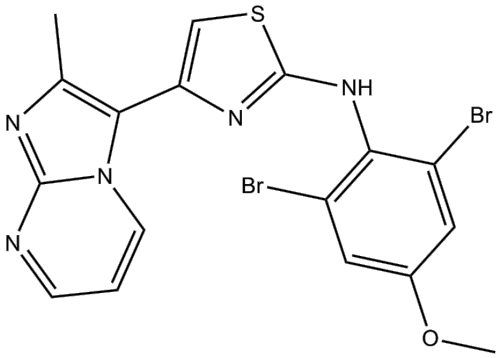
Product Data Sheet

Product Name: PTC-209
Cat. No.: GC15725

Chemical Properties

Cas. No.	315704-66-6		
Chemical Name	N-(2,6-dibromo-4-methoxyphenyl)-4-(2-methylimidazo[1,2-a]pyrimidin-3-yl)-1,3-thiazol-2-amine		
SMILES	CC1=C(N2C=CC=NC2=N1)C3=CSC(=N3)NC4=C(C=C(C=C4Br)OC)Br		
Formula	$C_{17}H_{13}Br_2N_5OS$	M.Wt	495.19
Solubility	≥ 24.75mg/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]:

Cell lines	U87MG and T98G human glioblastoma cell lines, TPC-1115 and TPC-0411 patient-derived primary glioblastoma cells

Product Data Sheet

Preparation Method	U87MG and T98G cells were maintained in high-glucose DMEM supplemented with 10% FBS and 1% penicillin-streptomycin at 37°C, 5% CO_2. TPC-1115 and TPC-0411 cells were maintained in serum-free DMEM/F12 supplemented with 75μg/mL BSA, N2 supplement, B27 supplement, 10μg/mL insulin, 20ng/mL bFGF and 20ng/mL EGF; sphere formation assay was performed in ultra-low attachment plates with serum-free DMEM/F12 containing B27 supplement, 5μg/mL insulin, 20ng/mL bFGF and 10ng/mL EGF. Cells were treated with 1μM or 10μM PTC-209 for corresponding assay durations.
Reaction Conditions	1μM or 10μM；2-4 day
Applications	PTC-209 downregulated BMI-1 protein and global H2AK119ub1 levels in U87MG and T98G cells. PTC-209 inhibited U87MG and T98G cell proliferation in a dose-dependent manner, arrested cells at G0/G1 and G2/M phases, reduced cell migratory capacity, downregulated mesenchymal markers (α-catenin, N-cadherin, Fibronectin, Vimentin) and mesenchymal-inducing transcription factors (Snail1, Slug). PTC-209 reduced the proportion of side population cells and CD133-high cells, decreased sphere-initiating cell frequency and formed smaller tumor spheres. PTC-209 reversed the transcriptional program altered by BMI-1 overexpression, reduced H2AK119ub1 enrichment at promoters of BMI-1-targeted tumor suppressor genes and upregulated their expression (e.g. CBX7, TIMP4, SFRP1, KLF9).

Animal experiment [2]:

Animal models	Male nude mice (8-week-old)

Product Data Sheet

Preparation Method	2×10^6 Cal27 or FaDu cells in 100μL PBS were subcutaneously injected into nude mice. Three weeks after inoculation when tumor volumes reached approximately 100mm³, mice were randomly divided into two groups (6 mice per group) and received daily subcutaneous injection of PTC-209 (30mg/kg) or vehicle (PBS) for consecutive 15 days. Tumor diameters were measured every 3 days using calipers, and tumor samples were harvested at the end of treatment for immunohistochemical and immunofluorescent staining.
Dosage form	30mg/kg; s.c.; daily for 15 days
Applications	PTC-209 administration significantly reduced tumor volume and final tumor weight in both Cal27 and FaDu xenografts. PTC-209 decreased the number of Bmi1-positive cancer cells and Ki-67-positive proliferating cells in tumor tissues, and reduced CD44-positive cell number as revealed by immunofluorescent staining.

References:

[1] Kong Y, Ai C, Dong F, et al. Targeting of BMI-1 with PTC-209 inhibits glioblastoma development. Cell Cycle. 2018;17(10):1199-1211.
[2] Wang Q, Li Z, Wu Y, et al. Pharmacological inhibition of Bmi1 by PTC-209 impaired tumor growth in head neck squamous cell carcinoma. Cancer Cell Int. 2017 Nov;17:107.

Background

PTC-209 is a cell-permeable BMI-1 inhibitor with an IC_{50} of 0.5μM in HEK293T cells. PTC-209 downregulates BMI-1 protein expression by inhibiting BMI-1 transcription and impairs RING1A-mediated epigenetic regulation of H2AK119ub1. PTC-209 suppresses tumor progression by reducing the self-renewal capacity of tumor-initiating cells. PTC-209 can be used in studies related to colorectal cancer, glioblastoma, multiple myeloma, and cardiac reprogramming[1-4].

In vitro, PTC-209 (1 or 10μM) treated U87MG and T98G glioblastoma cells and TPC-1115 and TPC-0411 primary glioblastoma cells for 2-4 days. PTC-209 downregulated BMI-1 protein and

Product Data Sheet

H2AK119ub1 levels, inhibited cell proliferation, and induced G0/G1 and G2/M phase arrest. PTC-209 suppressed cell migration and mesenchymal marker expression, and inhibited self-renewal and sphere-forming ability of glioblastoma stem cells[5]. PTC-209 (1μM) pretreated mouse embryonic fibroblasts and cardiac fibroblasts for 24h. PTC-209 reduced H2AK119ub enrichment at cardiac gene loci, upregulated Gata4, Isl1, Flk1, and downregulated Col1A1 (in embryonic fibroblasts). PTC-209 downregulated chemokines, interleukins, cytokines, and related JAK/STAT3 and MAPK/ERK1-2 pathway molecules[6].

In vivo, PTC-209 (0.5-1mg/g per week) alone or combined with cisplatin (0.5-1mg/g per week) was intraperitoneally injected into 4NQO-induced esophageal squamous cell carcinoma model mice for 4 consecutive weeks. PTC-209 monotherapy reduced ESCC lesion numbers, and combination with cisplatin further decreased lesion numbers and inhibited tumor growth compared to monotherapy[7]. PTC-209 (30mg/kg; once daily) was subcutaneously injected into Cal27 and FaDu head and neck squamous cell carcinoma xenograft nude mice for 15 consecutive days. PTC-209 significantly inhibited tumor growth, downregulated intratumoral Bmi1 and Ki-67 expression, and reduced CD44-positive cells[8].

References:
[1] Zhu M, Fan H, Deng J, et al. BMI1 Silencing Liposomes Suppress Postradiotherapy Cancer Stemness against Radioresistant Hepatocellular Carcinoma. ACS Nano. 2023 Dec 12;17(23):23405-23421.
[2] Bolomsky A, Schlangen K, Schreiner W, et al. Targeting of BMI-1 with PTC-209 shows potent anti-myeloma activity and impairs the tumour microenvironment. J Hematol Oncol. 2016 Mar 2;9:17.
[3] Mayr C, Wagner A, Loeffelberger M, et al. The BMI1 inhibitor PTC-209 is a potential compound to halt cellular growth in biliary tract cancer cells. Oncotarget. 2016 Jan 5;7(1):745-58.
[4] Elango R, Vishnubalaji R, Manikandan M, et al. Concurrent targeting of BMI1 and CDK4/6 abrogates tumor growth in vitro and in vivo. Sci Rep. 2019 Sep 23;9(1):13696.
[5] Kong Y, Ai C, Dong F, et al. Targeting of BMI-1 with PTC-209 inhibits glioblastoma development. Cell Cycle. 2018;17(10):1199-1211.
[6] Testa G, Russo M, Di Benedetto G, et al. Bmi1 inhibitor PTC-209 promotes chemically-induced direct cardiac reprogramming of cardiac fibroblasts into cardiomyocytes. Sci Rep. 2020 Apr;10(1):7129.
[7] Wang X, Li K, Cheng M, et al. Bmi1 Serves as a Potential Tumor-Initiating Cell Marker and Therapeutic Target in Esophageal Squamous Cell Carcinoma. Stem Cells Int. 2020

Aug;2020:8877577.
[8] Wang Q, Li Z, Wu Y, et al. Pharmacological inhibition of Bmi1 by PTC-209 impaired tumor growth in head neck squamous cell carcinoma. Cancer Cell Int. 2017 Nov;17:107.