Product Data Sheet

Product Name: Belinostat (PXD101)
Cat. No.: GC15962

Chemical Properties

Cas. No.	414864-00-9		
Chemical Name	(E)-N-hydroxy-3-[3-(phenylsulfamoyl)phenyl]prop-2-enamide		
SMILES	C1=CC=C(C=C1)NS(=O)(=O)C2=CC=CC(=C2)C=CC(=O)NO		
Formula	$C_{15}H_{14}N_2O_4S$	M.Wt	318.35
Solubility	≥ 15.92 mg/mL in DMSO, ≥ 44.1 mg/mL in EtOH with ultrasonic	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	Belinostat (PXD101)		

Protocol

Kinase experiment [1]:

Preparation Method	Reaction was carried out in a total volume of 150 µl of buffer [60 mm Tris (pH 7.4) containing 30% glycerol] containing 2 µl of cell extract and, where used, 2 µl of Belinostat. The reaction was started by the addition of 2 µl of [3H] labeled substrate (acetylated histone H4 peptide corresponding to the 20 NH2-terminal residues). Samples were incubated at 37°C for 45 min, and the reaction stopped by the addition of HCl and acetic acid (0.72 and 0.12 m final concentrations, respectively).

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Reaction Conditions	2 µl of Belinostat, incubated at 37°C for 45 min
Applications	Belinostat inhibited histone deacetylase activity in cell lysates with an IC50 in the range 9–100 nM

Cell experiment [1]:

Cell lines	The human ovarian cell line A2780, cisplatin (A2780/cp70) and doxorubicin (2780AD) resistant derivatives
Preparation Method	Cells were plated in 5 ml of medium at a density of 8 × 104 cells/25 cm2 flask and allowed to attach and grow for 48 h. Cells were exposed to Belinostat (five concentrations from 0.016 to 10 µm) for 24 h.
Reaction Conditions	0.016 to 10 µm, for 24 h
Applications	Belinostat inhibited the growth of a number of human tumor cell lines with IC50s determined by a clonogenic assay in the range 0.2–3.4 µm

Animal experiment [2]:

Animal models	female CD-1 athymic nude mice

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Preparation Method	Once tumors became established (~100 mm3 in size), animals were randomized (10 animals/group) and drug treatments were initiated. Belinostat was given by i.p. injection once daily for 15 consecutive days. Belinostat was prepared as a 50 mg/mL stock in Belinostat vehicle (pH ~9.4) and for administration was diluted in Belinostat vehicle to 10 mg/mL (for 100 mg/kg dose)
Dosage form	i.p , 20, 40, 100 mg/kg, for 15 d.
Applications	Belinostat monotherapy induced dose-proportional antitumor effects. When administered at 100 mg/kg, Belinostat inhibited tumor size by 47% at day 15 relative to vehicle-treated control animals.

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References:

[1]. Plumb J A, Finn P W, Williams R J, et al. Pharmacodynamic response and inhibition of growth of human tumor xenografts by the novel histone deacetylase inhibitor PXD101[J]. Molecular cancer therapeutics, 2003, 2(8): 721-728.

[2]. Qian X, LaRochelle W J, Ara G, et al. Activity of PXD101, a histone deacetylase inhibitor, in preclinical ovarian cancer studies[J]. Molecular cancer therapeutics, 2006, 5(8): 2086-2095.

Background

Belinostat (PXD101) is a novel hydroxamate-type inhibitor of histone deacetylase (HDAC) activity in HeLa cell extracts with an IC50 of 27 nM [1].

Belinostat(1-5 μM)for 48 h caused a dose-dependent inhibition of proliferation, with the most potent inhibitory effect occurring on 5637 cells (IC50 of 1.0 μM), and the least effect occurring on RT4 cells (IC50 of 10.0 μM). T24 and J82 cell lines had an IC50 of 3.5 and 6.0 μM, respectively [2]. Belinostat inhibited the proliferation of human bladder cancer T24 cells with IC50 of 3.5μM [3].

Belinostat (10-40 mg/kg/day i.p.) daily for 7 days causes a significant dose-dependent

growth delay with no obvious signs of toxicity to the colon tumor xenografts mice [1]. Gene expression analysis of belinostat-treated mice showed increased p21WAF1 gene transcript expression [3]. Belinostat monotherapy induced dose-proportional antitumor effects. When administered at 100 mg/kg, belinostat inhibited tumor size by 47% at day 15 on human ovarian cancer xenografts [4].

References:

[1]. Plumb J A, Finn P W, Williams R J, et al. Pharmacodynamic response and inhibition of growth of human tumor xenografts by the novel histone deacetylase inhibitor PXD101[J]. Molecular cancer therapeutics, 2003, 2(8): 721-728.
[2]. Buckley M T, Yoon J, Yee H, et al. The histone deacetylase inhibitor belinostat (PXD101) suppresses bladder cancer cell growth in vitro and in vivo[J]. Journal of Translational Medicine, 2007, 5(1): 1-12.
[3]. Buckley M T, Yoon J, Yee H, et al. The histone deacetylase inhibitor belinostat (PXD101) suppresses bladder cancer cell growth in vitro and in vivo[J]. Journal of Translational Medicine, 2007, 5(1): 1-12.
[4]. Qian X, LaRochelle W J, Ara G, et al. Activity of PXD101, a histone deacetylase inhibitor, in preclinical ovarian cancer studies[J]. Molecular cancer therapeutics, 2006, 5(8): 2086-2095.

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