AQX-435

Cat. No.: HY-136268

CAS No.: 1619983-52-6

Molecular Formula: $C_{27}H_{34}N_2O_4$

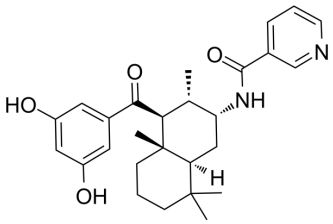
Molecular Weight: 450.57

Target: Phosphatase; Apoptosis

Pathway: Metabolic Enzyme/Protease; 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 (221.94 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2194 mL	11.0971 mL	22.1941 mL
	5 mM	0.4439 mL	2.2194 mL	4.4388 mL
	10 mM	0.2219 mL	1.1097 mL	2.2194 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 (5.55 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.55 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (5.55 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

AQX-435 is a potent SHIP1 phosphatase activator. AQX-435 reduces PI3K activation downstream of the B-cell receptor (BCR) and induces apoptosis of malignant B cells, and reduces lymphoma growth[1][2].

In Vitro

AQX-435 reduces CLL cell viability in a dose-dependent manner[1].
AQX-435-induced (5-30 μM; 24 hours) apoptosis is mediated via caspases since AQX435 induced PARP cleavage[1].
AQX-435 effectively inhibits PI(3,4,5)P3-mediated signaling downstream of the BCR in CLL and DLBCL cells[1]. AQX-435 and Ibrutinib combine effectively to enhanced inhibition of BCR signaling. AQX-435 induced TMD8 cell apoptosis in vitro with an

	IC_{50} of ~2 μM. AQX-435 reduces anti-IgM-induced AKT phosphorylation and induces apoptosis in DLBCL cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only. Cell Viability Assay[1]

Cell Line:	Chronic lymphocytic leukemia (CLL) cells
Concentration:	5-30 μM
Incubation Time:	24 hours
Result:	Reduced CLL cell viability in a dose-dependent manner.

In Vivo

AQX-435 (10 mg/kg; i.p.; 5 days) significantly reduced the volume of TMD8 tumors[1].
AQX-435 (50 mg/kg; ip) inhibits DLBCL PDX tumors growth[1].
AQX-435 reduced AKT phosphorylation and growth of DLBCL in vivo and cooperated with ibrutinib for tumor growth inhibition[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	NOD.Cg-Prkdc scidIl2rgtm1Wjl/SzJ mice (NSG mice) (TMD8 tumors)[1]
Dosage:	10 mg/kg
Administration:	I.p.; in 7-day cycles each comprising 5 days of AQX-435 followed by 2 days with no drug
Result:	Reduced the volume of TMD8 tumors.

REFERENCES

[1]. Lyoyd F. MACKENZIE, et al. Ship1 modulators and methods related thereto.WO2014110036A1.

[2]. Lemm EA, et al. Preclinical Evaluation of a Novel SHIP1 Phosphatase Activator for Inhibition of PI3K Signaling in Malignant B Cells. Clin Cancer Res. 2020;26(7):1700-1711.

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