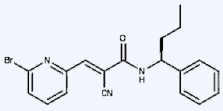
FOCUS on...

Deubiquitinating Enzyme Inhibitors



WP-1130

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

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] IC_{50}=0.6 µM, 125-fold selective over UCH-L1, IC_{50}=75 µM.[5] Cell permeable.

10-2428 10 mg, 50 mg

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

References

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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