产品名称：**AZD-8835**
产品别名：**AZD-8835**

生物活性：

Description	AZD8835 is a potent and selective inhibitor of **PI3Kα** and **PI3Kδ** with **IC_{50}**s of 6.2 and 5.7 nM, respectively.

IC_{50} & Target

PI3Kδ	PI3Kα	PI3Kα-H1047R	PI3Kα-E545K	PI3Kγ	PI3Kβ
5.7 nM (IC_{50})	6.2 nM (IC_{50})	5.8 nM (IC_{50})	6 nM (IC_{50})	90 nM (IC_{50})	431 nM (IC_{50})

In Vitro

The selectivity profile of AZD8835 (Compound 25) among the class I PI3K isoforms is tested in enzyme and cell based assays. At the enzyme level, AZD8835 is a potent mixed inhibitor of PI3Kα (IC50 6.2 nM) and PI3Kδ (IC50 5.7 nM), with selectivity against PI3Kβ (IC50 431 nM) and PI3Kγ (IC50 90 nM). AZD8835 is also a potent inhibitor of the commonly occurring PI3Kα mutants, PI3Kα- E545K (IC50 6 nM) and PI3Kα-H1047R (IC50 5.8 nM). In cell-based assays assessing the ability to inhibit Akt phosphorylation, AZD8835 is a potent inhibitor in cells sensitive to PI3Kα inhibition (IC50 57 nM in PIK3CA mutant human breast ductal carcinoma BT474 cell line) and in cells sensitive to PI3Kδ inhibition (IC50 49 nM in Jeko-1 B cell line, but not to cells sensitive to PI3Kβ inhibition (IC50 3.5 μM in PTEN null breast adenocarcinoma MDA-MB-468 cells) or to PI3Kγ inhibition (IC50 530 nM in monocytic RAW264 cell line)[1].

In Vivo

AZD8835 (Compound 25) displays good solubility, good permeability and low turnover in hepatocytes from various species. As expected from the in vitro data, low in vivo clearance associated with high bioavailability is seen in both rat and dog. AZD8835 shows high exposure following oral administration to SCID mice (AUC: 137 μM.h and Cmax 34 μM at 50 mg/kg p.o.) and is selected for further in vivo evaluation. In a pharmacodynamic experiment following chronic oral dosing (25 mg/kg b.i.d. or 6 mg/kg b.i.d. of AZD8835) in nude mice bearing mutant H1047R PI3Kα SKOV-3 tumour xenografts, target modulation is assessed by measuring Akt phosphorylation levels at Ser473 at 30 minutes and 8 hours. At both doses, strong inhibition of Akt phosphorylation is observed at the 30 minute timepoint. At 8 hours, significant inhibition is still seen at the 25 mg/kg dose, whereas no inhibition is seen at the lower dose of 6 mg/kg, consistent with the lower plasma concentrations observed[1].

Solvent&Solubility

In Vitro:

DMSO : 16 mg/mL (34.08 mM; Need ultrasonic and warming)

Preparing Stock Solutions (Solvent / Mass / Concentration)	1 mg	5 mg	10 mg
1 mM	2.1297 mL	10.6487 mL	21.2974 mL
5 mM	0.4259 mL	2.1297 mL	4.2595 mL
10 mM	0.2130 mL	1.0649 mL	2.1297 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。

References

[1]. Barlaam B, Discovery of 1-(4-(5-(5-amino-6-(5-tert-butyl-1,3,4-oxadiazol-2-yl)pyrazin-2-yl)-1-ethyl-1,2,4-triazol-3-yl)piperidin-1-yl)-3-hydroxypropan-1-one (AZD8835): A potent and selective inhibitor of PI3Kα and PI3Kδ for the treatment of cancers. Bioorg Med Chem Lett. 2015 Nov 15;25(22):5155-62.