

Product Data Sheet

Product Name: Panobinostat (LBH589)

Cat. No.: GC12257

Chemical Properties

Cas. No. 404950-80-7

Chemical Name (E)-N-hydroxy-3-[4-[[2-(2-methyl-1H-indol-3-yl)ethylamino]methyl]phenyl]prop-2-enamide

SMILES CC1=C(C2=CC=CC=C2N1)CCNCC3=CC=C(C=C3)C=CC(=O)NO

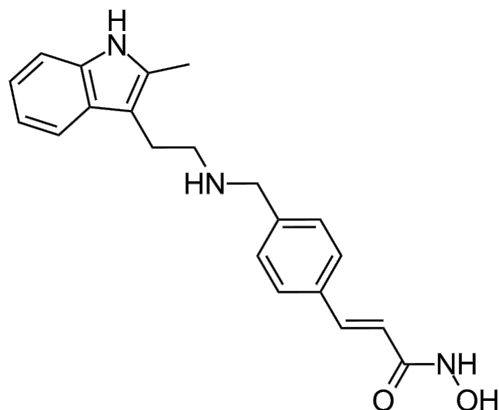
Formula $C_{21}H_{23}N_3O_2$ M.Wt 349.43

Solubility $\geq 17.47\text{mg/mL}$ 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 B16, WM793 and WM983A (melanoma cell lines)

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Preparation Method Two human (WM793 and WM983A) and one murine (B16) melanoma cell lines were plated in triplicate and treated for 72h with indicated doses of panobinostat (12.5, 25, 50, and 100nM). An MTS assay was used to determine relative amounts of metabolically active cells.

Reaction Conditions 12.5, 25, 50, and 100nM; 72h

Applications All treated cell lines displayed significant, dose-dependent impairment in growth, IC₅₀ values ranged from 25 to 100nM. And at the concentrations used, no impairment in the growth of normal melanocytes was observed.

Animal experiment [2]:

Animal models HH CTCL xenograft CB.17 SCID mouse model

Preparation Method Beginning at 13 days post-tumor implant, HH CTCL tumor-bearing mice were treated with panobinostat at 2 different doses. Mice bearing HH tumors were treated with 2 different doses (7.5mg/kg or 15mg/kg) of panobinostat i.v. daily, 5 days per week, for 2 weeks.

Dosage form 7.5, and 15mg/kg/day; 5 days/week; 2 week; i.v.

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Applications

Panobinostat treatment resulted in significant tumor regression of 41% and 94% at 7.5 and 15mg/kg, respectively. Mice treated with panobinostat showed some level of dose- and time-dependent body weight loss, but within the acceptable tolerability margin of -15%. Following treatment cessation, panobinostat-treated animals demonstrated delay of tumor growth and extended time to endpoint (TTE) of 41.8 and 61.6 days with 7.5 and 15mg/kg doses, respectively.

References:

- [1] WOODS D M, WOAN K, CHENG F, et al. The antimelanoma activity of the histone deacetylase inhibitor panobinostat (LBH589) is mediated by direct tumor cytotoxicity and increased tumor immunogenicity[J]. Melanoma Research, 2013, 23(5): 341-348.
- [2] SHAO W, GROWNEY J D, FENG Y, et al. Activity of deacetylase inhibitor panobinostat (LBH589) in cutaneous T-cell lymphoma models: defining molecular mechanisms of resistance[J]. International Journal of Cancer, 2010, 127(9): 2199-2208.

Background

Panobinostat (LBH589) is a potent, orally active, broad-spectrum histone deacetylase (HDAC) inhibitor with antitumor activity, exhibiting an IC_{50} value of 5nM^[1]. Panobinostat induces hyperacetylation of histones and other intracellular proteins, allowing the expression of previously suppressed genes, thereby inhibiting cell proliferation and inducing apoptosis in malignant cells^[2]. Panobinostat is commonly used in the treatment and research of diseases such as acute myeloid leukemia (AML), multiple myeloma (MM), Hodgkin's lymphoma (HL), and cutaneous T-cell lymphoma (CTCL)^[3].

In vitro, treatment of small cell lung cancer (SCLC) H69 cells with panobinostat (20nM) alone for 60h resulted in >70% cell death, accompanied by an increase in the proportion of sub-G₁ phase cells^[4]. Treatment of various human and mouse melanoma cell lines (e.g., B16, WM793, and WM983A) with panobinostat (12.5-100nM) for 72h effectively inhibited cell growth, with IC_{50} values ranging from 25 to 100nM, while showing no effect on the growth of untransformed normal melanocytes^[5]. Panobinostat (20nM) treatment of HUT78 and HH cells for 24h significantly induced caspase-3/7

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activation, with an EC₅₀ value of approximately 10nM^[6].

In vivo, intravenous administration of panobinostat (7.5 or 15mg/kg/day; 5 days/week) for 2 weeks in CB.17 SCID mice bearing HH cell CTCL xenografts induced significant tumor regression (41% and 94%, respectively) and prolonged survival time^[6]. Intraperitoneal injection of panobinostat (20mg/kg; 3 times/week) for 7 weeks in female nude mice inoculated with MDA-MB-231 cells significantly suppressed tumor volume growth, upregulated *APCL* gene expression in tumor xenografts, and downregulated β -catenin expression^[7].

References:

- [1] SCUTO A, KIRSCHBAUM M, KOWOLIK C, et al. The novel histone deacetylase inhibitor, LBH589, induces expression of DNA damage response genes and apoptosis in Ph⁻ acute lymphoblastic leukemia cells[J]. *Blood*, 2008, 111(10): 5093-5100.
- [2] ANNE M, SAMMARTINO D, BARGINEAR M F, et al. Profile of panobinostat and its potential for treatment in solid tumors: an update[J]. *OncoTargets and Therapy*, 2013, 6: 1613-1624.
- [3] PRINCE H M, BISHTON M J, JOHNSTONE R W. Panobinostat (LBH589): a potent pan-deacetylase inhibitor with promising activity against hematologic and solid tumors[J]. *Future Oncology*, 2009, 5(5): 601-612.
- [4] CRISANTI M C, WALLACE A F, KAPOOR V, et al. The HDAC inhibitor panobinostat (LBH589) inhibits mesothelioma and lung cancer cells in vitro and in vivo with particular efficacy for small cell lung cancer[J]. *Molecular Cancer Therapeutics*, 2009, 8(8): 2221-2231.
- [5] WOODS D M, WOAN K, CHENG F, et al. The antimelanoma activity of the histone deacetylase inhibitor panobinostat (LBH589) is mediated by direct tumor cytotoxicity and increased tumor immunogenicity[J]. *Melanoma Research*, 2013, 23(5): 341-348.
- [6] SHAO W, GROWNEY J D, FENG Y, et al. Activity of deacetylase inhibitor panobinostat (LBH589) in cutaneous T-cell lymphoma models: defining molecular mechanisms of resistance[J]. *International Journal of Cancer*, 2010, 127(9): 2199-2208.
- [7] QIN G, LI Y, XU X D, et al. Panobinostat (LBH589) inhibits Wnt/ β -catenin signaling pathway via upregulating *APCL* expression in breast cancer[J]. *Cellular Signalling*, 2019, 59: 62-75.

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