

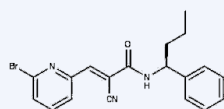
Deubiquitinating Enzyme Inhibitors

b-AP15

Abrogates the deubiquitinating activity of the 19S regulatory particle by inhibiting ubiquitin C-terminal hydrolase 5 (UCHL5) and ubiquitin-specific peptidase 14 (USP14) resulting in accumulation of polyubiquitin in cells. b-AP15 induces tumor cell apoptosis and tumor progression in four different solid tumor models *in vivo*.¹

10-1340

10 mg, 50 mg



WP-1130

WP-1130

A novel DUB inhibitor directly inhibiting USP9x, USP5, USP14 and UCH37 inducing rapid accumulation of polyubiquitinated proteins.² Induces apoptosis in tumor cell lines. Blocks Jak2 signaling via Jak2 ubiquitination.³

10-1351

5 mg, 25 mg

TCID

Inhibits ubiquitin C-terminal hydrolase L3 (UCH-L3).⁴ IC₅₀=0.6 μM, 125-fold selective over UCH-L1, IC₅₀=75 μM.⁵ Cell permeable.

10-2428

10 mg, 50 mg

References

1. D'Arcy, et al. (2011), *Inhibition of proteasome deubiquitinating activity as a new cancer therapy*; Nature Medicine **17** 1636
2. Kapuria et al. (2010), *Deubiquitinase inhibition by small-molecule WP1130 triggers aggresome formation and tumor cell apoptosis*; Cancer Res. **70** 9265
3. Kapuria et al. (2011), *A novel small molecule deubiquitinase inhibitor blocks Jak2 signaling through Jak2 ubiquitination*; Cell Signal. **23** 2076
4. Love et al. (2007), *Mechanisms, biology and inhibitors of deubiquitinating enzymes*; Nat. Chem. Biol. **3** 697
5. Mtango et al. (2012), *Essential role of ubiquitin C-terminal hydrolases UCHL1 and UCHL3 in mammalian oocyte maturation*; J. Cell Physiol. **227** 2022
6. Liu et al. (2003), *Discovery of inhibitors that elucidate the role of UCH-L1 activity in the H1299 lung cancer cell line*; Chem. Biol. **10** 837
7. Cartier et al. (2009), *Regulation of synaptic structure by ubiquitin C-terminal hydrolase L1*; J. Neurosci. **29** 7857

LDN-5744

Inhibits ubiquitin C-terminal hydrolase (UCH-L1) (K_i=0.4 mM).⁶ Decreases proteasome activity and increases levels of ubiquitinated proteins. Induces apoptosis. Causes dramatic alterations in synaptic protein distribution and spine morphology *in vivo*.⁷ Cell permeable.

10-1303

10 mg, 50 mg