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产品名称：Senexin B
产品别名：SNX2-1-165

生物活性：

Description	Senexin B 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].	
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].	
Solvent&Solubility	***In Vitro:*** **DMSO : 6 mg/mL** (**13.32 mM;** Need ultrasonic and warming)	

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2196 mL	11.0980 mL	22.1961 mL
	5 mM	0.4439 mL	2.2196 mL	4.4392 mL
	10 mM	0.2220 mL	1.1098 mL	2.2196 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

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

实验参考：

Animal Administration	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].
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