产品名称：

2-(2-fluoro-4-iodophenylamino)-N-(2-hydroxyethoxy)-1,5-dimethyl-6-oxo-1,6-dihydropyridine-3-carboxamide

产品别名： **AZD8330；ARRY-424704; ARRY-704**

生物活性：

Description	AZD8330 (ARRY-424704) is a potent, uncompetitive MEK1/MEK2 inhibitor, with an IC_{50} of 7 nM.	
IC_{50} & Target	MEK1	MEK2
	7 nM (IC_{50})	7 nM (IC_{50})
In Vitro	AZD8330 is a selective allosteric MEK1/ MEK2 inhibitor. Exposing human osteosarcoma cell lines MOS, U2OS, and 143B to a concentration of 0.5 μM of Trametinib, AZD8330 or TAK-733 for 6 hours, leads to loss of ERK phosphorylation indicating effective MEK inhibition.The activity of these three inhibitors is tested using concentration ranges in six osteosarcoma cell lines: MOS, U2OS, KPD, ZK58, 143b and Saos-2. All three inhibitors decrease viability of MOS and U2OS and strongly affect 143b. By contrast, viability of KPD, ZK58 and Saos-2 is not affected by any of the three inhibitors[2].	
In Vivo	In tumour xenograft models, AZD8330 demonstrates dose-dependent tumour growth inhibition of approximately 90% at tolerated doses (1.0 mg/kg once daily [OD])[1].	

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (216.81 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1681 mL	10.8406 mL	21.6812 mL
	5 mM	0.4336 mL	2.1681 mL	4.3362 mL
	10 mM	0.2168 mL	1.0841 mL	2.1681 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: ≥ 3.25 mg/mL (7.05 mM); Clear solution

此方案可获得 ≥ 3.25 mg/mL (7.05 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 32.5 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: ≥ 3.25 mg/mL (7.05 mM); Clear solution

此方案可获得 ≥ 3.25 mg/mL (7.05 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 32.5 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: ≥ 3.25 mg/mL (7.05 mM); Clear solution 此方案可获得 ≥ 3.25 mg/mL (7.05 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 32.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Cohen RB, et al. A phase I dose-finding, safety and tolerability study of AZD8330 in patients with advanced malignancies. Eur J Cancer. 2013 May;49(7):1521-9. [2]. Baranski Z, et al. MEK inhibition induces apoptosis in osteosarcoma cells with constitutive ERK1/2 phosphorylation. Genes Cancer. 2015 Nov;6(11-12):503-12.

实验参考：

Cell Assay	Human osteosarcoma cell lines MOS, U2OS, 143B, ZK58, KPD and Saos-2 are grown in RPMI1640 medium supplemented with 10% fetal bovine serum and 25 U/mL Penicillin and 25 μg/mL of Penicillin-Streptomycin. All cells are cultured in a humidified incubator at 37° C with 5% CO_2. Dose response curves for Trametinib, AZD8330 (10 nM, 100 nM, and 1 μM) and TAK-733 in 6 osteosarcoma cell lines as indicated. Cells are exposed for 72 hours. Cells are processed using the ATPlite 1Step kit, followed by luminescence measurement on a plate reader[2].
References	[1]. Cohen RB, et al. A phase I dose-finding, safety and tolerability study of AZD8330 in patients with advanced malignancies. Eur J Cancer. 2013 May;49(7):1521-9. [2]. Baranski Z, et al. MEK inhibition induces apoptosis in osteosarcoma cells with constitutive ERK1/2 phosphorylation. Genes Cancer. 2015 Nov;6(11-12):503-12.