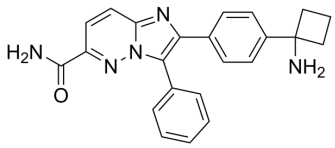
BAY1125976

Cat. No.:	HY-100018
CAS No.:	1402608-02-9
Molecular Formula:	$C_{23}H_{21}N_5O$
Molecular Weight:	383.45
Target:	Akt
Pathway:	PI3K/Akt/mTOR

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (65.20 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6079 mL	13.0395 mL	26.0790 mL
	5 mM	0.5216 mL	2.6079 mL	5.2158 mL
	10 mM	0.2608 mL	1.3040 mL	2.6079 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.52 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BAY1125976 is a selective allosteric Akt1/Akt2 inhibitor; inhibits Akt1 and Akt2 activity with IC_{50} values of 5.2 nM and 18 nM at 10 μM ATP, respectively.

IC_{50} & Target

Akt1	Akt2	Akt3
5.2 nM (IC_{50}, at 10 μM ATP)	18 nM (IC_{50}, at 10 μM ATP)	427 nM (IC_{50}, at 10 μM ATP)

In Vitro

BAY 1125976 is equally potent against Akt1 (IC_{50}=5.2 nM at 10 μM ATP and 44 nM at 2 mM ATP) and Akt2 (IC_{50}=18 nM at 10 μM ATP and 36 nM at 2 mM ATP) isoforms and up to 86 fold less potent against Akt3 (IC_{50}=427 nM at 10 μM ATP). It inhibits the Akt1 and Akt2 by binding into an allosteric binding pocket formed by kinase and PH domain. It inhibits cell proliferation in a broad panel of human cancer cell lines, particularly in breast and prostate cancer cell lines expressing estrogen or androgen receptors. It effectively blocks Akt signaling by inhibiting the phosphorylation of Akt and the downstream effectors, including eukaryotic translation initiation factor 4E binding protein 1 (4E-BP1), glycogen synthase kinase 3 beta (GSK3s),

	proline-rich Akt substrate 40 kDa (PRAS40), S6 ribosomal protein (S6RP), and 70 kDa ribosomal protein S6 kinase 1 (70S6K)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	BAY 1125976 targets tumors displaying activation of the PI3K/Akt/mTOR pathway. BAY 1125976 exhibits strong in vivo efficacy in both cell line and patient-derived xenograft models such as the KPL4 breast cancer model ($PIK3CA^{H1074R}$ mutant), the MCF7 and HBCx-2 breast cancer models, and the Akt^{E17K} mutant driven prostate cancer (LAPC-4) and anal cancer (AXF 984) models[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	PEG/water (60/40), pH 4.0, is used as a vehicle for BAY 1125976. The selectivity of BAY 1125976 is assessed using two different kinase panels: the 230 kinase panel; and the 468 kinase panel. In the 230 kinase panel, kinase activity is determined after incubation with 10 μM BAY 1125976. An additional incubation with 1 μM and 0.1 μM BAY 1125976 is performed for the kinases where 10 μM BAY 1125976 shows an inhibition over 70%. All tests are performed at 10 μM ATP. The 468-kinase panel covered AGC, CAMK, CMGC, CK1, STE, TK, TKL, lipid, and atypical kinase families. The profiling is performed by combining the test compound with DNA-tagged kinase and immobilized ligands. The final kinase concentrations are measured by quantitative PCR[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Female NMRI (nu/nu) mice s.c. injected with 3 x 10^6/100 μL KPL-4 breast cancer cells are used to study the mode-of-action of BAY 1125976. The treatment is started when tumors reaches 232-358 mm^3 in size and the mice receive a single oral dose of 25 or 50 mg/kg BAY 1125976. For determination of plasma concentration-time profiles, blood is drawn from the animals at different time points after compound administration[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Politz O, et al. BAY 1125976, a selective allosteric AKT1/2 inhibitor, exhibits high efficacy on AKT signaling-dependent tumor growth in mouse models. Int J Cancer. 2017 Jan 15;140(2):449-459.

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