

Product Data Sheet

Product Name: VU 0155069

Cat. No.: GC15888

Chemical Properties

Cas. No. 1130067-06-9

Chemical Name (S)-N-(1-(4-(5-chloro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidin-1-yl)propan-2-yl)-2-naphthamide hydrochloride

SMILES ClC1=CC=C2N(C(NC2=C1)=O)C3CCN(C[C@H](C)NC(C4=CC=C5C(C=CC=C5)=C4)=O)CC3.Cl

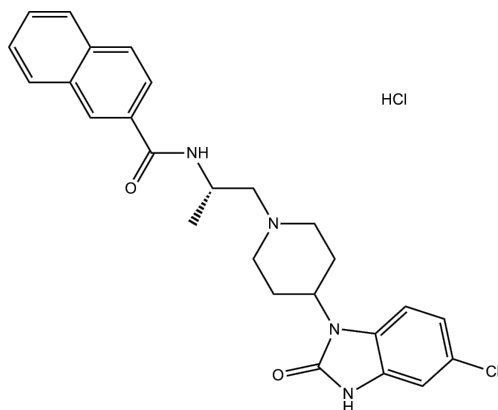
Formula $C_{26}H_{27}ClN_4O_2 \cdot HCl$ M.Wt 463

Solubility DMF: 30 mg/ml ; DMF:PBS (pH 7.2) (1:4): 0.2 mg/ml ; DMSO: 25 mg/ml Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines SW1990 cells (human pancreatic ductal adenocarcinoma cell line)

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Preparation Method	SW1990 cells were pretreated with VU 0155069 (100nM) for 24h, then treated with gemcitabine (500nM).
Reaction Conditions	100nM; 24 h pretreatment
Applications	VU 0155069 pretreatment significantly reversed the capability of SW1990 cells to tolerate gemcitabine cytotoxicity. VU 0155069 increased the apoptosis rate of PDAC cells induced by gemcitabine.

Animal experiment [2]:

Animal models	12-month-old 3xTg-AD mice (Alzheimer's disease model)
Preparation Method	3xTg-AD mice were administered VU 0155069 (1mg/kg) intraperitoneally every alternate day for a month beginning from ~11 months of age.
Dosage form	1mg/kg; i.p.; every alternate day for a month
Applications	VU 0155069 prevented AD-like cognitive decline affecting perirhinal cortex-, hippocampal- and amygdala-dependent behaviors. Glutamate-dependent HFS-LTP and LFS-LTD improved. Dendritic spine morphology showed preservation of mushroom and filamentous spine characteristics.

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References:

- [1] Fu D, Yan J, Zhang Z, et al. Nuclear PLD1 combined with NPM1 induces gemcitabine resistance through tumorigenic IL7R in pancreatic adenocarcinoma. *Cancer Biol Med*. 2023 Jun 27;20(8):599–626.
- [2] Natarajan C, Cook C, Ramaswamy K, et al. Phospholipase D1 Attenuation Therapeutics Promotes Resilience against Synaptotoxicity in 12-Month-Old 3xTg-AD Mouse Model of Progressive Neurodegeneration. *Int J Mol Sci*. 2023 Feb 8;24(4):3372.

Background

VU 0155069 is a selective phospholipase D1 (PLD1) inhibitor ($IC_{50}=46nM$). VU 0155069 inhibits inflammasome activation and reduces caspase-1 activation. VU 0155069 can be used in cancer research and sepsis treatment-related studies^[1-4].

In vitro, VU 0155069 was used to treat AML12 cells and mouse primary hepatocytes stimulated with oleic acid (500 μ M) or sodium palmitate (250 μ M) for 48 hours. VU 0155069 significantly reduced the proportion of CD36⁺ cells, CD36 mean fluorescence intensity, Cd36 mRNA levels, lipid droplet accumulation, triglyceride, and total cholesterol levels^[5]. After pretreating pancreatic cancer cell line (SW-1990) with VU 0155069 (100nM) for 24 hours, cells were incubated with Gemcitabine (500nM). VU 0155069 significantly reversed the ability of pancreatic cancer cells to tolerate Gemcitabine cytotoxicity and increased the apoptosis rate of pancreatic cancer cells induced by Gemcitabine^[6].

In vivo, VU 0155069 (10mg/kg; a total of 4 injections) was subcutaneously administered to septic mice at 2, 14, 26, and 38 hours after the establishment of the sepsis mouse model. VU 0155069 significantly improved the survival rate of mice and alleviated lung inflammation, leukocyte apoptosis, and bacterial load^[7]. VU 0155069 (1mg/kg; every other day) was intraperitoneally injected into 3xTg-AD mice for one month. VU 0155069 significantly prevented Alzheimer's disease-like cognitive decline in mice, improved glutamate-dependent HFS-LTP and LFS-LTD, and preserved dendritic spine morphology^[8].

References:

- [1] Scott SA, Selvy PE, Buck JR, et al. Design of isoform-selective phospholipase D inhibitors that modulate cancer cell invasiveness. *Nat Chem Biol*. 2009 Feb;5(2):108-17.

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- [2] Lewis JA, Scott SA, Lavieri R, et al. Design and synthesis of isoform-selective phospholipase D (PLD) inhibitors. Part I: Impact of alternative halogenated privileged structures for PLD1 specificity. *Bioorg Med Chem Lett*. 2009 Apr 1;19(7):1916-20.
- [3] Barclay Z, Dickson L, Robertson D, et al. Attenuated PLD1 association and signalling at the H452Y polymorphic form of the 5-HT(2A) receptor. *Cell Signal*. 2013 Apr;25(4):814-21.
- [4] Zhou YQ, Cheng XX, He S, et al. A positive feedback loop between PLD1 and NF- κ B signaling promotes tumorigenesis of nasopharyngeal carcinoma. *J Genet Genomics*. 2024 Oct;51(10):997-1006.
- [5] Wang H, Zhao Y, Pan Y, et al. Inhibition of phospholipase D1 ameliorates hepatocyte steatosis and non-alcoholic fatty liver disease. *JHEP Rep*. 2023 Mar 9;5(6):100726.
- [6] Fu D, Yan J, Zhang Z, et al. Nuclear PLD1 combined with NPM1 induces gemcitabine resistance through tumorigenic IL7R in pancreatic adenocarcinoma. *Cancer Biol Med*. 2023 Jun 27;20(8):599–626.
- [7] Lee SK, Kim YS, Bae GH, et al. VU0155069 inhibits inflammasome activation independent of phospholipase D1 activity. *Sci Rep*. 2019 Oct 4;9(1):14349.
- [8] Natarajan C, Cook C, Ramaswamy K, et al. Phospholipase D1 Attenuation Therapeutics Promotes Resilience against Synaptotoxicity in 12-Month-Old 3xTg-AD Mouse Model of Progressive Neurodegeneration. *Int J Mol Sci*. 2023 Feb 8;24(4):3372.

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