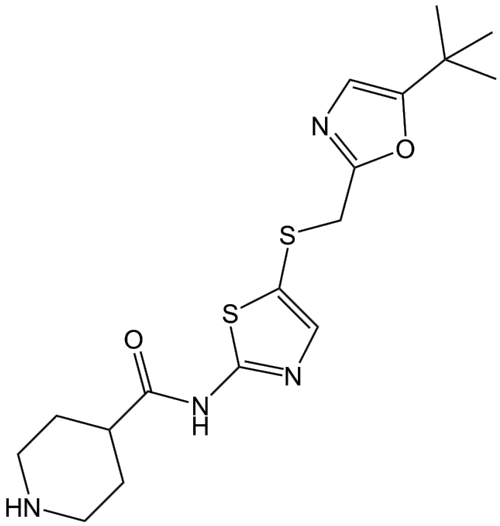
Product Data Sheet

Product Name: SNS-032 (BMS-387032)
Cat. No.: GC11396

Chemical Properties

Cas. No.	345627-80-7		
Chemical Name	N-[5-[(5-tert-butyl-1,3-oxazol-2-yl)methylsulfanyl]-1,3-thiazol-2-yl]piperidine-4-carboxamide		
SMILES	CC(C)(C)C1=CN=C(O1)CSC2=CN=C(S2)NC(=O)C3CCNCC3		
Formula	$C_{17}H_{24}N_4O_2S_2$	M.Wt	380.53
Solubility	≥ 19.05mg/mL in DMSO	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]:

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Cell lines	Chronic lymphocytic leukemia (CLL) cells
Preparation method	The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reaction Conditions	0.1, 0.3 and 1 μM; 6 or 24 hrs
Applications	CLL cells treated with SNS-032 for 6 or 24 hrs showed a decrease in the phosphorylation of Ser2 and Ser5 of the CTD of RNA Pol II, which appeared to be both time- and concentration- dependent, and remarkably consistent among samples. For the phosphorylation of Ser2, the inhibition of SNS-032 was greater than that for the phosphorylation of Ser5, this was consistent with the fact that IC50 for the inhibition of CDK9 was lower compared with that for the inhibition of CDK7 (4 nM vs 62 nM). After 6 hrs of SNS-032 exposure, protein levels of CDK7 and CDK9 were stable, but declined at 24 hrs.

Animal experiment [2]:

Animal models	MDA-MB-435 xenograft mouse model
Dosage form	15 mg/kg; i.p.; every 3 days for approximately one month
Applications	In SNS-032-treated nude mice, the volume of the xenografted breast tumor was significantly inhibited by 65.77% after 30 days of drug administration (eight SNS-032 injections).

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Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Chen R., Wierda W.G., Chubb S., et al. Mechanism of action of SNS032, a novel cyclin-dependent kinase inhibitor, in chronic lymphocytic leukemia. Blood, 2009, 113(19):4637-4645.

[2]. Xie G, Tang H, Wu S, Chen J, Liu J, Liao C. The cyclin-dependent kinase inhibitor SNS-032 induces apoptosis in breast cancer cells via depletion of Mcl-1 and X-linked inhibitor of apoptosis protein and displays antitumor activity in vivo. Int J Oncol. 2014 Aug;45(2):804-12.

Background

SNS-032 (BMS-387032) is a potent and selective inhibitor of cyclin-dependent kinases (CDKs) 2, 7, and 9 [1], with IC50 values of 38 nM, 62 nM and 4 nM, respectively [2].

CDKs mean a family of serine/threonine kinases regulating cell cycle process. Some CDKs are related to transcription control and are often perturbed in cancer cells [3].

Decrease in the phosphorylation at Ser5 and Ser2 in the C-terminal domain (CTD) of RNA Pol II can indicate the inhibition to CDK9 and CDK7 [1]. Chronic lymphocytic leukemia (CLL) cells treated with SNS-032 for 6 or 24 hours showed a decrease in the phosphorylation of Ser2 and Ser5 of the CTD of RNA Pol II, this appeared to be both time- and concentration- dependent, and remarkably consistent among samples. For the phosphorylation of Ser2, the inhibition of SNS-032 was greater than that for the phosphorylation of Ser5, this was consistent with the fact that IC50 for the inhibition of CDK9 was lower compared with that for the inhibition of CDK7 (4 nM vs 62 nM). After 6 hours of SNS-032 exposure, protein levels of CDK7 and CDK9 were stable, but declined at 24 hours [4].

In patients with chronic lymphocytic leukemia (CLL), infusion of SNS-032 in a total dose of 75 mg/m2 resulted in a decrease in the phosphorylation at Ser5 and Ser2 in the C-terminal domain of RNA Pol II. This indicated the inhibition to Cdk9 and Cdk7 by SNS-032. This inhibition was first seen 2 hours after the beginning of the infusion with SNS-032, was pronounced after 6 hours and returned to

baseline after 24 hours [1].

References:

[1]. Tong W.G., Chen R., Plunkett W., et al. Phase I and Pharmacologic Study of SNS-032, a Potent and Selective Cdk2, 7, and 9 Inhibitor, in Patients With Advanced Chronic Lymphocytic Leukemia and Multiple Myeloma. Journal of Clinical Oncology, 2010, 28(18):3015- 3022.
[2]. Chipumuro E., Marco E., Christensen C.L., et al. CDK7 Inhibition Suppresses Super-Enhancer-Linked Oncogenic Transcription in MYCN-Driven Cancer. Cell, 2014, 159:1-14.
[3]. Meng H., Jin Y.M., Liu H., et al. SNS-032 inhibits mTORC1/mTORC2 activity in acute myeloid leukemia cells and has synergistic activity with perifosine against Akt. Journal of Hematology & Oncology, 2013, 6:18.
[4]. Chen R., Wierda W.G., Chubb S., et al. Mechanism of action of SNS032, a novel cyclin-dependent kinase inhibitor, in chronic lymphocytic leukemia. Blood, 2009, 113(19):4637-4645.

Caution: Product has not been fully validated for medical applications. For research use only.
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