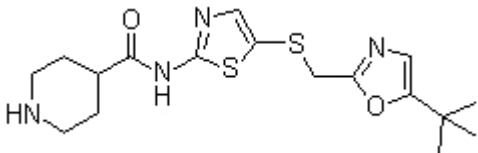


Product Introduction

SNS-032 (BMS-387032)

SNS-032 has firstly been described as a selective inhibitor of **CDK2** with **IC₅₀** of 48 nM and is 10- and 20-fold selective over CDK1/CDK4. It is also found to be sensitive to **CDK7/9** with **IC₅₀** of 62 nM/4 nM, with little effect on CDK6. Phase 1.

Technical Data:

| | | |
|---|--|--|
| Molecular Weight (MW): | 380.53 |  |
| Formula: | C ₁₇ H ₂₄ N ₄ O ₂ S ₂ | |
| Solubility (25°C) | DMSO 76 mg/mL | |
| * <1 mg/ml means slightly soluble or insoluble: | Water <1 mg/mL | |
| | Ethanol <1 mg/mL | |
| Purity: | >98% | |
| Storage: | 3 years -20°C Powder | |
| | 6 months -80°C in DMSO | |
| CAS No.: | 345627-80-7 | |

Biological Activity

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

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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. [4]

SNS-032 prevents tumor cell-induced VEGF secretion in a tumor coculture model. [2] SNS-032, a new CDK inhibitor, is more selective and less cytotoxic and has been shown to prolong stable disease in solid tumors. [4]

References

- [1] Chen R, et al. Blood, 2009, 113(19): 4637-45.
- [2] Ali MA, et al. Neoplasia, 2007, 9(5), 370-81.
- [3] Conroy A, et al. Cancer Chemother Pharmacol, 2009, 64(4), 723-32.
- [4] Walsby E, et al. Leukemia, 2011, 25(3), 411-9.



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