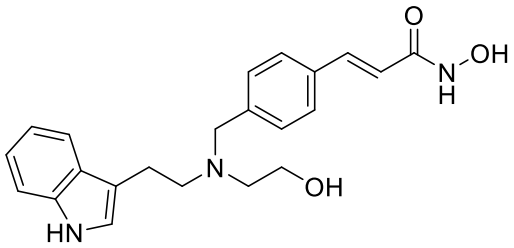
Product data sheet

MedKoo Cat#: 200845 Name: Dacinostat CAS#: 404951-53-7 (free base) Chemical Formula: $C_{22}H_{25}N_3O_3$ Exact Mass: 379.18959 Molecular Weight: 379.45	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Dacinostat, also known as LAQ824, is a hydroxamate histone deacetylase inhibitor with potential anticancer activity. LAQ824 sensitized nonsmall cell lung cancer to the cytotoxic effects of ionizing radiation. LAQ824 reduced clonogenic survival of the H23 and H460 cell lines five-fold compared with controls and four-fold compared with either agent alone ($P<0.001$). In phase I trials, LAQ824 was well tolerated at doses that induced accumulation of histone acetylation, with higher doses inducing changes consistent with HSP90 inhibition.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	56.0	147.58

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.64 mL	13.18 mL	26.35 mL
5 mM	0.53 mL	2.64 mL	5.27 mL
10 mM	0.26 mL	1.32 mL	2.64 mL
50 mM	0.05 mL	0.26 mL	0.53 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Fuino L, Bali P, Wittmann S, Donapaty S, Guo F, Yamaguchi H, Wang HG, Atadja P, Bhalla K. Histone deacetylase inhibitor LAQ824 down-regulates Her-2 and sensitizes human breast cancer cells to trastuzumab, taxotere, gemcitabine, and epothilone B. Mol Cancer Ther. 2003 Oct;2(10):971-84. PMID: 14578462.
2. Wang H, Cheng F, Woan K, Sahakian E, Merino O, Rock-Klotz J, Vicente-Suarez I, Pinilla-Ibarz J, Wright KL, Seto E, Bhalla K, Villagra A, Sotomayor EM. Histone deacetylase inhibitor LAQ824 augments inflammatory responses in macrophages through transcriptional regulation of IL-10. J Immunol. 2011 Apr 1;186(7):3986-96. doi: 10.4049/jimmunol.1001101. Epub 2011 Mar 2. PMID: 21368229; PMCID: PMC3998678.

In vivo study

1. Catley L, Weisberg E, Tai YT, Atadja P, Remiszewski S, Hideshima T, Mitsiades N, Shringarpure R, LeBlanc R, Chauhan D, Munshi NC, Schlossman R, Richardson P, Griffin J, Anderson KC. NVP-LAQ824 is a potent novel histone deacetylase inhibitor with significant activity against multiple myeloma. Blood. 2003 Oct 1;102(7):2615-22. doi: 10.1182/blood-2003-01-0233. Epub 2003 Jun 19. PMID: 12816865.

2. Leyton J, Alao JP, Da Costa M, Stavropoulou AV, Latigo JR, Perumal M, Pillai R, He Q, Atadja P, Lam EW, Workman P, Vigushin DM, Aboagye EO. In vivo biological activity of the histone deacetylase inhibitor LAQ824 is detectable with 3'-deoxy-3'-[18F]fluorothymidine positron emission tomography. Cancer Res. 2006 Aug 1;66(15):7621-9. doi: 10.1158/0008-5472.CAN-05-3962. PMID: 16885362.

7. Bioactivity

Biological target:

Dacinostat is a potent HDAC inhibitor, with an IC50 of 32 nM that also inhibits HDAC1 with an IC50 of 9 nM, and is used in cancer research.

In vitro activity

It was determined whether the acquisition of inflammatory properties by LAQ824-treated macrophages renders these cells better activators of antigen-specific CD4+ T-cells. PEMs were therefore treated with LAQ824, LPS or a combination of LPS plus LAQ824 for 24 hours. Following this treatment, naïve CD4+ T-cells specific for a MHC Class II restricted epitope of influenza hemagglutinin (HA) were added to the PEM monolayer and stimulated, or not, with cognate HA-peptide. LAQ824-treated PEMs triggered an enhanced effector function of clonotypic CD4+ T cells, as determined by their capacity to produce higher levels of IFN-γ in response to cognate peptide (Figure 5A-bottom). LAQ824-treated PEMs effectively prime naïve antigen-specific CD4+ T-cells and restore the responsiveness of anergic CD4+ T-cells. As shown in Figure 5D, IL-10 blockade was insufficient to enhance the APC function of LPS-treated macrophages to augment IFN-γ production by CD4+ T-cells (Fig. 5D, LPS alone, black bar versus gray bar), nor was it able to significantly enhance the effect of LAQ824 treatment (Fig. 5D, LAQ+LPS, black bar versus gray bar). Taken together, these data point to a contributory role of IL-10 inhibition in the enhanced APC function displayed by LAQ824-treated macrophages since this effect was reversed when recombinant IL-10 was added-back to the cultures.

Reference: J Immunol. 2011 Apr 1;186(7):3986-96. https://pubmed.ncbi.nlm.nih.gov/21368229/

In vivo activity

It was determined whether the in vitro effects correlate with the in vivo activity of NVP-LAQ824 using an immunodeficient mouse model. Immunodeficient BNX mice were inoculated subcutaneously in the flank with 3 × 107 RPMI 8226 MM cells in 100 μL RPMI 1640 medium, together with 100 μL Matrigel. Subcutaneous tumors became palpable in 90% of mice within 3 days and in all mice within 8 days, allowing randomization of mice to either treatment with NVP-LAQ824 or normal saline control cohorts. The data were log-transformed and modeled as a simple linear growth curve. There was no significant difference in the baseline intercept between control and treated groups (P = .83). Daily intraperitoneal administration of NVP-LAQ824 (25 mg/kg) significantly reduced MM tumor growth (Figure 8A-B) and increased survival (Figure 8C), compared with the control group treated with normal saline vehicle only. No significant toxicity, as evidenced by lack of weight changes, was observed in any treatment groups. Taken together, these findings provide the framework for NVP-LAQ824 as a novel therapeutic in MM.

Reference: Blood. 2003 Oct 1;102(7):2615-22. https://pubmed.ncbi.nlm.nih.gov/12816865/