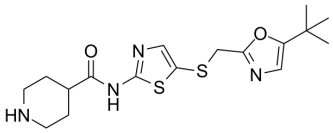
SNS-032

Cat. No.:	HY-10008
CAS No.:	345627-80-7
Molecular Formula:	$C_{17}H_{24}N_4O_2S_2$
Molecular Weight:	380.53
Target:	CDK; Apoptosis
Pathway:	Cell Cycle/DNA Damage; 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 : 62.5 mg/mL (164.24 mM; ultrasonic and warming and heat to 60°C)

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

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

In Vivo

1. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 25 mg/mL (65.70 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 10 mg/mL (26.28 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.47 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.47 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.47 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SNS-032 (BMS-387032) is a potent and selective inhibitor of CDK2, CDK7, and CDK9 with IC_{50}s of 38 nM, 62 nM and 4 nM, respectively. SNS-032 has antitumor effect[1].

IC_{50} & Target	CDK9 4 nM (IC_{50})	CDK2 38 nM (IC_{50})	CDK7 62 nM (IC_{50})	CDK1 480 nM (IC_{50})
	CDK4 925 nM (IC_{50})			
In Vitro	SNS-032 has low sensitivity to CDK1 and CDK4 with IC_{50} 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			

PROTOCOL

Cell Assay [2]	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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4]	Nude 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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cell Rep. 2021 Feb 9;34(6):108736.

- Int J Mol Sci. 2022 May 13;23(10):5476.
- Materials Express. August 2021.
- Patent. US20220175722A1.

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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.

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