Product Data Sheet

Product Name: BS-181
Cat. No.: GC12001

Chemical Properties

Cas. No.	1092443-52-1		
Chemical Name	5-N-(6-aminohexyl)-7-N-benzyl-3-propan-2-ylpyrazolo[1,5-a]pyrimidine-5,7-diamine		
SMILES	CC(C)C1=C2N=C(C=C(N2N=C1)NCC3=CC=CC=C3)NCCCCCCN		
Formula	$C_{22}H_{32}N_6$	M.Wt	380.53
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	BS-181		

Protocol

Cell experiment:	Cell viability is detected using Cell Counting Kit (CCK-8 kit) according to supplier’s introductions. Briefly, BGC823 cells are seeded at 104 cells per well for 48 hours with or without BS-181. Then, the absorbance is detected at 450 nm (reference at 650 nm) in each well.

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Animal experiment:	In total, 5×106 BGC823 cells (0.1 mL) are injected subcutaneously into the flank of the mice. Tumor measurements are performed two times per week, and volumes are calculated using the formula: tumor size= (length [mm] × width2 [mm])/2. Finally, 30 mice (tumor volume 100-200 mm3) are selected and randomLy assigned into three groups. As previously described, BS-181 is prepared in 10% dimethyl sulfoxide/50 mM HCl/5% Tween 20/85% saline. Micereceive BS-181 injection (ip) twice daily at indicated doses (BS-181 [10 mg/kg/d or 20 mg/kg/d] or roscovitine [20 mg/kg/d]) for a total of 14 days. Control mice are injected with vehicles. Animal weights and tumor volume are measured each day throughout the 14-day treatment. In addition, all rats are kept for another 30 days for survival observation. Mice are injected intraperitoneally twice daily with BS-181 at 5 mg/kg or 10 mg/kg.

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References:

[1]. Ali S et al. The development of a selective cyclin-dependent kinase inhibitor that shows antitumor activity. Cancer Res. 2009 Aug 1;69(15):6208-15.
[2]. Wang BY, et al. Selective CDK7 inhibition with BS-181 suppresses cell proliferation and induces cell cycle arrest and apoptosis in gastric cancer. Drug Des Devel Ther. 2016 Mar 16;10:1181-9.

Background

Normal progression through the cell cycle requires the sequential action of cyclin-

dependent kinases (CDK1, CDK2, CDK4 and CDK6). Deregulation of CDK activity is a feature of almost all cancers and has led to the development of CDK inhibitors as anticancer agents. As such, CDK7 is an target for the anticancer drug development. Computer modeling of CDK7 was used to design potential potent CDK7 inhibitor, which is BS-181.

In vitro: Testing of other CDKs as well as another 69 kinases showed that BS-181 only inhibited CDK2 at concentrations lower than 1 μM, with 35-fold less potently (IC50 880 nM) than CDK7. BS-181 inhibited the phosphorylation of CDK7 substrates in MCF-7 cells, led to cell cycle arrest and apoptosis to inhibit the growth of cancer cell lines, and showed antitumor effects in vivo [1].

In vivo: BS-181 was stable in vivo after i.p. administration of 10 mg kg-1. The same dose of drug inhibited the growth of MCF-7 human xenografts in nude mice. BS-181 is the first example of a potent and selective CDK7 inhibitor with potential as an anticancer agent [1].

Clinical trial: Currently no clinical data are available.

Reference:

[1] Ali S, Heathcote DA, Kroll SH, Jogalekar AS, Scheiper B, Patel H, Brackow J, Siwicka A, Fuchter MJ, Periyasamy M, Tolhurst RS, Kanneganti SK, Snyder JP, Liotta DC, Aboagye EO, Barrett AG, Coombes RC. The development of a selective cyclin-dependent kinase inhibitor that shows antitumor activity. Cancer Res. 2009;69(15):6208-15.