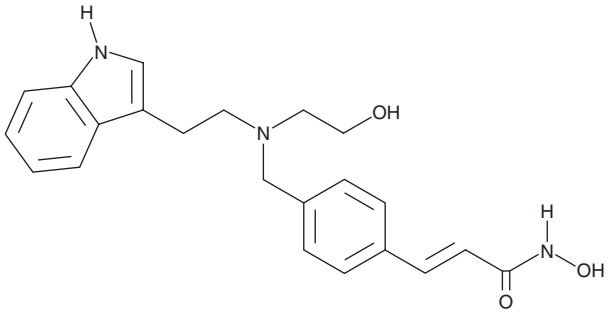
PRODUCT INFORMATION

LAQ824

Item No. 16427

CAS Registry No.:	404951-53-7
Formal Name:	(2E)-N-hydroxy-3-[4-[[(2-hydroxyethyl)[2-(1H-indol-3-yl)ethyl]amino]methyl]phenyl]-2-propenamide
Synonyms:	Dacinostat, NVP-LAQ824
MF:	$C_{22}H_{25}N_3O_3$
FW:	379.5
Purity:	≥95%
UV/Vis.:	λ_{max}: 222, 281, 352 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

LAQ824 is supplied as a crystalline solid. A stock solution may be made by dissolving the LAQ824 in the solvent of choice, which should be purged with an inert gas. LAQ824 is soluble in the organic solvent DMSO at a concentration of approximately 50 mg/ml.

Description

LAQ824 is a hydroxamate-based inhibitor of histone deacetylases (HDACs) with an IC_{50} value of 30 nM.[1,2] It inhibits the growth of colon, breast, prostate, and non-small cell lung cancer cell lines at concentrations of less than 1 µM.[1,3] LAQ824 augments the actions of fludarabine (Item No. 14128) and imatinib mesylate (Item No. 13139) in human leukemia cells.[4,5] Through its effects on HDACs, LAQ824 induces acetylation of histones, α-tubulin, and heat shock protein 90 (Hsp90).[5,6] Acetylation of Hsp90 blocks its chaperone function, resulting in changes in levels of several client proteins, including estrogen receptor-α, Hsp72, and Raf-1.[6,7]

References

1. Catley, L., Weisberg, E., Tai, Y.T., *et al.* NVP-LAQ824 is a potent novel histone deacetylase inhibitor with significant activity against multiple myeloma. *Blood* **102(7)**, 2615-2622 (2003).
2. Dokmanovic, M., Clarke, C., and Marks, P.A. Histone deacetylase inhibitors: Overview and perspectives. *Mol. Cancer Res.* **5(10)**, 981-989 (2007).
3. Zheng, Y.G., Wu, J., Chen, Z., *et al.* Chemical regulation of epigenetic modifications: Opportunities for new cancer therapy. *Med. Res. Rev.* **28(5)**, 645-687 (2008).
4. Rosato, R.R., Almenara, J.A., Maggio, S.C., *et al.* Role of histone deacetylase inhibitor-induced reactive oxygen species and DNA damage in LAQ-824/fludarabine antileukemic interactions. *Mol. Cancer Ther.* **7(10)**, 3285-3297 (2008).
5. Nimmanapalli, R., Fuino, L., Bali, P., *et al.* Histone deacetylase inhibitor LAQ824 both lowers expression and promotes proteasomal degradation of Bcr-Abl and induces apoptosis of imatinib mesylate-sensitive or -refractory chronic myelogenous leukemia-blast crisis cells. *Cancer Res.* **63(16)**, 5126-5135 (2003).
6. Fiskus, W., Ren, Y., Mohapatra, A., *et al.* Hydroxamic acid analogue histone deacetylase inhibitors attenuate estrogen receptor-α levels and transcriptional activity: A result of hyperacetylation and inhibition of chaperone function of heat shock protein 90. Clin. *Cancer Res.* **13(16)**, 4882-4890 (2007).
7. de Bono, J.S., Kristeleit, R., Tolcher, A., *et al.* Phase I pharmacokinetic and pharmacodynamic study of LAQ824, a hydroxamate histone deacetylase inhibitor with a heat shock protein-90 inhibitory profile, in patients with advanced solid tumors. *Clin. Cancer Res.* **14(20)**, 6663-6673 (2008).

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