# 产品名称：Pracinostat(SB939)
# 产品别名：Pracinostat

## 生物活性：

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| **Description** | Pracinostat is a potent histone deacetylase (HDAC) inhibitor, with $IC_{50}$s of 40-140 nM, used for cancer research. | | | | | |
| **$IC_{50}$ & Target** | HDAC10 | HDAC3 | HDAC5 | HDAC1 | HDAC11 | HDAC2 |
| | 40 nM ($IC_{50}$) | 43 nM ($IC_{50}$) | 47 nM ($IC_{50}$) | 49 nM ($IC_{50}$) | 93 nM ($IC_{50}$) | 96 nM ($IC_{50}$) |
| | HDAC7 | HDAC8 | HDAC6 | HDAC4 | HDAC9 | |
| | 137 nM ($IC_{50}$) | 140 nM ($IC_{50}$) | 1008 nM ($IC_{50}$) | 56 nM ($IC_{50}$) | 70 nM ($IC_{50}$) | |
| **In Vitro** | Pracinostat (SB939) is a potent novel hydroxamate-based inhibitor of HDACs class I, II, and IV, inhibiting the isolated enzymes with a $K_i$ of 19 to 48 nM (class I), 16 to 247 nM (class II), and 43 nM (class IV), but with no activity against the class III isoenzyme SIRT I. SB939 has effects on HCT-116 colon cancer cell line and the HL-60 acute myeloid leukemia cell line, with $IC_{50}$s of 0.48 μM and 70 nM, respectively. SB939 does not inhibit the proliferation of normal human dermal fibroblasts at concentrations up to 100 μM[1]. Pracinostat (SB939, compound 3) inhibits CYP2C19 with $IC_{50}$ of 5.78 μM. SB939 shows potent activities against A2780, COLO 205, HCT-116, and PC-3 cell lines, with $IC_{50}$s of 0.48 ± 0.21, 0.56 ± 0.08, 0.48 ± 0.27, and 0.34 ± 0.06[2]. Pracinostat downregulates JAK and FLT3 signaling in $JAK2^{V617F}$ and FLT-ITD cell lines, and shows synergy in combination with pacritinib. Pracinostat and pacritinib show in vitro synergy on STAT signaling and apoptosis. Pracinostat potently inhibits proliferation of different AML subtypes as a single agent and is synergistic with pacritinib in $JAK2^{V617F}$ or FLT3-ITD AML cell lines[3]. | | | | | |
| **In Vivo** | Pracinostat (SB939, 25-100 mg/kg) shows significant dose-dependent growth inhibition of HCT-116 xenografts. SB939 selectively accumulates in tumor tissue. SB939 (50 or 75 mg/kg) exhibits anti-tumor activities in the Apcmin genetic colon cancer mouse model[1]. Pracinostat (25 or 50 mg/kg per day for 21 days) induces significant inhibition of tumor growth (TGI), by 59 and 116%, respectively, in mice bearing MV4-11 xenografts. Pracinostat (75 mg/kg, q.o.d) in combination with pacritinib is efficacious and synergistic in vivo in two different models of human AML. Pracinostat and pacritinib have synergistic effects on AML-induced plasma cytokines/growth factors/chemokines[3]. | | | | | |

***In Vitro:***

**DMSO : 50 mg/mL** (**139.48 mM;** Need ultrasonic)

| **Preparing Stock Solutions** | Solvent / Mass / Concentration | **1 mg** | **5 mg** | **10 mg** |
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| | 1 mM | 2.7896 mL | 13.9478 mL | 27.8956 mL |
| | 5 mM | 0.5579 mL | 2.7896 mL | 5.5791 mL |
| | 10 mM | 0.2790 mL | 1.3948 mL | 2.7896 mL |

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

***In Vivo:***

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现

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| **Solvent&Solubility** | 用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶<br>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline<br>Solubility: ≥ 2.75 mg/mL (7.67 mM); Clear solution<br>此方案可获得 ≥ 2.75 mg/mL (7.67 mM，饱和度未知) 的澄清溶液。<br>以 1 mL 工作液为例，取 100 μL 27.5 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。<br><br>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)<br>Solubility: ≥ 2.75 mg/mL (7.67 mM); Clear solution<br>此方案可获得 ≥ 2.75 mg/mL (7.67 mM，饱和度未知) 的澄清溶液。<br>以 1 mL 工作液为例，取 100 μL 27.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。<br><br>3.请依序添加每种溶剂： 10% DMSO →90% corn oil<br>Solubility: ≥ 2.75 mg/mL (7.67 mM); Clear solution<br>此方案可获得 ≥ 2.75 mg/mL (7.67 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。<br>以 1 mL 工作液为例，取 100 μL 27.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 |
| **References** | [1]. Novotny-Diermayr V, et al. SB939, a novel potent and orally active histone deacetylase inhibitor with high tumor exposure and efficacy in mouse models of colorectal cancer. Mol Cancer Ther. 2010 Mar;9(3):642-52.<br>[2]. Wang H, et al. Discovery of (2E)-3-{2-butyl-1-[2-(diethylamino)ethyl]-1H-benzimidazol-5-yl}-N-hydroxyacrylamide (SB939), an orally active histone deacetylase inhibitor with a superior preclinical profile. J Med Chem. 2011 Jul 14;54(13):4694-720.<br>[3]. Novotny-Diermayr V, et al. The oral HDAC inhibitor pracinostat (SB939) is efficacious and synergistic with the JAK2 inhibitor pacritinib (SB1518) in preclinical models of AML. Blood Cancer J. 2012 May;2(5):e69. |

**实验参考：**

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| **Cell Assay** | Cells are seeded in 96-well plates at a predetermined optimal density, in the log growth phase, and rested for 24 h (adherent cells) or 2 h (suspension cells), respectively, before treatment with SB939. All experiments are done in triplicates for 96 h, with 1% solvent, using either the CyQUANT Cell proliferation assay kit for adherent cells or the CellTiter96 Aqueous One solution cell proliferation kit for suspension cells, in a total volume of 100 μL with SB939 concentrations from 100 μM to 1.5 nM in nine serial dilution steps. $IC_{50}$ are determined using the XLfit software[1] |
| **Animal Administration** | Male $Apc^{Min/+}$ mice and female C57BL/6 mice are fed a standard rodent diet. Mice with the confirmed mutation, between 16 and 20.5 wk of age, with a positive scoring in the hemocult assay are recruited to the experiment. During treatment, mice are injected i.p. with 40 mg/kg of 5-FU in a volume of 200 μL per 20 g body weight, once daily, for 5 d of treatment, followed by a 9-d recovery period and an additional 5 d of treatment. Treatment with SB939 per oral at 50 or 75 mg/kg once daily is given continuously for 21 d. At the last day of the treatment, the small intestine, caecum, and colon are removed; fixed by multiple injections of 4% PBS-buffered formaldehyde into the gut lumen; cut into |

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| | segments; and spread flat on a plastic film in a formaldehyde bath. Tumor load is measured in a dissection microscope. Assessment and analysis of the samples are done blinded[1] |
| **References** | [1]. Novotny-Diermayr V, et al. SB939, a novel potent and orally active histone deacetylase inhibitor with high tumor exposure and efficacy in mouse models of colorectal cancer. Mol Cancer Ther. 2010 Mar;9(3):642-52.<br>[2]. Wang H, et al. Discovery of (2E)-3-{2-butyl-1-[2-(diethylamino)ethyl]-1H-benzimidazol-5-yl}-N-hydroxyacrylamide (SB939), an orally active histone deacetylase inhibitor with a superior preclinical profile. J Med Chem. 2011 Jul 14;54(13):4694-720.<br>[3]. Novotny-Diermayr V, et al. The oral HDAC inhibitor pracinostat (SB939) is efficacious and synergistic with the JAK2 inhibitor pacritinib (SB1518) in preclinical models of AML. Blood Cancer J. 2012 May;2(5):e69. |