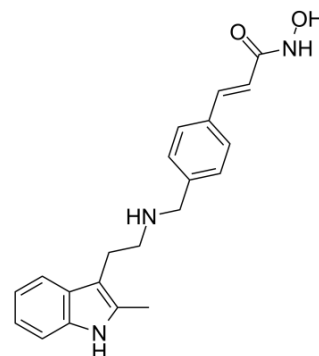


## Panobinostat

|                           |  |       |          |
|---------------------------|--|-------|----------|
| <b>Cat. No.:</b>          | HY-10224   |       |          |
| <b>CAS No.:</b>           | 404950-80-7  |       |          |
| <b>Molecular Formula:</b> | C <sub>21</sub> H <sub>23</sub> N <sub>3</sub> O <sub>2</sub>            |       |          |
| <b>Molecular Weight:</b>  | 349.43   |       |          |
| <b>Target:</b>            | HDAC; Autophagy; HIV; Apoptosis  |       |          |
| <b>Pathway:</b>           | Cell Cycle/DNA Damage; Epigenetics; Autophagy; Anti-infection; Apoptosis |       |          |
| <b>Storage:</b>           | Powder   | -20°C | 3 years  |
|                           |  | 4°C   | 2 years  |
|                           | In solvent   | -80°C | 6 months |
|                           |  | -20°C | 1 month  |



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 57 mg/mL (163.12 mM)  
 \* "≥" means soluble, but saturation unknown.

| Preparing Stock Solutions | Solvent       |      | 1 mg      | 5 mg       | 10 mg      |
|---------------------------|---------------|------|-----------|------------|------------|
|                           | Concentration | Mass |           |            |            |
|                           | 1 mM          |      | 2.8618 mL | 14.3090 mL | 28.6180 mL |
|                           | 5 mM          |      | 0.5724 mL | 2.8618 mL  | 5.7236 mL  |
|                           | 10 mM         |      | 0.2862 mL | 1.4309 mL  | 2.8618 mL  |

Please refer to the solubility information to select the appropriate solvent.

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 2.5 mg/mL (7.15 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.5 mg/mL (7.15 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.5 mg/mL (7.15 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline  
Solubility: ≥ 2.5 mg/mL (7.15 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)  
Solubility: 2.5 mg/mL (7.15 mM); Suspended solution; Need ultrasonic

### BIOLOGICAL ACTIVITY

#### Description

Panobinostat (LBH589; NVP-LBH589) is a potent and orally active non-selective HDAC inhibitor, and has antineoplastic activities<sup>[1][2]</sup>. Panobinostat induces HIV-1 virus production even at low concentration range 8-31 nM, stimulates HIV-1

expression in latently infected cells<sup>[4]</sup>. Panobinostat induces cell apoptosis and autophagy. Panobinostat can be used for the study of refractory or relapsed multiple myeloma<sup>[3]</sup>.

|                                     |   |       |
|-------------------------------------|---|-------|
| <b>IC<sub>50</sub> &amp; Target</b> | HDAC  | HIV-1 |
| <b>In Vitro</b>                     | Panobinosta (LBH589) induces apoptosis of both MOLT-4 and Reh cells in a time- and dose-dependent manner. Panobinosta treatment results in histone (H3K9 and H4K8) hyperacetylation and regulation of cell-cycle control genes in Reh cells <sup>[1]</sup> . Panobinostat exhibits potent antiproliferative activity in human NSCLC cell lines with the IC <sub>50</sub> ranging from 5 to 100 nM <sup>[2]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.  |       |
| <b>In Vivo</b>                      | Panobinosta (10, 20 mg/kg, i.p.) significantly slows tumor growth derived from Meso and NSCLC cells in vivo models. Panobinosta markedly increases acetylation of histone H3 and H4 of H69 human SCLC cells harvest from SCID mice <sup>[2]</sup> . Panobinostat (5, 10 and 20 mg/kg i.p.) demonstrates a clear benefit of decreased tumor burden, significantly improves TTE and reduces bone density loss in a disseminated multiple myeloma mouse model <sup>[3]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only. |       |

## PROTOCOL

### Cell Assay <sup>[1]</sup>

Cells are washed with ice-cold PBS containing 0.1 mM sodium orthovanadate, and total proteins are isolated using RIPA lysis buffer, which includes protease inhibitors (leupeptin, antipain, and aprotinin), 0.5 mM PMSF, and 0.2 mM sodium orthovanadate. Protein amounts are quantified using the Bio-Rad protein assay. Equal amounts of proteins are loaded onto an sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) gel, transferred onto nitrocellulose membrane, and probed with the antibody of interest: mouse monoclonal c-Myc and mouse monoclonal p21 antibodies; rabbit polyclonal phospho-Histone H2A.X, rabbit polyclonal acetyl-Histone H3 (Lys9), and rabbit polyclonal acetyl-Histone H4 (Lys8) antibodies; mouse monoclonal p27/KIP1 antibody; mouse monoclonal anti-β-actin; and mouse monoclonal anti-GADD45G. Membranes are then washed, reprobed with appropriate horseradish peroxidase-conjugated secondary antibodies, and developed with SuperSignal chemiluminescent substrate.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

### Animal Administration <sup>[1]</sup>

AE17 and TC-1 cancer cells (1×10<sup>6</sup> cells) are injected into the flanks of adult female C57Bl/6 mice and severe combined immunodeficiency (SCID) mice. M30 (10×10<sup>6</sup> cells), A549 (5×10<sup>6</sup> cells), H69 (2.5×10<sup>6</sup> cells), BK-T (6.5×10<sup>6</sup>), H526 (10×10<sup>6</sup>), and RG1 (10×10<sup>6</sup>) cells are also injected, but in the presence of matrigel, into the flanks of SCID mice. When tumors reach 100 to 500 mm<sup>3</sup>, panobinostat is administered via i.p. injections (10-20 mg/kg) on a daily schedule (5-days-on, 2-days-off regimen) for the entire duration of the experiment. Control mice receive i.p. injections with dextrose 5% in water. Every tumor is measured with a caliper at least twice weekly. For evaluation of the effects of combination therapy on SCLC-derived tumors, SCID mice with H69 tumors are administered panobinostat. Three days after the initiation of panobinostat, and again 1 wk later, etoposide (40 mg/kg) is administered i.p.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Cancer Res. 2016 Dec 1;76(23):7001-7011.
- Cancer Lett. 30 June 2021.
- PLoS Pathog. 2018 Sep 13;14(9):e1007267.
- J Clin Endocrinol Metab. 2021 Jan 1;106(1):e232-e246.
- Acta Pharmacol Sin. 2020 Aug 27.

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## REFERENCES

- [1]. Scuto A, et al. The novel histone deacetylase inhibitor, LBH589, induces expression of DNA damage response genes and apoptosis in Ph- acute lymphoblastic leukemia cells. *Blood*. 2008 May 15;111(10):5093-100.
- [2]. Crisanti MC, 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. *Mol Cancer Ther*. 2009 Aug;8(8):2221-31.
- [3]. Ocio EM, et al. In vitro and in vivo rationale for the triple combination of panobinostat (LBH589) and dexamethasone with either bortezomib or lenalidomide in multiple myeloma. *Haematologica*. 2010 May;95(5):794-803.
- [4]. Banerjee NS, et al. Vorinostat, a pan-HDAC inhibitor, abrogates productive HPV-18 DNA amplification. *Proc Natl Acad Sci U S A*. 2018 Nov 20;115(47):E11138-E11147.
- [5]. Barton K, et al. Broad activation of latent HIV-1 in vivo. *Nat Commun*. 2016;7:12731. Published 2016 Sep 8.
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**Caution: Product has not been fully validated for medical applications. For research use only.**

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