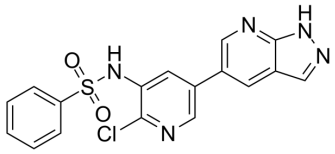
FD223

Cat. No.:	HY-132231
CAS No.:	2050524-24-6
Molecular Formula:	$C_{17}H_{12}ClN_5O_2S$
Molecular Weight:	385.83
Target:	PI3K; Apoptosis
Pathway:	PI3K/Akt/mTOR; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (259.18 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5918 mL	12.9591 mL	25.9182 mL
	5 mM	0.5184 mL	2.5918 mL	5.1836 mL
	10 mM	0.2592 mL	1.2959 mL	2.5918 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 (6.48 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.48 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

FD223 is a potent and selective phosphoinositide 3-kinase delta (PI3Kδ) inhibitor. FD223 displays high potency (IC_{50}=1 nM) and good selectivity over other isoforms (IC_{50}s of 51 nM, 29 nM and 37 nM, respectively for α, β and γ). FD223 exhibits efficient inhibition of the proliferation of acute myeloid leukemia (AML) cell lines by suppressing p-AKT Ser473 thus causing G1 phase arrest during the cell cycle. FD223 has potential for the research of leukemia such as AML[1].

IC_{50} & Target				
	PI3Kδ	PI3Kα	PI3Kβ	PI3Kγ
	1 nM (IC_{50})	51 nM (IC_{50})	29 nM (IC_{50})	37 nM (IC_{50})

In Vitro

FD223 exhibits notable anti-proliferative activities in the p110δ-positive AML cell lines HL-60, MOLM-16, EOL-1 and KG-1, with the IC_{50} of 2.25 μM, 0.87 μM, 2.82 μM, and 5.82 μM, respectively. FD223 shows weak anti-proliferative activity against p110δ

unexpressed MM.1R cell line, with the IC50 value of 23.13 μM[1].
FD223 (MOLM-16 cells; 0.1-5 μM; 16 hours) dose-dependently reduces phosphorylation of Akt (Ser473), which is consistent with the positive control Idelalisib, illustrating that the activity of PI3K/Akt pathway in MOLM-16 cell is blocked[1].
FD223 (MOLM-16 cells; 24 hours; 1-5 μM) arrests the cell cycle at the G1 phase similar to that of positive control Idelalisib[1].
FD223 (1-5 μM; 48 hours) dose-dependently induces cellular apoptosis[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	MOLM-16 cells
Concentration:	1-5 μM
Incubation Time:	48 hours
Result:	Dose-dependently induced cellular apoptosis, which is superior to that of positive control Idelalisib.

Western Blot Analysis[1]

Cell Line:	MOLM-16 cells
Concentration:	0.1-5 μM
Incubation Time:	16 hours
Result:	Dose-dependently reduced phosphorylation of Akt (Ser473).

In Vivo

FD223 (20 and 40 mg/kg; p.o, per day for 14 consecutive days) displays potent antitumor efficacy in MOLM-16 xenograft model with the tumor volume reduction of 49% at a dose of 40 mg/kg/day (po), and shows no significant toxicity in the preliminary safety assessment[1].
FD223 (i.v.; dose of 2 mg/kg; p.o.; 10 mg/kg rats) shows a moderate plasma clearance rate after intravenous administration with C =0.191 $L•h^{-1}•kg^{-1}$. In the po route, it shows a half-life ($t_{1/2}$) of 3.74 h and a Cmax of 1104 ng/mL, good oral plasma exposures ($AUC_{0-\infty}$>9000 h•ng/mL) and acceptable oral bioavailability (17.6%)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	MOLM-16 xenograft model of BALB/c nude mice[1]
Dosage:	20 and 40 mg/kg
Administration:	P.o, per day for 14 consecutive days
Result:	Showed a dose-dependent tumor growth inhibition (TGI) of 31% for 20 mg/kg and 49% for 40 mg/kg

REFERENCES

[1]. Yang C, et al. Bioisosteric replacements of the indole moiety for the development of a potent and selective PI3Kδ inhibitor: Design, synthesis and biological evaluation [published online ahead of print, 2021 Jun 21]. Eur J Med Chem. 2021;223:113661.

Caution: Product has not been fully validated for medical applications. For research use only.

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