产品名称：SNS-032 (BMS-387032)
产品别名：SNS-032

生物活性：

Description	SNS-032 (BMS-387032) is a selective inhibitor of CDK2, CDK7, and CDK9 with IC_{50}s of 38 nM, 62 nM and 4 nM, respectively.				
IC_{50} & Target	CDK9	CDK2	CDK7	CDK1	CDK4
	4 nM (IC_{50})	38 nM (IC_{50})	62 nM (IC_{50})	480 nM (IC_{50})	925 nM (IC_{50})
In Vitro	SNS-032 has low sensitivity to CDK1 and CDK4 with IC50 of 480 nM and 925 nM, respectively. SNS-032 effectively kills chronic lymphocytic leukemia cells in vitro regardless of prognostic indicators and treatment history. Compared with flavopiridol and roscovitine, SNS-032 is more potent, both in inhibition of RNA synthesis and at induction of apoptosis. SNS-032 activity is readily reversible; removal of SNS-032 reactivates RNA polymerase II, which led to resynthesis of Mcl-1 and cell survival[1]. SNS-032 inhibits three dimensional capillary network formations of endothelial cells. SNS-032 completely prevents U87MG cell–mediated capillary formation of HUVECs. In addition, SNS-032 significantly prevents the production of VEGF in both cell lines, SNS-032 prevents in vitro angiogenesis, and this action is attributable to blocking of VEGF. Preclinical studies have shown that SNS-032 induces cell cycle arrest and apoptosis across multiple cell lines[2]. SNS-032 blocks the cell cycle via inhibition of CDKs 2 and 7, and transcription via inhibition of CDKs 7 and 9. SNS-032 activity is unaffected by human serum[3]. SNS-032 induces a dose-dependent increase in annexin V staining and caspase-3 activation. At the molecular level, SNS-032 induces a marked dephosphorylation of serine 2 and 5 of RNA polymerase (RNA Pol) II and inhibits the expression of CDK2 and CDK9 and dephosphorylated CDK7[5].				
In Vivo	SNS-032 (15 mg/kg, i.p.) inhibits both xenografted BaF3-T674I cells and KBM5-T315I cells in vivo. SNS-032 abrogates the growth of tumors transplanted in nude mice with downregulation of T674I PDGFRα and T315I-Bcr-Abl[4].				

Solvent&Solubility

In Vitro:

DMSO : 33.33 mg/mL (87.59 mM; Need ultrasonic)

Preparing Stock Solutions (Solvent / Mass / Concentration)	1 mg	5 mg	10 mg
1 mM	2.6279 mL	13.1396 mL	26.2791 mL
5 mM	0.5256 mL	2.6279 mL	5.2558 mL
10 mM	0.2628 mL	1.3140 mL	2.6279 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。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

	Solubility: ≥ 2.5 mg/mL (6.57 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.57 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (6.57 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.57 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.57 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.57 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Chen R, et al. Mechanism of action of SNS-032, a novel cyclin-dependent kinase inhibitor, in chronic lymphocytic leukemia. Blood. 2009 May 7;113(19):4637-45. [2]. Ali MA, et al. SNS-032 prevents tumor cell-induced angiogenesis by inhibiting vascular endothelial growth factor. Neoplasia. 2007 May;9(5):370-81. [3]. Conroy A, et al. SNS-032 is a potent and selective CDK 2, 7 and 9 inhibitor that drives target modulation in patient samples. Cancer Chemother Pharmacol. 2009 Sep;64(4):723-32. [4]. Wu Y, et al. Cyclin-dependent kinase 7/9 inhibitor SNS-032 abrogates FIP1-like-1 platelet-derived growth factor receptor α and bcr-abl oncogene addiction in malignant hematologic cells.Clin Cancer Res. 2012 Apr 1;18(7):1966-78. Epub 2012 Mar 23. [5]. Walsby E, et al. The cyclin-dependent kinase inhibitor SNS-032 has single agent activity in AML cells. Leukemia. 2011 Mar;25(3):411-9. Epub 2011 Jan 7.

实验参考：

Cell Assay	Cell Titer-Glo (CTG) luminescent assay is performed to measure the growth curves of both HUVECs and U87MG cells. U87MG cells and HUVECs (2×10^3 cells/well) are seeded in a 96-well microplate in a final volume of 100 mL. After 24 hours, cells are treated with various doses of SNS-032 (0-0.5 mM) for 24, 48, or 72 hours. After completion of the treatment, 100 mL of CTG solution is added to each well and incubated for 20 minutes at room temperature in the dark. Lysate (50 mL) is transferred to a 96-well white plate, and luminescence is measured by POLARstar OPTIMA. Percent cell growth is calculated by considering 100% growth at the time of SNS-032 addition. [2]
Animal Administration	ude *nu/nu* BALB/c mice are housed in barrier facilities with a 12-hour light-dark cycle, with food and water available ad libitum. A mixture of 1×10^7 of BaF3-T674I cells with Matrigel or KBM5-T315I cells (3×10^7) are inoculated subcutaneously on the flanks of 4- to 6-week-old male nude mice. Tumors are measured every other day with use of calipers. Tumor volumes are calculated by the following formula: $a^2\times b\times0.4$, where a is the smallest diameter and b is the diameter perpendicular to a. Four days after subcutaneous inoculation, when tumors are palpable (appr 100 mm^3), mice are randomized to receive treatment with vehicle (tissue culture medium containing DMSO 0.1% v/v) or

	SNS-032 (15 mg/kg injected intraperitoneally every 2 days) for about 2 weeks. SNS-032 is dissolved in tissue culture grade DMSO before dilution. The body weight, feeding behavior, and motor activity of each animal are monitored as indicators of general health. The animals are then euthanized, and tumor xenografts are immediately removed, weighed, stored, and fixed. [4]
References	[1]. Chen R, et al. Mechanism of action of SNS-032, a novel cyclin-dependent kinase inhibitor, in chronic lymphocytic leukemia. Blood. 2009 May 7;113(19):4637-45. [2]. Ali MA, et al. SNS-032 prevents tumor cell-induced angiogenesis by inhibiting vascular endothelial growth factor. Neoplasia. 2007 May;9(5):370-81. [3]. Conroy A, et al. SNS-032 is a potent and selective CDK 2, 7 and 9 inhibitor that drives target modulation in patient samples. Cancer Chemother Pharmacol. 2009 Sep;64(4):723-32. [4]. Wu Y, et al. Cyclin-dependent kinase 7/9 inhibitor SNS-032 abrogates FIP1-like-1 platelet-derived growth factor receptor α and bcr-abl oncogene addiction in malignant hematologic cells.Clin Cancer Res. 2012 Apr 1;18(7):1966-78. Epub 2012 Mar 23. [5]. Walsby E, et al. The cyclin-dependent kinase inhibitor SNS-032 has single agent activity in AML cells. Leukemia. 2011 Mar;25(3):411-9. Epub 2011 Jan 7.