM	0.4324 mL	2.1620 mL	4.3240 mL
	10 mM	0.2162 mL	1.0810 mL	2.1620 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: ≥ 2.5 mg/mL (5.40 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.40 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 (5.40 mM); Suspended solution; Need ultrasonic and warming 此方案可获得 2.5 mg/mL (5.40 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 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。
References	[1]. Guichard SM, et al. AZD2014, an inhibitor of mTORC1 and mTORC2, is highly effective in ER+ breast cancer when administered using intermittent or continuous schedules. Mol Cancer Ther. 2015 Nov;14(11):2508-18.

实验参考：

Cell Assay	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration	Mice [1] MCF7 experiments: 5×10^6 MCF7 cells are injected s.c. in a volume of 0.1 mL in male SCID mice and are randomized into control and treatment groups when tumor size reach 0.2 cm^3. Vistusertib (AZD2014) is dissolved in captisol, and diluted to a final captisol concentration of 30% (w/v). Vistusertib (AZD2014) is administered by oral gavage (0.1 mL/10 g body weight). The control group receive vehicle only. Tumor volumes (measured by calliper), animal body weight and condition are recorded twice weekly for the duration of the study. The tumor volume is calculated (taking length to be the longest diameter across and width to be the corresponding perpendicular diameter) using the formula: (length×width)×√(length×width)×(π/6).
References	[1]. Guichard SM, et al. AZD2014, an inhibitor of mTORC1 and mTORC2, is highly effective in ER+ breast cancer when administered using intermittent or continuous schedules. Mol Cancer Ther. 2015 Nov;14(11):2508-18.