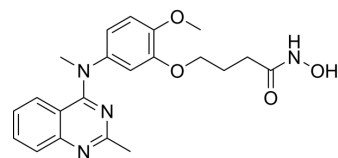


## SKLB-23bb

<b>Cat. No.:</b>	HY-18947		
<b>CAS No.:</b>	1815580-06-3		
<b>Molecular Formula:</b>	C <sub>21</sub> H <sub>24</sub> N <sub>4</sub> O <sub>4</sub>		
<b>Molecular Weight:</b>	396.44		
<b>Target:</b>	HDAC		
<b>Pathway:</b>	Cell Cycle/DNA Damage; Epigenetics		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



### SOLVENT & SOLUBILITY

<b>In Vitro</b>	DMSO : 32 mg/mL (80.72 mM; Need ultrasonic and warming)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	<b>Preparing Stock Solutions</b>	1 mM	2.5224 mL	12.6122 mL	25.2245 mL
		5 mM	0.5045 mL	2.5224 mL	5.0449 mL
10 mM		0.2522 mL	1.2612 mL	2.5224 mL	
Please refer to the solubility information to select the appropriate solvent.					
<b>In Vivo</b>	<ol style="list-style-type: none"> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 40% PEG300 &gt;&gt; 5% Tween-80 &gt;&gt; 45% saline Solubility: ≥ 2.5 mg/mL (6.31 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (6.31 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% corn oil Solubility: ≥ 2.5 mg/mL (6.31 mM); Clear solution</li> </ol>				

### BIOLOGICAL ACTIVITY

<b>Description</b>	SKLB-23bb is a potent and selective inhibitor for HDAC6 with an IC <sub>50</sub> of 17 nM and shows 25-fold and 200-fold selectivity relative to HDAC1 (IC <sub>50</sub> =422 nM) and HDAC8 (IC <sub>50</sub> =3398 nM), respectively.
<b>IC<sub>50</sub> &amp; Target</b>	IC <sub>50</sub> : 17 nM (HDAC6), 422 nM (HDAC1), 398 nM (HDAC8) <sup>[1]</sup>
<b>In Vitro</b>	SKLB-23bb (Compound 23bb) presents low nanomolar antiproliferative effects against panel of cancer cell lines. The antiproliferative activity is ton human malignant melanoma A375 cells and cervical cancer HeLa cells, SKLB-23bb shows the

most potent activities with IC<sub>50</sub> values of 50 and 49 nM on A375 and HeLa cells, respectively. The antiproliferative activities against 11 kinds of hematological tumors (myelomaU266, RPMI8226 cells, human leukemia MV4-11, K562 cells, and human B cell lymphoma Ramos cells) or solid tumors (ovarian cancer A2780s, SKOV-3 cells, breast cancer SKBR3 cells, liver cancer HepG2 cells, lung cancer H460, A549 cells, cervical cancer HeLa cells and colon cancer HCT116, HT29 cells) cell lines of SKLB-23bb are evaluated by MTT, and the SAHA and ACY-1215 are as positive control. SKLB-23bb shows significant antiproliferative potential with the IC<sub>50</sub> values ranging from 14 to 104 nM in these tumor cell lines<sup>[1]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### In Vivo

SKLB-23bb (Compound 23bb) reduces the tumor growth in both the hematological tumor MV4-11 xenograft model and solid tumor HCT116 xenograft model. The significant antitumor activities are observed by intravenous administration of SKLB-23bb at 50 mg/kg on MV4-11 and HCT116 xenograft models. The growth of MV4-11 and HCT116 cancer cell xenografts is suppressed by 55.0% and 76.3% (percent of tumor mass change [TGI] values) after iv administration of SKLB-23bb at 50 mg/kg. The HCT116 xenograft model is also established to investigate the antitumor activity of oral administration of SKLB-23bb. The TGI value of oral administration of SKLB-23bb (25 mg/kg) on HCT116 xenograft model is 60.4%, which is superior to the SAHA group (100 mg/kg, 59.2%). Additionally, the body weight decrease is acceptable and no other adverse effects are observed upon treatment with SKLB-23bb. Low clearance (CL=7.008 L/kg per hour for iv, CL=12.877 L/kg per hour for po) and long terminal half-life (t<sub>1/2</sub>=7.658 h for iv, t<sub>1/2</sub>=9.62 h for po) are observed in SKLB-23bb. The oral bioavailability of SKLB-23bb is excellent in rats and the bioavailability is up to 47.0%<sup>[1]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

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

A375, A2780s, SKBR3, HepG2, HeLa, HCT116, A549, and SKOV-3 cells are cultured in DMEM. RPMI8226, K562, H460, HT29, and Ramos cells are cultured in RPMI-1640 medium. MV4-11 cells are cultured in IMDM. All media contains 10% fetal bovine serum (FBS), 100 units/mL Penicillin, and 100 µg/mL Streptomycin. Cells are incubated at 37 °C in a humidified atmosphere of 5% CO<sub>2</sub>. Cells in logarithmic phase are seeded into 96-well culture plates at densities of 3000-5000 cells per well and subsequently treated with various concentrations of compounds (e.g., SKLB-23bb; 10, 100, 1000, and 10000 nM) for 72 h in final volumes of 200 µL. Upon end point, 20 µL of MTT (5 mg/mL) is added to each well, and the cells are incubated for an additional 1-3 h. After carefully removal of the medium, the precipitates are dissolved in 150 µL of DMSO via mechanically shaking, and then absorbance values at a wavelength of 570 nm are taken on a spectrophotometer. IC<sub>50</sub> values are calculated using percentage of growth versus untreated control<sup>[1]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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

**Mice<sup>[1]</sup>**  
For the MV4-11 and Ramos xenograft models, MV4-11 and Ramos cells (107 cells in 100 µL of serum-free IMDM) are injected subcutaneously into the right flanks of 5- to 6-week-old female NOD/SCID mice. For the HCT116 xenograft, HCT116 cells (107 cells in 100 µL of serum-free DMEM) are injected subcutaneously into the right flanks of 5- to 6-week-old female Balb/c nude mice. When the size of the formed xenografts reach 100-150 mm<sup>3</sup>, the mice are randomly divided (6 mice per group in MV4-11 model, 8 mice per group in Ramos model, and 7 mice per group in HCT116 model) into control group and treated groups. The mice in the experimental groups receive intravenous (iv) injection (50 mg/kg) or oral administration (25 mg/kg) of SKLB-23bb every 2 days. The mice in the vehicle group receive iv injection or oral administration of equal amount of physiological saline containing 5% ethanol and 5% Cremophor EL. Those in the SAHA or LBH-589 or ACY-1215 groups (positive controls) receive ip injection (50 mg/kg for SAHA and 10 mg/kg for LBH-589, dissolved in physiological saline containing 10% DMSO and 45% PEG400 to a concentration of 10 mg/mL) or oral administration (100 mg/kg for SAHA and 40 mg/kg for ACY-1215, dissolved in the same way described above) every 2 days. Tumor burden is measured every 2 days by a caliper. Tumor volume (TV) is calculated. The day that treatment started is defined as day 0. At the end of the experiment, mice are sacrificed and tumors are collected and weighed<sup>[1]</sup>.

**Rats<sup>[1]</sup>**  
SKLB-23bb is administered to SD rats intravenously (iv) at 12 mg/kg body weight and orally at 12 mg/kg body weight. Blood samples are taken, and the plasma is analyzed for concentration of SKLB-23bb using an LC-MS/MS system<sup>[1]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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## REFERENCES

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[1]. Yang Z, et al. Discovery of Selective Histone Deacetylase 6 Inhibitors Using the Quinazoline as the Cap for the Treatment of Cancer. J Med Chem. 2016 Feb 25;59(4):1455-70.

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**Caution: Product has not been fully validated for medical applications. For research use only.**

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