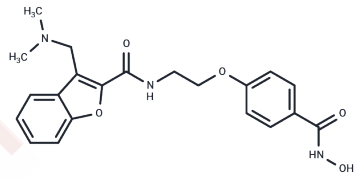
Data Sheet (Cat.No.T0431)

TargetMol

Abexinostat

Chemical Properties



CAS No. : 783355-60-2

Formula: C21H23N3O5

Molecular Weight: 397.42

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	PCI-24781 (Abexinostat (PCI24781)) is a new pan-HDAC inhibitor mainly targeting HDAC1 (Ki: 7 nM), also have moderate inhibitory for HDACs 2, 3, 6, and 10 and greater than 40-fold selectivity against HDAC8. Phase 1/2.
Targets(IC50)	HDAC
In vitro	HCT116 xenograft mice were treated with PCI-24781 for four consecutive days each week, followed by a three-day drug holiday, at dosages of 20, 40, 80, and 160 mg/kg, achieving inhibition rates of 48%, 57%, 82.2%, and 80.0%, respectively. Alternate-day treatment with 200 mg/kg PCI-24781 significantly inhibited the growth of both HCT116 and DLD-1 tumor cells, with inhibition rates of 69% and 59%, respectively.
In vivo	In CHO cells, PCI-24781 is consistent with the inhibition of homologous recombination (HR), leading to a decreased capability of homology-directed repair induced by I-SceI-mediated chromosomal breaks. The compound exhibits significant antitumor activity across various cancer cell lines, with GI50 values ranging from 0.15 μM to 3.09 μM. Treatment with PCI-24781 results in dose-dependent accumulation of acetylated histones/microtubule proteins, induction of PARP cleavage, p21 expression, and γH2AX accumulation in HCT116 and DLD-1 cell lines. PCI-24781 induces apoptosis in soft tissue cells, causes a deficiency in S phase, and arrests the cell cycle at the G2 phase. In STS cells, the compound likely induces transcriptional repression of Rad51 by enhancing E2F1 binding to the proximal promoter region of Rad51. Additionally, PCI-24781 prompts caspase and reactive oxygen species-dependent NF-κB-signaling-mediated apoptosis in non-Hodgkin's lymphoma and Hodgkin's lymphoma. PCI-24781 also inhibits the proliferation of human umbilical vein endothelial cells with a GI50 of 0.43 μM. Furthermore, it suppresses HDAC enzyme activity, leading to a noticeable decrease in transcription levels of HR-related genes, including RAD51.
Kinase Assay	HDAC Activity: HDAC activity is measured using a continuous trypsin-coupled assay. For inhibitor characterization, measurements are done in a reaction volume of 100 μL using 96-well assay plates. For each isozyme, the HDAC protein in reaction buffer [50 mM HEPES, 100 mM KCl, 0.001% Tween 20, 5% DMSO (pH 7.4), supplemented with bovine serum albumin at concentrations of 0% (HDAC1), 0.01% (HDAC2, 3, 8, and 10), or 0.05% (HDAC6)] is mixed with PCI-24781 at various concentrations and allowed to incubate for 15 minutes. Trypsin is added to a final concentration of 50 nM, and acetyl-Gly-Ala-(N-acetyl-Lys)-AMC is added to a final concentration of 25 μM (HDAC1, 3, and 6), 50 μM (HDAC2 and 10), or 100 μM (HDAC8) to initiate the reaction. Negative control reactions

	are done in the absence of PCI-24781 in replicates of eight. Reactions are monitored in a fluorescence plate reader. After a 30-minute lag time, the fluorescence is measured over a 30-minute time frame using an excitation wavelength of 355 nm and a detection wavelength of 460 nm. The increase in fluorescence with time is used as the measure of the reaction rate. Inhibition constants Ki(app) are obtained using the program BatchKi.
Cell Research	Cells are cultured for at least two doubling times, and growth is monitored at the end of PCI-24781 exposure using an Alamar blue fluorometric cell proliferation assay. PCI-24781 is assayed in triplicate wells in 96-well plates at nine concentrations using half-log intervals ranging from 0.0015 μM to 10 μM. The final DMSO concentration in each well is 0.15%. The concentration required to inhibit cell growth by 50% (GI50) and 95% confidence intervals are estimated from nonlinear regression using a four-parameter logistic equation.(Only for Reference)

Solubility Information

Solubility	DMSO: 3.97 mg/mL (9.99 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5162 mL	12.5811 mL	25.1623 mL
5 mM	0.5032 mL	2.5162 mL	5.0325 mL
10 mM	0.2516 mL	1.2581 mL	2.5162 mL
50 mM	0.0503 mL	0.2516 mL	0.5032 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Buggy JJ, et al. Mol Cancer Ther, 2006, 5(5), 1309-1317.
Adimoolam S, et al. Proc Natl Acad Sci U S A, 2007, 104(49), 19482-19487.
Lopez G, et al. Clin Cancer Res, 2009, 15(10), 3472-3483.
Bhalla S, et al. Clin Cancer Res, 2009, 15(10), 3354-3365.