Senexin B

Cat. No.: HY-101800

CAS No.: 1449228-40-3

Molecular Formula: $C_{27}H_{26}N_6O$

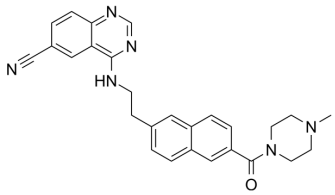
Molecular Weight: 451

Target: CDK

Pathway: Cell Cycle/DNA Damage

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 : 6 mg/mL (13.30 mM; Need ultrasonic and warming)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2173 mL	11.0865 mL	22.1729 mL
5 mM	0.4435 mL	2.2173 mL	4.4346 mL
10 mM	0.2217 mL	1.1086 mL	2.2173 mL

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

BIOLOGICAL ACTIVITY

Description

Senexin B (SNX2-1-165; BCD-115) is a potent, highly water-soluble and bioavailable CDK8/19 inhibitor, with K_ds of 140 nM for CDK8 and 80 nM for CDK19.

IC_{50} & Target

CDK19	CDK8
80 nM (Kd)	140 nM (Kd)

In Vitro

Senexin B inhibits CDK8/19 in low nanomolar range[1]. Senexin B is a newly optimized derivative of Senexin A. It has the same high selectivity for CDK8/19 and is more potent than Senexin A. Senexin B strongly reduces the emergence of estrogen independent cells. Senexin B shows synergy with fulvestrant in MCF7, T47D-ER/Luc and BT474[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Pretreatment of tumor-free mice with Senexin B significantly inhibits the growth of triple-negative breast cancer (TNBC) cells inoculated into mice subsequently to Senexin B administration, indicating a general chemopreventive effect on the normal tissue “soil”. Senexin B potentiates the tumor-suppressive effect of doxorubicin on established TNBC xenografts; this

effect is associated with the suppression of NFκB-mediated transcriptional induction of tumor-promoting cytokines. Senexin B inhibits invasive growth into the muscle layer in an orthotopic xenograft model of MDA-MB-468 TNBC cells. In a spleen-to-liver colon cancer metastasis model of syngeneic mouse CT26 tumors, Senexin B treatment of mice have the same effect as CDK8 knockdown in tumor cells: suppression of metastatic growth in the liver without a significant effect on primary tumor growth in the spleen[1]. Senexin B suppresses tumor growth and augmentes the effects of fulvestrant in ER-positive breast cancer xenografts[2].

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PROTOCOL

Animal Administration [2]

Mice: Once tumors reach 100-200 mm^3 volume, 4 groups of mice are treated with vehicle, Senexin B dimaleate (100 mg/kg; twice daily, oral gavage in 6.25% 2-Hydroxypropyl-β-cyclodextrin, 1% Dextrose buffer) alone or in combination with fulvestrant (5 mg/mouse; s.c; once/week). Tumor volumes are measured twice weekly with calipers and volumes are calculated. After 40 days mice are euthanized, tumors are excised and weighed[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Death Dis. 2021 Sep 29;12(10):889.

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REFERENCES

[1]. Porter D, et al. Abstract PR08: Targeting tumor microenvironment with selective small-molecule inhibitors of CDK8/19. Abstracts: AACR Special Conference on Cellular Heterogeneity in the Tumor Microenvironment; 2014 Feb 26-Mar 1; San Diego, CA. Philadelphia (PA): AACR; Cancer Res 2015;75(1 Suppl):Abstract nr PR08. doi:10.1158/1538-7445.CHTME14-PR08

[2]. McDermott MS, et al. Inhibition of CDK8 mediator kinase suppresses estrogen dependent transcription and the growth of estrogen receptor positive breast cancer. Oncotarget. 2017 Feb 21;8(8):12558-12575.

[3]. CDK8-CDK19 selective inhibitors and their use in anti-metastatic and chemopreventative methods for cancer. US 9321737 B2

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